The Role of Fibro-Adipogenic Progenitors in Musculoskeletal Disease

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SUMMARY
Skeletal muscle consists of heterogeneous cell populations that work in concert to support musculoskeletal homeostasis and regeneration in the context of acute injury and chronic disease. In this past decade, the recently discovered sub-population of muscle resident stem cells known as fibro-adipogenic progenitors (FAPs) have been implicated in the pathogenesis and regenerative response to a number of musculoskeletal conditions ranging from acute muscle injury to neurodegenerative disease, muscular dystrophy, rotator cuff tears, sarcopenia and heterotopic ossification. The purpose of this literature review is to synthesize a complete collection of basic, translational, and clinical science evidence implicating FAPs in the pathogenesis and regenerative response to acute and chronic musculoskeletal diseases. This study is an extensive literature review of papers recently published on FAPs in the development of acute and chronic musculoskeletal degeneration, and their potential role in therapeutic regeneration of these injuries. In this review, we highlight the multipotency of FAPs on a molecular level and review their role in the pathogenesis of acute, chronic, and degenerative musculoskeletal disorders with implications for the development of future novel therapeutic interventions.

KEY WORDS
Acute muscle injury; amyotrophic lateral sclerosis; cardiac fibrosis; chronic kidney disease; chronic obstructive pulmonary disease; fibro-adipogenic progenitors; heterotopic ossification; muscular dystrophy; neurodegenerative disease; obesity; rotator cuff tear; sarcopenia; spinal muscle atrophy.

INTRODUCTION
Fibrofatty degeneration of skeletal muscle is common to many disease and injury processes, but as yet lacks an effective treatment. Over the past decade, advances have been made in uncovering cellular and molecular processes that play a role in the degeneration of muscle. Fibro-adipogenic progenitors (FAPs) are a subpopulation of resident skeletal muscle stem cells arising from a distinct developmental lineage which have since been shown to play an important role in response to both acute injury and chronic musculoskeletal disease. Joe et al. (2010) defined this population as lin⁻/α7⁻/Sca1⁺ cells which were also uniformly positive for the surface marker PDGFRα. Uezumi et al. (2010) likewise noted ubiquitous PDGFRα⁺ expression of this population of mesenchymal progenitors (2). In healthy conditions in adult skeletal muscle in vivo, FAPs primarily localize to the interstitial space of skeletal muscle and are quiescent (1). Natarajan et al. (2010) summarized early findings that in the setting of an acute skeletal muscle injury, FAPs proliferate in the interstitial space between myofibers and produce trophic factors aiding in myofiber regeneration (3). However, when muscle fiber regeneration is impaired, FAPs continue to proliferate within injured muscle tissue and differentiate into adipocytes and myofibroblasts, leading to worsening muscle fatty degeneration and fibrosis. It
has therefore been recognized from early on that the skeletal muscle ‘niche’ in which FAPs are residing and proliferating is critical in determining their role in muscle degeneration versus regeneration. In this review, we present a summary of the role of FAPs in a wide range of musculoskeletal disease processes in an effort to better understand the complex, clinically relevant role of these cells in muscle degeneration and regeneration. We affirm that this literature review was synthesized in ethically in compliance with the international standards and required by Muscle, Ligaments, and Tendons Journal (4).

**Acute Muscle Injury**

FAPs were first recognized for the role that they play in response to a direct injury to muscle fibers. It was shown that a notexin (myotoxic venom) acute muscle injury in healthy mice results in rapid proliferation of FAPs in the injured muscle before a return to pre-damage levels between 4-5 days after injury (1). Similarly, in an acute injury setting created with either cardiototoxin (CTX) or glycerol, it was demonstrated that glycerol but not CTX led to adipogenic differentiation of FAPs (2). FAPs transplanted from the glycerol-injured muscle did not differentiate into adipocytes when transplanted into the CTX-injured muscle, while FAPs from the CTX-injured muscle underwent adipogenic differentiation when transplanted into glycerol-injured muscle (2). This highlights the importance of the local injury environment on FAP differentiation and suggests that adipogenic differentiation of FAPs primarily occurs when myogenic progenitor (MP) myofiber regeneration is impaired, as was seen with glycerol-mediated injury (2). It was further shown that hematopoietic cells partially mediate clearance of FAPs from muscle following a direct injury with NTX, and that this response is impaired in CCR2 knockout mice, in which bloodborne monocytes are unable to invade the parenchyma of the damaged muscle tissue following direct injury (5). This contraction of the FAP population that occurs several days after an acute muscle injury is thought to be largely mediated by TNF-α secreted by CD68+ macrophages, which leads to rapid apoptosis of FAPs following acute injury (5).

**Neurodegenerative diseases: ALS and SMA**

While FAPs may participate in a regenerative role in acute muscle injuries, their role in chronic, degenerative skeletal muscle diseases appears to be less beneficial. Here we will review the role of FAPs in the pathogenesis of neurodegenerative diseases such as amyotrophic lateral sclerosis (ALS), specifically in the disease characteristic wasting and scarring of muscle tissues (6-8). In ALS and spinal muscular atrophy (SMA), loss of the neuromuscular junction (NMJ) precedes progressive myofiber atrophy. FAPs play a key role in this progression from denervation to progressive myofiber atrophy (6-8).

In mouse models of mild acute muscle injury induced by cardiototoxin injection, FAPs were recruited to damaged muscle tissues and cleared between five to seven days, correlating with complete regeneration (6, 7, 9). In contrast, denervation by sciatic nerve transection, resulted in FAPs recruitment and retention at the injury site without concomitant macrophage infiltration or satellite cell-mediated regeneration (6, 7, 9). Denervation persistently activates STAT3 signaling in FAPs and simultaneously promotes their secretion of IL-6 through reciprocal positive feedback, promoting muscle atrophy and fibrosis (7). This muscle atrophy and fibrosis mediated by aberrant STAT3-IL-6 signaling in FAPs was also observed in murine models of spinal cord injury, SMA, and ALS and as well as in muscle samples from ALS patients (7). Thus, FAPs may represent a target for treatment of neuromuscular diseases. For example, antibody-mediated inhibition of FAP-specific STAT3-IL6 signaling prevents muscle atrophy and fibrosis in murine models of acute denervation and ALS.

FAPs also generate muscle fibrosis in these diseases by increasing extracellular matrix (ECM) deposition in the interstitial space between myofibers (6, 7). Induction of the TGF-β signaling pathway in skeletal muscle of murine models of ALS as well as in symptomatic ALS patient muscle is correlated with increased ECM deposition resulting in fibrosis (6, 10). FAPs and other mesenchymal progenitors residing in connective tissue express fibrotic genes: collagens, CTGF, and α-SMA, and deposit fibrotic ECM proteins in the interstitial space between muscle fibers resulting in muscle fibrosis (3, 6, 9). Because FAPs are sensitive to TGF-β signaling, one proposed model for the pathogenesis of fibrosis in ALS is that of a TGF-β-mediated increase in FAP cell number and FAP-mediated deposition of ECM in the muscle interstitium (6). Thus, inhibition of TGF-β may help prevent FAP-mediated skeletal muscle fibrosis in the setting of neurodegenerative diseases such as ALS. **Figure 1**, below, illustrates these molecular mechanisms promoting FAP mediated skeletal muscle atrophy and fibrosis in ALS.

**Muscular dystrophy**

Patients with muscular dystrophies suffer from characteristic progressive weakness and loss of muscle mass due to genetic perturbations of protein production requisite for healthy muscle development. Onset, signs, and symptoms of muscular dystrophies are dependent upon specific genetic
mutation-defined sub-classifications of these chronic myopathies. FAPs have been implicated in both the fibro-adipogenic remodeling of muscle and in some cases putative therapeutic intervention in Duchenne’s Muscular Dystrophy (DMD), Facioscapulohumeral Dystrophy, and Limb-girdle dystrophy.

**Duchenne’s Muscular Dystrophy**

Duchenne’s Muscular Dystrophy (DMD) is caused by an X-linked recessive mutation in the dystrophin gene which results in a complete loss of dystrophin in the sarcolemma. In healthy skeletal muscle tissue, dystrophin anchors the cytoskeletons of myofibers to the extracellular matrix by complexing with glycoproteins in the sarcolemma. In DMD, the unanchored sarcolemma is rendered vulnerable to mechanical stress. Therefore, DMD myofibers undergo permanent and asynchronous cycles of degeneration and regeneration which leads to chronic inflammation, fibro-adipogenic remodeling and atrophy of skeletal muscle tissues (11).

Myogenic progenitors (MP) and myotubes regulate the proliferation and fibro-adipogenic differentiation of FAPs, but this regulation is altered in DMD. Analysis of FAPs cultured in MP conditioned media revealed that MPs stimulate FAP proliferation by activation of the PI3K/Akt pathway, as further evidenced by reduction of Akt phosphorylation in FAPs and their proliferation rates in conditioned MP media with addition of an PI3Kinase inhibitor (12). However, the secretome of MPs is altered in a dystrophic environment. DMD MPs do not stimulate proliferation of DMD FAPs despite elevated Akt phosphorylation being observed in these FAPs, which was rescuable by healthy MP conditioned media (12). Further analysis of the MP secretome in healthy versus DMD muscle is necessary to elucidate specific factors responsible for FAP proliferation whose expression may be altered in the context of DMD, such as putatively platelet-derived growth factor-AA (3, 13). Whereas the MP secretome regulates FAP proliferation, the myotube secretome regulates FAP differentiation, inhibiting adipogenesis but promoting fibrogenesis. This is evidenced by mRNA expression of fibrotic and adipogenic markers in human FAPs treated with myotube-conditioned media compared to those treated with MP-conditioned media (12). Further molecular analysis of these cultures revealed that this anti-adipogenic and pro-fibrotic differentiation by myotube cytokines is mediated through activation of the ALK4/5/7 receptors, resulting in Smad2 phosphorylation and in parallel increasing GLI1 to activate Hedgehog signaling in FAPs (12, 14-16). Finally, these experiments revealed that MPs, rather than myotubes, secreted factors to inhibit FAP adipogenesis, and that DMD myotubes did not promote FAP-mediated fibrogenesis, suggesting that DMD alters the secretome of both MPs and myotubes (12). However, these findings...
suggest that non-myocyte cells are responsible for promoting FAP-mediated muscle degeneration in DMD. Chronic inflammation in DMD muscle involves the infiltration of pro-inflammatory macrophages, one subset of which is defined by Ly6C expression, found to be elevated in skeletal muscle of DMD patients and in Mdx mice (17). Elevated LTBP4 expression in DMD muscle stimulates Ly6C positive macrophages to produce latent-TGF-β1, which is activated by enzymes secreted by FAPs (17). Activated TGF-β1 then promotes FAP survival as well as myofibroblast differentiation and subsequent collagen deposition, thereby promoting pathological fibrosis of skeletal muscle (9, 17-19). Emerging evidence suggests that sub-populations of Vcam-1 expressing pro-fibrotic FAPs are persistent as DMD progresses (20). Furthermore, in early stages of DMD, FAPs can be reprogrammed to adopt pro-myogenic fates rather than fibro-adipogenic fates with histone deacetylase (HDAC) inhibitors, but lose this potency in late stages of the disease (21). HDAC inhibitors increase microRNA 206 in extracellular vesicles secreted by FAPs, which enhances satellite cell proliferation and differentiation and subsequent muscle regeneration in DMD human cells and Mdx mice (22). Similarly, TGF-β treatment of murine muscle progenitors and primary human cell cultures demonstrated increased expression of HDAC4, a key inhibitor of myogenic differentiation (23). However, HDAC4 expression can be directly attenuated by microRNA 206 and microRNA 29 through Smad3 inhibition, thereby supporting skeletal muscle regeneration in the context of aberrant TGF-β signaling (23). Since Metformin, an AMPK activator, reduces fibrosis and increases muscle regeneration and strength in murine models of DMD, it has been suggested that decreased AMPK expression in the DMD damaged myofiber niche initiates the macrophage and FAP mediated fibrosis of DMD skeletal muscle (17). Additionally, dysbiosis in macrophage subpopulation representation among the inflammatory infiltrate may support FAP adipogenesis. Whereas IL-4 polarized macrophages (M2) secrete cytokines to promote white adipocyte differentiation of FAPs, IL-1β macrophages (M1) secrete cytokines that promote phosphorylation of Smad2 in FAPs thereby inhibiting their adipogenic differentiation (18, 24). Thus, overrepresentation of IL-4 polarized macrophages within the inflammatory infiltrate in DMD tissues could support FAP-mediated white adipogenesis in skeletal muscle. In summary, the abnormal environment resulting from a lack of dystrophin creates an imbalance in IL-4 polarized macrophage-mediated signaling which ultimately results in increased white fat differentiation of FAPs, as illustrated in figure 2.

**Facioscapulohumeral Dystrophy**

Facioscapulohumeral muscular dystrophy (FSHD) is caused by an autosomal dominant mutation resulting in ectopic expression of the double homeobox 4 retrogene in skeletal muscle. This results in progressive weakness and wasting of muscles of the face, scapula, upper arms, trunk, and legs due to fibro-adipogenic remodeling of muscle. In a murine model of FSHD that closely recapitulates the pathophysiology of the disorder in humans, mice were observed to have a dose-dependent accumulation of intramuscular FAPs that positively correlated with inflammatory infiltrate, muscle fibrosis, and reduction in satellite cell numbers in diseased muscle (25).

FAPs that aberrantly accumulate in DUX4-expressing dystrophic muscle seem to be more sensitive to inflammatory stimuli during the progression of the disease as noted by differential gene expression of FAPs in acute vs. chronic doxycycline treated FSHD mice (25). The transcriptional profiles of the FAPs in FSHD patient muscles and from the hindlimbs of FSHD mice were strikingly similar (25). The transcriptional profile of these FAPs diverged from pro-myogenic FAPs seen in acute injury settings, and more closely resembled the transcriptional profiles of FAPs found pathologically in chronic disease (25). These findings suggest that DUX4-mediated dystrophy in FSHD results in the progressive fibrotic and adipogenic differentiation of FAPs. However, further studies are needed to further elucidate the molecular mechanisms through which such sub-population selection and fibro-adipogenic differentiation of FAPs supports the pathology of FSHD.

**Limb-Girdle Dystrophy**

Limb girdle muscular dystrophy 2B (LGMD2B) is a muscular dystrophy caused by mutations in dysferlin that manifests in weakness and atrophy of proximal muscles surrounding the hips and shoulders or limb girdles of patients (26). The paucity of dysferlin in the myofibers of these patients accounts for their impaired sarcolemmal repair, disrupted calcium homeostasis at t-tubes and immune dysbiosis in muscle tissues (27-32). This persistent myofiber damage positively correlates with accumulation of AnxA2, a dysferlin interacting protein that aids in its repair at the site of plasma membrane injury by inciting muscle inflammation (33, 34). AnxA2 levels progressively increases and correlates with disease severity in the ECM, creating a niche that results in FAP accumulation and subsequent adipogenic differentiation. This process is thought to occur through matrix metalloprotease 14 (MMP-14) signaling in myofibers which subsequently activates C/EBPd and PPARg expression in FAPs (35-37).
Rotator Cuff tears

Rotator cuff (RC) tears are among the most common musculotendinous injuries and their prevalence greatly increases with age (38, 39). Both the extent of muscle atrophy and fatty infiltration in injured RC muscles are independently predictive of worse outcomes after repair (40, 41). Although the pathophysiology of underlying muscle degeneration following RC tears remains under investigation, our group and others have found pathologic adipogenesis is commonly observed in RC, but no other musculotendinous injuries have been linked primarily to FAPs (42-44). We previously reported that TGF-β1 signaling is significantly increased in larger RC tendon tears, which not only promotes FAP survival, but also promotes both their fibro-adipogenic differentiation and remodeling of skeletal muscle (45, 46). All of these fibro-adipogenic effects of FAPs and their survival have been demonstrably attenuated with administration of a small molecular inhibitor of TGF-β1 in our group’s and other’s murine model of RC injury (43, 45). Additionally, the myokine IL-15 has been shown to activate the JAK-STAT pathway to stimulate FAP proliferation and the desert hedgehog pathway which inhibits FAP adipogenesis, such that IL-15 expression correlates with the severity of fibrosis and FAP abundance in chronic RC tears (47). However, a sub-population of FAPs known as beige FAPs, characterized by their UCP1 expression, have shown therapeutic efficacy in decreasing fibrosis, fatty infiltration, and atrophy and increasing vascularity and muscle function upon transplantation in murine models of RC repair (44, 48). Figure 3 highlights the heterogeneity of the FAP population in rotator cuff pathology and regeneration. Further investigation is required to elucidate molecular mechanisms that may be modulated to promote beige FAP differentiation in vivo.

Chronic disease processes

**Muscle fibrosis and sarcopenic obesity in Chronic Kidney Disease**

Muscle dysfunction serves as an important cause of morbidity among patients with chronic diseases including chronic kidney disease (CKD), chronic obstructive pulmonary disease (COPD), cardiovascular disease, and obesity. In patients with CKD, functional decline and loss of mobility, which precipitates falls, hospitalizations and morbidity may be in part due to skeletal muscle fibrosis (48-50). This excess collagen deposition in CKD patients is pathological and contributes to the skeletal muscle functional decline by reducing the transfer of force generated by myofibril contractile units per cross-sectional area of muscle tissue (49, 52-54).
Greater FAP abundance in human CKD muscle compared to controls was positively correlated with intrafibrillar collagen deposition (49). Compared to the muscles of healthy controls, muscles of CKD patients exhibited decreased macrophage abundances and associated decreased expression of TNF-α despite systemic inflammation in CKD patients (49). Therefore, skeletal muscle fibrosis in CKD patients may be linked to increased FAP abundance due to insufficient macrophage-produced TNF-α, which normally functions to promote FAP apoptosis. This results in increased intrafibrillar collagen deposition and subsequent decline in muscle function.

While reduced macrophage TNF-α signaling within skeletal muscle locally results in the aberrant survival of FAPs in muscle, increased systemic TNF-α and downstream effector signaling promotes FAP fibrotic differentiation (49, 55). Systemic elevation in TNF-α signaling in CKD stimulates production of myostatin through NF-κB at levels inversely proportional to patient’s eGFR (56-58). These elevated levels of myostatin are sustained through a signaling loop whereby myostatin signaling amplifies MAPK which in turn promotes IL-6 production followed by Stat3 activation which stimulates transcription factor C/EBPδ which results in production of myostatin (59). This augmented myostatin signaling promotes skeletal muscle atrophy by supporting satellite cell dysfunction and by stimulating Smad2/3 phosphorylation which in turn suppresses Akt phosphorylation, thereby activating the ubiquitin proteasome system, UPS (56, 60). Concomitant activation of UPS and dysfunction of satellite stem cells promotes skeletal muscle atrophy (55). This muscle atrophy has been shown to be suppressed by inhibition of myostatin in murine models of CKD (56).

Additionally, elevated myostatin promotes differentiation of FAPs into fibroblasts through Smad3 signaling (55). Because myostatin and FAP-mediated muscle fibrosis and atrophy can be suppressed by myostatin inhibition in murine models of CKD, this pathway may represent a therapeutic target for decreasing FAP-mediated muscle fibrosis in CKD (55).

FAPs are also stimulated to differentiate into adipocytes, resulting in sarcopenic obesity seen in CKD. The extracellular matrix protein CCN1 is a key driver of this fatty degeneration. CCN1 expression is positively correlated with muscle wasting, sarcopenia, and has recently been discovered to be upregulated in both serum and muscle of CKD patients relative to healthy controls (61). This expression increases in a dose dependent manner whereby CKD patients with sarcopenic obesity have higher serum and muscle CCN1 expression relative to CKD patients without sarcopenic obesity.

Figure 3. Rotator cuff tears result in sustained TGFβ-mediated survival of FAPs. However, FAPs are a heterogeneous population. One subpopulation contributes to fibrosis and fatty infiltration. The other subpopulation of UCP1+ FAPs may play a role in muscle regeneration and reduction of fatty infiltration.
In vitro treatment of FAPs with CCN1 promoted the growth of FAPs as well as their differentiation into adipocytes (61). CCN-mediated adipogenesis of FAPs was reversible with administration of a neutralizing CCN1 monoclonal antibody in the same cell culture conditions (61). However, further investigative studies are needed to elucidate the molecular mechanisms through which CCN1 is able to mediate FAP adipogenic differentiation and proliferation as well as satellite cell senescence.

In summary, myostatin and CCN1 inhibition may abrogate FAP-mediated pathogenesis of skeletal muscle fibrosis through differentiation into both adipocytes and fibroblasts, as well as satellite cell senescence.

Muscle atrophy in Chronic Obstructive Pulmonary Disease
Patients with COPD suffer from progressive and irreversible airway obstruction and chronic inflammation of the lungs (62). Skeletal muscle atrophy and dysfunction in these patients can be correlated with their physical inactivity, chronic inflammation, oxidative stress, and recurrent hypoxic episodes due to COPD exacerbations (63). Hypoxic stress in skeletal muscle due to COPD results in muscle degradation that may be mediated through aberrances in FAP recruitment or retention in skeletal muscle (1). FAPs and muscle progenitors express sialomucin CD34, which has been demonstrated to be necessary for skeletal muscle repair in response to acute-toxin-induced injury (1, 64). One study found that two days of exposure to hypoxic conditions is sufficient to induce muscle wasting and loss of lean mass similar to what is seen in COPD patients in mice and that this muscle wasting was notably worse in CD34 knockout mice (63). While expression of myogenic regulatory factors and protein degradation factor (Atrogin) were similar in both the CD34 knockout mice and wildtypes, the knockout mice’s extensor digitorum longus muscle was measured to have decreased maximal strength and recuperation capacity in response to hypoxia compared to that observed in wildtype mice (63). Moreover, FAP abundance in skeletal muscles of...
CD34 knockout mice were significantly decreased relative to in wildtype mice (63). Taken together these findings suggest that maintenance of muscle mass and function in response to recurrent hypoxemic insults as seen in COPD may be dependent on CD34-mediated accumulation of FAPs in injured skeletal muscle (63). However, further studies are needed to elucidate the molecular mechanisms that perturb FAP-mediated muscle homeostasis in the context of COPD.

**Cardiac muscle fibrosis and adipogenesis following acute or chronic injury**

Cardiovascular diseases categorically are the leading cause of morbidity and mortality worldwide (65). Cardiac fibrosis and fibro-adipogenic remodeling of the heart in response to acute or chronic ischemic injury that results in reduced ejection fraction, arrhythmogenicity, and heart failure may be mediated in part by FAPs. Post-myocardial infarction fibrogenic remodeling of cardiac tissue by cardiac stromal FAPs can be abrogated by administration of an anti-fibrotic tyrosine kinase inhibitor (66). Perivascular cells that co-express PDGFRα and Gli1 have been observed to differentiate into myofibroblasts and contribute to cardiac fibrosis in murine models following angiotensin-2-induced myocardial fibrosis and ascending aortic constriction (67). Furthermore, genetic models following angiotensin-2-induced myocardial fibrosis of myofibroblasts and contribute to cardiac fibrosis in murine models following angiotensin-2-induced myocardial fibrosis and ascending aortic constriction (67). Furthermore, genetic ablation of these FAPs ameliorates cardiac fibrosis and preserves ejection fraction in murine heart failure models (67). Additionally, in mice depleted of α-V integrins, which block TGF-β signaling in PDGFRα'/PDGFRβ' cardiac tissue resident FAPs, cardiac fibrosis was significantly reduced (68). Thus, TGF-β signaling mediates FAP fibrogenesis and subsequent fibrotic ECM deposition in both cardiac and skeletal muscle fibrosis (68).

Cardiac resident FAPs have additionally been implicated in the pathogenesis of cardiac fatty infiltration which precipitates arrhythmogenic disorders. In *in vitro* lineage tracing studies of human and mouse cardiac FAPs following genetic ablation of desmosome proteins, such as DSP, adipogenic but not fibrogenic FAPs underwent adipogenesis mediated by Wnt signaling (69). These FAPs account for at least 50% of the pathologically increased cardiac fibro-fatty infiltrate that results in ventricular arrhythmias, heart failure, and even sudden death in arrhythmogenic cardiomyopathy, a genetic disorder due to desmosomal protein aberrancies (69, 70). Furthermore, genetic ablation of the quiescence factor HIC1 in cardiac FAPs in an otherwise healthy murine heart also recapitulates the fibro-fatty infiltration and functional arrhythmogenicity observed in patients with arrhythmogenic cardiomyopathy (66).

Finally, cardiac FAPs mirror their skeletal muscle FAP counterparts’ multipotency as they contribute to cardiac fibrosis, cardiac fatty infiltration, and vascular calcification. Genetic fate mapping of murine epicardium in concert with immunostaining analysis of PDGRFα/Sca-1 distribution in fetal heart tissues indicate that cardiac FAPs arise from the epicardium (71). These FAPs primarily contribute to vascular compartments but also assist in cardiac tissue homeostasis (71). Aberrant FAP osteogenesis in the aorta may contribute to the vascular calcification notable in aortic stenosis leading to ventricular hypertrophy, chronic extremity ischemia, and heart failure (71). However, further investigation is needed to elucidate the molecular mechanisms underlying this aberrant osteogenic differentiation that mirrors that of skeletal FAPs in heterotopic ossification.

**Obesity-related fatty infiltration of muscle**

Obesity is a chronic condition defined by excessive fat accumulation that presents a risk to an individual’s health. Increased intramuscular fatty and fibrotic tissue in muscle of obese patients both decreases the force producing capacity of these tissues as well as glucose metabolism thereby contributing to both the pathogenesis of muscle remodeling and decreased sensitivity eventually leading to metabolic syndrome (72). FAP differentiation into fibroblasts or adipocytes in the context of metabolic stress are key contributors to the pathogenesis of obesity-related skeletal muscle fibrosis, degeneration, and metabolic decline. Several adipokines have been discovered to stimulate FAP-derived adipogenesis in obesity-related myopathies. Thrombospondin 1 (THBS1), a white adipokine secreted from expanded adipose tissue, promoted FAP proliferation in obese mice (73). TGF-β derived from expanded adiposity as well as other organs similarly modulates both FAP proliferation and fibrogenic differentiation *in vitro*. This finding is further substantiated by a reduction in collagen deposition and FAP abundance with TGF-β inhibition (5, 72, 74-77). Increased skeletal muscle adiposity not only contributes to decreased force-generation, but also contributes to insulin resistance of these same tissues.

Additionally, obesity and metabolic disorders such as diabetes are associated with chronic low-grade inflammation wherein macrophages sustain FAP survival, as seen in the other dystrophic states discussed above. In obesity-related fatty infiltration, macrophages secrete TGF-β1 which abrogates TNF-induced apoptosis of FAPs and instead promotes their fibrogenic differentiation and subsequent ECM deposition (17, 49, 72, 77). As discussed above, sub-populations of polarized M1 and M2 macrophages have opposite effects on FAP differentiation *in vitro*. While IL-1β polarized macrophages (M1) modulate a reduction in FAP adipogenic differentiation by stimulating Smad2 phosphorylation in FAPs downstream of TGFβ-1 signaling as assayed by decreased cellular lipid accumulation and reduced adipogenic gene expression but increased pro-inflammatory cytokines, IL-4...
polarized macrophages (M2) enhanced FAP adipogenesis (18). Thus, M1 and M2 macrophages likely sustain fibrogenesis and adipogenesis of FAPs in the pathogenesis of skeletal muscle fibrofatty degeneration in the setting of chronic inflammation associated with obesity and diabetes. Just as FAPs have been implicated in skeletal muscle fibrosis, degeneration and metabolic decline, they are implicated in the fibro-adipogenic remodeling of the diaphragm contributing to the pathogenesis of respiratory dysfunction of obese patients. This respiratory dysfunction characterized by impaired lung expansion and reduced central response to hypercapnia can contribute to increased cardiovascular morbidity and mortality that necessitates mechanical ventilatory support (73). Six months of high fat diet-induced obesity in mice was sufficient to reproduce shallow, short-interval breaths with increased duty cycle that are notable in obese humans (73). This respiratory dysfunction occurred in parallel with increased diaphragmatic adiposity, fibrosis and contractile dysfunction. Moreover, elevated circulating THBS1 and TGF-β3 within the diaphragm of obese mice mediated expansion of the FAP pool (73). The progressive adipogenic differentiation of FAPs within the diaphragm predominantly yielded white adipocytes but also produced some beige adipocytes (73). Further research is needed to fully elucidate the molecular mechanisms underlying FAP mediated fibro-adipogenic diaphragm remodeling and respiratory decline.

Sarcopenia and aging

Sarcopenia is the loss of muscle mass and function, frequently associated with normal aging as well as with chronic disease. Studies examining age-related sarcopenia highlight the important role of FAPs in the maintenance of muscle fiber mass through their crosstalk with MuSCs. Using transcriptome profiling of FAPs, it was shown that FAPs from aged muscle lose expression of WNT1 Inducible Signalling Pathway Protein 1 (WISP1), a matricellular signal that controls the expansion and asymmetric commitment of MuSCs through Akt signalling (78). This study further demonstrated that both transplantation of young FAPs to aged muscle as well as systemic administration of WISP1 to aged mice rescued the sarcopenic phenotype in aged mice (78). An in vitro study likewise showed that aged myogenic progenitors (MPs) failed to stimulate proliferation of FAPs through Akt phosphorylation as was observed with MPs from young donors (12). Taken together, these studies suggest that age-related sarcopenia is likely due to a failure of communication between FAPs and myogenic progenitors that occurs due to age-related changes in signaling in both populations of stem cells, as illustrated in figure 5.

**Heterotopic Ossification**

Heterotopic Ossification (HO) is defined as ectopic osteogenesis in non-skeletal tissues including muscle, tendons, and other soft tissues. This debilitating condition can be either a genetic or acquired disease from traumatic injury: soft tissue sports injuries, central nervous system damage, total hip arthroplasty, burns and in combat injuries (79-83). Osteogenic remodeling of muscle in trauma-induced HO precipitates joint ankylosis, impairs rehabilitation and

![Figure 5](image.png)

**Figure 5.** Failed crosstalk between FAPs and MPs promotes sarcopenic degeneration.
CONCLUSIONS AND PERSPECTIVE
As FAPs are a ubiquitous source of resident muscle stem cells, it can be expected that they play a diverse role in a variety of musculoskeletal disease processes, ranging from myopathies, to denervation-mediated processes, to chronic musculotendinous injuries. Upon reviewing the disease processes above, it is clear that FAPs play a nuanced role along with myogenic progenitors in maintaining normal muscle homeostasis, and when this balance is disrupted, FAP-mediated muscle degeneration may occur. The pathways highlighted above represent many potential therapeutic targets for the specific disease processes discussed, many of which are under active clinical investigation. However, many of these targeted interventions would likely carry broad systemic effects, in addition to potentially disrupting the nuanced balance between FAP-mediated muscle regeneration and adipogenic or fibrogenic differentiation of FAPs, particularly those that directly affect FAP cell number or viability. Future studies targeting muscle-specific therapeutics to decrease systemic effects may be the next step in ameliorating muscle degeneration.

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CONFLICT OF INTERESTS
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ABBREVIATIONS:
ActR1: Actin related protein 1
ACVR1: Activin receptor type 1
Akt: Protein kinase B
Alk2: Activin receptor-like kinase 2
ALK4/5/7: Activin receptor-like kinase 4/5/7
ALS: Amyotrophic lateral sclerosis
AMPK: Adenosine monophosphate activated protein kinase
BMP: Bone morphogenetic protein
BMP2: Bone morphogenetic protein 2
C/EBPδ:CCAAT enhancer binding protein delta
CCN1: Connective tissue growth factor nephroblastoma overexpressed 1
CD34: Cluster of differentiation 34
CKD: Chronic kidney disease
COPD: Chronic obstructive pulmonary disease
CTGF: Connective tissue growth factor
DMD: Duchenne’s muscular dystrophy
ECM: Extracellular matrix
eGFR: estimated glomerular filtration rate
FABP4: Fatty acid binding protein 4
FAPs: Fibro-adipogenic progenitor
FOP: Fibrodysplasia ossificans progressiva
GLI1: Glioma associated oncogene 1
HO: Heterotopic ossification
IL-15: Interleukin-15
IL-1β: Interleukin-1-beta
IL-4: Interleukin-4
IL-6: Interleukin-6
JAK: Janus kinase
LTBP4: Latent transforming growth factor beta binding protein 4
M1: Macrophage type 1
M2: Macrophage type 2
MAPK: Mitogen activated protein kinase
MP: Myogenic progenitor
Mrna: Messenger ribonucleic acid
MT: Myotube
NF-κb: Nuclear factor kappa beta
NMJ: Neuromuscular junction
NSAID: Nonsteroidal anti-inflammatory drug
p-Akt: phosphorylated protein kinase B
p-Smad2: phosphorylated smad protein
PDGFβR: Platelet derived growth factor receptor alpha
PI3K: Phosphoinositide 3-kinase
PPARγ: Peroxisome proliferator-activated receptor gamma
RARγ: Retinoic acid receptor gamma
RC: Rotator cuff
Scal: Stem cells antigen 1
SMA: Spinal muscle atrophy
Smad1/5/8: Smad protein 1/5/8; main signal transducers for receptors of transforming growth factor beta
Smad2: Smad protein 2; main signal transducers for receptors of transforming growth factor beta
Smad3: Smad protein 3; main signal transducers for receptors of transforming growth factor beta
STAT3: Signal transducer and activator of transcription 3
Tcf4: Transcription factor 4
TGF-β: Transforming growth factor beta
Tie-2: Angiopoietin-1 receptor
TNF-α: Tumor necrosis factor alpha
UCP1: Uncoupling protein 1
UPS: Ubiquitin proteasome system
Vcam-1: Vascular cell adhesion protein 1
α-SMA: alpha smooth muscle actin

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Effects of Traditional Srichiangmai dance on Balance and Mobility in the Elderly

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SUMMARY
Background. Previous research indicates that slow movement dance exercise can stimulate function of core muscles effectively may improve physical fitness and balance among older adults.

Methods. This study investigated the effects of Traditional Srichiangmai dance on balance and mobility in the elderly. Ninety participants aged 60-75 years, the data was normally distributed, were recruited and randomly assigned into two groups: A Traditional Srichiangmai dance group (TSD) (n = 45) and a walking group (WG) (n = 45). TSD program comprised 15 postures, 4 rounds of dance techniques sessions of 30 minutes, 3 time per week over the course of 12 weeks, while the WG kept their walking exercise. Before and after the training, the tests of health-related physical fitness (HRF) variables composed of body composition, general physiology, balance and mobility performance, were assessed using standardized tests including the Functional reach test (FRT), Timed Up and Go Test, (TUG), 6-minute walk test Chair stand test and Arm curl test for 30 seconds.

Results. The results revealed that in both groups, Physiological variables including heart rate rest, systolic blood pressure decreased while VO₂max increased, higher than the pre-test values (p ≤ 0.05). FRT and TUG was better for those in TSD compared to the WG. There was significant in the FRT (p ≤ 0.001) for those in the dance group. TSD had faster movement, took shorter time and performed a better score in the TUG after training (p ≤ 0.001).

Conclusions. After 12 weeks, Traditional Srichiangmai dance significantly improved balance and mobility among older community-dwelling as potentially prevent age-related mobility and balance decline as well as its related fall risk.

KEY WORDS
Traditional Srichiangmai dance; balance; mobility; elderly; physical fitness.

BACKGROUND
Presently, the medical development supports the people to live longer. The elderly’s physical change affects physical functions including muscular strength, cardiorespiratory endurance and flexibility as well as other congenital diseases (1, 2). The rate of physical fitness decreased when ages increased; the elderly’s balance also reduced (3). The physical performance reduces in functioning due to the reduction of mobility and balance. This causes the elderly’s related fall risk. (4, 5). It is found that among those who were 65 or older had 28-35% of fall risk whereas those who were 70 or older had 32-42% of fall risk, especially for the female elderly. Moreover, the statistics related to injury proposed by the Department of Disease Control, the ministry of public health in 2019 showed that the cause of death from fall was found the second whereas the first cause of death was road accident (6, 7). The activity to promote exercise to enhance muscles strength will help improve balance ability and reduce risk of for approximately 19 percent (8).
To enhance physical fitness with readiness and regular exercise can help reduce the risk of disease for the elderly and result in better physical fitness improvement heart function system work together efficiently (9). The researcher, addition, found that endurance training in elderly can increase heart muscles and strength, blood circulation in blood cells and blood flowing to heart better. When the amount of blood flowing to heart increased, physical organs will receive sufficient blood for functioning (10, 11). Moreover, regular exercise and continuation in the elderly will decrease heart rate and resistance of blood vessels which will result in the decrease of blood pressure (12, 13). Appropriate exercise for the elderly should be in form of aerobic with low impact within 20-30 minutes, 3-5 times a week in order to make the exercise most effective (14 - 16).

Different forms of aerobic dance exercise are very popular. It is the form of exercise that compose art, calisthenics, basic movement and dance step to be composed and applied to be a form of moment in music rhythm (17). Fon Ram or folk dance is mixed between movement in rhythm and the control of actions or postures. The pattern of dance needs the movement of all parts of the body to move slowly, then it helps improve all 3 systems of physical movement including central nerve system, sensory nerve system and muscular systems. These are good for core muscles which related to balance ability. The previous studies showed that slow movement exercise can stimulate function of core muscles effectively such as Waikru muaythai exercise (18), Tai Chi, Qigong (19, 20). Dance is a movement skill which is easy to control functional of balance. It is applied for exercise with beautiful postures with rhythm of slow movement to reduce impact. It is suitable for elderly. According to the field study in Pranprao sub-district, Srichaingmai district, Nongkai province, Thailand it was found that the community had their own dance postures as their identical uniqueness and the pattern of slow movement in rhythm which can be performed by all ages and genders, especially for the elderly. Consequently, this form of exercise is appropriate for being applied for the elderly in the community.

As mentioned earlier, the researcher had an idea to promote the beautiful culture along with physical and mental health and became interested in developing the model of aerobic exercise with low impact and folk-dance postures in rhythm of movement in folk music. This activity can link with the lifestyle of the local people and it is the way to conserve folk dance of the community to be promoted internationally. Consequently, the researcher was interested in studying the result of using folk dance for exercising which is called the activity in this research Traditional Srichangmai dance to enhance physical fitness including physiological, balance ability and mobility which are all important for daily-life activates and improving sustainable quality of life.

**MATERIALS AND METHODS**

This research is a Quai-experimental research design with two group pretest-posttest design, certified and proved by The Research Ethics Review Committee for Research Involving Human Research Participants, on 13th March 2017, project no. HE 0299/2560. The participants understood the details of practice during the experiment and signed consent letter to participate in the research.

**Participants**

The number of 90 participants were the older people residing in the elderly school Nongkai Province, males and females aged 60-75 years old, doing normal routines without having regular exercise. The simple random sampling technique was applying the balance and mobility abilities to rank and draw a random draw into two groups; the first group consisted of 45 participants performing Traditional Srichangmai dance and the second group consisted of 45 participants performing walking exercise. The participants were signed the consent document to participate in the research. All participants needed to pass the questionnaire for examining their general health history and physical activity readiness questionnaire (PAR-Q) specifying that they did not have any diseases involving with muscles and nerve systems. In addition, they were all able to walk. On the other hand, the participants who could not participate throughout the research project will be removed from the experiment.

**Experimental training**

In this study, the researchers designed both patterns of exercise as parts of health promotion activity for the elderly in the school for the older people. Both groups exercised for 30 minutes, 3 times a week, totally 12 weeks. For the details and instruction of exercise, the experimental group performed Traditional Srichangmai dance exercise including warm-up and stretching for 5 minutes, then began practicing 15 Traditional Srichangmai dancing postures techniques, each posture 32 continuous tempo and repeated 4 rounds for 20 minutes and practiced static stretching for 5 minutes. For the control group, the participants performed walking exercise beginning with warm-up, static stretching for 5 minutes and then walking with normal speed for 20 minutes and then doing static stretching for 5 minutes. Both
groups maintained an intensity of exercise 60-75% of maximum heart rate. There were sport scientists observing and suggesting the participants for correct positions and postures as well as breathing methods during the time of training.

Figure 1. Tha Buachufack.

Figure 2. Tha Manee.

**Measurement of outcomes**

**Physiological**

The data collection was conducted to test the variables regarding health at Sport Science and Exercise Laboratory in the faculty of Science and Technology, Loei Rajabhat University, Thailand from 08.30-12.00 am. The samples performed rest sitting for 5 minutes and were measured with Omron HEM-7320 to examine their heart rate, systolic blood pressure and diastolic blood pressure. Then, the samples were examined for their body composition using Bioelectrical Impedance Analysis (BIA), in body 370 model, including body weight (kilogram) and BMI (kg/m²).

**Balance and mobility assessment**

The researcher evaluated the reliability within the measure (research assistant) to measure all two balance abilities before the actual assessment. The measurement reliability was excellent (ICC = 0.964, 0.986, respectively). Then, the balance was tested:

- **method 1:** in a standing position, arms were stretched at shoulder width, reaching forward (functional reach test, FRT) for as far as possible;
- **method 2:** the fluency and balance were tested while moving (agility and dynamic balance) by sitting, standing, walking (Timed Up and Go Test, TUG). Upon hearing the “start” signal, samples stood up from the chair, walked at as fast a distance as 8 feet, turned back, walked back and sat in the same chair.

The researchers measured the timer (seconds) from getting up from the chair and until returning to the chair. In addition, the researcher tested walking ability with 6-minute walk test, 60 meters for each of walking round, for 6 minutes. Chair stand test 30 second was conducted to test the strength and endurance of lower body test and the final test upper body muscles. The samples sat with arm curled doing arm curl test for 30 seconds then counted the number of times in a fully practiced posture.

**Intensity control and Energy Expenditure**; In both groups, intensity was controlled, 60-75% of maximum heart rate throughout the duration of each exercise. Intensity and energy expenditure while training with Traditional Srichiangmai dance and walking exercise group were observed. All participants put on heart rate monitor (Polar Team Pro) in which the signal was connected to the receiver (Apple Ipad). The results were displayed on the screen while training including Heart Rate (bpm), percent of Average Heart Rate (%AVGHR), Percent of Maximum Heart Rate (%AVGHRmax) and Energy Expenditure of Exercise in Kilocalories (Kcal).

**Statistical analysis**

Descriptive statistics were used to describe the characteristics of the sample. A normal distribution test of data using the Kolmogorov-Smirnov Statistics Test (n > 50) found that the data was normally distributed. Changes within the group were analysed before and after the training with the Paired t-test and the differences between the groups were
analysed with Independent t-test statistics at the significant level $\alpha=0.05$ and with SPSS 17.0 (SPSS Inc. Released 2008. SPSS Statistics for Windows, Version 17.0 Chicago: SPSS Inc.).

**RESULTS**

There were 90 volunteers in this study divided into two groups. However, the two volunteers disappeared during the experiment, in which each group did not complete the program as specified. Initially, the basic data analysis results of the volunteers in both groups were of average age. Most of the female groups in both groups were overweight referred to the BMI. The general data of the volunteers before exercise showed that there was no significant difference.

The analysis with pair t-test revealed that heart rate, systolic blood pressure and VO$_{2\text{max}}$ of both groups had statistically significant difference when comparing between before and after exercise ($p \leq 0.05$). However, when analyzing between groups using Independent t-test statistics, using the mean values of change in physiological, there were no significant differences between the experimental groups. In addition, both groups were able to stabilize from the mobility of the lower body with the 6-minute walk test, strength and endurance of lower body with the chair stand test 30 second and upper body with the arm curl test for 30 second which was statistically improved within the group when comparing between before and after exercise ($p \leq 0.05$). When analyzing between groups using Independent t-test statistics, using the mean of the change in balance ability. It was found that the experimental group exer-

**Table I. Traditional Srichiangmai dance program.**

<table>
<thead>
<tr>
<th>Day</th>
<th>Unit of training</th>
<th>Traditional Srichiangmai dance</th>
<th>Duration of training</th>
</tr>
</thead>
<tbody>
<tr>
<td>Warm up</td>
<td>Static stretching of major muscle groups</td>
<td>5 minutes</td>
<td></td>
</tr>
<tr>
<td>Monday</td>
<td>Work out</td>
<td>Tha Maesri</td>
<td>15 Traditional Srichiangmai dancing posture techniques, each post 32 continuous tempo and repeated 4 rounds for 20 minutes</td>
</tr>
<tr>
<td>Wednesday</td>
<td></td>
<td>Tha Plangai</td>
<td></td>
</tr>
<tr>
<td>Friday</td>
<td></td>
<td>Tha Traven weha</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Tha Glang amporn</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Tha Sodsoi mala</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Tha Yonkeaw</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Tha Pisamai riangmon</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Tha Char nangnon</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Tha Orashon</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Tha Buuchufack</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Tha Kinarree</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Tha On-an</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Tha Srida</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Tha Manee</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Tha Nuaynard</td>
<td></td>
</tr>
<tr>
<td>Cool down</td>
<td>Static stretching</td>
<td></td>
<td>5 minutes</td>
</tr>
</tbody>
</table>

**Table II. General information of samples.**

<table>
<thead>
<tr>
<th>General information of samples</th>
<th>Experimental group (n = 45)</th>
<th>Control group Walking exercise (n = 45)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (male:female)</td>
<td>8:37</td>
<td>12:33</td>
<td>-</td>
</tr>
<tr>
<td>Age (year)</td>
<td>63.64 ± 4.6</td>
<td>64.20 ± 4.5</td>
<td>.641</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>153.60 ± 4.2</td>
<td>153.84 ± 4.0</td>
<td>.882</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>60.79 ± 10.0</td>
<td>61.26 ± 9.5</td>
<td>.526</td>
</tr>
<tr>
<td>Body mass index (kg/m2)</td>
<td>24.79 ± 3.1</td>
<td>24.81 ± 2.9</td>
<td>.721</td>
</tr>
<tr>
<td>Average Heart Rate (% AVGHR)</td>
<td>67.21 ± 12.9</td>
<td>66.06 ± 12.2</td>
<td>.825</td>
</tr>
<tr>
<td>Maximum Heart Rate (% AVGHRmax)</td>
<td>74.42 ± 16.8</td>
<td>74.10 ± 16.1</td>
<td>.925</td>
</tr>
<tr>
<td>Expenditure of Exercise (Kcal)</td>
<td>281.71 ± 21.4</td>
<td>280.20 ± 21.4</td>
<td>.831</td>
</tr>
</tbody>
</table>
cising with respect to Traditional Srichiangmai dance had a statistically significant in their balance ability and mobility (p ≤ 0.001). Additionally, the functional reach test and timed up and go test (TUG) showed faster movement time, walking speed, and a better score before training.

**DISCUSSION**

This research was conducted by integrating the knowledge of the art of traditional dancing to create aerobic exercise forms of exercise that are novel, safe, fun, challenging, suitable for health promotion activities of the elderly. The exercise style emphasizes various movement skills, combining the Traditional Srichiangmai dance style which is the national cultural heritage of Thailand. And the researcher has studied the effect of exercise training on health-related physical fitness, balancing ability and mobility in the elderly by comparing with exercise styles by walking which is the introduction of both forms of exercise activities as part of promoting physical activities in the elderly school Nongkai, Thailand. The research findings can be discussed as follows.

The physiological data report of the two experimental groups after 12 weeks showed that the body composition, consisting of body weight, body mass index compared and fat mass to before the experiment has a tendency to decrease. There was no significant difference found after exercise. The change of variables related to body composition showed that both forms of exercise did activate of large muscles for continuous movement, and the circulation of all muscle groups. It can be said that this form of exercise is aerobic exercise, which is a process that uses the energy system of the body at a time level as well as the right weight to use energy from fat for combustion as energy, which is related to weight loss (21, 22). In addition, the side physiological variables were related to the cardiovascular system and the ability to work better. In this study, we found that after exercise, the heart rate and systolic blood pressure decreased when comparing to before exercise. According to the change, it can be explained that exercise that can maintain the level of heart rate and control the proportion of respiration provide a good effect on the heart, circulatory system and respiration. In this study, it was found that both subjects reduced in heart rate resting and systolic blood pressure. In addition, maximum oxygen consumption (VO2max) increased

<table>
<thead>
<tr>
<th>Variable</th>
<th>Experimental group (n = 45)</th>
<th>Control group (n = 45)</th>
<th>t</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Traditional Srichiangmai dance</td>
<td>Walking exercise</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Pretest</td>
<td>12 weeks</td>
<td>Pretest</td>
<td>12 weeks</td>
</tr>
<tr>
<td>Physiological</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>60.78 ± 10.1</td>
<td>59.94 ± 8.0</td>
<td>61.04 ± 9.7</td>
<td>60.22 ± 9.0</td>
</tr>
<tr>
<td>Body mass index (kg/m2)</td>
<td>25.79 ± 3.1</td>
<td>25.65 ± 2.9</td>
<td>25.94 ± 2.5</td>
<td>25.62 ± 2.3</td>
</tr>
<tr>
<td>Muscle mass (kg)</td>
<td>23.00 ± 2.6</td>
<td>23.02 ± 2.7</td>
<td>22.87 ± 2.4</td>
<td>22.86 ± 2.4</td>
</tr>
<tr>
<td>Fat mass (kg)</td>
<td>27.15 ± 4.9</td>
<td>26.90 ± 4.4</td>
<td>27.75 ± 4.5</td>
<td>27.64 ± 4.4</td>
</tr>
<tr>
<td>Waist hip ratio (inc)</td>
<td>0.83 ± 0.1</td>
<td>0.83 ± 0.1</td>
<td>0.84 ± 0.1</td>
<td>0.85 ± 0.1</td>
</tr>
<tr>
<td>Basal metabolic rate (Kcal)</td>
<td>1208 ± 125.1</td>
<td>1209 ± 124.0</td>
<td>1215 ± 118.8</td>
<td>1215 ± 118.7</td>
</tr>
<tr>
<td>Heart rate (bpm)</td>
<td>79.51 ± 5.7</td>
<td>77.40 ± 4.1</td>
<td>78.80 ± 4.9</td>
<td>77.60 ± 4.3</td>
</tr>
<tr>
<td>Systolic blood pressure (mm/Hg)</td>
<td>128.4 ± 9.1</td>
<td>126.9 ± 8.8</td>
<td>129.3 ± 9.5</td>
<td>126.3 ± 8.2</td>
</tr>
<tr>
<td>Diastolic blood pressure (mm/Hg)</td>
<td>77.33 ± 7.9</td>
<td>75.78 ± 7.0</td>
<td>76.11 ± 8.1</td>
<td>77.89 ± 7.6</td>
</tr>
<tr>
<td>Maximum oxygen consumption</td>
<td>24.27 ± 1.3</td>
<td>26.07 ± 2.9</td>
<td>24.40 ± 1.1</td>
<td>26.29 ± 3.1</td>
</tr>
<tr>
<td>Balance and mobility</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Functional reach test (cm)</td>
<td>13.7 ± 1.3</td>
<td>16.6 ± 1.9</td>
<td>12.8 ± 1.2</td>
<td>14.2 ± 1.9</td>
</tr>
<tr>
<td>Timed Up and Go Test (second)</td>
<td>7.48 ± 2.3</td>
<td>7.17 ± 2.1</td>
<td>7.52 ± 2.4</td>
<td>7.24 ± 1.8</td>
</tr>
<tr>
<td>6-Minute walk test (meter)</td>
<td>489.23 ± 51.3</td>
<td>495.85 ± 54.9</td>
<td>476.07 ± 49.9</td>
<td>481.00 ± 53.0</td>
</tr>
<tr>
<td>Chair stand test 30 second (reps)</td>
<td>15.8 ± 1.2</td>
<td>18.7 ± 1.9</td>
<td>15.5 ± 1.1</td>
<td>18.2 ± 1.7</td>
</tr>
<tr>
<td>Arm curl test 30 second (reps)</td>
<td>18.07 ± 0.8</td>
<td>18.50 ± 1.3</td>
<td>19.47 ± 0.8</td>
<td>19.27 ± 1.6</td>
</tr>
</tbody>
</table>

The data are presented by means ± SD; * statistically significant difference when compared within group, mean scores at point comparisons from baseline: *p ≤ 0.05 and *t p ≤ 0.01 when comparing the difference between experimental groups.
when comparing to before exercise. The method of exercising with the ‘Traditional Srichiangmai dance is using the rhythm of the music which has the relationship of the rhythm of body movement continuously. The participants were advised for how to breathe and manage fatigue while exercising. Those who practiced exercise can control the intensity of heart rate continuously. This is consistent with the recommendations of Emiliano et al. (23) who described that the benefits of breathing exercises while exercising can affect the efficiency of the breathing and the cardiac muscles that help with compression. This is related to the function of controlling the baroreceptor system. Exercise will stimulate the vagal tone, resulting in slower heart rate. Lower peripheral vascular resistance helps promote the function of the artery wall which is an important reason for the decrease in blood pressure values (24, 25).

Traditional Srichiangmai dance is a new alternative exercise that can be added physical fitness for the elderly. The basic parameters of the structure of the body that promotes good physical fitness are 2 components, which are the strength and endurance of the muscles which has a positive effect on the structure of the body. In this study, the researcher realized that the training posture with the basic movement skills in daily life of the elderly. From the 6-minute walk test chair stand test 30 second and arm curl test 30 second, it was found that both experimental groups had an increased average when compared with before the experiment with statistical significance at the level of 0.05. In addition, the average post-exercise mean shows that Traditional Srichiangmai dance group have better balance ability and mobility with test the functional reach test (FRT) and movement time, walking speed with timed up and go test (TUG) than walking exercise groups when compared after 12 weeks of exercise. This is due to the use of Traditional Srichiangmai dance postures, using postures that use the power of the muscles of various parts of the body in rhythm, with the use of muscles in relation to the rhythm of the music that controls the movement. This helps control the muscles in various movements, postures and concentrate during practice. It is consistent to the study of Laophosri et al. (26) the study of exercise using Thai dance on the physical fitness and balance ability in the elderly. It was found that, after practicing Thai dance, there was a positive effect on balance ability. Similarly, Noopud et al. (27) described the benefits of Thai Dance to balance ability based on Berg balance score, strength of the muscles in lifting tests in the arms curl test for 30 seconds and Chair stand test for 30 seconds. The results are consistent to this result that Traditional Srichiangmai dance can help strengthen muscular strength which is a fundamental factor related to the ability to maintain a balanced body while moving effectively. In addition, Chen et al. (28) suggested that higher quadriceps strength was associated with better cognitive performance. This study focused on the study of variables related to balance in the elderly by the Functional reach test, which found that the samples had the ability to test the functional reach test in increasing range after exercise with statistical significance at the level of .001. There is also the test of agility and dynamic balance with Timed Up and Go Test, which are basic skills in daily physical movements. From the test results, it was found that experimental group was able to improve their mobility within movement time, walking speed the body according to the conditions of the test with shorter duration. Although this study does not include mechanisms that increases the ability to balance performance directly, but it can discuss the strength from the designed posture training of Traditional Srichiangmai dance with rhythm. This pattern requires the principle of transferring weight during movement in rhythm with various postures together with weighting on the heel and toes which will stimulate the senses and maintain a more balanced weight on the feet (2, 29).

Aging is an inevitable biological process that is characterized by a general decline in the physiological and biochemical functions of the major systems. In the case of the neuromuscular system, reductions in strength and mobility cause a deterioration in motor performance, impaired mobility and disability (30). Traditional Srichiangmai dance was applied by the researcher using rhythm to control body movement together, due to the muscles are the effectors of the descending orders from the CNS, thus, the sensorial integration and its output to the muscles (31). Affect to contracting the abdominal muscles and lower back muscle to help increase the stability of the core muscle while moving rhythmically at all times while performing the strength of the core muscles that are responsible for controlling body movement (32, 33). This causes the motion recognition mechanism to work harmoniously (coordination movement) both the arms and legs, resulting in the control of the coordination of muscles (neuromuscular control) awareness of joints (proprioceptive sense) according to the rhythm repeatedly throughout the training period (34). That is to say, exercise in a muscle group that is primarily responsible for controlling the movement of the arms, legs, or core muscle groups, including abdominal muscles, back, pelvic floor and diaphragm, resulting better balance of the participants (35, 36).

In this research, 15 Traditional Srichiangmai dancing postures techniques, each poste 32 continuous tempo and repeated 4 rounds of dance techniques were performed and repeatedly practiced with simple rhythm. Therefore, according to the above principles, it can be explained that the form of exercise by paying respect to Traditional Srichiangmai dance is to promote the mechanism of the relationship in the movement and develop the ability to maintain the balance of the body while in static (static balance) and the movement of the body (dynamic balance) as well as to practice learning and remem-
bering. This is consistent with the recommendations of Rektorova et al. (37) an action observation, visuomotor integration and action imitation, that is activities that are all important for motor learning and executing skilled movements. It also has a reduce depression, medical expenses and use of medical facilities, and prevent falls (38). In the case of the elderly who are unable to comply, basic movements should be used. By starting from the easy posture to the difficult posture or begin by using a slow tempo and increasing the tempo faster when the participant can follow, local, regional music may be selected for familiarity and rhythm to have fun, enjoy, or use rhythmic instruments instead of music, with rhythms that can be easily remembered. Finally, in this research, the researchers working within the 24 field of clinical and sport science research, with a focus on the declaration of Helsinki (39) that 25 specified in the agreement in all respects.

Suggestions for further research study
It is suggested that the elderly should perform regular exercise with various forms of movement to stimulate blood circulation to muscular and nerve cells. This physical activity will enhance the increase of nerve cells creation and the relation with blood quantity flowing to Dentate gyrus of Hippocampus which is important for learning and remembering. In addition, it is essential for the development neural stem cells which is very interesting the study in the future.

REFERENCES

CONCLUSIONS
This Traditional SriChiangmai dance is an alternative aerobic exercise with slowly rhyming movement and low impact. This exercise is appropriate to be applied for exercise activity in the school for the old people in order to promote health related physical fitness. The results of the research revealed that Traditional SriChiangmai dance positively resulted in strength and endurance of lower body and improved core stability which are main factors for balance and effectiveness of responsive muscular structures as well as body movement control which is a basic skill for doing daily-life activities among the older people with confidence.

ACKNOWLEDGMENTS
Deeply thanks to all participants at the elderly school, Nongkai Province, Thailand everyone who cooperated well in this research. And this research was funded by the Thai Health Promotion Foundation, Research and Development Institute Loei Rajabhat University.

CONFLICT OF INTERESTS
The authors declare that they have no conflict of interests.
Natural History of Patients with Acute Proximal Biceps Tendon Rupture

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SUMMARY

Purpose. To determine the natural history of patients presenting with acute proximal biceps rupture (APBR) and concomitant rotator cuff disease.

Methods. Prospective cohort study of patients with an APBR confirmed via magnetic resonance imaging (MRI) presenting to clinic within 8 weeks of injury. Visual Analog Scale (VAS) pain score, Simple Shoulder Test (SST) score, and the American Shoulder and Elbow Surgeons (ASES) score were the main outcome measures assessed at a minimum of two-years.

Results. Twenty-seven patients were included in the final analysis: seven females (26%) and 20 males (74%) (mean age: 61 years, range 42-78 years). Rotator cuff tears were found in 25 patients (93%). At two-year follow-up (SD 0.28), nine patients (33%) without improvement or dissatisfaction with conservative management opted to undergo shoulder surgery (all with rotator cuff tears), at a mean 4.5 months (range 1.2-24 months) after injury. Worker’s Compensation and a history of diabetes were significantly associated with having surgery. At the two-year follow-up, the median patient reported outcomes (PROs) were as follows: VAS pain- 0.0 (IQR 0.0-3.0); Disability subscale- 48.3 (IQR 34.2-50.0); ASES total- 89.2 (IQR 70.0-98.3); and SST-11.0 (IQR 9.0-12.0). There was no statistically significant difference in PROs between patients who went on to have surgery and those who did not.

Conclusions. Satisfactory PROs and low levels of pain were reported at the two-year follow-up in patients with an APBR, with no difference between those patients who underwent surgical intervention and those who did not.

KEY WORDS
Acute proximal biceps tendon; magnetic resonance imaging; observational study; rotator cuff pathology; shoulder; shoulder injuries.

BACKGROUND

The unique anatomy and biomechanics of the proximal long head biceps tendon (LHBT) place it at high risk for injury (1-5). Repetitive friction, traction and glenohumeral rotation, with subsequent pressure and shear forces at specific, anatomically constricted locations may account for its susceptibility to rupture (3, 6) (figure 1). Still, despite extensive research on the long head of the biceps tendon, controversy persists in regards to its function as well as operative and non-operative management of injury (7-9).

Acute proximal biceps rupture (APBR), presenting in isolation in a less physically demanding patient, can be treated successfully with benign neglect (10, 11). However, only recently has literature demonstrated a high prevalence of rotator cuff pathology in patients presenting with a chief complaint of APBR (figure 2). Kowalczyk et al. (12) reported an 85% prevalence of concomitant rotator cuff tear in the setting of APBR, while the current authors similarly found a 93% prevalence of rotator cuff pathology with approximately 50% of patients having a full thickness rotator cuff tear.
As this data suggests that APBR may be a harbinger of concurrent rotator cuff disease, Kowalczyk et al. recommends that clinicians be hypervigilant when presented with an APBR; however, the literature is sparse and the clinical course and outcomes after APBR with associated rotator cuff pathology is poorly understood.

The purpose of this study is to determine the natural history and outcomes of patients presenting with APBR. Our hypothesis was that the majority of patients with APBR would present with concurrent rotator cuff disease, but demonstrate low levels of pain and high patient reported outcome scores regardless of treatment. We also hypothesized that overall low proportion of patients would choose to undergo surgical intervention after failing conservative management strategies.

**MATERIALS AND METHODS**

After institutional review board approval, International Classification of Diseases codes (ICD-9) were used to prospectively collect data on 42 consecutive patients from five treating surgeons between September 2015 and February 2017. Patients 18 years or older with a diagnosis of an APBR were included. Acute, injury was defined as presenting to clinic within eight weeks of injury. Patients with a history of ipsilateral shoulder surgery were excluded, as were patients unable to undergo magnetic resonance imaging (MRI) due to contraindications. Patients with incomplete medical records were also excluded. A total of 15 patients were excluded: seven patients were excluded due to previous ipsilateral shoulder surgery, three patients were not seen within the eight-week window deadline, two patients did not have the correct diagnosis, two patients declined participation, and one patient’s Worker’s Compensation would not allow participation.

Demographics such as age, sex, body mass index (BMI), hand dominance, diabetes, tobacco use, Worker’s Compensation for the injured shoulder, and mechanism of injury were obtained. Patients underwent routine physical examination and plain radiography as part of their initial assessment. MRI was obtained to confirm the diagnosis of APBR, as well as to allow assessment of the rotator cuff. MRIs were interpreted by a Shoulder/Elbow or Sports Medicine Fellowship-trained orthopedic surgeon. The rotator cuff was recorded as the presence or absence of tearing, and if disrupted, to what degree (full or partial thickness tearing). A subset analysis was performed specifically for the subscapularis tendon.

Primary outcome variables included Visual Analog Scale (VAS) pain score, Simple Shoulder Test (SST) score, and the American Shoulder and Elbow Surgeons (ASES) score. Additional outcome variables included whether or not the patient underwent ipsilateral shoulder surgery for any reason, and risk factors for surgery. Outcomes were noted with a minimum follow-up of two-years. This study meets the ethical standards of the journal (14).
All data underwent descriptive statistical analysis using SAS version 9.4 (SAS Institute, Cary, NC; http://www.sas.com/software/sas9). Two groups were defined based on the severity of rotator cuff tear for comparative analysis. A Wilcoxon rank sum test was used for non-parametric continuous variables. A two-sample t test was used for normally distributed data. For categorical variables, a chi-square test (or Fisher’s exact test, where appropriate) was used for comparisons between groups. Significance was determined by an alpha level of 0.05. Study data was collected and managed using REDCap electronic data capture tools hosted at OrthoCarolina Research Institute (15).

**RESULTS**

Twenty-seven patients met the inclusion criteria and were included in the final analysis. The median time from injury to clinical evaluation was 21 days (interquartile range, IQR: 9 days, 37 days). There were seven females (26%) and 20 males (74%), with an average age of 61 years (SD: 10; range 42-78 years). The dominant extremity was affected in 20 shoulders (74%), while 11 patients reported antecedent shoulder pain (41%). Additional demographic data can be found in [table I](#).

Rotator cuff tears were found in 25 of the 27 patients (93%). Full thickness tears (N = 13; 52%) and partial thickness tears (N = 12; 48%) were seen in almost equal amounts. Seven patients had subscapularis tears in isolation, which were included in the “rotator cuff tear” group ([table II](#)). When stratified by rotator cuff tear, there was no significant difference between the full thickness and partial thickness tear groups in regard to gender, age, dominant extremity, diabetes or other demographic data and injury variables ([table III](#)). By the mean 2.2-year follow-up (SD 0.28, range 1.83-2.75 years), nine patients had undergone ipsilateral shoulder surgery (33%), at a mean time of 4.5 months from injury (range 1.2-24 months). Seven surgeries were arthroscopic, while two patients underwent reverse shoulder arthroplasty. The seven arthroscopic surgeries included: four rotator cuff repairs, one rotator cuff repair with biceps stump debridement, and two biceps stump debridement, subacromial decompressions, and distal clavicle excisions. The two reverse shoulder arthroplasties were performed for irreparable massive rotator cuff tears ([table IV](#)). Worker’s Compensation status and a history of diabetes were significantly associated with having surgery, compared to those who did not have surgery ([table V](#)).

Patient reported outcomes (PROs) were available on 27 patients at initial presentation to our clinic. The median overall PROs at initial examination were as follows: VAS pain 4 (IQR 1.6-6); disability subscale: 33.3 (IQR 15-43.3); ASES total: 66.7 (IQR 41.7-80.7); and SST: 8 (IQR 3-11). When stratified by patients managed by surgical or non-operative treatment, at initial presentation the patients treated non-operatively had significantly better PROs scores in: Disability subscale (P-value = 0.002), ASES total (P-value = 0.01), and SST (P-value = 0.006) ([table VI](#)). Although not statistically significant, VAS pain score at initial exam was lower in patients managed non-operatively.

PROs were available on 22 patients (full thickness: N = 10, partial thickness: N = 10, no tears: N = 2) at mean 2.2-year follow up. The median overall PROs scores were as follows: VAS pain: 0.0 (IQR 0.0-3.0); disability subscale: 48.3 (IQR 34.2-50.0); ASES total: 89.2 (IQR 70.0-98.3); and SST: 11.0 (IQR 9.0-12.0). There was no statistically significant difference

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**Table I.** Patient demographic data (N = 27).

<table>
<thead>
<tr>
<th>Demographic data for patients meeting inclusion criteria</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex, n (%)</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>20 (74.1%)</td>
</tr>
<tr>
<td>Female</td>
<td>7 (25.9%)</td>
</tr>
<tr>
<td>Age (years), mean (SD)</td>
<td>60.6 (9.9)</td>
</tr>
<tr>
<td>BMI (kg/m²), mean (SD)</td>
<td>28.9 (5)</td>
</tr>
<tr>
<td>Dominant Side Injury, n (%)</td>
<td>20 (74.1%)</td>
</tr>
<tr>
<td>Diabetes, n (%)</td>
<td>4 (14.8%)</td>
</tr>
<tr>
<td>Tobacco Use, n (%)</td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>15 (55.6%)</td>
</tr>
<tr>
<td>Past</td>
<td>11 (40.7%)</td>
</tr>
<tr>
<td>Currently</td>
<td>1 (3.7%)</td>
</tr>
<tr>
<td>Contralateral Shoulder Surgery, n (%)</td>
<td>4 (14.8%)</td>
</tr>
<tr>
<td>Antecedent Shoulder Pain, n (%)</td>
<td>11 (40.7%)</td>
</tr>
<tr>
<td>Worker’s Compensation, n (%)</td>
<td>4 (14.8%)</td>
</tr>
<tr>
<td>Mechanism of Injury, n (%)</td>
<td></td>
</tr>
<tr>
<td>Trauma</td>
<td>24 (88.9%)</td>
</tr>
<tr>
<td>Overuse</td>
<td>3 (11.1%)</td>
</tr>
</tbody>
</table>

BMI: Body Mass Index; SD: Standard Deviation.

**Table II.** MRI details (N = 27).

<table>
<thead>
<tr>
<th>MRI Variable</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rotator Cuff Tear</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>2 (7.4%)</td>
</tr>
<tr>
<td>Yes</td>
<td>25 (92.6%)</td>
</tr>
<tr>
<td>Full Thickness Tear</td>
<td></td>
</tr>
<tr>
<td>Full</td>
<td>13 (52.0%)</td>
</tr>
<tr>
<td>Partial</td>
<td>12 (48.0%)</td>
</tr>
<tr>
<td>Subscapularis Tear</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>20 (74.1%)</td>
</tr>
<tr>
<td>Partial</td>
<td>6 (22.2%)</td>
</tr>
<tr>
<td>Full</td>
<td>1 (3.7%)</td>
</tr>
</tbody>
</table>

When stratified by patients managed by surgical or non-operative treatment, at initial presentation the patients treated non-operatively had significantly better PROs scores in: Disability subscale (P-value = 0.002), ASES total (P-value = 0.01), and SST (P-value = 0.006) ([table VI](#)). Although not statistically significant, VAS pain score at initial exam was lower in patients managed non-operatively.

---

**Table III.** Patient demographics by rotator cuff tear status.

<table>
<thead>
<tr>
<th>Rotator Cuff Tear</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>2 (7.4%)</td>
</tr>
<tr>
<td>Yes</td>
<td>25 (92.6%)</td>
</tr>
<tr>
<td>Full Thickness</td>
<td></td>
</tr>
<tr>
<td>Full</td>
<td>13 (52.0%)</td>
</tr>
<tr>
<td>Partial</td>
<td>12 (48.0%)</td>
</tr>
<tr>
<td>Subscapularis</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>20 (74.1%)</td>
</tr>
<tr>
<td>Partial</td>
<td>6 (22.2%)</td>
</tr>
<tr>
<td>Full</td>
<td>1 (3.7%)</td>
</tr>
</tbody>
</table>

When stratified by patients managed by surgical or non-operative treatment, at initial presentation the patients treated non-operatively had significantly better PROs scores in: Disability subscale (P-value = 0.002), ASES total (P-value = 0.01), and SST (P-value = 0.006) ([table VI](#)). Although not statistically significant, VAS pain score at initial exam was lower in patients managed non-operatively.
Table III. Demographics and injury variables (stratified by rotator cuff status (N = 27)).

<table>
<thead>
<tr>
<th>Demographics and Injury Variables</th>
<th>Full Thickness Tear (N = 13)</th>
<th>Partial Tear (N = 12)</th>
<th>No Tear (N = 2)</th>
<th>P-value†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>8 (61.5%)</td>
<td>10 (83.3%)</td>
<td>2 (100%)</td>
<td>0.378</td>
</tr>
<tr>
<td>Female</td>
<td>5 (38.5%)</td>
<td>2 (16.7%)</td>
<td>0 (0%)</td>
<td></td>
</tr>
<tr>
<td>Age (years), mean (SD)</td>
<td>64 (9)</td>
<td>57.6 (10.5)</td>
<td>57 (8.5)</td>
<td>0.115</td>
</tr>
<tr>
<td>BMI (kg/m²), mean (SD)</td>
<td>27.9 (4.5)</td>
<td>30 (5.8)</td>
<td>28.5 (1.5)</td>
<td>0.328</td>
</tr>
<tr>
<td>Dominant Side Injury, n (%)</td>
<td>8 (61.5%)</td>
<td>11 (91.7%)</td>
<td>1 (50%)</td>
<td>0.160</td>
</tr>
<tr>
<td>Diabetes, n (%)</td>
<td>3 (23.1%)</td>
<td>1 (8.3%)</td>
<td>0 (0%)</td>
<td>0.593</td>
</tr>
<tr>
<td>Tobacco Use, n (%)</td>
<td></td>
<td></td>
<td></td>
<td>0.999</td>
</tr>
<tr>
<td>Never</td>
<td>7 (53.8%)</td>
<td>6 (50.0%)</td>
<td>2 (100%)</td>
<td></td>
</tr>
<tr>
<td>Past</td>
<td>6 (46.2%)</td>
<td>5 (41.7%)</td>
<td>0 (0%)</td>
<td></td>
</tr>
<tr>
<td>Currently</td>
<td>0 (0%)</td>
<td>1 (8.3%)</td>
<td>0 (0%)</td>
<td></td>
</tr>
<tr>
<td>Contralateral Shoulder Surgery, n (%)</td>
<td>1 (7.7%)</td>
<td>2 (16.7%)</td>
<td>1 (50%)</td>
<td>0.593</td>
</tr>
<tr>
<td>Antecedent Shoulder Pain, n (%)</td>
<td>7 (53.8%)</td>
<td>2 (16.7%)</td>
<td>2 (100%)</td>
<td>0.097</td>
</tr>
<tr>
<td>Worker’s Compensation, n (%)</td>
<td>1 (7.7%)</td>
<td>3 (25.0%)</td>
<td>0 (0%)</td>
<td>0.322</td>
</tr>
<tr>
<td>Mechanism of Injury, n (%)</td>
<td></td>
<td></td>
<td></td>
<td>0.999</td>
</tr>
<tr>
<td>Trauma</td>
<td>11 (84.6%)</td>
<td>11 (91.7%)</td>
<td>2 (100%)</td>
<td></td>
</tr>
<tr>
<td>Overuse</td>
<td>2 (15.4%)</td>
<td>1 (8.3%)</td>
<td>0 (0%)</td>
<td></td>
</tr>
</tbody>
</table>

BMI: Body Mass Index; SD: standard deviation. †Statistical significance tests were performed to look at differences between the Full Thickness Tear group and the Partial Tear group. The No Tear group was not included in the statistical test. Chi-square or fisher’s exact tests were used for categorical data and t-tests were used for continuous normally distributed data to determine statistical significance between groups at an alpha level of 0.05.

Table IV. Surgery data (N = 9).

<table>
<thead>
<tr>
<th>Group</th>
<th>Procedure</th>
<th>Time from Injury to Surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Full Thickness Tear (N = 6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>01</td>
<td>RCR, SAD</td>
<td>1.2 months</td>
</tr>
<tr>
<td>05</td>
<td>RCR, SAD, debridement of biceps tendon stump</td>
<td>2.8 months</td>
</tr>
<tr>
<td>06</td>
<td>Reverse total shoulder arthroplasty</td>
<td>24 months</td>
</tr>
<tr>
<td>13</td>
<td>RCR, SAD</td>
<td>1.4 months</td>
</tr>
<tr>
<td>27</td>
<td>Reverse total shoulder arthroplasty, latissimus tendon and teres major tendon transfer</td>
<td>1.4 months</td>
</tr>
<tr>
<td>29</td>
<td>RCR, SAD</td>
<td>3.3 months</td>
</tr>
<tr>
<td>Partial Thickness Tear (N = 3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>08</td>
<td>SAD, DCE, capsular release, debridement of biceps tendon stump</td>
<td>1.8 months</td>
</tr>
<tr>
<td>10</td>
<td>SAD, DCE, biceps tenodesis</td>
<td>1.6 months</td>
</tr>
<tr>
<td>11</td>
<td>RCR, SAD</td>
<td>3.2 months</td>
</tr>
</tbody>
</table>

RCR: rotator cuff repair; SAD: subacromial decompression; DCE: distal clavicle excision
### Table V. Risk factor analysis for surgery (N = 27).

<table>
<thead>
<tr>
<th>Demographics and Injury Variables</th>
<th>Had Surgery</th>
<th></th>
<th></th>
<th></th>
<th>P-value†</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No (N = 18)</td>
<td>Yes (N = 9)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Sex, n (%)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>13 (72.2%)</td>
<td>7 (77.8%)</td>
<td></td>
<td></td>
<td>0.999</td>
</tr>
<tr>
<td>Female</td>
<td>5 (27.8%)</td>
<td>2 (22.2%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Age (years), mean (SD)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.799</td>
</tr>
<tr>
<td>60.3 (11.3)</td>
<td>61.3 (6.7)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>BMI (kg/m²), mean (SD)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.220</td>
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<tr>
<td>28.1 (4.9)</td>
<td>30.6 (4.9)</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Dominant Side Injury, n (%)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.999</td>
</tr>
<tr>
<td>13 (72.2%)</td>
<td>7 (77.8%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Diabetes, n (%)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.007</td>
</tr>
<tr>
<td>0 (0%)</td>
<td>4 (44.4%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Tobacco Use, n (%)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.999</td>
</tr>
<tr>
<td>Never</td>
<td>10 (55.6%)</td>
<td>5 (55.6%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Past</td>
<td>7 (38.9%)</td>
<td>4 (44.4%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Currently</td>
<td>1 (5.6%)</td>
<td>0 (0%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Contralateral Shoulder Surgery, n (%)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.093</td>
</tr>
<tr>
<td>1 (5.6%)</td>
<td>3 (33.3%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Antecedent Shoulder Pain, n (%)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.231</td>
</tr>
<tr>
<td>9 (50.0%)</td>
<td>2 (22.2%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Worker's Compensation, n (%)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.007</td>
</tr>
<tr>
<td>0 (0%)</td>
<td>4 (44.4%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Mechanism of Injury, n (%)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.250</td>
</tr>
<tr>
<td>Trauma</td>
<td>17 (94.4%)</td>
<td>7 (77.8%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overuse</td>
<td>1 (5.6%)</td>
<td>2 (22.2%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Rotator Cuff Tear, n (%)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.411</td>
</tr>
<tr>
<td>Full Thickness Tear</td>
<td>7 (38.9%)</td>
<td>6 (66.7%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Partial Tear</td>
<td>9 (50.0%)</td>
<td>3 (33.3%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No Tear</td>
<td>2 (11.1%)</td>
<td>0 (0%)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

BMI: Body mass Index; SD: standard deviation. †Chi-square or fisher’s exact tests were used for categorical data and t-tests were used for continuous normally distributed data to determine statistical significance between groups at an alpha level of 0.05.

### Table VI. Patient reported outcomes at initial exam and at 2 year follow-up (stratified by surgical status).

<table>
<thead>
<tr>
<th>Surgery</th>
<th>Overall</th>
<th>No</th>
<th>Yes</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>At Initial Exam (N = 27)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VAS Pain, median (IQR)</td>
<td>4 (1.6, 6)</td>
<td>2.6 (1, 4.7)</td>
<td>4 (4, 6.3)</td>
<td>0.127</td>
</tr>
<tr>
<td>ASES - Function/Disability Subscale, median (IQR)</td>
<td>33.3 (15, 43.3)</td>
<td>40 (33.3, 45)</td>
<td>15 (11.7, 23.3)</td>
<td>0.002</td>
</tr>
<tr>
<td>ASES - Total, median (IQR)</td>
<td>66.7 (41.7, 80.7)</td>
<td>78.5 (59.8, 88.3)</td>
<td>43 (33.5, 51.7)</td>
<td>0.010</td>
</tr>
<tr>
<td>Simple Shoulder Test, median (IQR)</td>
<td>8 (3, 11)</td>
<td>9.5 (6, 12)</td>
<td>1 (1, 5)</td>
<td>0.006</td>
</tr>
<tr>
<td><strong>At 2 yrs post MRI (N = 22)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VAS Pain, median (IQR)</td>
<td>0.0 (0.0, 3)</td>
<td>0.0 (0.0, 3)</td>
<td>0.0 (0.0, 5)</td>
<td>0.817</td>
</tr>
<tr>
<td>ASES - Function/Disability Subscale, median (IQR)</td>
<td>48.3 (34.2, 50)</td>
<td>48.3 (31.7, 50)</td>
<td>45 (36.7, 50)</td>
<td>0.966</td>
</tr>
<tr>
<td>ASES - Total, median (IQR)</td>
<td>89.2 (70, 98.3)</td>
<td>89.2 (70, 98.3)</td>
<td>92.5 (71.7, 100)</td>
<td>0.757</td>
</tr>
<tr>
<td>Simple Shoulder Test, median (IQR)</td>
<td>11 (9, 12)</td>
<td>11 (7, 12)</td>
<td>11 (9, 12)</td>
<td>0.903</td>
</tr>
</tbody>
</table>
**Table VII.** Patient reported outcomes at 2-year follow-up (overall and stratified by rotator cuff status).  

<table>
<thead>
<tr>
<th>N; Median (IQR)</th>
<th>Full Thickness Tear (N = 10)</th>
<th>Partial Tear (N = 10)</th>
<th>P-value*</th>
<th>No Tear (N = 2)*</th>
<th>Overall (N = 22)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASES (Patient)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VAS Pain (0-10)</td>
<td>10; 0.0 (0.0, 2.5)</td>
<td>10; 1.8 (0.0, 4.0)</td>
<td>0.429</td>
<td>2; 0.0 (0.0, 0.0)</td>
<td>22; 0.0 (0.0, 3.0)</td>
</tr>
<tr>
<td>Function/Disability Subscale</td>
<td>9; 48.3 (31.7, 50.0)</td>
<td>9; 41.7 (38.3, 48.3)</td>
<td>0.999</td>
<td>2; 49.2 (48.3, 50.0)</td>
<td>20; 48.3 (34.2, 50.0)</td>
</tr>
<tr>
<td>ASES Total</td>
<td>8; 91.7 (78.3, 99.2)</td>
<td>9; 85.0 (68.3, 98.3)</td>
<td>0.539</td>
<td>2; 99.2 (98.3, 100)</td>
<td>19; 89.2 (70.0, 98.3)</td>
</tr>
<tr>
<td>Simple Shoulder Test</td>
<td>10; 10.5 (7.0, 12.0)</td>
<td>9; 10.0 (9.0, 12.0)</td>
<td>0.999</td>
<td>2; 12.0 (12.0, 12.0)</td>
<td>21; 11.0 (9.0, 12.0)</td>
</tr>
</tbody>
</table>

IQR: Interquartile Range; ASES: American Shoulder and Elbow Surgeons score; VAS: Visual Analogue Scale. *Time from injury to PRO: mean 2.2 years (SD: 0.28 years); range 1.83-2.75 years. Statistical significance tests were performed to look at differences between the Full Thickness Tear group and the Partial Tear group. The No Tear group was not included in the statistical test. Wilcoxon rank-sum tests were used for continuous non-normally distributed data to determine statistical significance between groups at an alpha level of 0.05. IQR= interquartile range. †Note: the IQR is also the range for this group.

in PROs between the full thickness and partial thickness tear groups (Table VII). Furthermore, at mean 2.2-year follow up, there was no statistically significant difference in PROs between patients who went on to have surgery and those who did not.

**DISCUSSION**

There is ample literature highlighting patients with rotator cuff tears with concurrent proximal long head biceps tendon pathology (16-19). It has been theorized that adjacent rotator cuff inflammation can lead to secondary biceps tenosynovitis, while subscapularis tears or rotator interval lesions could result in LHBUT instability and subsequent tearing (20-22). However, only recently has the literature reported the converse relationship: patients presenting with APBR with concomitant rotator cuff disease (12, 13). Furthermore, to our knowledge there is a lack of literature characterizing the natural progression of this specific population. In this prospective cohort study, nine patients (33%) had undergone ipsilateral shoulder surgery, at a mean time of 4.5 months from injury. In Kuhn et al.’s study of 319 patients with attempt at conservative treatment for rotator cuff tears, 82 patients eventually had surgery (26%), with most patients doing so within 12 weeks (23). Our study found that Worker’s Compensation status and a history of diabetes were significantly associated with having surgery. Kweon et al. observed younger age and lower BMI were predictive of eventual allocation to surgical treatment in the management of rotator cuff tears (although they did not specifically analyze the variables of Worker’s compensation and history of diabetes) (24). There is evidence showing a relationship between thyroid disease non-traumatic rotator cuff tears in females independent of age (25). We did not study the relationship between thyroid pathologies and outcomes in our study population. However, future studies may benefit by investigating if thyroid disorder in a similar cohort of patients to our study is a risk factor for poorer outcomes or predictive of failing conservative treatment and requiring surgery. There currently is no literature on the timeline of conservative treatment of acute proximal biceps ruptures that failed and were allocated to surgical management.

Patients who were treated non-operatively had significantly better PROs in disability subscale, ASES total, and SST at initial clinical presentation. Furthermore, the patients treated non-operatively had lower levels of pain, albeit statistical analysis did not show significance. Indications for surgery included failure to respond or patient dis-satisfaction with conservative treatment entailing physical therapy, non-steroids, and activity modifications. Of note, all nine patients that underwent surgical intervention had APBR with associated rotator cuff tears. The mean time of 4.5 months from injury to surgical intervention in our study is in accordance with Oliva et al.’s recommendations for treatment of long head of the biceps condition in association with lesions of the rotator cuff. The aforementioned guidelines recommend surgical exploration and possible treatment if symptoms persist for more than 3 months after conservative treatment (26). Lower scores in PROs are equivalent to a greater limitation in shoulder functioning and likely negatively affects patient’s motivation and willingness to continue conservative management. As a result, patients may have a lower threshold to seeking surgical treatment.

Our data reveals low levels of pain (VAS median-0.0, IQR 0.0-3.0) and satisfactory PROs (ASES median-89.2, IQR 70.0-98.3; SST median-11.0, IQR 9.0-12.0) at the two-year follow-up, with no difference between patients who went on to have surgery and those who did not. Kim et al. (27),
Koh *et al.* (28), Lee *et al.* (29) found similar outcomes in their studies of rotator cuff repairs with concurrent biceps pathology: SST 9.3 ± 1.6 and ASES 88.6 ± 8.9, ASES 79.6 ± 15.8, and VAS 2.0 and ASES 82.8, respectively.

We recognize several limitations to our study. It is well known that there is a high incidence of rotator cuff pathology in patients older than 60 years of age. As the average age of our cohort was 61 years, there is potential for confounding bias in our study. Also, each MRI was reviewed by one surgeon, with multiple surgeons (N = 5) included in the study. Intra-observer and inter-observer reliability would increase the validity of our study. However, all reviewers were shoulder/elbow or sports medicine fellowship-trained orthopedic surgeons. Lastly, as the overall sample size is small, it may not be large enough to detect differences between groups. Finally, there was heterogeneity with regard to surgical interventions for the nine patients. Seven patients underwent arthroscopic procedures with two patients receiving reverse shoulder arthroplasty. This may be due to the heterogeneous demographic characteristics of our study population and demonstrates that an individualized patient-centered care approach to this population yielded comparable outcomes at the two-year follow-up in patients with conservative or surgical management.

**CONCLUSIONS**

This is the first study, to our knowledge, to elucidate on the natural history and outcomes of acute proximal biceps ruptures. In this prospective, observational cohort, 93% of patients presented with concomitant rotator cuff tears, with 1/3 of patients eventually having surgery. However, low levels of pain and satisfactory PROs were reported at the two-year follow-up, with no difference between those who eventually had surgery and those who did not. These findings allow clinicians to have prognostic discussions with patients presenting with APBR.

**CONFLICT OF INTERESTS**

The authors declare that they have no conflict of interests.
**Dominant vs Nondominant Arm in Surgical Repair of Distal Biceps Tendon Rupture. A Case-Control Series of Isotonic Muscle Strength Evaluation**

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**LEVEL OF EVIDENCE:** 4

**SUMMARY**
**Background.** This case-control study investigated arm recovery from surgery for a ruptured distal tendon in terms of maximal strength, power, and endurance compared to the healthy contralateral arm, taking into account limb dominance.

**Methods.** An S-shaped single incision and suture anchor repair was used in all 15 patients. All patients were right-arm dominant and of them none participated in a specific postoperative physical therapy program. Outcomes were evaluated based on range of motion and with the Disability of the Arm, Shoulder and Hand (DASH) test, Mayo Elbow Performance Index (MEPI), and Bromberg and Morrey questionnaire. Muscle function was assessed with MuscleLab.

**Results.** Average test scores were as follows: DASH, 3.53/100; MEPI, 93/100; and Bromberg and Morrey, 90.87/100. There were significant differences in supination (P = 0.007), maximum lifted weight (P = 0.005763), strength during endurance exercise (P = 0.004366), and maximum strength in flexion (P = 0.045584) between impaired and healthy arms.

**Conclusions.** Limb dominance is not a critical issue for the choice of treatment and functional evaluation following surgical repair of ruptured distal tendon.

**KEY WORDS**
Distal biceps; handedness; outcomes; surgery; surgical repair.

**BACKGROUND**
Most biceps tendon ruptures involve the proximal long head or, more infrequently, the short head; 3% of biceps injuries involve the distal insertion (1, 2). Males between the ages of 30 and 60 years account for 95% of cases, and the prevalence is between 0.9 and 1.8 per 100,000 patients per year (1, 2). Additionally, 60% to 86% of injuries involve the dominant arm, which is more debilitating for patients (2, 3). Biceps injuries are caused by hypovascularization in the tendon, which results in isoxia and changes in tendon impingement on radial bone during pronosupination (2, 3). Other predisposing factors include high body mass index, tendinosis, osteophytes from mechanical overuse, prolonged steroid therapy, metabolic acidosis, smoking, and chronic inflammatory diseases (e.g., rheumatoid arthritis) (2, 3). Athletes who play contact sports are also prone to distal biceps tendon injuries (3). The increasing tendency of people of all ages to engage in sporting activities has led to increased rates of injury, prompting advances in surgical practices in the field of orthopedics to achieve better outcomes including more rapid restoration of function. In fact, conservative treatment of distal biceps ruptures can result in chronic pain, reduced grip strength, and weakness of flexion and supination (3-6).

Distal biceps tendon ruptures are relatively uncommon in clinical practice and there is no consensus regarding the optimal treatment and rehabilitation program, although surgery is
the preferred intervention for this type of injury; the literature on this topic is mostly limited to case series (3, 5-8). Surgery to repair distal tendon ruptures is traditionally performed through a single anterior incision or double incision. In addition to different surgical approaches, various methods and tools are used for reattachment including suturing through bone tunnels, suspensory fixation devices, suture anchors, and interference screws. While surgical reinsertion of the distal biceps tendon has good outcomes in terms of restoring strength and range of motion, complications are not uncommon (3-5, 7, 9). Although there have been studies comparing different surgical techniques, there are no clear guidelines regarding the optimal approach for reducing complications and achieving good clinical outcomes (3, 4, 7-9). Only a few studies have reported functional outcomes comparing the dominant and nondominant arms or impaired and healthy arms (1, 6, 10-18).

In this case-control study, we evaluated the recovery of biceps brachii following surgery for distal tendon rupture in terms of maximal strength, power, and endurance compared to the healthy contralateral arm, while taking into account limb dominance.

MATERIALS AND METHODS

Study subjects

The study meets the ethical standards of the journal (19). Approval for this study was obtained from the local bioethics committee (study no. 062951891, protocol no. 21883).

We retrospectively evaluated 15 male patients who underwent surgery to repair unilateral rupture of the distal biceps brachii tendon between January 2015 and December 2017. A single surgeon performed all of the surgeries using the same technique, which involved tendon reinsertion into the radial tuberosity with 1 or 2 suture anchors through a single S-shaped incision using an anterior elbow approach. With the arm in maximum supination, the suture anchors were placed into the tuberosity and the torn tendon was reapproximated to the anchors. In most cases, 2 anchors loaded with sutures were used (20, 21). The study participants were aged between 31 and 65 years (mean: 48 years). Seven patients had a left rupture and 8 had a right rupture. All patients were male and right-arm dominant.

The time from the traumatic event to surgery ranged between 2 and 15 days (mean: 5 days), and the time from surgery to follow-up was between 28 and 54 months (mean: 42.6 months) (table I). After surgery, none of the patients engaged in a specific physical therapy program for the recovery of range of motion, strength, power, and muscular endurance.

The participants were informed in detail of the scope and procedures of the study before being asked to take part in clinical evaluation, and provided written, informed consent prior to participating in accordance with National Health Council Resolution No. 196/96 and the 1975 Helsinki Declaration, as revised in 2000.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age</th>
<th>Injured side</th>
<th>Days since trauma</th>
<th>Follow-up, months</th>
<th>DASH</th>
<th>MEPI</th>
<th>B &amp; M</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>31</td>
<td>Left</td>
<td>7</td>
<td>45</td>
<td>0</td>
<td>100</td>
<td>94</td>
</tr>
<tr>
<td>2</td>
<td>45</td>
<td>Left</td>
<td>10</td>
<td>41</td>
<td>0</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>3</td>
<td>56</td>
<td>Right</td>
<td>6</td>
<td>46</td>
<td>0.8</td>
<td>100</td>
<td>94</td>
</tr>
<tr>
<td>4</td>
<td>50</td>
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<td>5</td>
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<td>12</td>
<td>85</td>
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<td>Left</td>
<td>11</td>
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<td>5.6</td>
<td>100</td>
<td>93</td>
</tr>
<tr>
<td>6</td>
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<td>29</td>
<td>0</td>
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<td>100</td>
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<tr>
<td>7</td>
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<td>73</td>
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<td>100</td>
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<tr>
<td>11</td>
<td>38</td>
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<td>6</td>
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<td>0</td>
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<tr>
<td>12</td>
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<tr>
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<td>2</td>
<td>60</td>
<td>1.6</td>
<td>85</td>
<td>86</td>
</tr>
</tbody>
</table>

B & M: Bromberg and Morrey; DASH: Disability of the Arm, Shoulder and Hand; MEPI: Mayo Elbow Performance Index.
Outcome measures

Patients completed questionnaires that examined different aspects of upper limb functioning including the Disability of the Arm, Shoulder and Hand (DASH) test and Bromberg and Morrey (B & M) rating scale, which evaluated upper limb disability; and Mayo Elbow Performance Index (MEPI), which assessed limitations in daily life activities caused by impaired elbow function.

The patients were also evaluated with physical/functional tests. The MuscleLab system (Ergotest Technology, Langesund, Norway) was used to measure muscle isotonic strength, speed of motion, and muscular power with a linear encoder during elbow flexion-extension of the right and left limbs against resistance. The theoretical maximum weight lifted by each upper limb of each participant was calculated using the following equation (22):

\[
\text{Theoretical maximum weight} = \frac{\text{weight lifted}}{(1.0278 - 0.0278 \times \text{no. of repetitions})}.
\]

This equation is reliable for a number of repetitions < 12. Measurements were first performed for the injured limb irrespective of whether it was the dominant one. Submaximal and isotonic muscle endurance testing against resistance was carried out for each arm with the MuscleLab system. In the submaximal test, participants performed 3 flexion-extension repetitions at 90% of the theoretical maximum weight. In the endurance test, participants performed as many repetitions as possible in 1 min at 50% of the theoretical maximum weight. Participants were allowed a 10-min rest period between tests. For each arm, we also recorded the range of motion for flexion, extension, supination, and pronation of the elbow.

Statistical analysis

Data are reported as mean ± standard deviation and were analyzed with the parametric Student’s t test for paired data between impaired and healthy arms of the same subject. Statistical analyses were performed with Excel software (Microsoft, Redmond, WA, USA). P < 0.05 was considered significant.

RESULTS

Clinical assessment

The patients were divided into 2 groups according to the side of the ruptured biceps tendon (left, n = 7; right, n = 8). Baseline demographic and clinical characteristics of the participants including age, time from trauma to surgery, time from surgery to follow-up, outcome scores, and functional test results/scores were normally distributed (table II). In terms of clinical outcomes, 5/15 patients reported bearable pain near the brachioradial muscle. Average scores for the clinical assessment scales were as follows: DASH: 3.53/100; MEPI: 93/100; and B&M: 90.87/100. There were no statistically significant differences between the 2 groups (table I). None of the patients reported functional limitations in daily life activities, and were eventually able to return to work and engage in sports.

Functional assessment

We compared functional parameters between the operated (injured) and non-operated (healthy) arms. There were no differences in flexion and extension, but average supination was 80.8° in the impaired arm vs 87° in the healthy arm (P = 0.007), and average pronation was 79.73° vs 86.66° (P = 0.02) (table III). The theoretical maximum weight lifted, maximum strength and power during endurance exercises, and average strength and power during submaximal tests were measured. Prior to statistical analysis of MuscleLab functional performance data, we subtracted 10% from the values of the dominant right arm to normalize the data for the 2 arms. The average maximum weight lifted with the impaired arm was 13.37 kg as compared to 14.52 kg with the healthy arm (P = 0.005763); the average strength during endurance exercise was 64.77% in the impaired arm and 70.34% in the healthy arm (P = 0.004366); and the maximum strength in flexion was 150.04% and 161.82%, respectively (P = 0.045584). There were no significant differences in power expressed during the submaximal test and endurance exercise between arms (table IV).

| Table II. Statistical parameters for patients’ baseline demographic and clinical characteristics. |
|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
|                | Age             | Months since rupture | Days since trauma | DASH            | MEPI            | B & M           |
| Avg left       | 50.28571        | 47.5714287         | 7.428571429       | 3.7714287       | 91.4285714     | 89.14285714     |
| Avg right      | 51.625          | 47.125             | 13.625            | 3.1             | 94.375          | 92.375          |
| SD left        | 10.93487        | 11.88636674        | 4.035556255       | 4.65822365      | 11.8019369     | 12.088956       |
| SD right       | 17.39301        | 25.32949532        | 11.1428228        | 47.8507523      | 9.9389805      | 23.25430068     |
| P value        | 0.793726        | 0.963724582        | 0.223680698       | 0.78418795      | 0.62935914     | 0.576004703     |
| Avg: average; B & M: Bromberg and Morrey; DASH: Disability of the Arm, Shoulder and Hand; MEPI: Mayo Elbow Performance Index; SD: standard deviation. |
DISCUSSION

This study evaluated clinical and functional outcomes following anatomic reinsertion of distal biceps tendon with an S-shaped single incision using anchors. Objective measures such as recovery of submaximal muscular strength, endurance, and range of motion along with subjective patient-reported outcome were evaluated. We also compared the results for dominant and non-dominant limbs.

The surgical technique used in our study yielded good results in all patients in terms of recovery of functionality and autonomy in daily life, as assessed using clinical outcome measures. We compared our results to those of case control studies that used comparable surgical technique and materials and methods (table V) and found that our clinical results and subjective patient-reported outcomes substantially overlapped with the findings of most of these studies. However, isokinetic assessment outcomes in these (23-29) as well as our own study were inconsistent, which may be attributable to the various assessment tools and testing protocols used and different isokinetic parameters that were evaluated, precluding direct comparisons.

Only 5 of the previous studies considered the issue of limb dominance when analyzing the results (9, 15, 18, 23, 29) (table V), with conflicting conclusions. We therefore compared all case-control studies that analyzed this factor regardless of the surgical approach, type of tendon fixation, evaluation method, average follow-up time, and sample size (table VI) and found that they yielded variable findings regarding the issue of dominance.

Isokinetic analyses are known to be affected by limb dominance (30); however, the ratio of strength and endurance during flexion, extension, pronation, and supination between dominant and non-dominant elbows is still debated (31). It has been suggested that the contralateral upper extremity can be used as a matched control in the evaluation of postoperative strength and endurance in biceps isokinetic testing, without adjusting the results for handedness (13). According to these indications, some studies assessing the contribution of limb dominance to surgical outcome (9, 14, 18, 23) did not normalize this ratio, since the strength difference favoring the dominant limb in isokinetic tests is in any case negligible. On the other hand, other studies (1, 6, 10, 11, 15, 16, 17) corrected for this factor using various methods (15).

All patients in our study were right-arm-dominant. Functional evaluation was performed with an isotonic strength test, and we subtracted 10% from right arm values to normalize data for the 2 arms according to Peterson et al. (32). This is based on the assumption that grip strength is an objective measure of upper extremity performance (33); it was shown that grip strength of the dominant hand was 10% greater than that of the non-dominant hand, although this was only true in the case of right-arm dominance. Therefore, the 10% rule is recommended for right-handed subjects, and the arms should be considered as having equal strength for left-handed subjects (32). This is partly supported by the findings of Gallagher et al. (34), who showed that for the elbow, dominance does not affect extension, pronation, or supination but significantly influences flexion in terms of mean peak torque, work, and power. In our analysis, we considered only flexion in isokinetic tests; by normalizing the results for the 2 arms, we circumvented the issue of dominance.
### Table V. Cases treated with the suture anchor technique.

| Study              | Pt no. | Average time from injury to surgery, days | Average follow-up, months | DASH, average | MEPI average | Evaluation tool for isokinetic analysis | Complications                                                                                   | Conclusions                                                                                      | Influence of dominance                                                                |
|--------------------|--------|------------------------------------------|----------------------------|---------------|--------------|------------------------------------------|-------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------|
| Luciani, 2020 (23) | 21     | < 10                                      | 12, 36, 60                | Not performed | 93.12 ± 6.30 | Biodex System 3                          | Transient paresthesia in LACN distribution (n = 2)                                             | No differences between injured and uninjured sides in terms of flexion and supination in isokinetic analysis | No difference in flexion between dominant and nondominant operated sides during follow-up |
| Suda, 2017 (24)    | 49     | 17.8                                      | 32                        | Yes (results not reported) | Not performed | BTE PrimerSTM                            | Permanent sensorial deficit in superficial ramus of radial nerve or LACN (n = 19)               | Strength in elbow flexion and extension as well as forearm pronation and supination were diminished on operated side | Not evaluated                                                                                     |
| Widkowski, 2017 (9)| 18     | 6.82 ± 9.90                              | 47                        | Not performed | 80.00 ± 15.00 | Biodex System 3                          | None                                                                                              | Isometric torque values of muscle flexion and forearm supination were comparable in the 2 limbs | Operated dominant limb did not regain its preoperative dominance in flexion and supination strength |
| Pangallo, 2016 (25)| 18     | 5                                        | 12                        | 4.2           | 92.1 ± 12.6  | Cybex isokinetic dynamometer             | Transient neuropraxia in LACN distribution (n = 3) Permanent deficit in superficial ramus of radial nerve distribution (n = 1) Symptomatic heterotopic ossification (n = 1) | No difference between injured and uninjured sides in terms of isometric strength                | Not evaluated                                                                                     |
| Siebenlist, 2014 (18)| 49   | 21.7 ± 31.4                              | 44                        | 7.9 ± 13.9    | 97.2 ± 4.9   | Isoforce Control®                        | Anchor failure (n = 4)                                                                           | Differences between injured operated arm and uninjured arm in terms of deficit in isometric strength for elbow flexion and supination | Mean strength measurements did not differ between patients with dominant vs nondominant arm injury |
| Gasparella, 2015 (26)| 18   | 5 ± 3                                     | 26                        | 4.7 ± 6.3     | 96.8         | Cybex isokinetic dynamometer             | Long-term paresthesia in LACN distribution (n = 2)                                             | Increase in average flexion strength by 10.2% compared to non-operated arm in isokinetic evaluation | Not evaluated                                                                                     |
Table V. Cases treated with the suture anchor technique.

<table>
<thead>
<tr>
<th>Study</th>
<th>Pt no.</th>
<th>Average time from injury to surgery, days</th>
<th>Average follow-up, months</th>
<th>DASH, average</th>
<th>MEPI average</th>
<th>Evaluation tool for isokinetic analysis</th>
<th>Complications</th>
<th>Conclusions</th>
<th>Influence of dominance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hansen, 2014</td>
<td>21</td>
<td>Not reported</td>
<td>&gt; 12</td>
<td>10 ± 7</td>
<td>Not performed</td>
<td>Biodex System 3</td>
<td>Flexion strength of repaired side equal to that of normal side in strength test</td>
<td>Supination strength and work performed were weaker on repaired side</td>
<td>Not evaluated</td>
</tr>
<tr>
<td>Mckee, 2005</td>
<td>53</td>
<td>16</td>
<td>21</td>
<td>8.2 ± 11.4</td>
<td>Not performed</td>
<td>BTE Work Simulator</td>
<td>Superficial wound infection (n = 1) Transient paresthesias in the LACN distribution (n = 2) Transient PIN palsy (n = 1)</td>
<td>No differences between injured and uninjured sides in terms of flexion strength and dynamic strength</td>
<td>Not evaluated</td>
</tr>
<tr>
<td>Balabaud, 2004</td>
<td>8</td>
<td>13</td>
<td>15</td>
<td>Not performed</td>
<td>Not performed</td>
<td>Cybex 6000 dynamometer</td>
<td>Isokinetic measurements showed a 5% strength deficit but 7% greater endurance, no strength deficit, and 13% more endurance for supination in flexion-concentric test</td>
<td>Dominant side had higher levels of peak torque, work, and power in the flexion-concentric test</td>
<td>No differences between dominant and nondominant sides in supination-concentric and flexion-eccentric tests</td>
</tr>
<tr>
<td>Lynch, 1999</td>
<td>6</td>
<td>21.8</td>
<td>24</td>
<td>Not performed</td>
<td>Not performed</td>
<td>Cybex isokinetic dynamometer</td>
<td>Isokinetic tests revealed elbow flexion strength for peak torque, total work, and average power of 107%, 103%, and 110%, respectively, for uninjured arm Forearm supination strength measured by peak torque, total work, and average power were 97%, 85%, and 88%, respectively, for uninjured arm Forearm supination endurance was 10% lower in the injured arm</td>
<td>In injured biceps of the dominant arm, flexion values were 111%, 111%, and 119% of the peak torque, total work, and average power values of the uninjured arm, respectively Flexion endurance ratio for dominant extremities was equal to that of uninjured side Supination strength values were 103%, 101%, and 98% of the peak torque, total work, and average power values of the uninjured side, respectively</td>
<td></td>
</tr>
</tbody>
</table>

BTE: Baltimore Therapeutic Equipment; DASH: Disability of the Arm, Shoulder and Hand; LACN: lateral antebrachial cutaneous nerve; MEPI: Mayo Elbow Performance Index; PIN: posterior interosseous nerve; Pt no.: patient number.
Table VI. Studies addressing the influence of dominance.

<table>
<thead>
<tr>
<th>Study</th>
<th>Pt no.</th>
<th>Average time from injury to surgery, days</th>
<th>Average follow-up, months</th>
<th>Surgical approach</th>
<th>Type of fixation</th>
<th>Evaluation tool for isokinetic analysis</th>
<th>Influence of dominance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Redmond, 2016 (14)</td>
<td>23</td>
<td>Not reported</td>
<td>80</td>
<td>Not reported</td>
<td>Cortical button</td>
<td>Biodex System 4</td>
<td>Arm dominance influenced the results: endurance in supination was greater when surgery was performed on dominant arm as compared to nondominant arm. Dominant arm did not affect results of other strength and endurance measures.</td>
</tr>
<tr>
<td>Dillon, 2011 (10)</td>
<td>27</td>
<td>Acute (&lt; 28 days) (n = 17) Chronic (&gt; 28 days) (n = 10)</td>
<td>30.9</td>
<td>Single anterior</td>
<td>Cortical button</td>
<td>BTE Work Simulator</td>
<td>Operated dominant limb recovered less maximal force in flexion and supination than operated nondominant limb. No difference in endurance.</td>
</tr>
<tr>
<td>Weinstein, 2008 (12)</td>
<td>32</td>
<td>29</td>
<td>42</td>
<td>2-Incision technique</td>
<td>Suture anchor</td>
<td>Biodex System 3</td>
<td>No differences in strength and endurance in flexion and supination after surgical repair between dominant and nondominant arms.</td>
</tr>
<tr>
<td>Bell, 2000 (17)</td>
<td>23</td>
<td>9</td>
<td>43</td>
<td>2-Incision technique</td>
<td>Pull-out (n = 11) Suture anchor (n = 5) Screws (n = 5) Tenodesis (n = 2)</td>
<td>Lido Isokinetic Workset</td>
<td>No differences in flexion strength and endurance or supination strength and endurance between dominant repaired and nondominant repaired groups.</td>
</tr>
<tr>
<td>Leighton, 1995 (1)</td>
<td>9</td>
<td>33</td>
<td>30</td>
<td>2-Incision technique</td>
<td>Pull-out</td>
<td>Cybex II System</td>
<td>Strength and endurance in both flexion and supination were completely restored in 3 repaired dominant extremities. Deficits in flexion, endurance, and supination strength in 6 nondominant repaired extremities.</td>
</tr>
<tr>
<td>Agins, 1988 (16)</td>
<td>10</td>
<td>0-14</td>
<td>23</td>
<td>2-Incision technique</td>
<td>Pull-out</td>
<td>Cybex system</td>
<td>No differences in flexion strength and endurance between dominant repaired and nondominant repaired groups. Differences in supination strength and endurance between dominant repaired and nondominant repaired groups.</td>
</tr>
<tr>
<td>Baker, 1985 (6)</td>
<td>10</td>
<td>10.4</td>
<td>24-60</td>
<td>2-Incision technique</td>
<td>Pull-out</td>
<td>Cybex system</td>
<td>No differences in flexion strength and endurance between dominant repaired and nondominant repaired groups. Differences in supination strength and endurance between dominant repaired and nondominant repaired groups.</td>
</tr>
</tbody>
</table>

BTE: Baltimore Therapeutic Equipment; Pt no., patient number.
of dominance vs non-dominance for isometric flexion muscle strength; additionally, we used the healthy contralateral arm as a matched control for the injured arm in each patient. We found that the healthy limb was superior in terms of maximum lifting weight, strength expressed during endurance exercise, and maximum strength during flexion; the impaired limb had less strength and lifted a lower weight. Muscle power during endurance and submaximal exercises was comparable; that is, while the impaired limb lacked explosive strength, muscle power during the endurance test was normal and adequate (table III).

Our study had 3 major limitations. Firstly, the small sample size and study design did not allow us to draw broad conclusions, especially regarding the application of the modified 10% rule. Secondly, we did not perform a detailed analysis of supination in terms of maximum strength and submaximal and endurance testing. Even after biceps tendon repair, a persistent loss of supination strength and range of motion are expected in both dominant and nondominant injured limbs (10, 12, 17, 18, 24, 27, 29). However, loss of supination strength and arc of motion in operated patients do not necessarily impact satisfaction scores, daily activities, or return to previous work (1, 10, 11, 12, 14, 17, 23, 24, 29). On the other hand, the considerable loss of supination strength (between 21% and 55%), endurance (up to 79%), and supination range of motion in injured biceps tendons that have not been surgically treated has been linked to lower satisfaction scores and can impede resumption of daily activities and work; this is true for both dominant and nondominant limbs (7, 35) and largely justifies surgical intervention in most cases. A third limitation of our study was the lack of a unified, comprehensive, and fully supervised postoperative physiotherapy program. Indeed, none of our patients followed a specific rehabilitation program after surgery, which may have biased our results. On the other hand, the good outcomes that were achieved highlight the value and effectiveness of the surgical technique.

A strength of our study was the normalization of isokinetic data for the 2 arms using the 10% rule, which allowed us to overcome the issue of dominance vs non-dominance for isometric flexion muscle strength; and the use of the healthy contralateral arm as a matched control, which obviated the need to test a group of normal subjects (1, 10, 11, 15, 17).

CONCLUSIONS

Based on this new method of evaluating results, we conclude that limb dominance is not a critical factor in the choice of treatment for distal biceps injury at midterm follow-up. Patients should be informed of the possibilities of a persistent loss of flexion strength and limited supination range after suture anchor repair via a single-incision approach. We also recommend an appropriate postoperative rehabilitation program that includes muscle strength and endurance exercises as soon as the sutures allow to promote good recovery of supination.

CONFLICT OF INTERESTS

The authors declare that they have no conflict of interests.
Comparison between Conservative and Surgical Treatment in Proximal Humeral Fractures. A Prospective Randomized Study with 5-Years Follow-Up

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SUMMARY

Background. There is no consensus on the optimal treatment of displaced proximal humeral fractures. The purpose of this prospective study was to present a 5-year follow-up of conservative treatment of proximal humeral fractures as compared to surgical treatment (ORIF).

Materials and methods. Fifty consecutive patients with a proximal humeral fracture (Neer types 2, 3, 4; hertel types 3 through 8) were enrolled in this study and randomized in two groups: conservative treatment (group A) and open reduction and internal fixation (ORIF) with a plate (group B). Twenty patients of group A and 15 patients of group B were available for the final follow-up. All patients were clinically evaluated at 1, 3, and 12 months, and at final follow-up with physical and radiological examination, functional scores (Constant-Murley, quick DASH, ASES, SF-12), and overall satisfaction (from 1 to 4).

Results. The groups were homogeneous with regard to demographic data and radiological classifications of fractures. At the final follow-up (5.21 ± 1.30 years), the Constant-Murley score was 82.0 ± 7.6 (group A) and 87.0 ± 5.4 (group B) (n.s.); quick-DASH was 8.7 ± 4.3 (group A) and 5.4 ± 0.37 (group B) (n.s.); ASES was 83.7 ± 7.0 (group A) and 96.1 ± 1.0 (group B) (p = 0.003); and SF-12 was 88.2 ± 5.9 (group A) and 90.1 ± 5.7 (group B) (n.s.). Eighty-five percent of patients in group A and 100% in group B were satisfied or very satisfied with their results (n.s.). One patient in group B reported wound dehiscence, which was treated with medical therapy.

Conclusions. Conservative treatment in proximal humeral fractures provides similar results in functional and symptom-related scores after 5 years, compared to ORIF. Indications for ORIF should be reserved only for patients with high functional demand.

KEY WORDS
Clinical outcomes; fracture; humerus; nonoperative treatment; ORIF; plate; radiological outcomes.

BACKGROUND

Proximal humeral fractures represent 4-5% of all fractures, the second most common fracture of the upper extremity after forearm fractures (1), and the third most common fracture in the elderly after Colles’ and hip fractures (2). Female sex and osteoporosis are the most important risk factors (3). In 87% of cases, fractures occur after low-energy trauma (4, 5).

There are different classification systems for proximal humeral fracture. The Neer classification (1970) (6) is probably the most frequently used, it divides fractures depending on an anatomic segmental classification. It is globally accepted that two-part fractures with minimal displacement can be treated conservatively. During the 8th ICSS (International Conference on Shoulder Surgery),
in 2001, Hertel presented a morphologic classification of proximal humeral fractures using a binary description system in which five basic planes were identified. Through a combination of blocks he managed to recognize 12 fracture patterns: between the greater tuberosity and the head, the greater tuberosity and the shaft, the lesser tuberosity and the head, the lesser tuberosity and the shaft, the lesser tuberosity and the greater tuberosity, six dividing the humerus into two fragments, five dividing the humerus into three fragments, and a single fracture dividing the humerus into four fragments (7).

Minimally displaced proximal humeral fractures could be treated nonoperatively; the treatment of displaced fractures is controversial and includes conservative treatment (immobilization with cast, Sling and Swathe brace or similar), percutaneous pinning, intramedullary nailing, open reduction and internal fixation (ORIF) with locking plate, and arthroplasty (8-14).

The aim of this study is to evaluate at 5-year follow-up, the clinical and radiological outcomes of conservative treatment of proximal humeral fracture types 2, 3, and 4 (not displaced in varus) according to the Neer classification and types 3 through 8 of Hertel’s system, compared to surgical treatment (ORIF with plate). The hypothesis is that there are no differences in clinical and radiological outcomes at final follow-up for these types of fractures.

MATERIALS AND METHODS

Eighty consecutive patients aged between 50 and 65 years who suffered proximal humeral fracture between 2013 and 2014 were enrolled in this prospective study. Each fracture was classified according to the Neer and Hertel classifications and was labeled in the study as one or more of the following fracture types: Neer type 2, 3, or 4 (not displaced in varus) and hertel types 3 through 8.

Exclusion criteria were the following: history of proximal humeral fracture; previous local and general infective disease; and previous surgery on the affected shoulder. After inclusion and exclusion criteria were applied, patients available for the study were randomly divided in two groups: group A, conservative group; and group B, surgical group.

The present study was approved by the ethics committees of both hospitals involved, in accordance with the ethical standards of the journal (15).

Conservative treatment protocol

Patients in group A were treated with Desault bandage immobilization for the first week. Shoulders were then immobilized with a Sling and Swathe shoulder brace from week 2 through week 4. At one month, mobilization was allowed after controlling bone healing with X-rays.

Surgical treatment protocol

The surgery was performed by the same surgeon for all patients of group B: the patient was placed in supine position; a deltopectoral approach was used; the fracture was identified and periosteum was debrided back from the fracture edges by 1-2 mm, just far enough for clear visualization of the fracture; reduction was achieved by using pointed reduction clamps, then a plate of sufficient length was fixed using screws. In the post-operative protocol, patients’ shoulders were immobilized with an abduction shoulder brace immediately after the surgery. At the 2-week clinical check, the shoulder brace was removed, and patients were encouraged to perform Codman’s pendulum exercises. An X-ray was performed after one month and full movement authorized, in the absence of contraindications.

Radiographic evaluation

Radiographic evaluation was performed obtaining both standard orthogonal planes of the anteroposterior shoulder and a lateral view of the scapula. Patients in group B were evaluated by X-ray postoperatively, and patients in both groups were evaluated at one week, at one, three, and twelve months; and at final follow-up (figure 1).

Clinical outcomes

All patients were clinically evaluated at one, three, and twelve months and at final follow-up with a physical examination. The Constant-Murley Score (CMS) (16), the Disabilities of the Arm, Shoulder and Hand Questionnaire (quickDASH) (17), the American Shoulder and Elbow Surgeons Shoulder Score (ASES) (18), and the Short-Form 12 (SF-12) health survey (19) were recorded at the final follow-up, along with a patient satisfaction rating: (1: disappointed; 2: moderately satisfied; 3: satisfied; 4: very satisfied).

Statistical analysis

Before treatment, patients were randomized into two groups (figure 2) through computer-generated blocked-randomization numbers (http://www.randomizer.org). All patients were informed of the advantages and disadvantages of both treatments. SPSS 22.0 (IBM, Armonk, NY, USA) was used for data analysis. Descriptive statistics were used to
summarize characteristics of the study patients (i.e., score results), including means and ranges. The Wilcoxon Test was used to detect significant differences in the evaluated scores at final follow-up. Results were compared with the Mann-Whitney U Test. Statistical significance was set at a p-value < 0.05.

RESULTS

From the initial sample, 20 patients of group A and 15 patients of group B were available for the final follow-up (Figure 2). The two groups were homogeneous with regard to age, gender, and dominance: group A was composed of eleven women and nine men (mean age, 60.45 ± 1.9); group B was composed of nine women and six men (mean age, 55.40 ± 3.48). Demographic data intergroup comparison were reported in Table I. The mean follow-up was 5.11 ± 1.30 years: 5.25 ± 1.34 years for group A, and 4.93 ± 1.24 years for group B (p = 0.143).

All fractures were classified according to the Neer’s and Hertel’s classifications, as summarized in Table II. No statistically significant differences, based on fracture classifications, were found between the two groups.

Clinical results at final follow-up showed: a median CMS of 82.0 ± 7.6 in group A, and 87.0 ± 5.4 in group B (p = 0.166); a median quickDASH of 8.7 ± 4.3 in group A, and 5.4 ± 0.4 in group B (p = 0.101); a median ASES of 83.7 ± 7.0 in group A, and 96.1 ± 1.0 in group B (p = 0.003); and a median SF-12 of 88.2 ± 5.9 in group A, and 90.1 ± 5.7 in group B (p = 0.327).

Table I. Demographic table. Intergroup comparison.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group A (Conservative) n = 20</th>
<th>Group B (ORIF) n = 26</th>
<th>p&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Follow-up ± SD</td>
<td>5.25 ± 1.34</td>
<td>4.93 ± 1.24</td>
<td>0.143</td>
</tr>
<tr>
<td>Average age ± SD</td>
<td>60.5 ± 1.9</td>
<td>55.4 ± 3.5</td>
<td>0.015</td>
</tr>
<tr>
<td>Gender (Male/Female)</td>
<td>9/11</td>
<td>6/9</td>
<td>0.409</td>
</tr>
<tr>
<td>Dominant side (Right/Left)</td>
<td>18/2</td>
<td>14/1</td>
<td>0.440</td>
</tr>
<tr>
<td>Affected side (Right/Left)</td>
<td>9/11</td>
<td>8/7</td>
<td>0.345</td>
</tr>
<tr>
<td>Complications</td>
<td>0</td>
<td>1</td>
<td>0.374</td>
</tr>
</tbody>
</table>

SD: Standard Deviation; <sup>b</sup>boldface indicates statistical significance (p < 0.05).
Seventeen patients of group A (85%) and 15 patient of group B (100%) were satisfied or very satisfied ($p = 0.058$). However, the results showed statistical significance only for ASES ($p = 0.003$). No statistical significance for the CMS (n.s.), quickDASH (n.s.), SF-12 (n.s.), or the Satisfaction rate (n.s.). Clinical data and intergroup comparison are reported in table III and IV.

One patients of group B reported wound dehiscence, which was successfully treated with medical therapy, and completely healed within four weeks of surgery. No other complications were reported. All patients in both groups showed bone healing without displacement and/or malunion.

### DISCUSSION

The most significant finding of this study was that, with regard to the treatment of proximal humeral fractures, there was no difference in outcomes between conservative and surgical treatment with conventional stainless steel plates. In accordance with the literature, outcomes showed a substantial equivalence of clinical and radiographic results between the two groups at 5.11 years of follow-up. In fact, a 2015 review by Xie et al. (20), which included nine articles and 518 patients, pointed out that operative treatment did not significantly improve the functional outcome and health-related quality of life.
In this study, there was only a slight difference with regard to the clinical evaluation forms between the two groups, yielding better results for the ORIF group. Again, in accordance with the literature, no statistically significant differences were found in the Costant-Murley and QuickDASH scores, or in the SF12 Questionnaire. On the other hand, the ASES score showed statistically significant outcomes; these results were correlated with a recovery of normal daily activities with both treatments. Patients with fractures in the dominant limb showed better functional outcomes, but this data is not relevant in this study since the two groups were homogeneous. The ORIF group, due to an early rehabilitation protocol, showed better outcomes in high demand activities. No differences between the two treatments were otherwise found in the radiographic evaluation. Bone healing was achieved in all patients. Only one patient reported a complication (surgical wound dehiscence), which could have been attributed to the small sample included in the study.

The limits of conservative treatment are: prolonged immobilization, and therefore the risk of articular stiffness; avascular necrosis; and malunion and/or nonunion. In the literature, these results are supported by several studies, such as the 2014 review by Mao et al. (21) and the 2018 review by Reinier B. Bekx et al. (22).

The former review included six studies and 287 patients, 144 of which were treated with conservative management: nonunion was identified in 5.47% (7/128); osteoarthritis in 14.6% (7/48); and avascular necrosis in 15.5% (20/128) of patients treated nonoperatively. The latter review included twenty-two studies and 1743 patients, 833 of which were treated conservatively. Specifically, 13 studies demonstrated a nonunion rate of 5.6% (25/45), and a rate of 8.0% (35/439) of avascular necrosis. In five studies, 4.8% of patients (20/457) underwent revision surgery due to impingement, displacement, or malunion. Even though surgical patients presented better functional outcomes, they ran into a higher incidence of infections, nerve injuries, and reintervention.

In a 2015 review by Xie et al. (20), operative and nonoperative treatments were compared. They reported that the surgical group had an infection rate five times higher than that of the non-surgical group; a nerve injury rate 1.57 times higher; and twice as high of reintervention and mortality rates, whereas, the rate of nonunion and displacement was reduced to almost half. Moreover, as stated by Panagiotopoulou et al. (23) in their 2019 review, and also by McMillan & Johnstone (24) in their 2018 review, implant-related complications such as screw perforations, screw cut-out, mobilization and plate bending, and breakage should not be overlooked.

In agreement with the significant rate of complications related to ORIF reported in the literature (25), this study suggests that the conservative approach leads to good clinical results and bone healing, and that it furthermore avoids the risks associated with surgery. On the other hand, patients with high activity demand could prefer the surgical option since operative treatment could lead to a faster recovery.

In accordance with the 2011 study by Olerud et al. (26), this study suggested that the choice of treatment in patients with proximal humeral fractures should be based on functional demands and comorbidities of the patients. The limitations of the study included the number of patients admitted to the study and the absence of comparison to other surgical treatments. Moreover, the follow-up period allowed us to draw conclusions only on the medium-term outcomes.

CONCLUSIONS

Conservative treatment is the gold standard for nondisplaced and minimally displaced proximal humeral fractures, whereas, in cases of majorly displaced humeral fractures, the treatment of choice in literature has yet to be defined. This prospective study showed that the comorbidity and functional demand of patients must be taken into consideration in the management of majorly displaced proximal humeral fractures.

Since the clinical and radiological outcomes in conservatively treated patients are comparable to the outcome of patients treated with ORIF, conservative treatment is therefore a viable option for patients with low functional demand, and furthermore, the associated risks of surgery are avoided. Operative treatment is best suited for younger and healthy patients with higher functional demand, where early mobilization of the affected limb can lead to faster recovery for activities demanding higher performance.

ETHICS

The study protocol was approved by the hospitals’ Ethical Review Board and it was conducted in accordance with the principles of the Declaration of Helsinki and its amendments. Patients were informed about the characteristics of the study and they gave their consent to participate.

CONSENTS

Consent was obtained from patients for publication of the study. No personal data was included in the manuscript.
CONTRIBUTIONS

All authors contributed equally to the manuscript and read and approved the final version of the manuscript.

REFERENCES

Can Supraspinatus Tears Contribute to Acquired Subcoracoid Impingement? A Radiological Study of Anterosuperior Cuff Tears

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SUMMARY

Background. Many subscapularis (SubS) lesions represent the result of the progression of anterosuperior cuff tears, although their pathophysiology is still relatively unknown. The goal of this paper was to determine the influence of supraspinatus tears in the development of subcoracoid impingement and therefore SubS tears.

Methods. This is a retrospective, controlled and single-blinded study. We analyzed 301 patients with rotator cuff pathology and an MRI study. The coraco-humeral distance and coracoid overlap were measured. The presence of supraspinatus and subscapularis lesions were also evaluated.

Results. Supraspinatus tears were found to be associated with the presence of subscapularis tears (p = 0.003). A significant relationship (p = 0.002) was achieved between supraspinatus tears and inferior coraco-humeral distance, with average values of 8.4 ± 2.9 mm and 10.2 ± 3.2 mm in shoulders with and without supraspinatus tears respectively. On the opposite side, there wasn't a significant association between supraspinatus tears and the coracoid overlap.

Conclusions. This paper is, to our knowledge, the first to study the influence of supraspinatus tears in different parameters implied in subscapularis tears pathology, representing also the largest published sample on this theme, including 301 patients. Finally, this study offers an explanation for anterosuperior cuff progression pathophysiology, confirming that supraspinatus full thickness tears can lead to a secondary subcoracoid impingement and thus subscapularis tears.

KEY WORDS
Coraco-humeral distance; coracoid overlap; rotator cuff tears; subscapularis; subcoracoid impingement; supraspinatus.

BACKGROUND

Rotator cuff tears pathophysiology remains controversial, with both probable contributions from degenerative processes, traumatic events and variants in shoulder anatomy (1-3). This is particularly true regarding subscapularis (SubS) tears, which pathophysiology and risk factors are still very much unknown (1, 2).

Although the understanding of degenerative rotator cuff pathology has evolved over the past decades, most of these studies focused on the more frequent posterosuperior cuff tears, including the infraspinatus and supraspinatus (SS) (3, 4). However, in recent years, there has been an increasing interest regarding anatomical risk factors for SubS tears, with the coracoacromial arch and the coracoid process being recognized as major players in anterior cuff tears (2, 5-7). Many
papers have recently showed that subcoracoid impingement can lead to SubS tears, and that smaller coraco-humeral distances (CHD) and greater coracoid overlaps (CO) are associated with greater risk of anterior cuff pathology (2, 7). Despite the fact that many of SubS tears occur in the context of progression of a previous SS tear, there are relatively few studies focusing on the progression of anterosuperior tears, as described by Warner et al. (8), affecting the SS and SubS (4, 9).

Some studies have showed that SS tears are risk factors, and could progress to a SubS tear. This progression was particularly evident with full thickness SS tears, larger SS tears, and SS tears that included the anterior cable (4, 10). Recently a few papers also re-established the previous notion that a rotator cuff tear would lead to the superior escape of the humeral head, because of the unopposed pull from the deltoid (10-12). Studies also agree that a superior cuff tear will lead to failing to compress the humeral head in the glenoid cavity, resulting in its superior migration (10, 12). On the other hand, papers have also showed that SubS tears do not cause a superior migration of the humeral head, more so, the addition of a SubS tear to a shoulder with previous SS tear didn’t result in aggravated superior humeral head escape (11, 13).

However there is still a sparse number of papers focusing in the process behind the progression of anterosuperior tears, although studies agree that a superior cuff tear will result in superior humeral head migration which will result in a decreased coraco-humeral distance (CHD) (10, 12). This association between superior cuff complete tears and smaller CHD, is explained by the superior migration of the humeral head, placing a part of the humeral head with greater cross section posteriorily to the coracoid, leading to a secondary subcoracoid impingement, defined by entrapment of the SubS between the coracoid process and the humerus (10, 12, 14). In a study conducted by Nove-Josserand et al. (15), the authors reported an association between patients with SS, SubS and infraspinatus tears and diminished CHD (15). In a previous paper by MacMahon et al. (10), the authors compared the effect of complete SS tears in CHD and the association of these with SubS tears (10). They concluded that SS tears were associated with increased risk of SubS tears (p < 0.05). They also found that patients with SS tendentially showed narrowing of the CHD, however without significant differences between the study and control group (10).

Similarly, to the subacromial impingement role in posterosuperior cuff tears, decreased CHD could be an etiologic factor in progression of SS tears anteriorily into the SubS (7, 12, 16-18). Besides the CHD, studies also showed that the CO is also a very strong predictor of SubS tears (2). The CO is used to describe the coracoid shape as it measures the distance from the glenoid fossa to the most prominent aspect of the coracoid process (2). However, none of the previously published papers established if the presence of SS tears would influence the CO.

The main goal of this study was to evaluate the influence of SS full thickness tears in the CHD and CO. We postulated that a full thickness SS tear would result in a secondary subcoracoid impingement and help explain the pathophysiology of anterosuperior cuff tears.

**MATERIALS AND METHODS**

We performed a retrospective, controlled, single-blinded study. Patient data were collected retrospectively from our institution’s outpatient orthopedics clinical files, and included all patients with suspected rotator cuff pathology evaluated between 2009 and 2019. The study group included patients with full thickness SS tears, while the control group included patients with normal MRIs. Patients without an MRI study, with inflammatory arthropathy, rotator cuff tears other than full thickness SS tears, rotator cuff arthropathy, shoulder instability, or congenital deformities were excluded.

Our institution’s standard MRI shoulder protocol was applied, including T1- and T2-weighted fat-saturated images, with the patient in supine position with the arm alongside the body, elbow extended, and forearm supinated. All MRI scans were performed in our institution’s radiology department, using similar MRI models with equivalent gantries. The CHD and CO were measured in transversal sections of T1 weighted images to take advantage of its better definition of the cortical margins. The CHD consists in the minimal distance between the humeral cortex and the coracoid cortex. The CO represents the distance from the glenoid to the tip of the coracoid process (figures 1, 2). The axial images were acquired where the subcoracoid space was at its minimum (5).

The presence of SS tears, the presence and type of injury to the SubS and long head of the biceps (LHB), gender and laterality were also recorded. A standardized measurement technique was developed, these measurements were recorded by the same orthopedic surgeon, blinded to the MRI report. The final recorded value was the average of three separated evaluations of each index.

**Statistical analysis**

Statistical analysis was performed using SPSS software (version 24; IBM, Armonk, NY, USA). Categorical variables are presented as absolute and relative frequencies, whereas continuous variables are characterized by the mean and
standard deviation. The statistical tests used were the χ² test to evaluate the association between categorical variables and 1-way analysis of variance test to compare means of continuous variables. The value with the highest Youden index was considered the cutoff with the best precision. Statistical significance was considered at P < .05.

Ethical commission approval was obtained regarding this paper.

RESULTS
The sample was comprised of 301 shoulders, including 143 female (47.5%) and 158 male (52.5%). The study group included 272 shoulders with complete SS tears, and corresponded to 90.4% of the sample.

The sample included 145 shoulders with SubS injuries (tendinopathy or tear), corresponding to 48.2% of the sample, with 99 (32.9%) presenting a SubS tear (complete or partial). Regarding the LHB, 93 shoulders presented a lesion of this tendon, including tendinopathy, rupture or instability.

The sample included 158 right (52.5%) and 143 left shoulders (47.5%). The left shoulder was associated with more SS tears (p = 0.008).

Comparing the type of rotator cuff injuries in both genders, we didn’t find any statistically significant relationship between the presence of a SS lesion and gender.

Analyzing the presence of simultaneous lesions of the SS, SubS or LHB, we found a significant association between SS lesions and lesions of the SubS (p = 0.003) or LHB (p = 0.045).

The CHD and CO were measured in 301 shoulders, with an average CHD of 8.6 ± 3 mm and an average CO of 16.4 ± 4.8 mm. There were no significant differences in CHD or CO variables according to gender. Regarding joint laterality, the CHD was significantly smaller in the left shoulder (p = 0.04); no statistical significance was obtained in the comparison between CO and joint laterality (p = 0.34).

Comparing the CHD and CO with the presence of a SS lesion, we found that only the CHD showed a statistically significant association with the presence of a SS tear (p = 0.002). The mean CHD in the presence of a SS tear was 8.4 ± 2.9 mm, contrasting with an average CHD value of 10.2 ± 3.2 mm in the control group.

Regarding the CO, the average values were 16.5 ± 4.7 mm and 15.1 ± 4.7 mm in the shoulders with and without SS tears respectively. This difference didn’t achieve statistical significance (p = 0.12).

DISCUSSION
The role of subacromial and subcoracoid impingement in SS and SubS tears is extensively studied, however there are no published studies able to establish the exact pathophysiology of these two entities, that often are present simultaneously.

In this paper we confirmed the relationship between the presence of SS full thickness tears and SubS tears, and even LHB injuries, with a statistical significant association between these lesions. Comparing both groups, we can see that the control group presents a healthy SubS in 82.8% of shoulders, and
that only 48.5% of shoulders in the study group present a normal SubS. Besides that, 34.9% of the study group presented a SubS tear, contrasting with 13.7% in the control group. Regarding the CHD, we found a significant relationship between SS tears and decreased CHD, with average values of 10.2 ± 3.2 mm and 8.4 ± 2.9 mm, for the control and study group respectively (p = 0.002).

On the other hand, no statistical significant relationship was established between the CO and the presence of SS tears. To our knowledge, our paper presents the largest sample on this topic, including 301 patients, being also the first to evaluate the different influence of the CHD as well as the CO in shoulders with SS tears and their roles in SubS tears pathology. However, there are some limitations to our study. Although our MRI protocol stated that the arm should be in a predefined position, variation in patient positioning is always a possibility and may influence the measurements. Also, our control group was relatively small when compared to the study group, due to the strict inclusion criteria for this group, which only included patients with completely normal MRI. In addition, our study was designed as a retrospective study, with its inherent limitations, and a prospective longitudinal study would be of value to confirm our preliminary conclusions.

It is known that many SubS tears originate from the anterior extension of SS tears, and many authors have already proved that SS tears are risk factors for SubS pathology (3, 9, 10). More so, numerous papers have showed that SS tears result in superior migration of the humeral head with decreased acromio-humeral distance (10-12). Differently, only a few study groups were able to establish the effect of SS tears in CHD, with complete SS tears associated with inferior CHD, and none of these searched the effect on other known SubS predictors, such as CO (10, 12). Our results allow us to extrapolate that the humeral head superior migration results in a secondary subcoracoid impingement, resulting in increased risk of SubS tears in the context of SS full thickness tear.

As it is also known, both the CO and CHD are very strong predictors of SubS tears, with studies showing ROC Curves with areas under the curve of 93.8% and 80.6% (2). Both these parameters demonstrated being excellent SubS lesion predictors in several studies, however they translate different anatomic particularities of the shoulder gridle. The CHD corresponds to the smaller distance between the humerus lesser tuberosity and the coracoid, and represents the space available for the SubS (2, 7, 19-21). This space can be altered by pathologies affecting the humerus lesser tuberosity or the coracoid, such as fracture mal union, osteophytes, cysts or anomalies of the lesser tuberosity, SS tendon calcifications or even abnormal coracoid anatomy (2, 7, 19-21). As stated previously, other papers have also showed that the CHD can also be influenced by the presence of SS tears, and the phenomenon is explained by superior subluxation of the humeral head in these patients, that results in a greater humeral cross-section posteriorly to the coracoid process, and secondary subcoracoid impingement (10).

On the other hand, the CO represents the medial to lateral projection of the coracoid process, in regard to the glenoid fossa (2). This measurement is less susceptible to alterations caused by traumatic, iatrogenic or degenerative processes as it only depends on the coracoid projection, and the superior migration of the humeral head should not influence this measurement, as proved by our study.

The fact that the study group, with increased risk of SubS tears, was associated with inferior CHD but not with greater CO, suggests that this subcoracoid impingement is secondary to subluxation of the humeral head and not a result of coracoid process morphology. This can represent one more clue in explaining the physiopathology of SubS tears as a progression of SS tears, in the context of anterosuperior rotator cuff tears.

Our results shed light in anterior superior cuff progression pathophysiology, confirming the hypothesis that SS full thickness tears lead to a secondary subcoracoid impingement and consequently SubS tears. However future prospective longitudinal studies are needed to further explain this complex relationship. The study meets the ethical standards of the journal (22).

**CONFLICT OF INTERESTS**

The authors declare that they have no conflict of interests.

**REFERENCES**

Objective. Although the trigger point injection (TPI) is the most widely used treatment method in myofascial pain syndrome (MPS), other treatment methods have also been proven to be influential. Even if a certain level of pain relief is achieved after the TPI, this effect persists for a short time and a few treatment sessions are generally required. Hence, a multidisciplinary approach to treatment seems to be most useful. Therefore, this study aimed to evaluate the efficacy of the combination of TPI with kinesio taping (KT) on the trapezius muscle in the treatment of MPS.

Methods. 50 patients with MPS were randomly separated into two groups (25 patients per group): Group 1: TPI plus KT; Group 2: TPI plus sham KT. Visual analog scale (VAS) and neck disability index (NDI) were recorded at baseline and 1, 3 months post-treatment.

Results. The mean age of patients was 42.5 ± 13.89 and 43.8 ± 12.23 years in Group 1 and Group 2, respectively. In Group 1, pre- and post-treatment (at 1 and 3 months) VAS/NDI scores were 8.0 ± 0.45/40.96 ± 1.27, 0.08 ± 0.28/7.51 ± 2.55, and 0.44 ± 0.51/8.96 ± 3.27, respectively. In Group 2, pre- and post-treatment (at 1 and 3 months) VAS/NDI scores were 8.0 ± 0.54/41.21 ± 1.54, 0.25 ± 0.44/8.35 ± 2.75, and 2.33 ± 1.44/13.98 ± 5.63, respectively. VAS and NDI scores at 3 months were significantly lower in Group 1 versus Group 2 (p < 0.05).

Conclusions. The complex pathology with underlying peripheral and central neural mechanisms of MPS might contribute to the difficulties within the treatment of MPS, especially within the chronic period. The combined therapy appears to generate a more influential outcome for a long run than monotherapy in alleviating pain and reforming functional amelioration in the management of MPS.

KEY WORDS
Myofascial pain syndrome; trigger point injection; kinesio taping.

INTRODUCTION
Myofascial pain syndrome (MPS) is a musculoskeletal pain condition defined by local and referred pain sensed as deep and aching and with the existence of myofascial trigger points in skeletal muscles or fascia in any part of the body. A myofascial trigger point (MTrP) is a hyperirritable spot in skeletal muscle or muscle’s fascia that is linked by a hypersensitive palpable nodule in a taut band (1).

The major symptoms of MPS are tenderness to palpation with referred pain to the other muscles of the body or joints, limited range of motion and hassle to relax or fully lengthen the muscle, longer-lasting muscle pain, weakness and stiffness, sleep disturbance, and autonomic phenomena such as vasomotor and temperature disturbance, sweating, lacrimation, dermal flushing, coryza, salivation, pilomotor erection, proprioceptive disorder. Cervical myofascial pain may be linked by neuro-otologic symptoms such as dizziness, imbalance, and tinnitus. It might attend with a sensory ingredient of paresthesias or dysesthesias. Additionally, it could simulate other pains such as radicular pain or visceral pain (1).

Myofascial pain is an important health cause influencing as much as 85% of the general population sometime in their
lifetime while the estimated overall prevalence is ~46%. Common etiologies of MPS could be from exposure to cumulative and repetitive strain, spine pathology, postural dysfunction, and physical deconditioning, and direct or indirect trauma. The affected muscles are frequently the muscles in the neck, shoulders, and pelvic girdle such as the trapezius, sternocleidomastoid, levator scapulae, scalene, infraspinatus, quadratus lumborum, and gastrocnemius, which are used to preserve body posture. The trapezius is the muscle in which MTrPs consist frequently. MTrPs in trapezius muscle might produce chronic upper-quarter pain, neck pain, migraine, headache, tinnitus, temporomandibular joint pain, eye symptoms, torticollis, or shoulder pain (1, 2).

The natural course of MPS is spontaneous recovery, persistence without progression, and additional TrP and chronicity. The prime aims of the management are alleviating pain with the inactivation of TrPs, fixing a range of motion (ROM) of the joints, prevention of recurrence, and extinguishing predisposing factors (mechanical factors such as poor posture, structural abnormality, systemic factors such as vitamin deficiency, hypothyroidism, chronic infection/infestation and psychological factors such as psychosomatic diseases, depression and secondary gain) for MTrPs. The major governance choices contain management of predisposing factors, patient education, medications by analgesics, myorelaxants and anti-depressants, stretch and spray, therapeutic massage, ischemic compression, biofeedback, hot pack, transcutaneous electrical nerve stimulation (TENS), interferential (IFA) current, ultrasound (US), extracorporeal shock wave therapy (ESWT), low energy light amplification by stimulated emission of radiation (LASER), trigger point injections (TPIs, with local anesthetics (LAs), corticosteroids, nonsteroidal anti-inflammatory drug, saline or botulinum toxin), dry needling and acupuncture (3). Although there are wide variations in application models, there is no obvious consensus on when and how to use these interventions. Even though TPI is the most widely used treatment method, other treatment methods have also been proven to be influential. In clinical practice, even if a certain level of pain relief is achieved after TPI, this effect persists for a short time and a few treatment sessions are generally required. Hence, a multidisciplinary approach to treatment seems to be most useful (1, 4). Moreover, a few studies are supporting the efficacy of KT for MPS in the trapezius muscle (5). Hence, this study aimed to evaluate the effectiveness of the combination of TPI with KT on the trapezius muscle in the management of MPS.

MATERIALS AND METHODS
The randomized sham-controlled clinical trial was directed at the patients with MPS in an outpatient ambulatory setting who applied to Kocaeli Government Hospital, Kocaeli, Turkey, between March 2019 and May 2019. The study protocol was approved by the Ethical Committee of Kocaeli University (Trial Registration: KU GOKAEK 2018/197). Written informed consent was obtained from all patients.

Participants
A total of 50 patients (32 female, 18 male) were contained in this trial. The diagnosis of MPS was made in accordance with the diagnostic criteria of Travell and Simon. These criteria include five major and three minor criteria. Major criteria are: 1) regional pain complaint in the neck, 2) pain complaint or altered sensation in the expected distribution of referred pain from a myofascial trigger point, 3) taut band palpable in accessible muscle, 4) excruciating spot tenderness at one point along the length of the taut band and 5) some degree of restricted range of motion when measurable. Minor criteria are: 1) reproduction of clinical pain complaint, or altered sensation, by pressure on the tender spot, 2) elicitation of a local twitch response by transverse snapping palpation at the tender spot or by needle insertion into the tender spot in the taut band and 3) pain alleviated by elongating (stretching) the muscle or by injecting the tender spot (trigger point) (1). Inclusion criteria were the patients who had an active MTrP in the trapezius region and taut palpable band and failed to respond to previous medication, age between 20 and 65 years, and neck and/or upper back pain in the normal range with symptom duration of at least one month. Exclusion criteria were the patients diagnosed with fibromyalgia, history of pregnancy, systemic diseases such as hypertension, diabetes mellitus and rheumatic illness or bleeding disorders, trauma and neck surgery, the patients with cervical disc lesions and radiculopathy or myelopathy, using the anticoagulant medication, a history of allergy to LAs and previous history of TPI within the preceding six months (table I). All patients were randomly separated into two groups (25 patients per group) through random allocation using a computer-generated random number: Group 1: TPI plus KT; Group 2: TPI plus sham KT. Firstly, Groups 1 and 2 were treated by TPI of 1 ml of 20 mg betamethasone dipropionate combined with 3 ml of 2% lidocaine and 1 ml of saline solution. In both groups, the point with a pinch between the thumb and index finger or between the index and middle finger was isolated. Then, a TrP was located and the overlying skin was sterilized with povidone-iodine solution. The needle was then inserted 1 to 2 cm away from the TrP and was advanced into the trigger point at an acute angle of 30 degrees to the skin. The plunger was pulled before injection to guarantee that the needle is not in a blood vessel. A small amount (1 ml) of...
the mixture was injected after the needle got into the TrP. Then, the needle was pulled to the level of subcutaneous tissues. It was redirected medially, laterally, inferiorly and superiorly. Needling and injection were repeated in all directions until the local twitch response no longer appeared or resisted muscle tautness (figure 1). Before the KT application, the skin was shaved if required, cleaned with alcohol, and dried. KT (VZN Tape Kinesiology) with a width of 10 cm and a thickness of 0.5 mm was used in both groups. In Group 1, four tapes were applied to a horizontal stripe across each other the most painful area with a maximum stretch on the injected trigger point (figure 2). In Group 2, the same application (four tapes in a star shape) without tension was applied over the same point. KT was applied five times by intervals of 3 days for two weeks. All injections and applications were performed by the same physician (EY). The participants in both groups received home-based exercise programs including neck isometric exercises and trapezius muscle strengthening and stretching exercises. All patients were instructed about the exercises by physiotherapists and the first set of exercises were performed under the supervision of clinical physiotherapists. These exercises were performed three times with 10 repetitions daily for two weeks. No adverse side effects were reported.

Data extraction
Data collected including age, sex, duration of symptoms, affected side of the trapezius muscle. The pain intensity using visual analog scale (VAS) and neck disability using neck disability index (NDI) were recorded at baseline and 1, 3 months post-treatment. VAS and NDI scores were recorded by a nurse. The nurse who collected the VAS and NDI scores was blinded to the assignment of groups.

Statistical analysis
Sample size and power calculation determined that 18 patients in each group were sufficient to power (power of 0.80, \( \alpha = 0.05 \), and \( \beta = 0.20 \)). The calculation of sample size was based on a mean difference of 2 points with 2.5 points standard deviation in the VAS according to previous data

<table>
<thead>
<tr>
<th>Inclusion criteria</th>
<th>Exclusion criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>The patients had an active myofascial trigger point in the trapezius region and taut palpable band</td>
<td>The patients with fibromyalgia, cervical disc lesions and radiculopathy or myelopathy</td>
</tr>
<tr>
<td>The neck and/or upper back pain in the normal range</td>
<td>A history of pregnancy, trauma and neck surgery, systemic diseases such as hypertension, diabetes mellitus and rheumatic illness or bleeding disorders</td>
</tr>
<tr>
<td>The presence of these symptoms for at least 1 month</td>
<td>A history of using the anticoagulant medication</td>
</tr>
<tr>
<td>The patients who are between 20 and 65 years of age</td>
<td>A history of allergy to local anesthetics</td>
</tr>
<tr>
<td>The patients failed to respond to previous medication</td>
<td>Previous history of trigger point injection within the preceding six months</td>
</tr>
</tbody>
</table>

Figure 1. The injection technique used for trigger point.

Figure 2. The technique used for kinesio taping.
(20) using the PASS (power analysis and sample size) system. All statistical analyses were performed using IBM SPSS Statistics for Windows, Version 20.0 (IBM Corp., Armonk, NY, USA). For continuous data (age, symptom duration, VAS, and NDI score) descriptive statistics were expressed as mean ± standard deviation (SD). For categorical data (sex, affected side of the trapezius muscle) were expressed as frequency and percentage. Relations among categorical variables were assessed by Chi-square analysis. Kolmogorov-Smirnov tests were used to determine whether or not the variables were normally distributed. Normal distributions of continuous variables were assessed by Student’s t-test. Non-normally distributed metric variables were analyzed by Mann-Whitney U tests. Repeated non-normal VAS and NDI scores were compared using Friedman Two way ANOVA. P values < 0.05 were considered statistically significant.

RESULTS
The demographic characteristics of patients including age, sex, duration of symptoms, affected side, and part of the trapezius muscle were presented in Table II. The mean age of patients was 42.5 ± 13.89 and 43.8 ± 12.23 years in Group 1 and Group 2, respectively. Of all patients, 64% (n = 16) was female and 36% (n = 9) was male in Group 1, 64% (n = 16) is female and 36% (n = 9) was male in Group 2. The mean duration of symptoms is 17.36 ± 17.59 and 17.24 ± 16.86 months in Group 1 and Group 2, respectively. There was no statistically significant difference between groups regarding age, sex, symptom duration, and affected side (p > 0.05).

In Group 1, pre- and post-treatment (at 1 and 3 months) VAS/NDI scores were 8.0 ± 0.45/40.96 ± 1.27, 0.08 ± 0.28/7.51 ± 2.55, and 0.44 ± 0.51/8.96 ± 3.27, respectively. In Group 2, pre- and post-treatment (at 1 and 3 months) VAS/NDI scores were 8.0 ± 0.54/41.21 ± 1.54, 0.25 ± 0.44/8.35 ± 2.75, and 2.33 ± 1.44/13.98 ± 5.63, respectively. The change in VAS and NDI scores compared with the initial evaluation was shown in Table III and Table IV. VAS and NDI scores in 1 and 3 months significantly decreased in both groups compared to baseline (p < 0.05). However, the VAS and NDI scores at 3 months were significantly lower in Group 1 versus Group 2 (p < 0.05) (Tables III and IV, figure 3 a, b).

DISCUSSION
Recently, the most extensively admitted strategy for the management of MPS is to treat the underlying etiology. MTrPs might reactivation and MPS might sustain if the main cause is not warrantably treated. Different procedures can be utilized alone or in combination with varying degrees of success in the treatment of MPS. Moreover, the combined therapy rather than monotherapy is usually utilized to manage MPS in routine clinical practice (1, 6). In the regions of MTrPs, there is a muscle spasm due to an aberrant enhancement in the production and release of acetylcholine within the motor endplate at rest, resulting in reduced blood circulation because of the compression of nearby blood vessels. Additionally, nociceptors and peripheral nerve endings can be affected by several inflammatory factors, thus creating a vicious cycle of events and the autonomic symptoms of MPS owing to the activation of sympathetic fibers (1, 7). This study was hypothesized that the combination of TPI (by providing anti-nociceptive effect) and KT (by improving blood circulation) may produce better results. According to the results of this study, TPI plus KT group had significantly reduced pain and improved functional status compared to the TPI plus sham KT group.

Table II. Patients’ characteristics of groups

<table>
<thead>
<tr>
<th>Variables</th>
<th>Group 1 (n = 20) Trigger point injection (TPI) plus kinesio taping (KT)</th>
<th>Group 2 (n = 20) TPI plus sham KT</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>42.5 ± 13.89</td>
<td>43.8 ± 12.23</td>
<td>0.53</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>16 (64%)</td>
<td>16 (64%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Male</td>
<td>9 (36%)</td>
<td>9 (36%)</td>
<td></td>
</tr>
<tr>
<td>Symptom duration (months)</td>
<td>17.36 ± 17.59</td>
<td>17.24 ± 16.86</td>
<td>0.46</td>
</tr>
<tr>
<td>Affected side</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right</td>
<td>8 (32%)</td>
<td>8 (32%)</td>
<td>0.78</td>
</tr>
<tr>
<td>Left</td>
<td>11 (44%)</td>
<td>10 (40%)</td>
<td></td>
</tr>
<tr>
<td>Bilateral</td>
<td>6 (24%)</td>
<td>7 (28%)</td>
<td></td>
</tr>
</tbody>
</table>

All values are expressed as mean ± standard deviation (SD), number and percentage. P < 0.05, significant difference.
TPIs are a widespread and efficacious therapy because of mechanical disruption by the needle and the ending of the dysfunctional activity in motor endplates. The effects of the applications of TPIs are: 1) to block nerve sensitizing substances, 2) to decrease hypersensitivity, 3) to release intracellular potassium depolarizing and disturbing nerve conduction, 4) to enhance circulation at the TrP via local vasodilation impact, 5) to block the passage of noxious inputs in the dorsal horn of spinal cord, 6) to activate the endogenous opioid system and 7) to break the vicious cycle of ischemia-pain-muscle spasm. TPI is an injection technique in which some materials are injected into the TrP. LAs are the most widely injected materials. Outside of LAs, corticosteroids are commonly used for injection.

Table III. Changes in VAS in before treatment and 1 and 3 months after treatment in Group 1 and 2.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Group 1 (n = 20) Trigger point injection (TPI) plus kinesio taping (KT)</th>
<th>Group 2 (n = 20) TPI plus sham KT</th>
<th>P value²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before injection</td>
<td>8.0 ± 0.45</td>
<td>8.0 ± 0.54</td>
<td>1.000²</td>
</tr>
<tr>
<td>1 month after the injection</td>
<td>0.08 ± 0.28</td>
<td>0.25 ± 0.44</td>
<td>0.289²</td>
</tr>
<tr>
<td>3 months after the injection</td>
<td>0.44 ± 0.51</td>
<td>2.33 ± 1.44</td>
<td>0.006²</td>
</tr>
</tbody>
</table>

P ¹ value < 0.001 a,b,c < 0.001 a,b
All values are expressed as mean ± SD. P < 0.05, significant difference. ¹: By Friedman Two way ANOVA. ²: By Mann-Whitney U-test. a: there is differences between before injection and 1 month after injection. b: there is differences between before injection and 3 months after injection. c: there is differences between 1 month after injection and 3 months after injection.

Table IV. Changes in NDI in before treatment and 1 and 3 months after treatment in Group 1 and 2.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Group 1 (n = 20) Trigger point injection (TPI) plus kinesio taping (KT)</th>
<th>Group 2 (n = 20) TPI plus sham KT</th>
<th>P value²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before injection</td>
<td>40.96 ± 1.27</td>
<td>41.21 ± 1.54</td>
<td>0.883²</td>
</tr>
<tr>
<td>1 month after the injection</td>
<td>7.51 ± 2.55</td>
<td>8.35 ± 2.75</td>
<td>1.000²</td>
</tr>
<tr>
<td>3 months after the injection</td>
<td>8.96 ± 3.27</td>
<td>13.98 ± 5.63</td>
<td>0.002³</td>
</tr>
</tbody>
</table>

P¹ value < 0.001 a,b,c < 0.001 a,b, c
All values are expressed as mean ± SD. P < 0.05, significant difference. ¹: By Friedman Two way ANOVA. ²: By Mann-Whitney U-test. a: there is differences between before injection and 1 month after injection. b: there is differences between before injection and 3 months after injection. c: there is differences between 1 month after injection and 3 months after injection.

Figure 3. The median changes of VAS and NDI scores in TPI plus KT group (Group 1) and TPI plus sham KT group (Group 2).
TPI is utilized for patients with symptomatic active TrPs showing a twitch response to pressure and produce a pattern of referred pain (3, 6). Even though corticosteroid injections in TrPs are still controversial owing to being little evidence to promote an underlying inflammatory pathophysiology, triamcinolone plus lidocaine has been found to induce a relatively higher rate of pain relief compared to lidocaine monotherapy (8). Besides, it is reasonable to do these injections with LAs considering the possible side effects of corticosteroids. In one study, it was shown that corticosteroids selectively block the transmission of nociceptive fibers, whereas local anesthetics can relax the muscles and break the cycle of pain and spasms (9, 10). Sonne et al. evaluated the effect of the injection of steroid and LA as therapy for low-back pain and found significant reductions in pain score and patients’ self-assessments (11).

Hossain et al. also demonstrated that the concomitant use of steroids and LA injection was better than only LA injection in intensity and duration of pain relief. They proposed that the pain-relieving impact of a locally injected steroid is largely dependent on local anti-inflammatory action and partially its central effect. Corticosteroid has also a strong irritant effect on peripheral nerve ending. Moreover, it awakens its act in pain modulation mechanism in the central nervous system inducing its analgesic action. What’s more, corticosteroid owns characteristic softening and stretching impacts on the collagen, assists the growth of new fibrocytes, and ultimately decreases tissue tension (10). Therefore, in this study, the combination of LA and corticosteroid was chosen for TPI and a short-acting steroid was preferred because of possible side effects. The complications of TPI are muscle spasm, tenderness, and local infection sustaining for several hours to days (9, 10). There was no adverse effect in this study.

Today, KT is generally utilized as an assistance method in the rehabilitation of musculoskeletal disorders, prevention of injuries, treatment of fascia, muscles or joints dysfunctions, and lymphoedema. Moreover, it is demonstrated that KT could improve the ROM, diminishment of pain, decrease swelling, inflammation, and contusion, increase blood circulation, raise strength and muscle tone, and be employed in muscle spasms and prevention of cramping and speed up the healing of overused muscles (5, 12). KT could also be accustomed to deal pain within patients with MPS (5). There are several hypotheses that indicate a possible analgesic effect of KT. One of these might be associated with the reduced subcutaneous nociceptor pressure in the skin through lifting the skin with the application of KT. An additional hypothesis is the gate control theory. The cutaneous stretch stimulation initiated by KT could affect nociceptive stimuli achieving the central nervous system and prevent the pain (13). Moreover, KT enhances blood and lymphatic fluid circulation under the taped area by a lifting effect that forms a wider area between the skin and the muscle. According to the theory of the action of KT on fascial tissues, the transmission of the relative tension created by the KT band to the appropriate receptors reveals the muscle response due to the direct connection between the fascia and the muscles. These might influence muscle functions and lead to the improvement in pain and ROM (14, 15). It is believed that the pressure and stretching impact of KT on the skin stimulates cutaneous mechanoreceptors which transmit information about joint position and movement. In this way, it can increase proprioception (16).

The application techniques of KT contain inhibition, facilitation, field correction, fascia correction, functional correction, and mechanic correction techniques. The practitioner of KT must decide which muscle group should be treated with which type of technique. Furthermore, the proper technique should be performed after full examination of the affected muscle. In practice, the inhibition technique used for muscle dysfunction induced by microtrauma or tension is generally preferred (5). In this study, the field correction technique was performed to improve the circulation of tissue.

Gonzales-Iglesias et al. investigated the effect of KT application on whiplash injury and demonstrated improvements in terms of pain level (17). Hernandez et al. compared the efficacy of cervical manipulation and KT application in patients with mechanical neck pain. They found results similar to those of Gonzalez-Iglesias et al. (18). Karatas et al. examined the efficacy of KT application on mechanical neck pain. They showed that patients treated with KT exhibited improvements in terms of pain (19). Ozturk et al. determined the short- and mid-term effects of KT on the trapezius muscle in individuals with MPS. They compared KT with sham KT application and found improvements in terms of pain level after KT application (20). Ay et al. compared the effects of KT and sham taping with 2 weeks follow-up and demonstrated that KT is successful for the improvement of findings including pain, pressure pain threshold, cervical range of motion, and neck disability (21). Considering these studies, it is thought that the combination of TPI and KT, which act at different points, may increase the duration of symptomatic effective in MPS. Ata et al. evaluated the efficacy of KT with that of local anesthetic injection alone on the degree of pain and quality of life in MPS and indicated that KT may be useful to increase the efficacy of lidocaine injection in MPS (22). The results of the study were in accordance with this study. This can be explained by an additive synergic effect of KT.
When MTrP injection is used as the primary therapy, patients are at risk for becoming dependent on this treatment for pain relief because of the limited role of this treatment in the long-term management of MPS (23). Therefore, it has seemed that TPI plus KT on the trapezius muscle in the treatment of MPS may contribute to interrupting the progression of chronic process and prohibiting recurrence and blocking a vicious cycle of pain.

Study Limitations

Some limitations of the present study include sample size and the absences of the KT group, placebo group, long-term consequences, and using inhibition technique via KT. Further studies are needed to design with a placebo group and inhibition technique via KT to clarify the efficacy of this combination in the treatment of MPS.

REFERENCES


CONCLUSIONS

The complex pathology with underlying peripheral and central neural mechanisms of MPS might conduce to the difficulties within the treatment of MPS, especially within the chronic period. Furthermore, the presence of TrP related symptoms in some patients indicates that the treatment may require more than a single approach of injections. The combined therapy appears to generate a more influential outcome for the long run than monotherapy in alleviating pain and reforming functional amelioration in the management of MPS. The study meets the ethical standards of the journal (24).

CONFLICT OF INTERESTS

The author declares that she has no conflict of interests.

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Cross-Cultural Adaptation and Measurement Properties of the Brazilian Portuguese Version of Two Scales Which Measure Function and Disability in People with Achilles Tendinopathy

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SUMMARY

Background. Achilles tendinopathy can be disabling and is one of the most common chronic lesions among conditions affecting athletes’ feet and ankles. The clinical recommendation to measure self-reported limitations and functional capacity of patients with Achilles tendinopathy suggests the use of the Victorian Institute of Sport Assessment-Achilles (VISA-A) for pain and stiffness and the Foot and Ankle Ability Measure (FAAM) or the Lower Extremity Functional Scale (LEFS) to assess activity and participation. The Tendon Grading System and the Classification System for the Effect of Pain on Athletic Performance together measure the basic outcomes of VISA-A, FAAM, and LEFS, but is short, concise, and can be applied quickly in clinical practice. However, the scales were not adapted and validated for a Brazilian Portuguese version. The purpose of the present study is to validate and culturally adapt these scales to the Brazilian Portuguese language.

Methods. A cross-cultural adaptation and validation study were performed. The recommendations presented on standardized methods for the cross-cultural adaptation of self-administered questionnaires was followed. The recommendations define this process in six phases: translation, synthesis, back translation, expert committee review, pretesting, and a Delphi study to obtain the consensus of a group of experts on the quality of translation. The construct validity was tested in 17 non-athletes and asymptomatic participants, 50 amateur and professional athletes who are practitioners of modalities that place a great demand on the Achilles tendon, and 39 amateur and professional athletes diagnosed with Achilles tendinopathy.

Results. The Spearman correlation between the Tendon Grading System and VISA-A-Br was -0.79 (p = 0.001); between Tendon Grading System and LEFS, -0.72 (p = 0.001); and between Classification System for the Effect of Pain on Athletic Performance and LEFS - 0.68 (p = 0.001), demonstrating a strong correlation in both comparisons. The results between Classification System for the Effect of Pain on Athletic Performance and VISA-A-Br were - 0.81 (p = 0.001), indicating a very strong correlation.

Conclusions. The Tendon Grading System and Classification System for the Effect of Pain on Athletic Performance are similar to their original versions. The scales were valid for assessing pain and stiffness (Tendon Grading System) and activity and participation (Classification System for the Effect of Pain on Athletic Performance) in a Brazilian population with Achilles tendinopathy.

KEY WORDS
Achilles tendinopathy; activity; pain; participation; patient reported outcome.
BACKGROUND
Achilles tendinopathy can be disabling and is reported as one of the most common chronic lesions among the conditions affecting athletes’ feet and ankles (1). The annual incidence of Achilles tendinopathy in runners is 7 to 9% (2), and in soccer players a new case occurs every 4000 hours of training (3). It can also occur in sedentary individuals, affecting about 30% of this population (4). The overall incidence of Achilles tendinopathy is approximately 1.85 per 1000 people (5). The clinical recommendation to measure self-reported limitations and functional capacity of patients with Achilles tendinopathy suggests the use of the Victorian Institute of Sport Assessment-Achilles (VISA-A) for pain and stiffness (6). The Foot and Ankle Ability Measure (FAAM) or the Lower Extremity Functional Scale (LEFS) are suggested to implement to assess activity and participation in patients with Achilles tendinopathy (6, 7). In addition to assessing the effectiveness of the proposed intervention using standardized instruments, these measures are important for comparing individual and collective results (6). The VISA-A was recently adapted and the Brazilian version validated (VISA-A-Br) (8). The VISA-A-Br had good internal correlation, good test-retest validity (ICC2.1 = 0.84), and good construct validity when compared to the LEFS (Spearman’s coefficient with LEFS = 0.73) (8).

Besides that, the Tendon Grading System and Classification System for the Effect of Pain on Athletic Performance are potential instruments for use in clinical practice. The scales were cited in the English (7), Swedish (11) and German (12) versions of VISA-A, although their original version had not been validated in other languages. The Tendon Grading System (9) uses an ordinal variable that grades pain and function levels as excellent, good, reasonable, and poor. The Classification System for the Effect of Pain on Athletic Performance (10) evaluates the influence of tendon pain on limitations in sports performance and classifies this influence at six levels, ranging from no pain and unrestricted performance to pain during activities of daily living and the inability to play sports (12). The Tendon Grading System has the potential to measure pain and function in participants with Achilles tendinopathy and the Classification System for the Effect of Pain on Athletic Performance to measure the impact on the activity and performance of participants with Achilles tendinopathy. Together, the scales measure the basic outcomes of VISA-A, FAAM, and LEFS but is short, concise, and can be applied quickly in clinical practice. However, the Tendon Grading System and Classification System Scales for the Effect of Pain on Athletic Performance were not adapted and validated for a Brazilian Portuguese version. Thus, due to the use of the Tendon Grading System and Classification System for the Effect of Pain on Athletic Performance in international studies of versions of VISA-A and its potential to aggregate information on pain, function, and limitations in sports activity, the purpose of the present study is to validate and culturally adapt these scales to Brazilian Portuguese.

MATERIALS AND METHODS
The study procedures were carried out according to the ethical standards of the journal (13). We conducted the study at the Federal University of Ceará with the Research Group of Prevention, Evaluation, and Intervention in Tendon Alterations (Tendon Research Group-Brazil). The study protocol was approved by the research ethics committee following all due procedures.

Cross-cultural adaptation
The process of cross-cultural adaptation followed the recommendations of international guidelines (translation, synthesis, back translation, expert committee review, pretesting) (14). We added a Delphi study with to obtain the consensus of a group of experts on the quality of translation and finally, the scales were tested with 15 university students who pointed out possible difficulties in understanding items on the scales. If three or more college students, representing 15%, noted a particular difficulty on a scale it would be reviewed and applied again. And so, we get the final version of the translations (figures 1, 2).

Sample
The study included 105 active participants, both men and women. The participants were between 18 and 60 years of age and participation in various sports. The sample was classified according to the level of participation in sports in general, the level of participation in sports with a high risk of developing Achilles tendinopathy, and the presence of Achilles tendinopathy. According to these criteria, three groups were formed. The control group included participants who were physically active, non-athletes and asymptomatic for Achilles tendinopathy (n = 17). The risk group included amateur and professional athletes asymptomatic for Achilles tendinopathy and practitioners of modalities that place greater demands on the Achilles tendon (n = 50). The tendinopathy group was composed of amateur and professional athletes diagnosed with Achilles tendinopathy (n = 39). Participants were recruited in amateur and professional sports clubs, training centers, dance companies, orthopedic outpatient clinics, physiotherapy clinics. Individuals were recruited by direct contact and responded
to self-administered Tendon Grading System and Classification System for the Effect of Pain on Athletic Performance VISA-A-Br and LEFS. All participants were informed about the objectives, risks, and benefits of participating in the research and signed a free and informed consent form. Personal data such as name, age, gender, type of activity, and medical diagnosis (if any) were then collected.

We take into account the clinical history of pain reported with the Achilles tendinopathy associated with calcaneal tendon overload by sports practice was taken into account when characterizing the participants with Achilles tendinopathy. In addition, participants with Achilles tendinopathy had pain by palpation in the medial portion (2-6 cm proximal to the insertion) (15), and/or a nosological diagnosis by an orthopedic specialist in the area, which may or may not have been accompanied by complementary tests such as ultrasonography and magnetic resonance imaging. We considered as asymptomatic participants for Achilles tendinopathy if they did not present spontaneous complaints of pain and stiffness in the region of the calcaneal tendon and obtained a negative result in the palpation test of the calcaneal tendon. Subjects who presented bilateral tendinopathy of the calcaneus were excluded from the study. Also excluded, those with any musculoskeletal lesion on the lower limbs, low back pain with radiculopathy, or surgery on the lower limbs.

Collection of data and instruments used
After the participants signed the free and informed consent form (TCLE), we completed a brief questionnaire and we performed a physical evaluation to identify the participants with Achilles tendinopathy. Then, the Tendon Graduation System and Classification for the Effect of Pain on Athletic Performance scales and the VISA-A-Br (8) and LEFS (16) were distributed.

The Tendon Graduation System is an ordinal variable scale. The scale classifies the tendon as excellent if there is total function and no residual disability; good if there is total function, no disability and minimal pain; reasonable if there are some limitations during activities; and bad if there is severe weakness and marked lameness (9). The Classification for the effect of pain on athletic performance is a continuous variable scale that classifies the influence of pain on the limitation of athletic performance at six levels. The scale defines level 1 as no pain and unrestricted performance. Level 2 occurs if there is pain with extreme exertion and unrestricted performance. Level 3 occurs if there is pain with extreme exertion or after 1 or 2 hours of activity with normal or slightly reduced performance. Level 4 occurs if there is pain during and after vigorous activity and reduced performance. Level 5 occurs if there is pain during sports activity, forcing an interruption with a marked decrease in performance. Level 6 occurs if there is pain during daily life activity and the inability to participate in sports (10).

The VISA-A-Br is a self-administered scale that assesses the intensity of symptoms and their impact on the individual’s physical activity. The VISA-A-Br consists of eight questions. Questions 1 to 3 are about pain, 4 to 6 about function, and 7 and 8 about activity. Six questions are scored using a Likert scale, ranging from 0 to 10. Question 7 is scored on a Likert scale, but with four possible answers, 0, 4, 7, or 10. The eighth question is divided into three items, but only one is answered. The item is chosen according to the perception of pain during sports activities, and the score can range from 0 and 30. The total score of the scale varies between 0 and 100. A score of 0 represents the highest severity of the disease, and 100 represents no pain or dysfunction (8).

The LEFS scale is self-applied and assesses the function of the lower limbs related to activities and tasks. LEFS can be used in various musculoskeletal conditions, such as Achilles Tendinopathy. The scale consists of 20 items graded on a Likert scale (0 to 4 points). The total score ranges from 0 to 80 points. A score of 80 represents the best possible function (16).

Properties of measurements
We defined the measurement properties according to the COSMIN manual (17) and Terwee et al. (18). We have previously defined four hypotheses for construct validity: 1) Moderate to strong correlation between the Tendon Grading System and LEFS; 2) Moderate to strong correlation between Classification System for the Effect of Pain on Athletic Performance and LEFS; 3) Very strong correlation between Tendon Graduation System and VISA-A-Br; 4) Very strong correlation between Classification System for the Effect of Pain on Athletic Performance and VISA-A-Br. We categorize the correlation force according to the classification: very weak (0.0-0.19); weak (0.2-0.39); moderate (0.4-0.59); strong (0.6-0.79); and very strong (> 0.8) (19). Good construct validity was based on meeting the criteria in at least 75% (3/4) of the indicated hypotheses (17).

Statistical analysis
We used the software packages SPSS Version 20 (IBM Corporation, Armonk, NY) and to perform the statistical analyzes. The construct validity was tested by correlating the translated Tendon Graduation System and Classification System for the Effect of Pain on Athletic Performance
RESULTS

Cross-cultural adaptation and consensus
We did not experience any conflicts during the phases of cross-cultural adaptation. We obtained 10 responses from experts in the Delphi study and the agreement rate was between 80 and 100% on the translation of the Tendon Grading System and Classification System for the Effect of Pain on Athletic Performance scales. No volunteers reported difficulty in understanding the scales. The results of the cross-cultural adaptation of the scales is found in figures 1 and 2.

Characterization of the sample
A total of 105 volunteers were included in the study. The data is presented in table I. The groups were composed of individuals who participated in basketball (24.8%), running (14.3%), soccer (12.4%), and other modalities ranging from 1% (CrossFit) to 11.4% (volleyball).

Construction validity
The Spearman correlation between the Tendon Grading System and VISA-A-Br was -0.79 (p = 0.001), and between Tendon Grading System and LEFS - 0.72 (p = 0.001) (table II), demonstrating there is a strong correlation in both comparisons. The Spearman correlation between Classification System for the Effect of Pain on Athletic Performance and VISA-A-Br was - 0.81 (p = 0.001), indicating a very strong correlation. Between Classification System for

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Sistema de graduación do tendão

- Excelente: función total e nenhuma incapacidade residual
- Bom: función total, nenhuma incapacidade e com dor mínima
- Razoável: algumas limitações durante atividades
- Ruim: apresenta fraqueza severa e claudicação acentuada

Figure 1. Final version of Tendon Graduation System.

Sistema de classificação para o efeito da dor no desempenho atlético

- 1: nenhuma dor e desempenho irrestrito
- 2: dor no esforço extremo e desempenho irrestrito
- 3: dor no esforço extremo ou após 1 a 2 horas da atividade, com desempenho normal ou levemente reduzido
- 4: dor durante e após qualquer atividade vigorosa e redução no desempenho
- 5: dor durante atividade esportiva forçando uma interrupção com diminuição acentuada do desempenho
- 6: dor durante AVD e incapacidade de praticar esportes

Figure 2. Final version of Classification for the Effect of Pain in Athletic Performance.
Table I. General characteristics of the sample.

<table>
<thead>
<tr>
<th>Characteristics of the sample</th>
<th>Mean ± standard deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>26.43 ± 8.08</td>
</tr>
<tr>
<td>Gender (male %)</td>
<td>61.90</td>
</tr>
<tr>
<td>Weight (Kg)</td>
<td>74.19 ± 14.50</td>
</tr>
<tr>
<td>Height (m)</td>
<td>1.73 ± 0.09</td>
</tr>
<tr>
<td>Duration of injury (months)</td>
<td>35.46 ± 47.71</td>
</tr>
</tbody>
</table>

Table II. Psychometric properties of the Tendon Grading System and Classification System for the Effect of Pain on Athletic Performance.

<table>
<thead>
<tr>
<th>Measurement properties - Validity of construct (105 patients)</th>
<th>Spearman correlation coefficient (Rho)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TGS</td>
<td></td>
</tr>
<tr>
<td>ρ, using VISA-A-Br as a comparison</td>
<td>- 0.794*</td>
</tr>
<tr>
<td>ρ, using o LEFS as a comparison</td>
<td>- 0.724*</td>
</tr>
<tr>
<td>CSEPAP</td>
<td></td>
</tr>
<tr>
<td>ρ, using VISA-A-Br as a comparison</td>
<td>- 0.809*</td>
</tr>
<tr>
<td>ρ, using LEFS as a comparison</td>
<td>- 0.678*</td>
</tr>
</tbody>
</table>

TGS, Tendon Graduation System; VISA-A-Br, Victorian Institute of Sport Assessment - Achilles Questionnaire Brazilian Portuguese; CSEPAP, Classification for the Effect of Pain in Athletic Performance; LEFS, Lower Extremity Functional Scale. * ρ < 0.05.

The Effect of Pain on Athletic Performance and LEFS was - 0.68 (p = 0.001) (Table II), indicating a strong correlation. We confirmed 3 of the priori hypotheses, formulated resulting in 75% agreement.

DISCUSSION

The purpose of the study was to validate and culturally adapt the Tendon Grading System and Classification System for the Effect of Pain on Athletic Performance scales for the Brazilian Portuguese language. The results indicate that the Portuguese versions of the scales present idiomatic and semantic equivalence with the original English versions.

All steps proposed by the guidelines for transcultural adaptation of self-administered questionnaires were followed (14). The Delphi study provided the trusted opinion of a group of experts on the quality of translation. Although the sample from the risk group was higher than from the tendinopathy group, the number of participants was similar to other validation studies (12, 20). The pre-final versions of the scales were not tested in subjects with Achilles tendinopathy, but were applied to 25 healthy subjects to assess their comprehension of the scales. The scales were applied in a single moment. The Cronbach’s alpha coefficient assesses internal consistency of a set of items, scale or subscale, corresponding to a single clinical dimension (21). Thus, the internal consistency could not evaluate because the two translated scales are composed by a single question (12). Baseline information and results were not divided into groups, but other studies support this analysis (8, 16, 22, 23).

The sample size of this research was compatible with the samples used in similar studies on translation and validation of functional scales. In addition, COSMIN recommendations address samples with at least 100 individuals in study designs like ours as satisfactory (17). The absence of others validation studies of these scales makes not possible to compare with other researches.

The Brazilian version of the Tendon Grading System and Classification System for the Effect of Pain on Athletic Performance scales presented satisfactory construct validity, as 75% of our hypotheses were met according to the criterion indicated by Terwee (17). Our findings corroborate information from the article by Robinson et al. that found a significant correlation between Classification System for the Effect of Pain on Athletic Performance and VISA-A in the English language versions (7).

Our article found a strong correlation between Tendon Grading System and VISA-A-Br. One possible explanation is that VISA-A-Br is a questionnaire that presents eight questions divided into three domains, pain, functional status, and activity (7), therefore, it evaluates the Achilles tendinopathy in a more specific manner. The Tendon Grading System covers all domains in only one item, so it is a broader classification. Our results are similar to those found in the original version of VISA-A, where a moderate correlation was found between Tendon Grading System and VISA-A (7).

The information provided by the LEFS and Classification System for the Effect of Pain on Athletic Performance scales would be complementary in the evaluation of an individual with Achilles tendinopathy. We highlight that VISA-A-Br is considered the most important scale for determining the severity of calcaneal tendon injuries (12) and has strong construct validity with the two scales translated. The Tendon Grading System and Classification System for the Effect of Pain on Athletic Performance are easy to apply and understand, providing an Achilles tendinopathy severity index with the advantage of being faster than the VISA-A. Therefore, the scales can be used to screen for the severity of Achilles tendinopathy more quickly and may obtain a similar result to the VISA-A-Br.
CONCLUSIONS
We suggest that future studies be performed using the two scales as an outcome in the evaluation of individuals with Achilles tendinopathy. The Tendon Graduation System and Classification Scales for Effect of Athletic Performance Pain are similar to their original versions. The scales were valid for assessing pain and stiffness (Tendon Graduation System) and activity and participation (Classification Scales for Effect of Athletic Performance Pain) in the Brazilian population with Achilles tendinopathy.

CONFLICT OF INTERESTS
The authors declare that they have no conflict of interests.

REFERENCES
TGF-β1 Expression in Contractured Achilles Tendon among Diabetic Foot Patients: a Semi-Quantitative Study

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SUMMARY
Background. Increased plantar pressure when walking is among the pathogenesis of diabetic foot ulceration. Contractured Achilles tendon will biomechanically result in increased plantar pressure. In this study, we summarize the correlation between increased transforming growth factor β1 (TGF-β1) expression and the development of Achilles tendon contracture in diabetic foot patients.

Methods. Thirty diabetic foot patients with indication for surgery were enrolled to this study and divided to two groups. Case group consisted of patients presenting Achilles tendon contracture, in contrary with control group. During surgery, the specimens of Achilles tendon were taken and analysed semi-quantitatively by immunohistochemical (IHC) examination. Achilles contracture as a dependent variable was concluded from physical examination, and later by histological findings.

Results. IHC revealed that the positive TGF-β1 expressions were found in all case and control group cases, respectively. There were different results between both groups regarding the expression strength, specifically 2/15 vs 8/15 for +3 result, 10/15 vs 6/15 for +2 result, and 3/15 vs 1/15 for +1 result. Linear regression analysis showed significant result (p < 0.05) of age and TGF-β1 expressions as the determinants of Achilles tendon contracture, while the results for sex, body mass index (BMI), and HbA1c were insignificant.

Conclusions. Chronic hyperglycemia was thought to be one of the etiology of Achilles tendon contracture through the cascade involving the advanced glycation end products (AGEs) accumulation. However, these results suggested that the HbA1c level is not a sole determinant, and TGF-β1 should be considered as a contributing factor for Achilles tendon contracture during the development of diabetic foot ulcerations.

KEY WORDS
Achilles tendon; contracture; diabetes; immunohistochemistry; TGF-β1.

BACKGROUND
Diabetes mellitus (DM) is a chronic metabolic condition characterized by persistent hyperglycemia with resultant morbidity and mortality related to its microvascular and macrovascular complication (1). Such a profound demographic shift is likely to yield a corresponding increase in the prevalence of diabetes chronic complications, including those in the lower extremity, the diabetic foot (2). Diabetic foot is a complication of DM leading to most feared non-traumatic lower limb amputation. As many as 15% of diabetic patients will suffer from ulcer in their lifetime, and 12-24% will undergo amputation (3). Since most diabetic patients who have an amputation have foot ulcers, if foot ulcers can be eliminated, most amputations in diabetics could potentially be prevented (4).
Tendon imbalance, especially due to Achilles and gastrocnemius-soleus tightness, may cause an increased stress in the forefoot. Increased stress in the forefoot can cause a callus, followed by a forefoot ulcer (4). Prior comparison between diabetic and nondiabetic patients suggests that equinus may be more prevalent in diabetic patients. Coombes et al. had also concluded that Achilles tendon from individuals with type 2 diabetes were thicker compared to inactive individuals without diabetes (5). Nonetheless, these data are insufficient to prove causality and lack the required power to prove or disprove these relationship (4, 6).

Hyperglycemia in diabetic patients is responsible for the presence of high levels of nonenzymatically produced advanced glycation end-products (AGEs) in patients with diabetes. AGEs play an important role in cell signaling by interacting with specific receptors that link to the activation of adhesion molecules, proinflammatory cytokines and growth factors, thus contributing to the pathogenesis of diabetic complications (7). AGEs are able to stimulate directly the production of extracellular matrix (ECM) (8). However, despite the recognized importance of AGEs in the development of age and diabetes related conditions, there are still several important open questions regarding their role in the onset and progression of connective tissue disease (9). Why contracture is not commonly found in all diabetic patients is not yet fully understood. Other than hyperglycemia, factors that regulate ECM formation include multiple forms of growth factor such as transforming growth factor-beta (TGF-β). The important role of growth factors in the pathogenesis of diabetic long-term complications was suggested by their increased concentrations in target tissues. An excess of growth factor is implicated in tissue where fibrosis predominates, whereas a lack of growth factors occurs in diabetic neuropathy and wound healing (7). Among the TGF-β isoforms, TGF-β1 has been known to promote wound healing and also fibrosis (10, 11).

In our literature review, there is still insufficient study on pathogenesis of diabetic ulcer focusing on the development of equinus due to contracture of Achilles tendon. In this study, we evaluated immunohistochemical expression of TGF-β1 in Achilles tendon tissue by comparing between contractured and non-contracted tendon.

**MATERIALS AND METHODS**

This was a case-control study of 30 subjects admitted to Hasan Sadikin Hospital, Bandung, Indonesia from January to September 2020. Target population is diabetic foot ulcer patients with indication for surgery such as debridement or deformity correction including Achilles tendon lengthening. Achilles tendon lengthening procedures were performed by Z-lengthening in open manner to facilitate the tendon specimen collection. Study group consists of diabetic foot ulcer patients with Achilles tendon contracture, and control group consists of diabetic foot ulcer patients without Achilles tendon contracture. We reckoned the Achilles tendon contracture if the ankle dorsiflexion was less than 10° with the knee flexed as described in a definition of equinus (12). Subjects were taken in accordance to inclusion and exclusion criteria and selected by consecutive sampling. Demographic characteristics and other information were extracted from the electronic medical records. This study was conducted ethically according to international standards as described by Padulo et al. (2018) (13).

Inclusion criteria for study group included: 1) confirmed type 2 diabetes mellitus, 2) incur foot ulceration less than 4 weeks onset, 3) sustain indication for surgery, 4) present Achilles tendon contracture, and 5) age not less than 18 years old. Inclusion criteria for control group is the same for criteria number 1, 2, 3 and 5. The distinction between both groups is at number 4, which was without Achilles tendon contracture. Exclusion criteria for both groups consisted of 1) prior ankle deformity due to congenital disease or trauma, 2) prior Achilles contractures attributed to scarring, 3) any medical comorbidities causing drop foot e.g., spinal problem, 4) patient with contraindication for surgery, and 5) patient who refuse to participate in the study.

Demographic data and related clinical characteristics were collected, including body mass index (BMI) and HbA1c levels. Independent variable in this study was TGF-β1 in Achilles tendon, analysed semi-quantitatively using immunohistochemical studies by an experienced histopathologist. Dependent variable was the contracture of Achilles tendon, concluded from ankle range of motion measurement using a goniometer with 90° knee joint flexion and expression of fibronectin, a glycoprotein which is normally present in ECM and plasma with thrombotic, inflammatory, angiogenic, and fibrogenic functions. Fibronectin was observed for its crucial role in cell adhesion, growth, migration, and differentiation (14-16).

**Sample Collection and analysis**

During the surgery, a 5 mm × 5 mm × 5 mm specimen of the Achilles tendon was obtained from each patient at the mid-substance (figure 1). Immunohistochemical analyses of TGF-β1 and fibronectin were performed using the avidin-biotin complex method. The specimens were fixed in neutral buffered formaldehyde and processed into paraffin wax by standard histological methods prior to immunostaining. Three microns thick sections were cut and placed, then dried overnight. The sections were incubated...
with the primary antibodies against TGF-β1 and fibronectin for 1 hour in a humidity chamber. Biotin-labelled secondary antibodies were utilized for 7 minutes at 45 °C. The streptavidin-horseradish peroxidase detection system was then applied to the capillary channels. After drainage, the tissue sections were ready for the chromogen reaction with 3-amino-9ethyl carvazole. The sections were counterstained with hematoxylin subsequently. The specimens were reviewed by an expert histopathologist. The stained slides were scanned at low power view. Cytoplasmic staining of TGF-β1 was scored by the percentage of positive cells (0: < 10%, 1: 10-25%, 2: 26-50%, and 3: > 51%) (17). Assessment of fibronectin staining included initial low power view and subsequent high-power observation. The observations were graded according to the following pattern: negative staining (0), focal weak staining (1 +), intense patchy staining (2 +), and intense diffuse staining (3 +).

**Statistical analysis**

Demographic and clinical characteristics were summarized in frequencies and percentages for categorical variables and in appropriate measures of central tendency and dispersion for continuous variables. Linear regression analysis was used to examine the associations between selected variables and outcomes of interest (development of Achilles tendon contracture). A p-value was less than 0.05 was considered to be statistically significant. All statistical analyses were performed using IBM SPSS Statistics for Windows, version 25 (IBM Corp., Armonk, N.Y., USA).

**Ethics permission**

This study was conducted after the ethical clearance had been granted from the Research Ethics Committee of Universitas Padjadjaran (Institution Review Board No. 00008626), No.780/UN6.KEP/EC/2019. Ethical aspect was applied to all subjects, including respect for person, beneficence, non-maleficence, and justice. The copy of ethical approval would be available upon request.

**RESULTS**

**Clinical characteristics**

The 15 patients presenting Achilles tendon contracture in the case group included 8 men and 7 women aged from 51 to 72 years (mean age: 63.13 ± 6.91 years). The 15 patients in the control group had diabetic foot without Achilles tendon contracture, including 6 men and 9 women aged from 46 to 68 years (mean age: 57.2 ± 6.07 years). BMI mean in case and control group were 26.88 ± 4.02 kg/m² and 24.54 ± 4.87 kg/m², respectively. HbA1c level median were similar, specifically 7.8% (range 5-14) in case group and 7.8% (range 5.6-13) in control group.

**Immunohistochemical findings**

Each slide was reviewed by an expert histopathologist and scored in areas with the highest score based on the scoring system disregarding the dimensions of the stained areas (table I):

1. TGF-β isoforms: the TGF-β expression score, as illustrated in figure 2, was significantly higher in the case group than in the control group (p = 0.025). The median score was 2 (+ 2) in the control group versus 1 (+ 1) in the control group.

2. Fibronectin: with regard to fibronectin expression (figure 3), four types of expression patterns were interpreted. Most common appearance found in case group was intense diffuse staining (11/15), in contrary with 0/15 in the control group.

**Determinant analysis**

The results from logistic regression analysis on the factors associated with Achilles tendon contracture and increased fibronectin expression are presented in table II. Among the tested variables, age and TGF-β1 expression score were significantly associated with the contracture (p = 0.036 and p = 0.031, respectively), while sex, BMI, and HbA1c level were not.
DISCUSSION

The main characteristics of diabetes mellitus is hyperglycaemia. Persistent overnutrition creates a steady level of high blood glucose that is toxic to macrovascular and microvascular systems. Skin and soft-tissue infections are of particular concern in patients with diabetes mellitus, especially those with comorbid peripheral vascular disease (18, 19). One possible cause of wound healing defects in diabetes patients has been associated with altered biology of bone marrow-derived endothelial progenitor cells. Pathological analysis has revealed abnormal microvessels that can be cuffed with collagen, laminin, fibronectin, or fibrin (20). Altered immune function is one potential effect in diabetic patients. Changes in leucocyte function figure prominently.

Table 1. Clinical and histological findings.

<table>
<thead>
<tr>
<th>No</th>
<th>Age</th>
<th>Sex</th>
<th>BMI</th>
<th>HbA1c</th>
<th>TGF-β expression</th>
<th>Fibronectin expression</th>
<th>Ankle RoM</th>
<th>Contracture</th>
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<td>67</td>
<td>F</td>
<td>29.9</td>
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<td>+ 3</td>
<td>PF 25° - DF 0°</td>
<td>+</td>
</tr>
<tr>
<td>2</td>
<td>64</td>
<td>F</td>
<td>32.47</td>
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<td>+ 2</td>
<td>+ 1</td>
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<td>-</td>
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<td>+ 1</td>
<td>PF 30° - DF 10°</td>
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<tr>
<td>4</td>
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</tr>
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<td>+ 1</td>
<td>+ 2</td>
<td>PF 30° - DF 15°</td>
<td>-</td>
</tr>
</tbody>
</table>

BMI: Body mass index; HbA1c: Glycated haemoglobin level; TGF-β: Transforming growth factor-β; RoM: Range of motion; DF: dorsiflexion; PF: plantarflexion.
Table II. Linear regression analysis for contracture development.

<table>
<thead>
<tr>
<th>Variables</th>
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<th>Non-contracture</th>
<th>p value</th>
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<td>Age (years)</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 60</td>
<td>4</td>
<td>11</td>
<td>0.036</td>
</tr>
<tr>
<td>≥ 60</td>
<td>11</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
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</tr>
<tr>
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<td>8</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>7</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 25</td>
<td>3</td>
<td>7</td>
<td>0.216</td>
</tr>
<tr>
<td>≥ 25 and &lt; 30</td>
<td>7</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>≥ 30</td>
<td>5</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 6</td>
<td>1</td>
<td>3</td>
<td>0.356</td>
</tr>
<tr>
<td>≥ 6 and &lt; 8</td>
<td>7</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>≥ 8</td>
<td>7</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>TGF-β expression</td>
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<td>10</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>3</td>
<td>1</td>
<td></td>
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</table>

and are believed to result from hyperglycemia (19). Decrease of sensation and increased sensory phenomena are also an important major expressions of varieties of diabetic polyneuropathies that contribute to foot ulceration due to loss of protective sensibility to external pressure or trauma (21). Chronic non-healing ulcers are frequently observed at pressure points of the lower extremities (20). Soft tissue plantar to the forefoot is normally subjected to vertical ground reactive and shear forces (4, 22). In those cases in which propulsive phase pronation is great, minute haemorrhages develop in the skin at points of the greatest concentration of force. Limited joint mobility may predispose the diabetic foot to ulceration by producing high plantar pressure during gait. Equinus is the primary mechanical common denominator that leads to the majority of acquired non-traumatic foot and ankle problems by indirect leveraged means as well as direct forces along the posterior/plantar chain (23). Combination of high plantar pressures and sensory neuropathy has been well linked to plantar ulceration. The management of limited joint mobility resulting from tendon contracture included non-operative by regular stretching, and operative such as tendon lengthening. Bezerra et al. reported that the exercise protocol shown to be possible to prevent the progression of diabetic tendon stiffness and reduce blood glucose levels in some animal during the experiments (24).
The pathogenesis of limited joint mobility is complex and multifactorial, including angiopathy and the correlation with AGEs accumulation due to hyperglycemia (25). All the above are the predispositions of diabetic foot ulceration. Notwithstanding, not all the diabetic patients present plantar ulcerations. Certain comorbidities are considered play a role in pathogenesis of diabetic foot ulceration.

This study found no significant association between HbA1c level and Achilles tendon contracture. The finding was counterintuitive because higher HbA1c level would be expected to exhibit the highest risk of developing complications including tendon contracture. Predominantly, diabetes is still considered as etiological factor of Achilles equinus contracture. However, chronic hyperglycemia and subsequent AGEs accumulation seems not to be the sole source of fibrosis of the affected tendons.

ECM turn-over is characterized by a balance between matrix formation and matrix degradation. AGEs is not the sole cause of ECM turn-over. Factors that regulate ECM formation include multiple forms of growth factors such as TGF-β1. TGF-β is generally accepted to be the main pro-fibrotic factor in diabetic nephropathy (11). Diabetic environment up-regulated TGF-β1 expression and bioactivity in glomerular mesangial and proximal tubule cells (7, 26). Certain comorbidities has been known to affect TGF-β expression, for example cigarette smoking, in which sustained oxidative stress induces a chronic inflammation and cause further release of active TGF-β1 (27).

TGF-β is a family of growth factors involved in a number of essential cellular functions and contributes to the pathogenesis of tissue fibrosis in most organs (28). High glucose levels and mechanical stretch, particularly in a cyclic fashion, increases production of TGF-β by mesangial cells and vascular smooth muscle cells (29). Similarly, fluid shear stress, as would be induced by mechanical loading, increased production of TGF-β by cultured osteoblasts. Extracellular signalling molecules that act to increase TGF-β production include angiotensin II and thromboxane, as shown in diabetic nephropathy (11). Stimuli that activate latent TGF-β include plasmin, thrombospondin, and reactive oxygen species (28).

The three isoforms of TGF-β (TGF-β1, β2, and β3) are secreted as inactive latent precursors that require activation prior to binding to the TGF-β receptors (30). TGF-β1 and 3 play essential roles in cell proliferation and differentiation, immune response, angiogenesis, and tissue repair. While TGF-β1 promotes wound healing, it may promote fibrosis when checked. In contrast, TGF-β3 may have an anti-fibrotic role in wound healing.

Identification of TGF-β1 as a key factor in the cascade of Achilles tendon contracture development and thorough understanding of its regulation will contribute into not only prevention but also treatment the contracture. Neutralizing the actions of TGF-β with highly specific monoclonal antibodies or with application of antisense technology can effectively prevent the fibrosis (11). One approach is to reduce TGF-β gene expression, either by suppressing the initiation of gene transcription or by altering mRNA stability. TGF-β mRNA expression is reduced by anti-sense oligonucleotide, interferon α, and anti-oxidants such as α-tocopherol (28). Another approach directly targets circulating TGF-β. Thus, administration of anti-TGF-β antiserum at the time of induction of experimental mesangial proliferative glomerulonephritis suppresses the accumulation of ECM and histologic manifestation of disease (28, 31).

Along with TGF-β1 expression, age was found to be a significant determinant of contracture in this study. The common use of the terms “decrease flexibility” or “increased stiffness” in association with the decrease in maximal passive dorsiflexion ROM implies that shortened calf muscle-tendon unit may become stiffer with aging, even in active adults without related pathologies (32). Prior studies has also reported some contributing factors to increased TGF-β1 level, such as the duration of cigarette smoking (33).

This study has limitations. We identified our patients based on the surgery indication, thus, other than small sample size we cannot account for patients without wound who had not presented for evaluation. We were unable to adjust our analyses for multiple factors such as vascular status, neuropathic severity, and smoking habits due to relatively small group sizes. The more objective parameters should be done to assess the clinical examination of tendon contracture, for example, using ultrasound techniques as described by Kuo et al. (34). However, this study may provide the framework to define the diabetic foot management algorithm, particularly regarding the role of TGF-β1 in Achilles tendon contracture pathogenesis.

The results of this study revealed that TGF-β1 play a role in the pathogenesis of Achilles tendon contracture in diabetic foot other than chronic hyperglycemia. The involvement of TGF-β1 in contracture or tissue fibrosis suggest that TGF-β1-mediated pathways may be one of therapeutic targets for diabetic foot managements. This study research can contribute a more detailed understanding of the role of TGF-β1 in pathogenesis of equinus contracture of Achilles tendon in diabetes population, which leads to the development of plantar ulcerations. Further studies to identify the determinants of increasing TGF-β1 expression and tissue level, can be performed based on this study. Clinical benefits of this study include yielding information on significance of increasing TGF-β1 activity in Achilles tendon contrac-
tures, thus the clinician can identify and control the causative factors, as well as the therapeutic interventions.

**FUNDINGS**

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**REFERENCES**


**ACKNOWLEDGEMENTS**

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**CONFLICT OF INTERESTS**

The authors declare that they have no conflict of interests.
Anterior Tibial Tendon Transfer for Treatment of Recurrent Congenital Clubfoot Initially Treated According to Ponseti Method. Update and Systematic Review Of Literature

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Division of Orthopaedic Surgery, Department of Clinical Sciences and Translational Medicine, University Tor Vergata, Rome, Italy

INTRODUCTION

The Ponseti conservative method for treatment of idiopathic clubfoot deformity is actually adopted all over the world. This method allows to obtain excellent results, although, as stated by Ponseti, the clubfoot has a stubborn tendency to relapse regardless the mode of treatment and “its wrongly assumed that relapses occur because the deformity has not been completely corrected” (1). The reliability of this conservative method has been proved by several clinical and radiological studies (2-6). The incidence of recurrence after a complete initial correction of the deformity using Ponseti method ranges from 7% to 56% (7). In a recent survey of the POSNA member, the incidence of clubfoot relapses managed by Ponseti method, was < 10% by 22% of the respondents, between 10% to 20% by 52% and between 20% to 40% by 25% (8). Anterior tibial tendon transfer...
TATT for Treatment of Recurrent CCF

(TATT) is commonly used for treatment of recurrent clubfeet, since extensive surgery has a high rate of poor results (9-12). Garceau (13) first described the surgical technique of TATT to the lateral side of the foot to correct relapsing clubfoot deformities. The author proposed to perform the TATT to the fifth metatarsal bone or the cuboid by three different incisions, pulling out the tendon from the extensor retinaculum at the ankle. Twenty years later, Ponseti and Smoley (14) modified the original technique, proposing to transfer the tendon on the third cuneiform, by only two incision leaving the tendon under the retinaculum. Hoffer et al., in two subsequent studies (15, 16) further modified the technique transferring the lateral half of the anterior tibial tendon by splitting it, to the cuboid to correct equinovarus deformity in cerebral palsied patients. These three different surgical techniques are tested in a cadaveric foot model in which the authors concluded that all three techniques may be useful and deliver varying degrees of increased forefoot pronation (17). However, currently the most common TATT procedure provides to reinsert the tendon to the third cuneiform, through a hole drilled in the ossified bone using two Kite’s needles. The transferred tendon was prepared with a Bunnell-type suture and anchored to the plantar sole with a button (figure 1 A-E). A recent cadaver study suggests passing the sutures with a blunt needle to prevent damage to nerves and vessels of the plantar side of the foot (18). Ponseti and Smoley technique is performed making only two limited incisions on the dorsum of the foot instead of the three more invasive incisions proposed by the original Garceau technique, avoiding to pull out the tendon from the extensor retinaculum. Regarding the anchor of the transferred tendon to the bone, some authors suggested different technique using bone anchors instead bone tunnel or bioabsorbable screw (19, 20).

Several retrospective studies reported that TATT seems to be the best EBM surgical procedure for treatment of recurrent clubfeet originally managed by Ponseti method; however, to the best of our knowledge, the majority of reported articles had level of evidence of III or IV. Only three studies were categorized as level II. Equally satisfactory results are observed by other authors that using TATT in recurrent clubfeet in patients initially treated by extensive posteromedial release or in rigid residual deformities (11, 12, 21-26). The aim of our study was to analyze a series of papers published from 2000 to present to evaluate the effectiveness of the anterior tibial tendon transfer for treatment of recurrent congenital clubfoot initially treated according to Ponseti method.

METHODS

To guide the review the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRIS-MA) guidelines were used and adhered to (27, 28).

Studies comparing non-operative management to surgical management of recurrent clubfeet originally managed by Ponseti method were evaluated against the set inclusion criteria. To formulate the inclusion and exclusion criteria, the PICOT method was used (29) (table I).

Search strategy and sources of information

Authors of this review (VDL, AC, GG, MM, FDM, PF) performed a literature search about the topic by querying online databases. Studies were located by searching the databases Medline (Pubmed) and Cochrane Library. The search strategy covers PICO and was performed independently by each author on January 2021. Keywords and MeSH Terms were identified by a preliminary search and selected by discussion. The search was conducted using the following keywords assembled in various combination to obtain most pertinent articles: clubfoot, club foot, club-foot, clubfeet, club feet, congenital clubfoot, talipes equinovarus, pes equinovarus, equinovarus, recurrent, relapse, relapsed, relapsing, residual, tendon transfer, anterior tibial tendon transfer, tibialis anterior tendon transfer, anterior tibial tendon, tibialis anterior, tatt, attt, att, dynamic supination. The following search queries were used: 1) (“2000/01/01”[Date - Publication]: “3000”[Date
Table 1. Inclusion and exclusion criteria (PICOT).

<table>
<thead>
<tr>
<th></th>
<th>Inclusion criteria</th>
<th>Exclusion criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Population</strong></td>
<td>Patients affected by recurrent congenital clubfoot originally managed by Ponseti method.</td>
<td>Patients affected by non-idiopathic congenital clubfoot. Patients affected by residual deformities or neglected congenital clubfoot.</td>
</tr>
<tr>
<td><strong>Intervention</strong></td>
<td>TATT in patients originally managed by Ponseti method. TATT in patients originally treated by surgical methods.</td>
<td>Other surgical techniques.</td>
</tr>
<tr>
<td><strong>Comparison group</strong></td>
<td>Studies reporting patients originally treated by surgical methods.</td>
<td>Not applicable.</td>
</tr>
<tr>
<td><strong>Outcome</strong></td>
<td>Studies reporting clinical, radiographic and pedobarographic evaluation (Laaveg and Ponseti score; Dimeglio score; AOFAS score).</td>
<td>Not applicable.</td>
</tr>
<tr>
<td><strong>Language</strong></td>
<td>English.</td>
<td>Other languages.</td>
</tr>
</tbody>
</table>

The reviewers (VDL, AC, GG, MM, FDM, PF) retrieved the data and independently analyzed each selected study; instances of disagreement were resolved by the senior investigator (PF).

The articles were screened for the presence of the following inclusion criteria:
1. patients affected by recurrent congenital clubfoot originally managed by Ponseti method;
2. anterior tibial tendon transfer surgical technique;
3. studies providing an adequate level of evidence, including retrospective studies;
4. availability of full text.

The researches were excluded if providing information regarding:
1. studies on different technique than anterior tibial tendon transfer;
2. studies on patients affected by non-idiopathic congenital clubfoot;
3. studies on patients affected by residual deformities or neglected congenital clubfoot.

Figure 2 shows the PRISMA flowchart for study selection.

**RESULTS**

The initial search produced 123 studies from Medline database and 22 studies from Cochrane library database. One more article was included by the search after that the references were screened. Duplicated were filtered out and a total of 84 unique studies were obtained (68 from Medline...
After detailed evaluation based on inclusion and exclusion criteria, articles were screened and only 11 studies fulfilled the eligibility criteria of our study (30-40). The other studies were excluded for the following reasons: 70 articles did not meet the study design because the topic was not pertinent or have insufficient data or the deformities were initially treated by surgical procedures while 6 articles were published in a different language than in English. In conclusion, a total of 11 articles were enrolled in the present review (30-40). All the selected articles were published from 2006 to 2020 and they included overall 331 patients (481 clubfeet). Table II presents the list of reference of the studies, level of evidence, number of patients and clubfeet, age at surgery, surgical technique performed, combined TAL, age at follow-up, results analysis, possible second recurrence after TATT and conclusions.

DISCUSSION

Recurrent congenital clubfoot is caused by the same pathology that initiated the deformity. Stiff clubfeet with a severe atrophy of the leg muscles have a greater tendency to recur, in comparison to more flexible deformities (1, 41-45). The incidence of recurrence of congenital clubfoot is considerably decreased in the last 20 years for two main reasons, the greater widespread of the Ponseti method instead of surgical procedures and the better parent’s compliance with bracing after casting. However, recurrence is still observed independently of the method of treatment performed, and usually occurs between 2 and 5 years of age; it generally rare after 5 years of age and extremely rare after 7 years of age (1). Few long term follow-up studies have been reported on the effectiveness of the anterior tibial tendon transfer to the lateral side of the foot to correct relapsed or relapsing clubfeet, initially treated according to Ponseti method based on a serial of casting performed following Ponseti technique and possible Achilles tendon tenotomy. In all these studies, the surgical technique of Ponseti and Smoley had been used. Farsetti et al. (30) reported satisfactory results in a series of 12 patients (16 clubfeet) surgically treated by TATT at an average age of 3.9 years. The results were clinically evaluated, according to the Laaveg and Ponseti point system based on pain, function, satisfaction, ROM, forefoot alignment and ability to walk. All the patients were also evaluated by radiographs and CT scan examinations. The authors concluded that TATT corrects and stabilizes relapsing clubfeet by restoring their normal function of foot dorsi-flexion/eversion. Radiographic examinations and CT scan showed some anatomic anomalies in the treated clubfeet, in fact the cuneiforms and the cuboid were shifted more laterally than normal in spite of a persistent subluxation of the navicular bone. The authors pointed out the importance of the flexibility of the foot that represents the main condition for a successful final result, since this surgical procedure is based on the dynamic muscle balance of the forefoot. Similar results have been reported more recently in another long term follow-up study (35), in which the authors analyzed 14 patients (25 clubfeet) from the clinical and radiographic point of views and using pedobarographic analysis (peak pressures, total force distribution) and surface electromyography. The authors concluded that TATT is very effective at preventing additional relapse without affecting long-term foot function. The radiographic changes commonly observed in the operated feet did not correlate with the long-term functional outcomes. The third long-term follow-up study (32) reported the treatment results of late relapsing idiopathic clubfeet previously treated by the Ponseti method. The authors divided their 39 patients (60 feet) in five groups with an average age that ranged from 6 to 8.3 years; 56 clubfeet were surgically treated by TATT, in some cases associated to other surgical procedure as plantar fasciotomy, extensor hallucis longus recession or limited posterior release. They reported that only 5 cases needed a revision surgery and two of them a triple arthrodesis. The authors concluded that TATT is effective in late relapsed deformities, in some cases combined to other surgical procedures.
<table>
<thead>
<tr>
<th>References</th>
<th>Level of evidence</th>
<th>Follow-up</th>
<th>Number of patients</th>
<th>Number of clubfeet</th>
<th>Age at surgery</th>
<th>Surgical technique</th>
<th>Achilles tendon/</th>
<th>Age at follow-up</th>
<th>Results analysis</th>
<th>Second recurrence</th>
<th>Conclusions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Farsetti et al., JPO, 2006, Italy</td>
<td>retrospective study level IV (long term)</td>
<td>12</td>
<td>16</td>
<td>3.9 y</td>
<td>Ponseti and Smoley</td>
<td>3 feet</td>
<td>19 y</td>
<td>Lauveg and Ponseti score</td>
<td>Clinical evaluation</td>
<td>11 feet (9 feet treated conservatively and 2 feet surgically)</td>
<td>TATT corrects and stabilizes relapsed CCF. Importance of CCF flexibility</td>
</tr>
<tr>
<td>Masrouha and Morea, JPO, 2012, Iowa (USA)</td>
<td>case-control study level III (medium term)</td>
<td>66 (64)</td>
<td>102 (98)</td>
<td>3.1 y (2nd relapse)</td>
<td>Ponseti and Smoley</td>
<td>34 y</td>
<td>6.8 y</td>
<td>Clinical evaluation</td>
<td>-</td>
<td>Relapsed clubfeet treated by TATT at younger age seems to have an increased risk of a second relapse</td>
<td></td>
</tr>
<tr>
<td>McKay et al., JPO, 2012, Iowa (USA)</td>
<td>therapeutic study level IV (long term)</td>
<td>36</td>
<td>36</td>
<td>5 groups</td>
<td>Ponseti and Smoley</td>
<td>32 feet</td>
<td>23.3 y</td>
<td>Clinical evaluation</td>
<td>5 feet (revision surgery)</td>
<td>TATT is effective in late relapsed CCF. In some cases combined to other surgical procedures</td>
<td></td>
</tr>
<tr>
<td>Gray et al., CORR., 2014, Westmead, Sidney (Australia)</td>
<td>therapeutic study level III (short-term)</td>
<td>20</td>
<td>23</td>
<td>4.4 y</td>
<td>Ponseti and Smoley</td>
<td>5 feet</td>
<td>5.4 y</td>
<td>Foot alignment (Dimeglio score/foot posture index)</td>
<td>Strength Function</td>
<td>2 feet (treated conservatively)</td>
<td>TATT was an effective procedure, restoring the balance eversion-to-inversion strength</td>
</tr>
<tr>
<td>Jeans et al., JPO, 2014, Florida (USA)</td>
<td>therapeutic study level II (short-term)</td>
<td>30</td>
<td>37</td>
<td>4.3 y</td>
<td>TATT (whole): 28 feet; (split): 9 feet, 3rd c.; 18 f, cuboid: 4 f, 1st/2nd c. or base 3rd met.: 3 f</td>
<td>18 feet</td>
<td>6.5 y</td>
<td>Planar pressure testing pre and post operatively (EMED ST Platform)</td>
<td>-</td>
<td>Relapsed CCF following TATT are better aligned (distribution of pressure through the foot), but are not fully normalized</td>
<td></td>
</tr>
<tr>
<td>Holt et al., JBJS Am, 2015, Iowa (USA)</td>
<td>therapeutic study level III (long term)</td>
<td>14</td>
<td>25</td>
<td>5 y</td>
<td>Ponseti and Smoley</td>
<td>10 feet</td>
<td>48 y</td>
<td>AOFAS and Lauveg and Ponseti score</td>
<td>Radiog. and Pedob. analysis</td>
<td>no</td>
<td>TATT is very effective at preventing additional relapse without affecting long-term foot function</td>
</tr>
<tr>
<td>Luckett et al., JPO, 2015, Kentucky (USA)</td>
<td>prognostic study level II (medium term)</td>
<td>60</td>
<td>85</td>
<td>2 groups</td>
<td>Ponseti ans Smoley</td>
<td>-</td>
<td>8.1 y</td>
<td>Clinical evaluation</td>
<td>-</td>
<td>Patients with young age at TATT and with brace noncompliance are at an increased risk of 2nd recurrence</td>
<td></td>
</tr>
<tr>
<td>Wallace et al., JPOB, 2016, Kentucky (USA)</td>
<td>retrospective level IV (medium term)</td>
<td>28</td>
<td>39</td>
<td>3.2 y</td>
<td>Ponseti e Smoley</td>
<td>20 feet</td>
<td>6.2 y</td>
<td>Pedobuographic analysis</td>
<td>no</td>
<td>TATT resulted in improvements of pedobuographic parameters and in a more balanced foot post-operatively</td>
<td></td>
</tr>
<tr>
<td>Agarwal et al., J Clin Orthop and Traumatology, 2018, Delhi (India)</td>
<td>prospective randomized study level II</td>
<td>30</td>
<td>46</td>
<td>6.3 y</td>
<td>Garceau: 12 feet Ponseti and Smoley: 17 feet Hoffer: 17 feet</td>
<td>-</td>
<td>7 y</td>
<td>Clinical evaluation (physical ex.)</td>
<td>-</td>
<td>No significant differences for foot or ankle function could be detected in short term follow-up</td>
<td></td>
</tr>
<tr>
<td>Yasin et al., JPOB, 2019, Cairo (Egypt)</td>
<td>retrospective study level IV (short term)</td>
<td>18</td>
<td>26</td>
<td>3.6 y</td>
<td>Modified Ponseti and Smoley (2 incisions) transfusing wire</td>
<td>-</td>
<td>5 y</td>
<td>Clinical evaluation (tension tendon and active dorsiflexion)</td>
<td>-</td>
<td>The proposed technique appeared simple, feasible, economic and reliable, but could not detect significant differences for foot or ankle function</td>
<td></td>
</tr>
<tr>
<td>Mindler et al., JPO, 2020, Vienna (Austria)</td>
<td>therapeutic level II (short term)</td>
<td>17</td>
<td>25</td>
<td>6.8 y</td>
<td>Modified Garceau (3 incisions) Bioteno des screw and plantar button</td>
<td>7 feet</td>
<td>7.5 y</td>
<td>Gait analysis (Oxford foot model)</td>
<td>-</td>
<td>Gait analysis showed normalization of the main components of CCF recurrence after TATT</td>
<td></td>
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</table>
Despite 55% having residual deformity, at final follow-up, 80% of patients were without functional limitation. Three further studies reported the medium-term follow-up results in as many series of patients affected by relapsed clubfeet treated by TATT, according to Ponseti and Smoley technique (31, 36, 37). In two of them, the authors identified the deformities who presented further relapses after TATT procedure (31, 37). In both these articles, in which a considerable number of clubfeet were analyzed (98 + 85 feet), the authors agreed that clubfeet treated by TATT at younger age, showed an increased risk of a second relapse. However, the majority of the second relapses observed were treated conservatively. In the third study of this second group (medium-term follow-up study), the authors reported a series of 39 recurrent clubfeet treated by TATT and evaluated through a pedobarographic analysis and concluded that TATT resulted in improvements of pedobarographic parameters and in a more balanced foot postoperatively. The remaining articles are short term follow-up studies (33, 34, 38-40), that analyzed overall 115 patients (158 relapsed clubfeet) treated by TATT; contrary to previous studies, in these articles, the surgical techniques used were different (Ponseti and Smoley, Garceau and Hoffer) and some surgical technique variations have been proposed. Also these studies emphasized that TATT procedure is effective, restoring the balance eversion/inversion strength of the foot with an improvement of the distribution of the plantar pressure of the foot (34) and, at the gait analysis, a normalization of the main components of dynamic clubfoot recurrence was observed (39). Among them, Argawal et al. (40) conducted a prospective randomized study on three groups of patients with relapsed clubfoot (30 patients; 46 clubfeet), treated by TATT performed by Ponseti and Smoley technique in 17 feet, by Garceau technique in 12 feet and by Hoffer technique in another 17 feet. The average patient’s age at surgery was 6.48 years and the average follow-up 5.49 months. The authors concluded that no significant differences for foot or ankle function could be detected using the three different surgical technique in short-term follow-up. Other two studies proposed a variation technique of the Ponseti and Smoley and Garceau technique respectively, reporting satisfactory results; Yasin et al. (38) performed two incisions as in the Ponseti and Smoley technique, but modified the anchor of the transferred tibialis anterior tendon using a transfixing wire, while Mindler et al. (39), performed a three incisions as in the Garceau technique, but they fixed the tendon using both a Bio-Tenodesis screw and a plantar button. Regarding the comparison group of studies including patients originally treated by surgical methods (11, 12, 21-26) instead of Ponseti method, the authors reported equally satisfactory results. However, they suggested to perform a recasting, according to Ponseti method, before TATT with the aim to soften the foot recurrent deformity that after surgery often appear to be stiff. Regarding the biases and limitations, this systematic review focused on 1 prospective randomized study, 1 prognostic study, 5 therapeutic study, 3 retrospective studies and 1 case-control study. Therefore, only few high quality evidence studies were included in this review. Literature search was performed with the aim to include all possible keywords to retrieve all published studies regarding our topic, however it is possible that some studies eligible for review were not identified due to publication bias. A language bias was also introduced as studies written in languages other than English were excluded.

In conclusion, from an accurate review of the literature, we believe that TATT is an effective surgical procedure to treat relapsed clubfeet. The majority of the authors prefer the Ponseti and Smoley technique, that has been used in all the studies with a long or medium follow-up, although the only paper that prospectively analyzes possible differences between the various techniques did not show any difference between them. A second recurrence is absolutely uncommon, however it is more frequent when TATT is performed in younger patients. TATT seems to be effective also in late relapse, although in some cases an associated surgical procedure is necessary. The pedobarographic analysis performed in some studies, showed an improvement of the plantar pressure after surgery as well as the only study on gait analysis performed with the Oxford foot model, showed a normalization of the main components of CCF recurrence after TATT.

CONFLICT OF INTERESTS
The authors declare that they have no conflict of interests.

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An adaptive Model of Achilles Tendon Mechanical Properties during Adolescence: Effect of Sex

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LEVEL OF EVIDENCE: 1B

SUMMARY
Background. This longitudinal study aimed to quantify the relative effects of body mass, peak muscle force, maturation and sex on Achilles tendon (AT) mechanical properties and to examine the external factors that trigger mechanical changes, or intrinsic tendon adaptations during adolescence.

Methods. We measured AT mechanical properties and dimensions during pre-pubertal and adolescent growth in 41 participants (20 boys and 21 girls). Participants were tested over 18 months; longitudinal changes were examined through linear mixed modelling.

Results. Sex and maturation were found to be the major factors influencing AT mechanical changes. Their effects were largely exerted through increases in muscle force, which imposed greater stress on AT and strongly predicted changes in stiffness and Young’s modulus in boys and girls, while strain was consistent.

Conclusions. The more rapid increase in stiffness before the age of peak height velocity in boys was associated with an increase in force at that time, which may have evoked the molecular signaling required for adaptations to internal tendon structure leading a different adaptive response between sexes. The present data are suggestive of an adaptive model in which increases in muscle force production impose greater mechanical loading, on the tendon to trigger increases in stiffness as children mature through adolescence.

KEY WORDS
Tendon stiffness; stress; strain; adaptation; sex; adolescence.

BACKGROUND
The human Achilles tendon (AT) is a spring-like, load-bearing structure that transmits muscular forces directly to the calcaneum of the foot, playing an essential role during daily tasks such as walking, running and jumping. AT would theoretically need to adapt rapidly to changes in body mass and strength, such as during periods of body growth and maturation. In the present study we investigated the longitudinal changes in the properties of the Achilles tendon in adolescent girls and boys during a time period around growth-spurt. Cross-sectional data from human studies suggests that the timing and rate of maturation during growth from childhood varies greatly between individuals (1), with a rapid period of growth associated with the peak height velocity (PHV) being clearly observed in the pubertal phase. However, the limited existing data obtained by cross-sectional analyses suggests that significant increases in both tendon stiffness and Young’s modulus occur with maturation to adulthood (2, 3), with a rapid increase in stiffness at or around PHV resulting partly from increases in cross-sectional area (2, 3), potentially alongside a slowing in the rate of increase in tendon length (4). Collectively, these data provide an uncomplicated picture of the growth characteristics of important, energy-storing tendons such as the human AT. However, it is not yet known whether cross-sectional analyses accurately describe the longitudinal adaptive process.

The mechanical properties of the Achilles tendon also have been shown to differ based on both sex (5) and growth...
Despite asynchronous growth rates, stress, strain, and stiffness of AT, especially in the PHV period, growth itself may not be a major factor influencing muscle-tendon unit (MTU) strain, and thus mechanical change. Indeed, the cross-sectional data of Mogi, Torii (2) indicated that the calf-Achilles MTU length increases concurrently with the longitudinal growth of bones even in the period of rapid adolescent growth. In the only longitudinal study thus far completed, Neugebauer and Hawkins (6) did not detect changes in peak AT strain, stiffness or modulus over a 6-month period, and no statistical relationships with sex, growth rate or physical activity levels were observed in a sample of 10-12 years old girls and 12-14 years old boys. However, it is not known whether changes, if present, can be reliably detected over a 6-month period using current testing methods. Furthermore, we do not perfectly know whether boys and girls adapt similarly, whether their changes occur at the same rate relative to PHV, or whether changes are similar in low or high force levels. By tracking changes over a longer time period, age- and maturation-related changes could be clarified.

Body mass increases significantly around PHV (1), which results in rapid increases in muscle force and consequently a greater mechanical load on tendons (7). These changes have been associated with increased stiffness ($k$) and Young's modulus ($E$) (3, 6), but it is not clear yet whether body mass, strength or both are explanatory factors of tendon adaptation. Furthermore, increases in Young's modulus, are related to either repeated stress (8) or high strain magnitudes (9). Whereas the strain at tendon failure is more or less constant during maturation the stress to tendon failure is dependent on the tendon's material properties. Peak AT stress increased over a 6-month period due to a decrease in AT CSA in the study of Neugebauer and Hawkins (6) whereas greater (by percentage) increases in tendon stiffness and cross-sectional area than both muscle size and strength were observed over 2 years in the patellar tendon of adolescent volleyball players, suggesting that growth was associated with a reduced peak tendon stress (10). However, it is not certain whether the peri-adolescent period is associated with significant increases in stress or strain that might predispose to adaptation and injury (11). Therefore, the examinations of AT properties over a similar period might allow for the rates of changes in mechanical variables to be more clearly established and for associations with variables such as sex, maturation, body mass and peak muscular strength to be explored. The current literature remains limited primarily to cross-sectional studies, thus a more complete picture of tendon adaptation could then be feasibly drawn from the simultaneous tracking of children at different ages and levels of maturation at the start of the 1.5-year period.

Complicating matters is that tendon exhibits highly non-linear axial force-displacement behavior at low force (low strain) levels and linear behavior at higher forces (higher strain). Little is known about the relative changes in the low-force region of the force-length (stress-strain) relation in AT or other energy-storing tendons, which is problematic given that in vivo loading of the human AT typically lies within the low-strain region in most activities of daily living. Therefore, it is of great interest to specifically examine age-related changes in tendon properties, in both sexes, in the low-to-moderate force level region.

Given the above, the purpose of the present longitudinal study was to quantify the relationships between body mass, peak muscle force (strength), maturation and sex with AT mechanical properties including stiffness, Young's modulus, stress and strain. It was hypothesized that changes in both body mass and strength would be strongly associated with longitudinal changes in AT mechanical properties in both low- and high-force regions, but that these would be underpinned by the maturation process in a sex-dependent manner which may varies at different force levels during the adolescent growth spurt.

**MATERIALS AND METHODS**

Fifty-seven prepubertal children volunteered for the study, while forty-one participants (20 boys: $12.6 \pm 0.4$ years, $48.7 \pm 7.2$ kg, and $157.6 \pm 5.1$ cm; 21 girls: $10.6 \pm 0.5$ years, $36.6 \pm 6.8$ kg, and $146.4 \pm 8.1$ cm) were found to be close to the age of PHV, 16 participants were excluded since no PHV was observed. The predicted age of PHV was based on the equation of Mirwald, Baxter-Jones (12). The observed age of PHV that was closer to the best predicted age of PHV was accepted as the age of peak height velocity (APHV) in each participant. In order to determine the degree of reliability of the above assumption, the intraclass correlation coefficient (ICC) between the two ages (best predicted and APHV) was calculated. The ICC rate for boys was 0.97 ($p < 0.001$) and for girls 0.77 ($p < 0.001$). The acceptable limit of the coefficient is $> 0.75$ (13), thus the best predicted age of PHV did not differ significantly from the approximate APHV defined in the present study.

Complete anthropometric characteristics for each sex at each testing time point are shown in table I. The age range represent one standard deviation around the average age at which peak height velocity (PHV) occurs for boys and girls, respectively. Finally, the maturation progress was classified into 4 stages: 12, 6 mo before, and then 0, and 6 months after, the age of PHV (corresponding to $1^{st}$, $2^{nd}$, $3^{rd}$ and $4^{th}$ time point of measurement, respectively). The difference of 6 mo in the predicted PHV was accepted.
within the acceptable range (< 1 year) as recommended by Mirwald, Baxter-Jones (12). All participants were recruited from public schools and were healthy, without any disability or leg injury. All students and parents provided informed consent. Research protocol and measurement techniques were approved by Local Ethics Research Committee (ERC-003/2020). The study was conducted in accordance with the ethical guidelines and recommendations for the clinical and field science research (14).

Experimental design – measurements

Participants were tested in a random order over 18 months by performing the same measurements under similar conditions at 6-month intervals. Anthropometric data including standing height, sitting height, leg length, body mass and age were recorded at each testing session (every six months, 4 time points) and used to ensure the validity of procedure and calculate the maturity offset. Subsequently, the participants laid prone on the dynamometer bench (Cybex Humac Norm, CSMI, MA, USA) for strength measurements (figure 1). The instrument and measurement accuracy were ± 0.5% full-scale maximum. The foot was positioned perpendicular to the tibia (ankle in the neutral position, knee fully extended) and placed in the dynamometer’s foot plate with right ankle in the neutral position (0°: foot was perpendicular to the longitudinal axis of the tibia). The foot was tightly secured with straps to the footplate and the hips were tightly strapped to the seat. The rotation axis of the ankle joint was carefully aligned to be parallel to the axis of the lever arm of the dynamometer and passing through the midpoint of the line connecting both malleoli, as described by De Monte, Arampatzis (15). B-mode ultrasonography (US) (SSD-3500, Aloka, Tokyo, Japan) using a 60-mm electronic linear-array probe (7.5 MHz wave frequency) was used to measure the displacement of the distal myotendinous junction (MTJ) of the medial gastrocnemius (MG) during ramped, maximal isometric plantar flexions. The probe was placed longitudinally at the position specified by a marker attached on the skin surface. An echo-absorptive marker was attached to monitor possible motion of the probe on the skin during the measurement. Analog signals from the dynamometer were amplified and synchronized with data from the ultrasound system using a DA 100 B amplifier (Biopac Systems, Inc., Goleta, CA, common mode rejection ratio > 90 db, bandwidth = 0.05-500 Hz). Torque data were recorded by the dynamometer at a sampling frequency of 100 Hz.

Familiarization

Prior to testing, each participant performed warm-up exercise consisting of 3-5 sub-maximal isometric plantar flexions.

Table I. Anthropometric characteristics of participants per stage of maturity (months from predicted age of PHV): age (years), body mass (kg), height (cm). A significant change in height (* 0.001 < p < 0.01) was observed in the interval between 1 year before and the predicted age of PHV.

<table>
<thead>
<tr>
<th>Maturity stage</th>
<th>- 12</th>
<th>- 6</th>
<th>0</th>
<th>+ 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Boys (N = 21)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>12.6 ± 0.4</td>
<td>13.4 ± 0.4</td>
<td>13.9 ± 0.4</td>
<td>15.2 ± 0.7</td>
</tr>
<tr>
<td>Body mass</td>
<td>48.7 ± 7.2</td>
<td>53.2 ± 7.3</td>
<td>59.1 ± 7.2</td>
<td>61.3 ± 8.3</td>
</tr>
<tr>
<td>Height</td>
<td>157.6 ± 5.1</td>
<td>162.1 ± 7.2</td>
<td>169 ± 7.5*</td>
<td>173.2 ± 10.7</td>
</tr>
<tr>
<td>Girls (N = 20)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>10.6 ± 0.5</td>
<td>11.5 ± 0.5</td>
<td>12 ± 0.5</td>
<td>13.05 ± 0.5</td>
</tr>
<tr>
<td>Body mass</td>
<td>36.6 ± 6.8</td>
<td>41.6 ± 7.9</td>
<td>46.8 ± 8</td>
<td>50.0 ± 8.5</td>
</tr>
<tr>
<td>Height</td>
<td>146.4 ± 8.1</td>
<td>151.4 ± 7.9</td>
<td>158.1 ± 6.9*</td>
<td>162.2 ± 4.0</td>
</tr>
</tbody>
</table>

Figure 1. Experimental setup, showing the ultrasound probe fixed to the muscle-tendon junction during ankle joint moment data collection. Upper left corner: torque-time trace (raw data) showing linear torque (Nm) increase over time (s).
ion contractions to pre-condition the tendon. Thereafter, three ramped isometric plantar flexions (IPF) with maximal effort were done to familiarize the participants with the IPF required for testing. A 5-min passive rest was given between the familiarization phase and the testing protocol to minimize fatigue.

**Torque measurement during plantar flexion**

Upon the instructor’s request, participants performed two 10-s isometric ramp plantar flexion contractions increasing from 0% to 100% of the maximum torque at 20% of maximum torque every 2 s and holding maximally for 5 s (30-s inter-trial rest). In addition to continuous verbal encouragement, the participant was provided visual feedback of the torque signal on screen to allow execution of the effort as accurately as possible. Torque values were obtained from the best effort in which the ramp was properly achieved and torque-time relations were linear in the ramp period without energy loss (resulting from notable decreases in torque) in the test.

**Measurement of tendon elongation**

Ultrasound images were digitally recorded at a sampling frequency of 25 Hz. Max TRAQ software (Max Traq Lite version 2.09, Innovision Systems, Inc. Columbiaville, Michigan, U.S.A) was used to digitize the spatial location of the MTJ in order to generate MTJ position-time data from the ultrasound video. 25 position points (1 position point every 0.4 s) were recorded for each 10-s ramp contraction. AcqKnowledge Acquisition & Analysis Software (BIOPAC Systems, Inc., USA) was used to synchronize the torque signal and ultrasound imaging data. MG MTJ displacement was assumed to represent the change in the length of the AT. An example of Torque-elongation relationship obtained during ramped plantar flexion contractions for an adolescent girl (12 years old) during age of peak height velocity is shown in figure 2.

As reported elsewhere (16), both a shift of the foot from the initial position and a change in ankle joint angle were observed during the measurements. The detection of possible heel movement during contraction was provided by capturing high-speed digital video (JVC 9800, frame rate = 120 Hz) with a high-speed shutter to record plantar flexion motion. Five reflectors (2.5-mm radius) were placed on the 5th metatarsal, lateral malleolus, and lower extremity of the heel and two markers were placed on the foot plate. The video camera was placed opposite the ankle in the frontal plane at the middle of the dynamometer’s foot plate. Despite foot stabilization with the elastic straps and bandages, displacement of the ankle joint was recorded during contraction, resulting in loss of alignment with the dynamometer rotation axis. To accurately calculate the angle of rotation in two dimensions, the positions of the reflectors were recorded during the ramp isometric plantar flexion contraction and coordinate data from high-speed camera were down-sampled to match the ultrasound sampling frequency. The additional MTJ positional change (ΔL; mm) due to ankle rotation was calculated from the angle Δφ (rad) recorded by the camera and the torque moment arm’s length (d; mm) according to the equation: ΔL = Δφ × d. The additional MTJ displacement was subtracted from recorded elongation (ΔL) to compensate for the influence of ankle joint rotation.

**Moment arm measurement**

The perpendicular distance from the center of rotation to the line of AT action was defined as AT moment arm (MA), which was calculated with the excursion method. Following the execution of the measurement protocol, without changing the participant’s position or the position of the ultrasound probe, passive AT behavior assessment was performed with the dynamometer rotating passively between 20° dorsiflexion and 20° plantarflexion at a speed of 5°/s. The instruction was given to the participants to relax their leg muscles during the dynamometer’s foot plate movement to minimize muscle activity. Six trials were executed, and data were collected from the rotation in which the MTJ location was best visualized. MTJ position data were collected initially as video

![Figure 2. Example of Torque-elongation relationship obtained during ramped plantarflexion contractions for an adolescent girl (12 years old) during age of peak height velocity.](image-url)
recordings and Acknowledge software was used to synchronize the MTJ movement and angular position. A 3rd-order polynomial was fitted to describe the relationship between angular position and elongation of AT, and the first derivative of the polynomial for angle 0° was calculated to find the slope of the curve which represents the moment arm. Previous studies have not detected any difference between AT moment arm estimations between rest and MVC using the tendon excursion method over any given foot rotation step (17). This was attributed to the fact that although both elongation (ΔL) and angular displacement (dq) were altered during MVC compared with rest at any angle, their ratio, which determines the magnitude of moment arm value, remained constant between contraction conditions.

Calculation of the AT force
The tendon’s force was estimated by the equation: F = M / d, where:
- M is the plantar flexion moment;
- d the AT MA length.

In this study, the isometric plantar flexion force was calculated at angle 0°. The force resulting from this calculation represents the total force of all the ankle muscles transferred through the AT. In order to estimate the antagonistic moment of tibialis anterior (TA), moment and EMG signals from tibialis anterior were measured during ramped isometric dorsiflexions. The TA, as the major dorsiflexor muscle, was assumed to represent antagonist co-activation during plantarflexion. The EMG signals were recorded using pre-gelled Ag-AgCl surface circular electrodes with 10 mm diameter placed 20 mm apart located at 1/3 between the tip of fibula and the tip of medial malleolus and placed parallel to the TA fibers, in conformity with European recommendations for the surface EMG assessment of muscles. Reference electrodes were placed around the ankle. EMG signals captured by each of the electrode pairs over tibialis anterior were smoothed using a digital low-pass filter. The maximal plantar flexor moment was corrected by the antagonistic moment values. The plantar flexor moment was calculated by finding the sum of the resultant joint moment and antagonistic moment.

Tendon stiffness calculation
The stiffness k (N/mm) was defined as the slope of the linear portion of force (F) - elongation (ΔL) relation. The area of the linear trend (F-ΔL) was accepted as the area between 60% and 90% of the peak force (3, 17). In order to plot the F-ΔL relation, data from the force-time calculation and data from the MTJ position-time relation were combined in each ramp isometric plantar flexion for all measurements. Subsequently, muscle force (N) and the MTJ length change (mm) data were synchronized and the slope of the F-ΔL relation was calculated: k = dF / dL (N/mm). Force-elongation values ranged from 10% to 40% and 60% to 90% (linear region) of the maximum force. A 1st-order polynomial was applied where the slope of the low-force and linear regions of the F-ΔL relation was equal to AT stiffness. Stiffness in the 10% to 40% region was measured from the length in relaxed muscle at a 0° joint angle (that is, at the length during standing but with no muscle activity) and that during contraction. The ankle angle was thus tested under identical conditions at each time point and between individuals.

Measurement of AT test length and cross-sectional area (CSA_{AT})
Slack length is usually assumed to be the length measured either with the joint in its mid-position or when the net joint torque is zero and the resting length can only be defined when the muscle is completely slack. There is currently no method to characterize tendon resting length in vivo, i.e., it cannot be ascertained whether force was zero, hence in our study the ‘test’ length was measured. Therefore, a standardized joint configuration was set to control tendon length before muscle contraction. With the leg muscles relaxed, the MTJ was located with the ultrasound probe placed on the skin above and parallel to GM. Measurements were performed by sagittal imaging where the tendon boundaries were defined from AT insertion on the calcaneal tuberosity to the GM MTJ. The positions of the MTJ and the insertion of the tendon onto the calcaneal tuberosity were carefully marked on the skin and then the distance measured as a straight line. The vertical distance to the contact surface of the probe from the MTJ was measured by ultrasound. The test length of AT was defined as the hypotenuse of the Pythagorean triangle. Two main imaging techniques have been used to estimate in vivo CSA_{AT}: magnetic resonance imaging and B-mode ultrasound. To measure CSA_{AT}, a transverse section was visualized using B-mode ultrasound. A special gel patch (gel pad Aquaflex, 2 × 9 cm Parker Laboratories, Inc., Fairfield, NJ USA) was used to enhance acoustic conductivity and obtain clearer images where CSA_{AT} is smaller and receives the greatest pressure. The minimum CSA_{AT} was the one accepted for the measurement. The area evaluated as minimum CSA_{AT} was the mean value of three recorded measurements by subtracting and replacing the gel patch each time. This ultrasonography technique is widely used to measure AT cross-sectional area (18). However, Bohm, Mersmann (19) showed that
US measurements were smaller (19%) than those obtained using MRI method. We therefore ran the analysis with and without the 19% correction and found the same outcome, so any potential underestimation would not have influenced the results as long as that error was consistent. The reliability of CSA_{AT} measurements was investigated in a pilot study of 6 participants aged 10.5-15.5 years who performed the same test on two different days by two experienced observers. There were no significant differences between the test and retest CSA_{AT} values. The CV was 2.6 ± 1.2% and the RMSE was 2.1 mm²; a CV of < 5% is deemed acceptable.

Calculation of AT Peak Stress, Strain and Young’s Modulus
Stress (σ), determined as the force per unit area, was calculated using the minimum recorded CSA (i.e., CSA_{AT}) from each participant according to the equation: σ = F / A, where:
- F was the AT force (N);
- A was the minimum CSA_{AT} (mm²).

Tendon strain (ε) was defined as tendon’s elongation normalized to its test length according to the following equation: ε = (ΔL / L₀) × 100% where L₀ and ΔL represent the test length and elongation of the Achilles tendon, respectively. The ‘peak strain’ was not defined as the strain before failure of the tendon but the peak strain that could be induced by voluntary contraction (e.g., how much an individual might be able to induce strain by themselves). The Young’s Modulus was calculated as the slope of stress (σ) - strain (ε) curve according to the equation: E = dσ / dε.

Over the 1.5-year project period, standing height, sitting height, leg length, body mass, AT test length and minimum CSA_{AT} were re-measured every 6 months. Achilles tendon moment arm, force, stiffness, Young’s Modulus, strain and stress were calculated every 6 months. The maturation stage of 0 was defined as the age of PHV for all participants (N = 41). Table II shows combined data and percentage changes between successive maturation stages for tendon cross-sectional area, force, and tendon mechanical properties per stage of maturity.

<table>
<thead>
<tr>
<th>Maturity stage</th>
<th>-12</th>
<th>-6</th>
<th>0</th>
<th>+6</th>
</tr>
</thead>
<tbody>
<tr>
<td>CSA_{AT}</td>
<td>44.5 ± 3</td>
<td>47 ± 3 (5.6%)</td>
<td>49 ± 3 (4.3%)</td>
<td>51.5 ± 3 (5.1%)</td>
</tr>
<tr>
<td>F_{peak}</td>
<td>1966.2 ± 505.4</td>
<td>2108.5 ± 501.8 (7.2%)</td>
<td>2586.7 ± 696.5^{±}(22.7%)</td>
<td>2980 ± 746.0 (15.2%)</td>
</tr>
<tr>
<td>k_{low}</td>
<td>101.5 ± 30.25</td>
<td>121.7 ± 51.8 (20.0%)</td>
<td>142.5 ± 62.2 (17.1%)</td>
<td>156.4 ± 59 (9.8%)</td>
</tr>
<tr>
<td>E_{low}</td>
<td>338.3 ± 105.85</td>
<td>409.5 ± 178.2 (21.0%)</td>
<td>494.1 ± 212.0 (20.7%)</td>
<td>530.5 ± 205.7 (7.3%)</td>
</tr>
<tr>
<td>ε_{low}</td>
<td>3.8 ± 0.6</td>
<td>3.9 ± 0.6 (2.6%)</td>
<td>3.9 ± 0.6 (0.0%)</td>
<td>3.9 ± 0.6 (0.0%)</td>
</tr>
<tr>
<td>σ_{low}</td>
<td>18.64 ± 6.8</td>
<td>23.3 ± 10.2 (25.0%)</td>
<td>27.8 ± 12.5 (19.3%)</td>
<td>29.25 ± 11.3 (5.2%)</td>
</tr>
<tr>
<td>k_{lin}</td>
<td>199.5 ± 47.3</td>
<td>311.9 ± 151.7^{±}(56.3%)</td>
<td>372.2 ± 153.9 (19.3%)</td>
<td>448.3 ± 165.6 (20.4%)</td>
</tr>
<tr>
<td>E_{lin}</td>
<td>664.0 ± 162.5</td>
<td>1049.2 ± 519.2^{±}(58.0%)</td>
<td>1290.6 ± 524.5^{±}(23.0%)</td>
<td>1519.0 ± 574.1 (17.7%)</td>
</tr>
<tr>
<td>ε_{peak}</td>
<td>6.5 ± 5.0 (0.0%)</td>
<td>6.8 ± 1.1 (4.6%)</td>
<td>6.7 ± 1.0 (-1.5%)</td>
<td>6.88 ± 1.0 (2.7%)</td>
</tr>
<tr>
<td>σ_{peak}</td>
<td>36.3 ± 13.2</td>
<td>40.9 ± 14.8 (12.7%)</td>
<td>45.8 ± 15.4 (12.0%)</td>
<td>49.9 ± 13.2 (9.0%)</td>
</tr>
</tbody>
</table>

CSA_{AT}: minimum cross-sectional area (mm²), F_{peak}: peak force (N), k: stiffness (N/mm), E: Young’s modulus (MPa), σ: stress (MPa), ε: strain (%), (low) and (lin) indicate the low force level (10%-40% of peak force) and high force level (60%-90% of peak force; linear) region of force-elongation relationship. Significant change between consecutive stages of maturity in total sample: *: p < 0.01 total sample, ^: p < 0.01 within boys, -: p < 0.01 within girls.

Table II. Mean ± SD values (combined data) and percentage changes between successive maturation stages (months from predicted age of PHV), for tendon cross-sectional area, force, and tendon mechanical properties per stage of maturity (months from predicted age of PHV).

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Statistical analyses
Maturation offset values were quantified to the nearest semester and grouped to integers such as -12, -6 months before and 0, +6 months after predicted age of PHV in order to present the mean values (combined data) for AT dimensional and mechanical properties. Linear mixed models (LMM) were used to analyze inter-individual and intra-individual differences in changes in AT mechanical properties over maturity stages using SPSS statistical software (v. 25.0, SPSS Inc., Chicago, USA). A diagonal covariance structure was used due to heterogeneous variances for each repeated measure and zero correlation between other repeated measures. An unstructured covariance structure was used as the most general covariance structure with no assumptions about the pattern of measurement errors within individuals. The estimation method of -2 Restricted Log Likelihood (-2RLL) was used as the main criterion for comparison with other models and according to the best fit of the model. Additionally, -2RLL was more accurate than Full Maximum Likelihood as the number of participants (N = 41) is small. Dependent variables (DVs) were peak force (Fpeak), stiffness (klow, klin), Young’s modulus (Elow, Elin), stress (σlow, σpeak) and strain (εlow, εpeak) in low (10%-40% of Fpeak) and high (60%-90% of Fpeak) linear region, respectively. Sex was used as a potential 2-level predictor (factor) for all dependent variables. Pairwise comparisons between two consecutive stages were conducted using Bonferroni confidence interval adjustment for each sex (tables I, II). Statistical significance was accepted at a p-value < 0.05.

RESULTS
Mean ± SD values (combined data) for age, body mass and body height per stage of maturity are shown in table I. A significant change in height (p < 0.01) was observed in the interval between 1 year before and the predicted age of PHV. Measured and calculated variables relating to AT mechanical properties are shown in table II.

AT test length (ltest) and cross-sectional area (CSAAT)
Analysis showed that ltest and CSAAT were greater in boys than girls (b = 1.53 95% CI [1.2-1.9], p < 0.001; b = 4.90 [4.18-5.57], p = 0.023) although the rate of increase in ltest and CSAAT (b = 0.05 [-1.40-0.3], p = 0.594; b = 0.31 [-0.13-0.8], p = 0.176) in boys and girls was similar. A significant increase in ltest at PHV was observed in boys with limited increase thereafter (see table II). Increases in both ltest (b = 0.68 [0.55-0.82], p < 0.001) and CSAAT (b = 1.55 [1.23-1.87], p < 0.001) were associated with maturation. No other significant increases in ltest or CSAAT occurred between consecutive states of maturity in boys or girls (table II).

AT Stiffness and Young’s Modulus
As shown in figure 3, stiffness (klow) and Young’s modulus (Elow) measured in the low-force region were greater in boys than girls (b = 44.18 [24.03-64.32], p < 0.001; b = 145.6 [73.4-217.7], p < 0.001, respectively). klow and Elow increased significantly with age relative to maturation offset (b = 9.63 [4.21-15.04], p = 0.001; b = 34.41 [14.32-54.51], p = 0.001, respectively), but the rate of change over time (sex x maturation interaction) was not different between boys and girls (p = 0.104; p = 0.118, respectively). klow increased with force at 40% of Fpeak (b = 0.07 [0.03-0.11], p < 0.001) but was not related to changes in ltest, CSAAT, the ratio of CSAAT and ltest, or body mass. Thus, changes in klow may be explained by changes in Elow as evidenced by its similar temporal response.

Both stiffness (klin) and Young’s Modulus (Elin) measured in the linear region was greater in boys than girls (see figure 3; b = 88.90 [38.56-139.25], p < 0.001; b = 287.98 [108.71-467.25], p = 0.002, respectively). klin and Elin increased significantly with maturation (b = 39.97 [23.95-52.00], p < 0.001; b = 132.67 [81.85-183.48], p < 0.001, respectively), although the rates of increases in klin and Elin were greater in boys than girls (b = 23.37 [4.68-41.79], p = 0.015; b = 80.49 [12.97-148.01], p = 0.020, respectively). klin increased with Fpeak (b = 0.08 [0.05-0.12], p < 0.001), but the trend towards increase with body mass was not significant (b = 1.42 [-0.13-3.00], p = 0.072). klin also decreased with ltest (b = -14.07 [-27.36-0.78], p = 0.038), but was not associated with changes in CSAAT. Furthermore, klin was not related to the ratio between CSAAT and ltest. Significant increases in klin (p = 0.002) and Elin (p < 0.001) were observed before PHV in boys while Elin increased significantly (p = 0.044) at PHV in girls (table II). Elin increased with body mass (b = 5.95 [0.47-11.42], p = 0.034). The strain, as the ratio between elongation and ltest, was not different between the two groups (p > 0.05). Mean strain difference was null between boys and girls at all stages of maturity, indicating that stiffness was calculated in similar stain sectors between sexes (figure 3).
Sex Differences in Adolescent Tendon Adaptation

associated with maturation, while the response between the sexes was similar and body mass had no effect. $\sigma_{\text{low}}$ also increased with increasing $k_{\text{low}}$ and $E_{\text{low}}$ ($b = 0.19 \ [0.17-0.20]$, $p < 0.001$; $b = 0.06 \ [0.05-0.07]$, $p < 0.001$, respectively), and $\sigma_{\text{peak}}$ increased with increasing $k_{\text{lin}}$ and $E_{\text{lin}}$ ($b = 0.18 \ [0.01-0.03]$, $p = 0.005$; $b = 0.01 \ [0.002-0.009]$, $p = 0.003$, respectively) when sex and $k_{\text{lin}}$ or $E_{\text{lin}}$ were entered as independent variables. As expected mathematically, $\sigma_{\text{peak}}$ was strongly related to $F_{\text{peak}}$ ($p < 0.001$). As shown in table II, $e_{\text{low}}$ and $e_{\text{peak}}$ were consistent across maturity stages as a result of parallel increases in length and tendon peak elongation.

AT force
Peak isometric plantar flexor force, and thus AT force ($F_{\text{peak}}$), was greater in boys than girls ($b = 879.38 \ [697.50-1061.28]$, $p < 0.001$), and increases were associated with both maturation ($b = 147.95 \ [80.21-215.70]$, $p < 0.001$) and body mass ($b = 9.86 \ [2.07-17.64]$, $p = 0.013$). The response differed between sexes such that force increased more in boys than girls ($b = 98.21 \ [10.10-186.31]$, $p = 0.029$). $F_{\text{peak}}$ showed a significant increase at PHV in boys ($p < 0.001$) but increased relatively linearly in girls (table II).

DISCUSSION
The present longitudinal study describes changes in mechanical properties of an important energy-storing tendon, the Achilles tendon (AT), in boys and girls during pre-pubertal and adolescent developmental phases. Individuals were followed for 18 months (with testing at 0, 6, 12 and 18 months) and the data were combined to form a longitudinal data set for linear mixed model analysis. The results of the analysis, which are summarized in figure 4, indicate that stiffness in both the low-force ($k_{\text{low}}$) and high-force (linear; $k_{\text{lin}}$) regions of the force-length (stress-strain) relation was greater in boys than girls and increased similarly with age relative to peak height velocity (PHV), although boys showed a more prominent increase in $k_{\text{lin}}$ in the year before PHV. These changes in $k_{\text{low}}$ and $k_{\text{lin}}$ were most strongly related to changes in Young’s modulus ($E_{\text{low}}$ and $E_{\text{lin}}$) rather than AT cross-sectional area (CSA AT); stiffness and Young’s moduli in both low force and linear regions were also greater in boys than girls but increased similarly with age except for the more notable increase in the year before PHV in boys. Similarly, force increased rapidly 6 months before PHV in boys. Therefore, changes in stiffness $k_{\text{low}}$ and $k_{\text{lin}}$ with age as well as differences between sexes were most strongly associated with changes/differences in maximal plantar flexor peak strength ($F_{\text{peak}}$), speculatively through a greater potential for force application to the tendon. Changes in $F_{\text{peak}}$, CSA AT and tendon length ($l_{\text{test}}$) – or CSA AT/$l_{\text{test}}$ – did not change consistently with $F_{\text{peak}}$, so age-related changes in tendon stress ($\sigma_{\text{low}}$ and $\sigma_{\text{peak}}$) were strongly related to the changes in $F_{\text{peak}}$. However, since both muscular strength and AT stiffness increased simultaneously with age, the maximum tendon strain ($e_{\text{peak}}$) was constant across ages. Therefore, boys had greater AT stiffness than girls around PHV as a result of force changes rather than morphological changes. These results have important implications for our understanding of adaptation of energy-storing tendons during growth and maturation, and these are discussed below.
Regarding to sex differences, linear mixed model analysis revealed that boys had greater k and E than girls in both force level regions. These results are consistent with several cross-sectional studies showing a lesser (patellar) tendon stiffness in young women than men (21, 22) but not consistent with others that observed no differences in AT between boys and girls cross-sectionally (3) or over a short (6 month) time period (6). One possibility is that our longitudinal analysis using LMM minimized the effects of between-subject variability, and thus statistical error, whilst allowing changes in AT to be tested over a period of several years. This analysis indicates that changes in muscle force production, with a small influence from body mass change, may underpin the observed sex differences.

The present analysis also leads to the assumption that the age-related increases in Achilles tendon k and E were likely predominately triggered by an increase in maximal planatar flexor force capacity (F peak). This assumption is partly based on the findings that: 1) the rate of change in F peak increased significantly just prior to PHV (table II), which followed the rapid increase in both k and E in boys and is also temporally aligned with the rapid increase in E in girls in the linear region; 2) robust statistical relationships were observed between k, F peak, and E; and 3) the significant association between force with maturation, body mass, sex and the interaction between sex and maturation, showing that force increased with maturation. However, boys produced greater force at all ages than girls and had correspondingly greater slopes of their force-, k- and E- maturation relations compared to girls. The present analysis also leads to the assumption that the peak mechanical stimulus for tendon adaptation (9), our findings indicate that muscle strength and body mass stimuli for tendon adaptation, and therefore E measured in the linear region (60%-90% of F peak), was greater in boys and changed earlier than in girls. It would be of interest to compare adaptive changes in girls who perform a significant amount of physical activity (possibly including strength training) to those in the present study to determine whether adaptation might then be more similar between boys and girls.

Although tendon strain is commonly considered an important mechanical stimulus for tendon adaptation (9), our findings that ε peak (6.5-6.9%) was constant across maturation stages whilst σ low and σ peak were strongly related to E low and E lin (as well as k low and k lin), respectively, is more consistent with the hypothesis that peak force, drives tendon stiffness adaptation. One possibility is that increases in tendon strain resulting from increases in muscle force production with maturation triggered rapid adaptations that subsequently limited tendon strain, i.e., strain was a predomi-

![Figure 4. Model of adaptation according to our longitudinal data.](image-url)
nate trigger, which then restricted strain to constant values. The exact mechanism by which mechanical loading (force) might trigger adaptive change is not yet clear, however it might 1) result from tendon-specific molecular signaling in response to high forces imposed on local mechanosensitive molecules (24), or 2) relate to ubiquitous molecular signaling events in both the muscle and its associated connective tissues, including the tendons, triggered when high muscular forces are generated. By this latter mechanism, muscle (i.e., muscle strength) and tendon would undergo synergistic growth and adaptation during maturation in order to optimize muscle-tendon congruity (25). Thus, a link between muscle molecular signaling and tendon adaptation may exist. This concept is consistent with data showing a correlation between increases in muscle size and (patellar) tendon stiffness after a period of strength training in adult humans (26), as well as increases in both tendon CSA and stiffness in response to low-load (i.e., low tendon strain) blood flow-restricted exercise training leading to significant muscle hypertrophy (27). As the strategies for increasing tendon mass and altering mechanical function rely on a better understanding of the triggers for adaptation, molecular signaling and mechanical adaptation in energy-storing tendons may an important area for future study.

In this study there are some limitations. Firstly, the foot was accepted to be rigid. Thus, the effect of foot deformation on the changes in MTU length during contractions was considered negligible (28). In addition, there are no studies measuring the range of foot deformation in adolescents. Therefore, it was not investigated if foot deformation may cause incorrect results. Secondly, the ultrasound measurement may underestimate the CSA_{AT} and the calculated stress may thus be overestimated. Previous research reported 5.5% (29) smaller CSA_{AT} measured with the ultrasound than the MRI method. Given that we measured the difference in Young’s modulus between boys and girls in a longitudinally context, the methodological choice would not have strongly affected our finding that Young’s modulus was greater between boys and girls at and/or around PHV. However, further analysis using MRI methods or 3D ultrasound may be needed to provide accurate CSA_{AT} values.

CONCLUSIONS

In conclusion, Achilles tendon mechanical properties change throughout the adolescent growth period, although with a more rapid change before the age of peak height velocity in boys and with greater magnitude in boys than girls. The more rapid increase before PHV in boys was associated with an increase in force at that time, which may have evoked the molecular signaling required for adaptations to internal tendon structure. These mechanical changes were observed in both low- and high-force regions of the force-elongation relation. Our data are most consistent with a model in which increases in muscle force capacity (with a smaller effect of body mass, particularly for mechanical properties of the linear region of the force-elongation relation) trigger increases in modulus and thus stiffness. While both Achilles tendon CSA and length increase approximately linearly during adolescence, their changes appear to contribute little to changes in tendon stiffness. These data are the first to quantify longitudinal changes in the mechanical properties of an energy-storing, load-bearing tendon in humans as well as the factors that may influence them.

CONFLICT OF INTERESTS

The authors declare that they have no conflict of interests.

REFERENCES


Identifying Differences in Elastographic Properties of Calf Muscles and Tendons Across Subsets of Tennis Players

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SUMMARY

Objective. Calf strain occurs frequently in tennis players and has been termed “tennis leg”. To date, there is a lack of information showing how injury history, age, gender, or level of play, may predispose tennis players to injury (1, 2). The purpose of this study was to investigate the elastographic properties of the gastrocnemius-soleus complex in a group of club-level tennis players. We hypothesized that elastographic properties of the gastrocnemius-complex are affected by age and sport specificity (tennis only vs multi-sport).

Methods. Participants were recruited through contact personnel of a local tennis club. At the club’s annual summer tournament, each participant voluntarily consented and completed a survey to obtain information about age, level of play, length of play, participation in other sports, relevant injuries, and relevant surgeries. Participants underwent ultrasonography that included visualization of the medial gastrocnemius musculotendinous junction, soleus muscle, and Achilles tendons, bilaterally. Shear wave speed (SWS) was gathered from ultrasonography for all tissues to provide a comparative standard unit of measurement. The data was analyzed with a mixed effects model.

Results. 20 participants with mean age 33.5 years old (range, 14-61) were evaluated. There was a statistically significant trend in medial gastrocnemius SWS depending on age, participation in sports other than tennis, and two different metrics for skill level (highest level of competitive play and USTA NTRP rating). There was a statistically significant trend between Achilles tendon SWS and highest level of competitive play. Results showed no significant trends for any of the tissues and serving hand, whether the ultrasound was conducted before or after a match, or for any of the four metrics for tennis experience (times playing tennis per week, overall tennis experience, years playing > 3 times per week, and whether a player had > 10 or < 10 years of experience). No statistically significant trends were observed for the soleus muscle when compared to any of the demographics.

Conclusions. Age, exclusively playing tennis as opposed to other sports, and two metrics of skill level (highest level of competitive play and USTA NTRP rating) significantly affected gastrocnemius SWS. Highest level of competitive play was the only metric found to affect Achilles tendon SWS. Soleus SWS exhibited no significant changes with any of the variables, despite following similar trends with gastrocnemius SWS.

KEY WORDS
Achilles tendon; calf strain; Gastrocnemius-Soleus Complex; tennis leg; tennis.
INTRODUCTION

Tennis elbow, or lateral epicondylitis, is a well-known activity-related injury, but less discussed is tennis leg, or calf-strain. Like lateral epicondylitis, calf strain commonly occurs in tennis players, but also occurs in people who do not play tennis (1, 3). It was first described by Powell in 1883 as a tissue rupture at the distal and medial musculotendinous junction where the AT meets the gastrocnemius muscle (4). “Tennis leg” has been commonly described among tennis players and is most often seen in people between ages of 30–45. Risk factors that predispose this population to calf strain are unknown. Clinical presentation commonly involves a middle-aged patient who has acute activity-related pain in the medial portion of their calf, accompanied by a “popping” sound when stretching their gastrocnemius muscle through dorsiflexion of their foot (5). There are various stages of injury severity, ranging from minor structural injury to complete tear of the muscle from the tendon (6). Treatment is largely conservative, consisting of “RICE,” or rest, ice, compression, and elevation, to promote tissue healing (5).

Ultrasound is an effective method of quantifying the elastographic properties of various tissue types and has previously been used in muscle and tendon studies of athletes such as volleyball players and distance runners, where cross-sectional area, elongation, and force were obtained and analyzed (7, 8). In this study, ultrasound has been used to identify elastographic differences of the gastrocnemius-soleus complex across tennis players according to age, gender, level of play, and length of play. While it is observed that the injury occurs more often in middle-aged tennis players than younger tennis players or their non-tennis-playing counterparts, little is known about specific risk factors related to calf strain.

The objective of this study is to evaluate the elastographic properties of the Achilles tendon in club-level tennis players. We hypothesized that elastographic properties of the gastrocnemius-complex are affected by age and sport specificity (tennis only vs multi-sport).

METHODS

This study was ethically conducted according to the international standards described in (9). It was performed as a pilot study with a level of evidence of V. It was conducted at an academic medical center and approved by the Institutional Review Board according to Protocol for Human Subject Research (9). Once approval was obtained, permission from a local tennis club was granted to recruit participants and collect ultrasound data during the first two consecutive days during their 2019 Summer Tennis Tournament. If they were willing to participate, the tennis players were first screened according to the inclusion and exclusion criteria. Inclusion criteria were competitive male and female tennis players with minimum age of 14 and under the age of 65. Exclusion criteria were previous injury or surgery to the lower extremity. Once consent was obtained, each participant completed a survey pertaining to participant age, gender, level of play, length of play, participation in other sports, relevant injuries, and relevant surgeries. While in an unloaded plantarfexion position, participants underwent ultrasonography of their medial muscle-tendon junction of the Achilles tendon and gastrocnemius, bilaterally, either before or after partaking in their tennis match. This set-up is shown in figure 1. Excellent interobserver correlation, at several locations of the Achilles tendon, including the muscle-tendon junction, has been reported when the lower leg is in the unloaded plantar flexion position (10).

A Verasonic ultrasound system (Verasonics Inc., Redmond, WA, USA) with a L7-4 transducer (center frequency = 5.2080 MHz, and beam width = 4.7 MHz) was used. A customized supersonic shear wave elastography (SWE) method was used to measure shear modulus within lower leg muscles (11). The technique was validated using calibrated homogeneous elasticity phantom having various shear modulus values (Model 040GSE, CIRS, Norfolk, Virginia, USA) as well as other musculoskeletal tissues with the intraday and day-to-day reliability of 0.72 (95% Confidence Interval (CI) = 0.59-0.83) and (0.95 with 95% CI = 0.88-0.98), respectively (12). The ROI size of 7.39 mm × 7.39 mm was selected for the measurement of lower leg shear modulus in the gastrocnemius and soleus muscles, while the ROI height for the Achilles tendon measurements was adjusted to include just the tendon (ROI size = Tendon thickness × 7.39 mm) (13). After data collection, ultrasound data was analyzed to identify the elastographic properties of the Achilles tendon-gastrocnemius junction. Shear wave speed (SWS) was the primary measurement used to compare tissue properties between all three tissues. SWS was used to analyze muscle in addition to tendon to keep analysis consistent, instead of comparing tendon SWS to muscle shear modulus.

The analyzed data was subject to statistical analysis using a mixed effects model to identify any significant differences in Achilles tendon-gastrocnemius junction properties based on age, gender, level of play, and length of play. The effect of age on SWS was also analyzed by dividing the participants into two groups: young (under 35 years old) or older (35 years old or older). All tests were two-sided, with p-values < 0.05 being considered statistically significant.

RESULTS

Twenty participants with a mean age 33.5 years (range, 14-61 years old) participated in this study. Table I depicts
SWS values obtained for all participants and illustrates each participant’s tennis profile, including duration of experience, highest level of play, other sports played, and whether ultrasound scan occurred before or after a match. Table II organizes this data and states the highest, lowest, and average values for tissue SWS. Table III shows a summary of the significant and non-significant associations between the variables tested against gastrocnemius, soleus, and Achilles tendon SWS.

**Age**

There was a significant negative correlation between age and gastrocnemius SWS \( p = 0.047 \). As age increased, gastrocnemius SWS decreased. Gastrocnemius SWS was also significantly different for participants older than 35 compared to those younger than 35 \( p = 0.039 \). Subjects in the older group exhibited a lower average gastrocnemius SWS (2.14 and 1.81 m/s for the right and left legs, respectively) compared to the younger group (2.38 and 2.33 m/s for the right and left legs, respectively).

There were no significant positive or negative correlations when age was compared to soleus SWS \( p = 0.361 \) or Achilles SWS \( p = 0.127 \). There were also no significant differences for soleus SWS \( p = 0.11 \) or Achilles SWS \( p = 0.744 \) when participants over 35 years old were compared to participants under 35 years old. The data pertaining to age can be seen in **figure 2**.

**Tennis experience**

There was no significant positive or negative trend between the number of years that an athlete played tennis and gastrocnemius SWS \( p = 0.747 \), soleus SWS \( p = 0.257 \), or Achilles tendon SWS \( p = 0.241 \). We also found no significant difference between SWS of tennis players with greater than or equal to 10 years of experience compared to those with less than 10 years of experience for the gastrocnemius \( p = 0.380 \), soleus \( p = 0.287 \), or Achilles tendon \( p = 0.311 \).

There was no significant positive or negative trend between the frequency of tennis play per week and gastrocnemius SWS \( p = 0.248 \), soleus SWS \( p = 0.725 \), or Achilles tendon SWS \( p = 0.363 \). When comparing players’ cumulative number of years of playing greater than 3 times per week to tissue SWS, no significant trend was observed for gastrocnemius \( p = 0.810 \), soleus \( p = 0.280 \), or Achilles tendon \( p = 0.968 \).

**Effect of match timing**

Match timing had no significant effect on elastographic properties of the gastrocnemius \( p = 0.446 \), soleus \( p = 0.834 \), or Achilles tendon \( p = 0.663 \).

**Other sports**

There was a significant difference between gastrocnemius SWS of the right leg *versus* the left leg depending on wheth-
Table I. Demographic and measurement details for each participant.

<table>
<thead>
<tr>
<th>Number</th>
<th>Age</th>
<th>Gender</th>
<th>Serving-Hand</th>
<th>Years playing tennis</th>
<th>Years playing &gt; 3 times per week</th>
<th>Level of competitive play</th>
<th>USTA NTRP rating</th>
<th>Scan before/after match?</th>
<th>Times playing per week</th>
<th>Other sports played?</th>
<th>Left Gastroc.</th>
<th>Right Gastroc.</th>
<th>Left Soleus</th>
<th>Right Soleus</th>
<th>Left Achilles</th>
<th>Right Achilles</th>
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<tbody>
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<td>M</td>
<td>Right</td>
<td>10</td>
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<td>D3 college</td>
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<td>2.5</td>
<td>yes</td>
<td>2.54</td>
<td>2.9</td>
<td>3.34</td>
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<td>9.52</td>
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<td></td>
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<tr>
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<td>Right</td>
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<td>after</td>
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<td>Right</td>
<td>13</td>
<td>8</td>
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<td>3.5</td>
<td>after</td>
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<td>high school</td>
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<tr>
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<td>before</td>
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<td>2.06</td>
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<td>before</td>
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<td>no</td>
<td>2.58</td>
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<td>3.77</td>
<td>2.68</td>
<td>4.52</td>
<td>6.8</td>
</tr>
</tbody>
</table>

Table I depicts the demographics for all subjects. Three were female and 17 were male. Only one subject served with his left hand, while 19 subjects were right-hand dominant for serving. 12 subjects were younger than 35 years old and 8 were older than 35 years old. The SWS values can also be found for each patient and each tissue.
Table II. Organized demographics of participants.

<table>
<thead>
<tr>
<th></th>
<th>Highest</th>
<th>Lowest</th>
<th>Average</th>
<th></th>
</tr>
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<td>Age</td>
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<td>14</td>
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<td>Male</td>
</tr>
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<td>Total years</td>
<td>35</td>
<td>4</td>
<td>15.9</td>
<td>Female</td>
</tr>
<tr>
<td>Years &gt; 3 times/week</td>
<td>26</td>
<td>0</td>
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<td>Recreational</td>
</tr>
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<td>Gastrocnemius SWS</td>
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<td>1.28</td>
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<td>Soleus SWS</td>
<td>5.70</td>
<td>1.34</td>
<td>2.66</td>
<td>D3 college</td>
</tr>
<tr>
<td>Achilles SWS</td>
<td>36.60</td>
<td>1.69</td>
<td>10.06</td>
<td>D2 college</td>
</tr>
</tbody>
</table>

Table II gives an organized picture of the demographics that were collected. The average age was 33.6 years old, and the average number of years that a participant played tennis was 15.9 years. The average SWS values for each tissue are also shown.

Table III. Summary of data.

<table>
<thead>
<tr>
<th></th>
<th>Gastrocnemius SWS</th>
<th>Soleus SWS</th>
<th>Achilles tendon SWS</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>p value (sig = p &lt; 0.05)</td>
<td>p value (sig = p &lt; 0.05)</td>
<td>p value (sig = p &lt; 0.05)</td>
</tr>
<tr>
<td>Age</td>
<td>Age correlation by side</td>
<td>Age correlation - overall</td>
<td>Age correlation - overall</td>
</tr>
<tr>
<td></td>
<td>Right 0.231</td>
<td>Left 0.096</td>
<td>0.047</td>
</tr>
<tr>
<td></td>
<td>&gt; 35 yo vs. &lt; 35 yo</td>
<td>0.056</td>
<td>0.101</td>
</tr>
<tr>
<td>Tennis Experience</td>
<td>Times playing tennis / week</td>
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<td>0.2566</td>
</tr>
<tr>
<td></td>
<td>Tennis experience correlation</td>
<td>0.8104</td>
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</tr>
<tr>
<td></td>
<td>Years playing &gt; 3 times per week</td>
<td>0.3798</td>
<td>0.2867</td>
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<td></td>
<td>Experience &gt; 10 years vs. &lt; 10 years</td>
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<td>0.434</td>
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<td></td>
<td>Other sports: R vs. L SWS</td>
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<td>0.834</td>
</tr>
<tr>
<td></td>
<td>Serving hand</td>
<td>0.137</td>
<td>0.1866</td>
</tr>
<tr>
<td></td>
<td>Skill Level</td>
<td>Level of competitive play</td>
<td>0.0062</td>
</tr>
<tr>
<td></td>
<td>USTA NTRP Rating</td>
<td>0.0183</td>
<td>0.8829</td>
</tr>
</tbody>
</table>

Table III summarizes the data that was analyzed for all three tissues compared to each demographic. Gastrocnemius SWS was significantly correlated with age and was significantly different for age > 35 years old vs. age < 35 years old, whether or not other sports were played, and both skill level metrics. Soleus SWS was not found to significantly correlate with any demographics. Achilles tendon SWS was significantly different compared to the level of competitive play.

Tennis players played other sports (p = 0.039). For tennis players who did not play other sports, gastrocnemius SWS ranged from (1.54-3.84) in the right leg and (1.38-2.87) in the left leg. For tennis players who did play other sports, gastrocnemius SWS ranged from (1.68-3.24) in the right leg and (1.28-2.89) in the left leg. These trends can be seen in figure 3.

No significant difference was identified between soleus SWS (p = 0.834) or Achilles tendon SWS (p = 0.663) of the right versus left leg between participants who played only tennis when compared to multi-sport participants.

Serving hand
There was no significant trend between serving handedness and SWS of a player's right leg compared to their left leg for any tissue analyzed; gastrocnemius (p = 0.137), soleus (p = 0.187), or Achilles tendon (p = 0.843).

Skill level
Interestingly, a tennis player's highest level of competitive play had a significant trend with gastrocnemius SWS (p = 0.006) and Achilles tendon SWS (p = 0.010), but not with...
soleus SWS (p = 0.925). Gastrocnemius SWS ranged from (1.38-2.89) for recreational tennis players, and (1.74-3.84) for college tennis players. Achilles tendon SWS ranged from (1.69-13.35) for recreational tennis players, and (4.64-36.6) for college tennis players.

A tennis player’s USTA NTRP rating also significantly correlated with gastrocnemius SWS (p = 0.180), but not for soleus SWS (p = 0.883) or Achilles tendon SWS (p = 0.280).

DISCUSSION
This study quantified tissue characteristics in tennis players of varying tennis backgrounds to identify differences in elastographic properties between demographics. SWE was carried out on healthy tennis participants of an annual local tennis tournament either before or after match play. The gastrocnemius muscle was the only tissue that was found to have significant correlations with multiple variables. Achilles tendon SWS was found to be significantly different based on a player’s skill level metrics. Soleus SWS was not found to have significant associations with any of the demographics, despite following a similar pattern seen in gastrocnemius SWS. SWE proved to be an effective technique to measure elastographic properties of the medial gastrocnemius musculotendinous junction.

Compared to the other tissues of the medial gastrocnemius musculotendinous junction, the gastrocnemius was most significantly affected by the metrics that were studied. This suggests that the gastrocnemius muscle is more likely to be affected by age and by movements performed in tennis compared to the soleus muscle or the Achilles tendon. Gastrocnemius SWS was also significantly affected by both metrics that measured a tennis player’s skill level: highest level of competitive play and USTA NTRP rating. The high
involvement of the gastrocnemius was also seen in a study by Delgado (14), where ultrasonography was used to identify the precise etiology of 141 patients’ tennis leg symptoms (14). Of the cases they analyzed, 66% were caused by rupture of the medial gastrocnemius, 21% by joint involvement of the medial gastrocnemius and soleus, and only 0.7% were due to rupture of the soleus alone.

Our data shows that as age increased, gastrocnemius SWS significantly decreased. Additionally, gastrocnemius SWS was significantly lower in participants over 35 years old compared to those under 35 years of age, indicating that older aged players exhibited significantly less gastrocnemius tissue stiffness compared to younger tennis players. A similar result was observed by Yoshida (15), whereby SWE of the medial gastrocnemius musculotendinous junction resulted in greater elastic moduli in younger participants compared to older participants (15). Their participants were not specifically tennis players, so the observed negative correlation between gastrocnemius SWS and age is seen in populations other than tennis players. This negative correlation between age and gastrocnemius SWS can potentially be a factor related to injury. Calf strain occurs more frequently in older athletes compared to their younger counterparts (16). From a biomechanical point of view, tissues with lower mechanical strength are more likely to fail when loaded, which may explain the higher incidence of gastrocnemius tears compared to the Achilles tendon or soleus muscle. However, this contradicts conventional wisdom that considers musculotendinous stiffness a risk factor for musculoskeletal injury (17, 18). Younger individuals tend to exhibit lower joint stiffness and muscle tightness (19, 20). However, joint stiffness and muscle tightness are the result of the interaction of muscle with connective tissues such as tendons and ligaments. Aging affects each of those tissues differently, with tendons and ligaments exhibiting higher stiffness in older individuals (21). Therefore, it is possible that although muscle properties (shear modulus or SWS) decrease with age, joint stiffness and muscle tightness increase due to the stiffening of tendons and ligaments. Additionally, a review article from Murphy (17) reveals that many characteristics that are generally thought of as risk factors actually are not significantly correlated to risk (17).

Our study demonstrated a positive association between each of the two skill level metrics and gastrocnemius SWS, but not between any of the four tennis experience metrics and gastrocnemius SWS. Achilles tendon SWS also exhibited an increasing trend with a player’s highest level of competitive play. It is counterintuitive that gastrocnemius stiffness would significantly increase with increasing skill level, but lack a significant relationship when compared to experience; it is likely that players competing at a high skill level had to gain significant experience in the sport to reach that level and may not currently be playing as much tennis as they had in the past. Furthermore, extended low level tennis experience does not require these tissues to undergo the same changes as engagement at a high level of intensity. This is in accordance with studies investigating the relationship between muscle strength and elastic properties. Lima (22) used elastography to compare elastic properties of the gastrocnemius and soleus muscles to force generated by them (22). They concluded that elasticity of these muscles does not correlate to force. According to their conclusions, the demographic factors that we found to significantly correlate with increased stiffness do not relate to the force that can be generated by those tissues. Tennis involves eccentric, concentric, and isometric contractions; for example, Rafael (23) found that there is significant isometric contraction of the serratus anterior during tennis serve, forehand, and backhand swings (23). Gatz (24) found a significant difference in stiffness of the Achilles after a rehabilitation program limited to eccentric exercises, compared to a program that included eccentric and isometric movements (24). In their study, eccentric exercises yielded stiffer Achilles SWS measurements after a 12-week rehabilitation program for Achilles strain, while a combination of eccentric and isometric maneuvers did not produce significant changes in tissue stiffness. Tennis players who exhibit demographics that correlate with stiffer gastrocnemius tissue could consider incorporating isometric movements in their routines to mitigate further tissue stiffening. However, more research correlating isometric exercise, calf muscle stiffness, and calf strain needs to be conducted to study the efficacy of such exercise.

To our knowledge, there have been no other studies that analyzed structural tissue changes in comparison to the skill level of tennis players. However, a study conducted by Agresta (25) investigated how a runner’s “stride-to-stride fluctuations” can adapt to changing demands based on the runner’s length of experience in the sport (25). They found that increased experience allowed runners to modify gait more skillfully in response to changing demands. Experience alone was enough to correlate with significant changes in a runner’s stride. In contrast, our study found that experience alone was not sufficient to elicit significant changes in tissue stiffness.

Limitations
The multiple comparison issue arises when looking at multiple variables simultaneously, which could result in false positives. The multiple effects model was chosen to carry out data analysis to combat this phenomenon. The small sample size of the study is itself a limitation, but this does not affect the significance of the results due to the method of...
analysis being the mixed effects model. Further, all subjects were of male gender, which keeps the sample homogenous. It is a good representation of the male tennis population because of the wide age range of participants.

CONCLUSIONS
In conclusion, SWE was used to measure elastographic properties of the tissues comprising the medial musculotendinous junction of the Achilles tendon in tennis players. Age, exclusively playing tennis as opposed to other sports, and two metrics of skill level (highest level of competitive play and USTA NTRP rating) significantly affected gastrocnemius SWS. Highest level of competitive play was the only metric found to affect Achilles tendon SWS. Soleus SWS exhibited no significant changes with any of the variables, despite following similar trends seen with gastrocnemius SWS. The results suggest that the gastrocnemius muscle is disproportionately involved in the movements conducted in tennis compared to the other tissues comprising the medial Achilles musculotendinous junction.

ACKNOWLEDGEMENTS
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CONFLICT OF INTERESTS
The authors declare that they have no conflict of interests.

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Ligamentum Teres and its Analog in the Hip Endoprosthesis – Necessary or Superfluous? A Systematic Review

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INTRODUCTION

Hip arthroplasty has been widely used since the mid-1940s-early 1950s (1-5). Soon after the start of a wide use of both cups and the more familiar endoprostheses, however, surgeons began to report cases of their dislocation and subluxation (6-13). Dislocation after hip replacement is a serious and devastating complication of such surgical interventions (14, 15). According to literature data, the incidence of dislocation reached 15% in the 1970s-1980s (16). These days, dislocation after primary arthroplasty occurs in 0.2-10% of the cases, more often for prostheses implanted after femoral neck fracture (17-22). The incidence of dislocation after revision surgeries can reach 25-31% (20, 22, 23). The risk of dislocation increases with time, regardless the type of surgery and in spite of adequate restoration of soft tissues (24, 25). At the same time, no relationship has been noted between the dislocation rate, on the one hand, and the patients’ sex, age, diagnosis, and the type of endoprosthesis, on the other (26). Surgery for dislocation increases the treatment costs and health risks for the patient (15). This problem has important clinical and social implications and has no clear solution so far.

SUMMARY

Background. Dislocation of hip endoprosthesis remains a common and serious complication of arthroplastic interventions. One of the ways to prevent endoprosthesis dislocation is to integrate a ligamentum teres analog into its design.

Purpose. Reviewing international experience in the design, development and insertion of hip endoprosthesis with the native ligamentum teres or its analog.

Materials and methods. A systematic patent and non-patent search and analysis of publications on hip endoprostheses with native ligamentum teres or its artificial analog. The search was done on relevant online platforms and in available libraries.

Results. To date, there are 20 identified patents on endoprosthesis designs with the native ligamentum teres or its analog. Ligamentum teres analogs are proposed to be created using auto-, allo- or xenografts, synthetic materials and metals. We have found two subtotal endoprosthesis with ligamentum teres analogs that are used in clinical practice. The long-term outcomes of such surgeries are not known. There are no commercially available endoprostheses with ligamentum teres analogs.

Conclusions. A ligamentum teres analog integrated into a hip endoprosthesis can help prevent dislocation in the post-operative period. Further theoretical, experimental, biomechanical and clinical studies are needed to develop such endoprostheses for a wider use.

KEY WORDS

Hip joint; ligamentum capitis femoris; ligamentum teres; endoprosthesis; complication; dislocation of a hip joint prosthesis.
A technical solution that can apparently prevent dislocation of endoprosthesis head is to make a non-detachable ball-and-socket joint. In 1952, H. G. Van Steenbrugge was among the first to propose a total endoprosthesis of such a design, with the femoral component fixed by neck (27). In order to – among other things – reduce the risk of displacement for the acetabulum component, J. Charnley has begun implanting prostheses with a smaller head since 1960, but he still reports a dislocation rate of 1.5% in the early postoperative period (28, 29). Dislocation is currently prevented by using non-detachable systems. While solving the main problem, however, their use is associated with excessive wear of the friction pair, degradation of the bone-cement and cement-metal bonds, leading to aseptic loosening and a catastrophic failure of the acetabulum component (14). Even at the early stages of implant arthroplasty, one of the ways for solving the problem of hip implant dislocation was by completing the implant design with an analog of the ligamentum teres (LT). The first hip endoprosthesis of this type was proposed by Leon L. Pellet in 1954 (30).

The use of native LT or its analog as a binding element in the endoprosthesis design has not been fully developed yet. The purpose of this paper was to review relevant international experience, from the concept formation to the development and practical use of hip prostheses with native LT or its analogs, and to understand the prospects for their use and improvement. Currently, there are no systematic reviews on design of hip endoprostheses with the LT or its analogs, registered as projects in PROSPERO and COCHRANE.

MATERIALS AND METHODS

This systematic review was done in accordance with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analyses) Guidelines (31). The Protocol of Systematic Review of the topic in question was prepared and discussed by the team of authors. The Protocol are available upon request from the corresponding author. The Protocol are formally examined by reading the text and viewing the illustrative material. If the document met the eligibility criteria, the related documents were evaluated for compliance with these criteria: patent and non-patent publications cited therein, patent documents that cited this document, as well as similar documents from the lists available on the viewed Internet page (Patent Citations, Non-Patent Citations, Cited By, Similar Documents). Where the initial search failed to find the full-text view of a document, the search switched to the electronic platforms EPO, WIPO and FIPS. These databases were also used to ascertain the dates of the earliest publications of eligible patent documents. The search for eligible non-patent scientific publications mentioned in the related documents cited in patents was done on the Google Scholar electronic platforms (https://scholar.google.com/), PubMed (https://www.ncbi.nlm.nih.gov/pubmed/), and in available libraries.
As the result of our search on these resources, we obtained a cohort of publications that passed the final screening. Of these, we excluded patent abstracts and abstracts of scientific reports. Then, from the number full-text publications, we excluded the descriptions of applications for invention. Next, we identified and excluded duplicates among the remaining patent descriptions evaluated as eligible and non-patent publications discussing the installation of the devices. Thus, we obtained a list of publications for the final analysis.

All the identified sources of patent information are listed in Table 1, in the order of their earliest priority. The nationality of patent authors was derived from the two-letter codes of countries, administrative divisions and intergovernmental organizations (WIPO ST.3). The risk of bias regarding the applicability and the rational technical essence of the identified hip prosthesis designs with native LT or its analog was ranked according to the following criteria: 1) commercial devices used in clinical practice; 2) small-batch devices used in clinical practice; 3) individually produced devices used in clinical practice; 4) concepts presented as a text description of the device design and installation method, with explanatory graphic material, never used in clinical practice. The maximum risk of bias rating was assigned to endoprostheses that fell under criterion 4, the minimum, to those under criterion 1. The risk-of-bias assessment took into account the short-term outcomes of arthroplasty described in both patent and non-patent documents. All the identified designs were grouped by the type of endoprosthesis and by the type of friction pair. Where the materials of friction pairs were either not specified, or specified too broadly or not quite clearly, the friction pair was assigned to the most likely type based on the description of the technical essence of design. Next, we analyzed the options for using native LT or its analogs in the hip endoprosthesis design, as well as analogs of the external ligaments of the hip, if available. This systematic review had no external source of funding.

### RESULTS

The systematic search among 9178 patent publications identified 130 patents and applications for inventions dedicated to hip endoprostheses with native LT or its analog. Of these,

<table>
<thead>
<tr>
<th>No.</th>
<th>Earliest priority</th>
<th>Earliest publication</th>
<th>Inventor/s</th>
<th>Patent number</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1954-08-02</td>
<td>1956</td>
<td>Pellet LL (30)</td>
<td>US2765787A</td>
</tr>
<tr>
<td>2</td>
<td>1975-06-26</td>
<td>1976</td>
<td>David T (34)</td>
<td>US4092741A</td>
</tr>
<tr>
<td>3</td>
<td>1986-10-29</td>
<td>1990</td>
<td>Dudko GE (35)</td>
<td>SU1551366A1</td>
</tr>
<tr>
<td>4</td>
<td>1987-07-06</td>
<td>1990</td>
<td>Perepichka V.D. (36)</td>
<td>SU1572603A1</td>
</tr>
<tr>
<td>5</td>
<td>1990-05-03</td>
<td>1992</td>
<td>Neverov VA, Shilnikov VA (37)</td>
<td>SU1743595A1</td>
</tr>
<tr>
<td>6</td>
<td>1996-01-22</td>
<td>1997</td>
<td>McCandliss R (38)</td>
<td>US5702474A</td>
</tr>
<tr>
<td>7</td>
<td>1996-07-01</td>
<td>1998</td>
<td>Dennis DA, Komistek RD (39)</td>
<td>US5951605A</td>
</tr>
<tr>
<td>8</td>
<td>1998-04-30</td>
<td>2000</td>
<td>Shah MK (40)</td>
<td>US6010535A</td>
</tr>
<tr>
<td>12</td>
<td>2007-09-17</td>
<td>2010</td>
<td>Linares MA (44)</td>
<td>US8211182B</td>
</tr>
<tr>
<td>13</td>
<td>2007-09-17</td>
<td>2009</td>
<td>Linares MA (45)</td>
<td>US7887586B2</td>
</tr>
<tr>
<td>17</td>
<td>2011-07-08</td>
<td>2013</td>
<td>Castro FF, Fisher JMO, Moskovitz AP $ (49)</td>
<td>US9060862B2</td>
</tr>
<tr>
<td>19</td>
<td>2015-08-07</td>
<td>2015</td>
<td>Haining Z (51)</td>
<td>CN105105873B</td>
</tr>
<tr>
<td>20</td>
<td>2015-09-09</td>
<td>2015</td>
<td>Boroumand S, Halwai I (52)</td>
<td>DE202015006363U1</td>
</tr>
</tbody>
</table>
26 abstracts, 28 applications for inventions and 56 duplicate patent descriptions were excluded at the stages of final screening and eligibility assessment. Finally, 20 patent documents were included in the systematic review. From the 55 initially identified non-patent sources discussing various aspects of hip arthroplasty with an LT analog, including those describing short-term outcomes of the surgery, we selected two publications in Russian meeting the eligibility criteria (32, 33).

The flowchart for selecting information sources (Figure 1) follows the recommendations of Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) (31).

Eligible patent documents selected for the systematic review are presented in Table I. Of the 20 patents selected for the systematic review, 15 were in English, 3 in Russian, 1 in German and 1 in Chinese. The selected patents on hip endoprostheses with native LT or its analogs were grouped by the earliest priority date and presented in Figure 2. The main numbers of patents coming from 90th years to current time. Therefore, it is possible to conclude that interest to type of hip endoprostheses with native LT has been grow up from 90th and still remain at this level.

Figure 1. Flowchart of literature search according to PRISMA guidelines (31).
We identified 40 authors of patents for invention of hip endoprostheses with native LT or its analog, their nationalities are shown in figure 3. The dominated activity – 60% of patents was registered at the US, the second place is 17.5 – Denmark, third (10%) Soviet Union. All the others are less than 3%.

The risk of bias regarding the applicability and the rational technical essence of identified hip prosthesis designs with native LT or its analogs is ranked in table II. It is no commercial endoprostheses with LT in this time. A few construction were applied at clinics, however, results are not clear.

The identified designs of endoprostheses with native LT or its analogs were grouped by type and presented in table III (see also figures 4-6).
Table II. Risk of bias regarding endoprosthesis applicability.

<table>
<thead>
<tr>
<th>Bias assessment criteria</th>
<th>Patent document</th>
<th>Non-patent document</th>
<th>Risk of bias (1 – min; 4 – max)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Commercial production and use in clinical practice</td>
<td>Not found</td>
<td>Not found</td>
<td>1</td>
</tr>
<tr>
<td>Small-batch production and use in clinical practice</td>
<td>[35]</td>
<td>[32]</td>
<td>2</td>
</tr>
<tr>
<td>Individual production and use in clinical practice</td>
<td>[37]</td>
<td>[33]</td>
<td>3</td>
</tr>
<tr>
<td>Design description without use in clinical practice</td>
<td>[30, 34, 36, 38–52]</td>
<td>Not found</td>
<td>4</td>
</tr>
</tbody>
</table>

Table III. Distribution of endoprostheses by the type of design.

<table>
<thead>
<tr>
<th>Type</th>
<th>Description of design</th>
<th>Description of practical use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spacer prosthesis</td>
<td>[46]</td>
<td>Not found</td>
</tr>
<tr>
<td>Surface replacement arthroplasty</td>
<td>[41, 43, 45, 50]</td>
<td>Not found</td>
</tr>
<tr>
<td>Partial endoprosthesis</td>
<td>[41, 46]</td>
<td>Not found</td>
</tr>
<tr>
<td>Unipolar partial hip endoprosthesis</td>
<td>[30, 34-37]</td>
<td>[32, 33, 35, 37]</td>
</tr>
<tr>
<td>Bipolar partial hip endoprosthesis</td>
<td>Not found</td>
<td>Not found</td>
</tr>
<tr>
<td>Total hip endoprosthesis</td>
<td>[38-40, 42, 44, 45, 47-49, 51, 52]</td>
<td>Not found</td>
</tr>
<tr>
<td>Revision endoprosthesis</td>
<td>Not found</td>
<td>Not found</td>
</tr>
<tr>
<td>Tumor endoprosthesis</td>
<td>Not found</td>
<td>Not found</td>
</tr>
</tbody>
</table>

Figure 4. Unipolar partial hip endoprosthesis with an artificial LT, which is indicated by the number 36 (30).

Figure 5. Total hip endoprosthesis with an artificial LT, which is indicated by the sing TL (52).
Figure 6. Surface replacement arthroplasty with the native LT, which is indicated by the number 56 (43).

The friction pair characteristics and combination of materials are of great importance for the endoprosthesis functioning. The designs of the reviewed hip prostheses with native LT or its analog were grouped by friction pair materials and presented in Table IV.

DISCUSSION

Most of the hip endoprostheses designs with native LT or its analog that passed the final screening date back to the first decade of the 21st century. That was the period of extensive introduction of methods for hip arthroscopy and a growing use of magnetic resonance and computed tomography, and the number of publications mentioning the LT increased significantly. Another possible explanation for the fact is that the growing number of hip replacements was associated with the growing number of implant dislocations. This, again, stimulated the efforts to improve anti-luxation prostheses.

Based on the risk of bias regarding the applicability criterion, most of the proposed devices have the maximum risk rating of 4. We have failed to identify any commercially available endoprostheses with native LT or its analog, and hence any devices with the minimum risk rating of 1. Only two subtotal hip endoprostheses with an LT analog are known to have been used in clinical practice. The first one – a subtotal endoprosthesis designed by G.E. Dudko – has been implanted since 1984, and its risk-of-bias can be rated as 2 (35). The second one – proposed by V.A. Neverov and V.A. Shilnikov – has been used since 1990 and is assigned a risk-of-bias rating of 3 (37). The short-term outcomes of their medical use were assessed as satisfactory (32, 33, 35, 37). We have not succeeded in finding any long-term outcomes of these surgical interventions in the literature. Scanty publications about the practical use of hip endoprostheses with an LT analog do not allow any firm conclusions about their benefits and drawbacks. Of all known endoprostheses designs that propose the use of native LT or its analog, 18 have never been implanted and there are no available reports on their laboratory and clinical trials. The endoprostheses with native LT and its analog included in the review fall under the existing classification of implants for hip arthroplasty. However, the specific nature of patent documentation allowed the authors to claim their proposed technical solution as belonging to several types and, in some cases, not to specify the type of design at all. We classified 11 of the identified endoprostheses as total hip endoprostheses (Table III), 5 as unipolar partial hip endoprostheses (subtotal endoprosthesis, subtotal hip prosthesis system), 4 as surface replacement arthroplasty (mould arthroplasty), 2 as partial endoprostheses, and 1 as a spacer prosthesis.

We failed to identify any bipolar partial hip endoprostheses, revision endoprostheses or tumor endoprostheses (e.g., pelvis tumor-prosthesis) with an LT analog. Some of the identified devices (Table III) for surface replacement arthroplasty, partial acetabular rim arthroplasty and spacer endoprostheses are claimed as intended for retention of the LT (41, 43, 46, 50). These endoprostheses repeat the form of a part of the femoral head articular surface or the lunate surface of the acetabulum and, generally, have a horseshoe shape. However, there are some similar devices, of a similar shape (C-shaped, U-shaped, lunate), whose description has no mentioning of the LT. The technical idea behind the C-shape is to help preserve the fat pad in the acetabular fossa, preserve its blood supply, and ensure normal functioning and natural lubrication of the joint (53, 54).

Most of the proposed hip endoprostheses with native LT or its analog are supposed to use a metal head, less often, a polymer one, and quite rarely, a ceramic one (Table IV). Some authors propose various embodiments of friction pair, which do not exclude the use of native cartilage for one of the components (45, 46, 50). Although some inventions do not specify the type of friction pair, it can be assumed from
the context that their proposed endoprosthesis has a metal head (30, 36, 38, 39, 51, 52). Yet other designs do not clearly state it either, but one can surmise that the endoprosthesis head or the acetabular liner is made of a polymer material (35, 48, 52). We have found design embodiments with a non-detachable articulating system in the form of an industrially manufactured monobloc (42, 47, 49). In some endoprostheses, the articulation system is supposed to be enclosed by an analog of the joint capsule: a cuff or a cover made of a synthetic material (38). In rare cases, it is proposed to use a lubricant in the friction pair (43, 47). Some endoprostheses use native LT, others, a modified one, and still others replace it by a specially designed analog. It is proposed that healthy native LT should be retained in surface replacement arthroplasty, spacer prosthetics and in total hip arthroplasty (41, 43, 46, 48, 50). If the native LT is not healthy, it can be reinforced with an artificial structure (48). As noted in the device descriptions, an LT can be reconstructed using biological tissues (auto-, allo- or xenografts), polymer materials, and combination thereof (35-37, 39, 42, 44, 45). There are known proposals to make LT analogs of metal, in the form of rods, chains or cords (30, 34, 38). Some designs provide LT analogs with a protective coating (45, 47), others, with a coating that carries a drug, e.g., an antibiotic (52). It has also been proposed to make an external deformable coating for LT analog and put antibiotics inside (45). Assuming that an LT analog can be damaged during its use, various methods for its repair are discussed (47).

Some endoprostheses are proposed to be supplemented with artificial analogs of external ligaments (39, 44, 48). Here, we should note that there is a method for creating artificial external ligaments to prevent post-arthroplasty dislocation. The method was tested in practice and proved useful (55-60). The above-said supports the feasibility of supplementing hip prosthesis with native LT or its analog, analogs of external ligaments, and retaining them whenever possible during arthroplasty. The most tricky and highly specialized aspect of creating endoprostheses with an LT analog is to provide conditions for the element functioning, proper positioning of its attachment areas, its geometric and mechanical properties. The lack of fundamental experimental and clinical studies of these issues makes it impossible to evaluate properly all data presented in the reviewed sources.

**CONCLUSIONS**

Among patents for inventions, we have identified 20 descriptions of various hip endoprosthesis systems which include native LT or its analog. At the same time, there is an apparent new trend in arthroplasty – creation of endoprostheses that are structurally similar to the natural joint and include the ligamentous apparatus as their structural component. There is need for further studies of mechanical impacts on an LT analog and its attachment area, the nature of its connection with the other parts of the endoprosthesis. These issues are among the least developed in this field. Prevention of post-operative dislocations requires developing new surgical approaches and methods for placing an endoprosthesis while retaining or adequately reconstructing the natural ligamentous apparatus. The variety of the already available designs demonstrates multiple potential solutions to the pressing problems of arthroplasty, on the one hand, and the scarcity of basic data, on the other. Creating such endoprostheses seems quite realistic. However, it requires extensive preliminary research and development efforts. These devices can likely make a line of implants for staged arthroplasty, from simple and small ones, requiring minimal removal of native tissues, to complex and massive reconstructive and oncologic endoprostheses. The common distinguishing feature of the new-generation endoprostheses should be the ideology of retaining or reconstructing the ligamentous apparatus of the hip joint.
DECLARATIONS
This work submits to the ethical standards of the Muscles, Ligaments and Tendons Journal (61). All data and material are available upon request from the corresponding author.

CONTRIBUTIONS
S.V.A: design of investigation, collecting the data and its systematization, analysis the data, writing a draft; D.V.S: conception and design of investigation, system analysis the data, revising the text; S.V.A and D.V.S: writing text; all authors discussed the results and commented on the manuscript at all stages.

CONFLICT OF INTERESTS
The authors declare that they have no conflict of interests.

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Estimating the Dynamic Ratio of the Lateral/Medial Hamstrings. A Case Control Study

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INTRODUCTION
The hamstring muscles comprise the biceps femoris muscle laterally and the semimembranosus and semitendinosus muscles medially. Crossing both the hip and knee joints, they produce both hip extension and knee flexion. Muscle strain injuries of this group are common in running based sports and are the most frequently reported injury in track and field (1). At the 2011 IAAF World Championships, hamstring strains were the most common injury, with 67% of them resulting in absence from sport. Increased repeated use of the hamstring was the predominant cause of injury (1) and approximately...
80% of hamstring strains involve the long head of the biceps femoris (2).

A systematic review of hamstring muscle strain injuries in sport found the most consistent risk factors for this injury to be intrinsic factors such as age, previous hamstring injury and an increase in quadriceps peak torque (3-5). The available evidence for hamstring weakness as a risk factor for injury is conflicting: a recent meta-analysis did not support strength deficit as a risk factor (3), but the aetiology of hamstring injuries is multifactorial (6), and hamstring strengthening is an important component of injury prevention programmes (7). Isokinetic dynamometry is widely used in the assessment of the hamstring strength (8). In 614 soccer players (9) there was a small but significant association between lower hamstring eccentric strength and increased risk of injury. Using isokinetic strength testing, side to side differences in hamstring peak torque and decreased strength of the hamstrings to quadriceps, or H:Q ratio, have been suggested as risk factors for hamstring injury (10). Although it is difficult to generalise and no definite consensus exists, the normal H:Q ratio is considered to be 50% to 80% over the full range of knee motion (11). A side-to-side difference of > 10% is generally considered abnormal (12). In 6 sprinters with an acute hamstring injury, Sugiyama et al. reported a significantly decreased eccentric and concentric peak torque in the injured vs non-injured limb and in H:Q ratio (13). Electromyography (EMG) records and quantifies the electrical activity associated with contracting skeletal muscle fibres (14). Each of the hamstring muscles has different properties in terms of architecture (15) and contraction activation patterns on EMG, depending on whether they act as knee flexors (16) or hip extensors (17). Heterogeneous hamstring activation patterns are evident during different strength training exercises and during the gait cycle or sprinting (18), indicating complex neuromuscular coordination patterns. Previously injured hamstrings exhibit altered muscle activation patterns, with earlier EMG onsets for both the biceps femoris and medial hamstrings in preparation for single leg standing compared to the control group (19). In contrast, the rate of torque development and onset of muscle activity as measured by EMG is not associated with future hamstring injury (20). Using functional MRI, a more symmetrical activation of the lateral (biceps femoris longus, BFL) and medial (semitendinosus, ST) hamstrings during a maximal voluntary isometric contraction. This information may be used to prevent hamstrings unilateral overuse and secure their kinetic activation and function.

MATERIALS AND METHODS

Participant characteristics

Eighteen male elite track and field athletes (ten sprinters, five long jumpers, three triple jumpers; mean age 24.4 ± 4.1 years; mean height of 177.4 ± 6.5 cm; mean body mass 78.8 ± 5.6 kg) from the Greek national team gave their written informed consent to participate in this study. None of them had reported a hamstring injury during the previous 6 months according to the clinic archives. Informed consent has been obtained from all individuals included in the study. The current study has been complied with the ethical standards of the journal (23) and all the relevant national regulations, institutional policies and in accordance the tenets of the Helsinki Declaration, and has been approved by the ethics committee of the Greek Track and Field Federation.

Methodology

The participants executed an isokinetic test to estimate the dynamic ratio between the Flexors and Extensors of the knee joint (H:Q ratio). Following that, an EMG of the biceps femoris longus and semitendinosus muscles during maximal voluntary isometric contraction (MVIC) was performed. The hamstrings dynamic ratio (HDR) was determined from the individuals who presented a isokinetic H:Q ratio within the range 55-70% and with a side to side difference in the ratios no greater than 6 units.

Isokinetic test

An isokinetic dynamometer (CSMI, Lumex, Ronkonkoma, NY, USA) was used. The participants completed a warm up of 10 minutes of submaximal cycling and 10 minutes of static stretching of the thigh muscles (quadriceps/hamstrings and adduction/abduction), preceded by familiarization with the isokinetic dynamometer with five submaximal repetitions performed at low, medium and high angular velocities (90-120-180°/sec). The subjects were strapped in the dynamometer according to standard practice. The range...
of motion was set at 120° (0° full extension). The angular
velocity of both flexion and extension was set at 60°/sec, for
5 repetitions at the highest possible effort. Visual (screen)
and verbal (tester) feedback were used to encourage that
each athlete performed at his maximum.

EMG recording
EMG recording was performed using the 8-channel
Biomonitor ME6000 (Mega Electronics Ltd, Linton, UK).
Prior to EMG recording, the skin of each participant was
shaved, sand-papered, and carefully cleaned with 70% alco-
hol. The biceps femoris longus and semitendinosus muscles
were sampled, as they are the most commonly affected
muscles in case of injury to the posterior thigh muscles.
Disposable pre-gelled self-adhesive bipolar surface elec-
trodes (Ag/AgCl, 0.8 cm in diameter, Blue Sensor N-00-S,
Medicotest A/S, Ølstykke, Denmark) were placed on the leg
with an inter-electrode distance of 2 cm in accordance with
SENIAM (Surface ElectroMyoFigurey for the Non-Invasive
Assessment of Muscle) guidelines (http://www.seniam.org).
This protocol was used to measure the electrical
activity of the relevant muscle during MVIC.

Each participant was given a detailed presentation of the
procedure for the MVICs and allowed to familiarise with
the isometric test on the isokinetic dynamometer. The
participants were prone, with the knee stabilized at 45°
of flexion, with neutral rotation of the tibia. The subjects
performed two or three isometric contractions at almost
50% of maximum perceptual effort as a warm-up. During
the actual test, they performed three MVICs lasting five
seconds each, with a five second rest between each contrac-
tion. The EMG signal (µV) from the two recorded channels
was averaged. Standardized verbal encouragement and
visual feedback from the monitor was given to each partic-
ipant. After a root-mean-square (µV) adjustment, the trial
with the highest averaged EMG signal was chosen, and then
the 80% value of the last 3 seconds of this trial, was used
as the final MVIC value (figure 2). The hamstrings dynamic
ratio (HDR) between the BFL and ST muscles was calcu-
lated based on the BFLEMG/STEMG percentage value.

Statistical analysis
Group separation for comparison analysis
Based on the isokinetic H: Q ratio, the participants were
separated in two groups: Group 1 (N = 10): athletes with a
H: Q ratio range 55-70% and no side to side difference of the
ratios more than 6 units; and Group 2 (N = 8) athletes with a
H: Q ratio outside of the 55-70% range and/or a side to side
difference of the ratios greater than 6 units (figures 3, 4 A).
Descriptive statistics were performed to calculate mean/
median/range/percentiles and SD of the (HDR) and Isoki-
netic H:Q ratio, for each group. A paired samples t-test was
also performed, between the groups, for each variable.

RESULTS
The athletes in Group 1 had a dynamic ratio of BFL/ST,
based on the EMG, of 78.4 (SD = 5.1). The mean BFL/ST
Figure 3. H:Q Isokinetic ratio in Group 1 (A) and in Group 2 (B).

Figure 4. (A) Isokinetic H:Q ratio for the Right and Left leg between groups. (B) Hamstring dynamic ratio (HDR): medians and range between groups.
ratio for the Group 2 was 69.3 (SD = 18.9) (figure 5). There were no statistically significant differences in the BFL/ST ratio between the groups (p = .179). The values in Group 1 athletes showed less variation (r = 18.5), with a median of 79.9 compared with the values in Group 2 athletes (r = 51.9) with a median of 69.3 (figure 4 B). The results in Group 1, coupled with the specified bilaterally dynamic balance (H:Q ratio), show that the Hamstring dynamic ratio (HDR) between BFL and ST muscles is around 78% (figures 4 B, 5).

**DISCUSSION**

The main result of the present study is that, in elite uninjured track and field athletes with H:Q ratios within the normal range and no side-to-side asymmetry, the HDR of BFL/ST muscle activity during isometric hamstring contraction is around 78%. Although not significantly different in this population of elite track and field athletes in the present investigation, the HDR in athletes with strength asymmetries or H:Q ratios out of the normal range were lower, around 69%.

These results are in part in keeping with the study by Scheurmans et al. (21), who used functional MRI to assess individual hamstring muscle activation during eccentric exercise. In that investigation, the biceps femoris and semitendinosus muscles engage in complex synergistic activation patterns during eccentric exercises, with more symmetrical degrees of activation in the injured group, together with higher overall levels of metabolic activity in the hamstring group. This would suggest that a more symmetrical muscle activation pattern during a hamstring task may imply a less efficient maladaptive compensatory mechanism.

**Practical implications**

The lateral to medial ratio difference in our population may imply a change in muscle activation patterns in those athletes possibly more prone to hamstring injury, as suggested by altered H:Q ratios and side to side strength asymmetries. Obviously, the design of the study does not allow to ascertain which factor is causative or reactive. However, the present study contributes to a greater understanding of the characters of hamstring muscles contraction in healthy athletes.

**CONCLUSIONS**

A proposed HDR of 78% between lateral to medial hamstrings could be used as a risk factor for hamstring injuries in athletes with hamstring muscle imbalances. Better characterisation of the normal patterns of hamstring muscle activation will allow targeted rehabilitation to address specific neuromuscular coordination patterns, using exercises that preferentially target individual muscles of the hamstring group.
Limitations
In the present study, we did not investigate the pattern of activation of the semimembranosus muscle (SM), which acts together with the semitendinosus as a medial knee flexor. This was because of the difficulty to collect clear EMG signal from this muscle. We therefore assumed that the dynamic EMG outputs collected from the ST muscle are representative of the activity of the SM, given their analogous mechanical and physiological function.
We acknowledge that the current study was relatively small. However, they were all elite track and field athletes who regularly competed in international competitions up to world and Olympic level. In this respect, it would be difficult to recruit a larger population. We nevertheless acknowledge that further work to examine muscle activation during hamstring contractions with larger cohorts is needed. Additionally, recent literature (24) has shown different incidence rate and different hamstring injury distribution in younger athletic population, and therefore the results could be different in according to the age of the athletes. Another limitation is that the study entry criteria did not exclude other peripheral injuries in the ipsilateral lower extremity, which could be a factor of potential alterations in hamstring muscle activity (25).
In the future, it would be interesting to examine not only the amount of muscle activity but the timing of muscle activity as well. EMG would allow assessing the timing of muscle activation to be assessed, an advantage over functional MRI. Then, following athletes longitudinally would allow understanding whether altered synergistic relationship between the medial and lateral hamstrings on isokinetic testing is associated with injury development. However, such study would necessitate large number of athletes, and relatively long periods of observation.

CONTRIBUTIONS
Nikolaos Malliaropoulos planned the study and contributed to write the manuscript. Panagiotis Tsaklis performed the data collection and statistical analysis. Georgios Bikos, Dev Pyne and George Kakavas contributed to write the manuscript. Nicola Mafulli contributed to interpret the data, and wrote and edited the manuscript. All authors have read and approved the final version of the manuscript, and agree with the order of presentation of the authors.

ETHICS
The ethics committee of the Greek Track and Field Federation approved the study.

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CONFLICT OF INTERESTS
The authors declare that they have no conflict of interests.

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A 90 Minute Soccer Match Induces Eccentric Hamstring Muscles Fatigue

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SUMMARY
Background/Purpose of the study. Hamstring injuries are the most prevalent muscle injuries in both amateur and professional soccer (football) players. Eccentric strength deficits and muscle strength imbalances have been associated with an increased risk of muscle injuries. The current study is a non-randomised observational study investigating whether fatigue significantly reduces peak eccentric strength of the hamstring muscle group.

Methods. Twenty-two right leg dominant professional football players participated in this study. None were injured or were rehabilitating from an injury at the time of testing. The eccentric strength of the hamstring muscles was determined using the Nordic exercise on a Norbord device prior to a 90 minute soccer match and after its end.

Results. There was a significant decrease in eccentric strength at the end of the match (before the match: M = 306.91, SD = 59.26; after the match: mean = 277.77 ± SD = 60.35 p = .000, Cohen’s d = .50). The imbalance in eccentric hamstring muscle strength between dominant and non-dominant limb before the match remained unchanged after its end.

Conclusions. A professional football match significantly impacts on the ability of players to produce high speed eccentric strength in the hamstring muscle groups. Resistance to fatigue and eccentric strength, particularly at high speeds, are considerable factors in conditioning of professional soccer players. Eccentric muscle strength fatigue of the hamstring muscle group after a 90 min soccer match may provide a possible explanation for the greater risk of hamstring injuries under fatigue conditions.

KEY WORDS
Adaptation; hamstring; injury prevention; risk factors scheduling.
BACKGROUND

Participation in a single football match leads to acute fatigue, with a decline in physical performance over the following hours and days. In elite professional soccer, players can play up to 70 competitive matches per season. Hamstring injury (HI) is the most prevalent injury in both amateur (1) and professional (2) soccer (football) players, with an increase in the annual incidence of 2.4% between 2010 and 2014 (3). Modifiable HSI risk factors such as eccentric knee flexor weakness (4) and muscle architecture, specifically biceps femoris fascicle length (4), are potential focus areas for HI injury prevention programs. A popular exercise choice for prevention of HI is the Nordic hamstring exercise (NHE), as it can influence both eccentric knee flexor strength and muscle architecture (4). Though ranked in the top five injury prevention modalities, compliance with the exercise is poor (5).

The adaptive response to eccentric strength training is multifactorial: it may include increases in motor unit discharge rate (6) and changes in muscle architecture, including hypertrophy and increase in fascicle length (7). The stimulus for hypertrophy is governed by mechanical tension and intramuscular metabolic stress (8), the degree of which may be influenced by the muscle status at either the beginning or end of football activity. Neuromuscular fatigue has central and peripheral origins. Central fatigue, preponderant during long-duration low-intensity exercises, may involve a drop in the central command (motor, cortex, motoneurons) elicited by the activity of cerebral neurotransmitters and muscular afferent fibers. Peripheral fatigue, associated with an impairment of the mechanisms from excitation to muscle contraction, may be induced by a perturbation of the calcium ion movements, an accumulation of phosphate, and/or a decrease of the adenosine triphosphate stores (8).

The present study examined the changes in eccentric strength of the hamstring muscle group to ascertain whether the fatigue induced by a 90 minute match by elite professional soccer players influences two of the major risk factors for hamstring injury, namely 1) eccentric strength of the hamstring muscle group and 2) between limb imbalance in eccentric strength of the hamstring muscle group (9). Therefore, the current study tested the null hypothesis that a 90 minute match by elite professional soccer players did not produce any changes in the eccentric strength of the hamstring muscle group and did not result in changes in between limb imbalance in eccentric strength of the hamstring muscle group.

MATERIALS AND METHODS

Twenty-two professional football players (Mean ± SD: Age: 19.3 ± 2.9 year; Height 185.0 ± 8.7 cm; Body Mass 81.6 ± 6.7 kg) participated in this study. All players were right dominant (defined as their preferred kicking leg). Subjects were included in the study if they were not injured or rehabilitating from an injury at the time of testing. Ethics approval for the study was granted by our University. Written informed consent was obtained from each player or their legal guardian prior to data collection. Participants were blinded to the study hypothesis. The study was carried out in accordance with the ethical standards of the journal (10) and with the Declaration of Helsinki, and was approved by our local Ethics Committee.

The game was played in the second half of the competition season. The eccentric hamstring strength of players was assessed using the NORDBORD (Vald Performance, Queensland, Australia) device prior to the 90 minute football match. The Nordic board test was used to measure hamstring strength based on the NHE. We used 2 NORDBORDS per each team, and each athlete undertook a NORDIC exercise on the NORDBORD. The 11 players in each team completed the testing procedure within 20 min before and after the match.

Data analysis

The Shapiro-Wilk test confirmed that the data followed the normal distribution. We tested whether the eccentric force of the right and left hamstring muscle group in each player changed before and after the match, using a paired sample t-test and one sample t-test. Cohen’s d index was used to estimate the intensity of the difference whenever that was necessary. The statistical analysis was conducted by using the statistical software SPSS 23.0.

RESULTS

There was a significant difference in the eccentric strength of the hamstring muscle group before a match (M = 306.91, SD = 59.26) compared to after the match (mean = 277.77 ± SD = 60.35, p = .000, Cohen’s d = .50). The 95% confidence interval (24.00, 34.68) showed a decrease of 7.82% to 11.30% from the pre-match eccentric force (M = 306.91) of the athletes (figure 1). There was no statistical difference between the mean value of hamstring imbalance between the right and left hamstring (M = 1.49, SD = 8.96) and zero value; t(21) = .777, p = .446. Also, the bootstrap 95% confidence interval (−2.18, 5.11) suggest that there is no hamstring imbalance (figure 2).
Figure 1. Eccentric strength before and after the exercise, 95% confidence intervals.

Figure 2. Hamstring testing imbalance (after the exercise), 95% confidence intervals.
DISCUSSION

Soccer involves sprinting, changes in direction and running speed, jumps and tackles, as well as technical actions such as dribbling, shooting and passing. Fatigue may induce a decline in performance. In soccer, fatigue occurs temporarily after short-term intense periods in both halves, towards the end of the match, and persists after the match. Rampinini et al., for example, observed reductions in knee extensor maximal voluntary activation and electromyographic activity and a decrease in knee extensor peak torque responses to paired stimulations after a match (11). Match-related fatigue results from a combination of central and peripheral factors, involving mechanisms from the central nervous system to the muscle cell itself and energy production. The present investigation showed a significant decrease in eccentric strength of both right and left hamstring muscle groups after the game, with no change in muscle imbalance detected between the left and right hamstring muscle groups. Factors associated to an increased risk of muscular strain injury include poor muscle strength, particularly eccentric strength deficits, and ipsilateral muscle strength imbalances (12). The temporal pattern of injury during match play also suggests that fatigue is a factor in injury causation, with 47% of match-play hamstring strains incurred during the latter stages of each half (11). Soccer is characterised by an irregular and intermittent activity profile; this intermittent nature places great emphasis on acceleration and deceleration phases of sprinting (13).

Fatigue has become a hot topic in football, and is regarded as a complex and multi-factorial phenomenon (11). There is growing interest as to how fatigue relates to recovery, player fitness and effort during matches. To avoid exhaustion before the final whistle, players may adopt a pacing strategy that allows them to be involved in demanding and critical moments, even during the final stages of a match (14). The regulation of self-chosen high intensity activity is also an important product of training, as players need to learn to adopt pacing strategies that will allow a high effort even during the final stages, and whenever required of the match situation (15). Fatigue during a soccer match has been associated with decreased eccentric hamstring strength, and this may be related to increased hamstring injury risk: nearly half of all hamstring injuries occur during the final 15 min of each half. Therefore, it could be hypothesized that fatigue during the later stages of a soccer match may increase the predisposition to hamstring strain injury by negatively altering the biomechanics of sprinting in relation to muscle flexibility, muscle strength, or body mechanics (16).

There is a significant decrease in eccentric hamstring strength during simulated soccer match-play (17). A complex neuro-muscular coordination pattern is necessary during the running cycle (18). Therefore, if the hamstrings are not able to produce sufficient strength to decelerate the limb during the latter part of the swing phase, eccentric overload could cause tears at the musculotendinous unit (19). Hamstring injuries are most frequently sustained at the end of matches and training sessions (11). This would support the notion that fatigue may be a predisposing factor for such injuries. Any factor that adversely affects the appropriate running pattern may result in injury. The dual innervation of the biceps femoris may cause asynchrony, as poor coordination may allow separate parts of the muscle to activate at different times. The observed decline in eccentric hamstrings strength might be attributed to the greater contribution of the hamstrings in controlling the intermittent running profile (2). Additionally, as sprinting is a primary mechanism of injury, the frequency of speed changes places greater emphasis on the acceleration and deceleration phases of the running cycle (20). The increased muscle contribution from the biceps femoris in maintaining running mechanics during the intermittent protocol, in parallel with the decrease in peak eccentric strength, may further increase the risk of injury.

The test-retest reliability of the NORBORD device (4) is high to moderate when NHE measurements were performed bilaterally, but there is poor reliability during unilateral testing. Also, elite athletes with a unilateral history of hamstring injury within the previous 12 months displayed significant eccentric knee flexor weakness in their injured limb and to the limbs of uninjured recreational athletes (21). In our setting, the results obtained were valid and reliable. Most biceps femoris injuries occur at the end of matches and training sessions (2). Moreover, when soccer players become fatigued during maximal sprinting (22), early activation of the biceps femoris and semitendinosus muscles occurs during the swing phase of the cycle (23). This recruitment pattern may result from local muscle fatigue, and may be causative of hamstring strains (24). In agreement, as fatigue increases, so does biceps femoris activity during knee extension (concentric quadriceps contraction) movements in recreational soccer players (24).

All these studies highlight a possible positive relationship between fatigue and hamstring strains. Despite this plausible link, however, to our knowledge no study examines these variables in elite athletes. However, in vitro animal studies further support such hypothesis (15). The extensor digitorum longus muscles from 48 rabbits were fatigued to different levels of severity, then stretched to failure, and compared with their non-fatigued contralateral controls. Fatigued muscles are able to absorb less energy before reaching the degree of stretch that causes injury, suggest-
ing that fatigue is an important factor in the pathogenesis of acute muscle strains (23). However, it should also be noted that muscles were injured at the same length, regardless of fatigue. Fatigued player may become more susceptible to both muscular strain injury and impaired joint stability (22). Coaching and medical staff need to ensure that players are sufficiently warmed up before the start of the second half of the match, and that their eccentric hamstrings strength is well developed and resistant to fatigue.

Limitations
We are aware that this investigation included a relatively small number of participants, and this would limit the generalizability of our findings. However, we point out that our study included only elite professional players who were extremely well trained, and that the index match occurred in mid-season.

CONCLUSIONS
Soccer specific fatigue can influence the eccentric strength of the hamstring muscle group, and thus exert an influence of the propensity of football players to injury to these muscles. However, it does not exert any influence on the imbalance of the hamstrings between the dominant and non-dominant leg. These findings highlight not only the susceptibility of eccentric hamstrings strength to fatigue but also the influence imposed by movement speed. The present study confirms previous findings (25) but was performed in real match play conditions, and therefore is even more specific and valid.

Strength work is a fundamental component of the conditioning program in professional soccer. However, strength and speed training tend to be addressed only when the players are well rested. Such practices may not provide the best mode of intervention to prevent the increased injury incidence observed late in the game. Resistance to fatigue and eccentric strength, particularly at high speeds, should be given greater consideration in conditioning for soccer.

Practical implications
There was a significant decrease in eccentric strength of both hamstrings before and to after the game.

There was no effect on muscle imbalance between the dominant and non-dominant hamstring muscle group. Coaches, fitness coaches, rehabilitation specialists and sports medicine doctors should be made aware that a single match impacts negatively on the ability of football players to develop eccentric strength in the hamstring muscle group, so that they can plan training and prevention programmes adapted to these findings. Soccer specific fatigue affects the eccentric strength of the hamstring muscle group. There is significant decrease in eccentric strength of both hamstring muscle group after a match. Future injury prevention strategies may need to consider reducing negative effects of fatigue.

CONTRIBUTIONS
All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by Georgios Kakavas. The first draft of the manuscript was written by Georgios Kakavas and Tim Gabbett, Michail Mitrotasios, Nicol Van Dyk, Nikolaos Malliaropoulos, Georgios Bikos and Nicola Maffulli participated to review and editing of the manuscript. All authors read and approved the final manuscript.

RIGHTS
All procedures performed in the current study involving human participants were in accordance with the ethical standards of the Atromitos Fc Ethics Committee (reference number 1023) and with the 1964 Helsinki declaration and its later amendments.

INFORMED CONSENT
Written informed consent was obtained from each player or their legal guardian prior to data collection.

CONFLICT OF INTERESTS
The authors declare that they have no conflict of interests.

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Quick Recovery and No Arthrofibrosis in Acute Anterior Cruciate Ligament Reconstruction: a Prospective Trial of Early versus Delayed Reconstruction

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INTRODUCTION

The annual anterior cruciate ligament (ACL) injury incidence reported rates for professional athletes ranges from 0.15% to 3.67% and it is higher than national population rates (median rate of 0.03%) (1). Although ACL reconstruction (ACLR) is considered a safe and effective procedure regardless of age (2), most reconstructions are performed in young active athletes or in patients with physically demanding occupational pursuits who are keen to resume sports or work activities as soon as possible (3). Early surgery and rehabilitation were considered as important prerequisites for a quick recovery, however, the timing of reconstruction is a debated topic (3). Historically, delayed ACLR has been recommended since some studies reported a risk of arthrofibrosis and suboptimal clinical outcomes associated with early surgery, accordingly ACLR is often delayed recovering range of motion (ROM) and muscle strength through a preoperative rehabilitation protocol (4, 5).
Recent studies, otherwise, reported no risk of arthrofibrosis with acute reconstruction showing similar or better outcomes than delayed ACLR (6, 7). Furthermore, early surgery seems to be more cost-effective and can decrease the risk of subsequent meniscal or cartilage lesions by reducing the time between injury and reconstruction (8-10). Systematic reviews tried to answer this question, however, because of the lack of high-level studies and considerable overlap in the definition of acute versus delayed reconstruction, it was difficult to come to conclusions (3, 11-13).

In more recent systematic reviews and meta-analysis, with the definitions for early and delayed reconstruction set at < 3 weeks and ≥ 3 weeks respectively, the authors found no differences regarding patient reported outcome measures (PROMs) and objective clinical assessments comparing early and delayed ACLR (14, 15). The aim of this study was to compare clinical outcomes following ACLR performed in a very early phase post injury (maximum 2 weeks injury-surgery interval) with those of surgery performed at least 3 weeks post injury and to evaluate ROM difference at different follow-ups.

METHODS

All patients with a clinical and magnetic resonance imaging (MRI) diagnosis of ACL complete lesion, examined in the emergency department or the clinic of our hospital, were eligible for inclusion during a 1-year period beginning September 2018. Inclusion criteria applied were unilateral primary ACL complete lesion diagnosed by positive Lachman and Pivot shift test and confirmed by MRI, age between 18 and 50 years, contralateral healthy knee, availability for early reconstruction and supervised rehabilitation protocol. Exclusion criteria were as follows: fibular collateral or posterolateral corner injury requiring surgery, medial collateral ligament (MCL) lesion greater than grade 1, posterior cruciate ligament (PCL) insufficiency, cartilage damage (grade 3 or 4 according to Outerbridge classification) (16); any prior surgery in the involved or contralateral knee, BMI > 30, no radiographic signs of osteoarthritis, rheumatological disorders, associated malalignment (severe valgus > 7 degree or varus knee deviation > 10 degree), genu recurvatum (> 5°), Beighton score 4 or more (hyperlaxity).

Patients meeting the eligibility criteria were prospectively enrolled in the study after informed consent was obtained. Patients who underwent surgery within 14 days of injury were assigned to group 1 (early ACLR) while patients who came to visit after two weeks from trauma or who chose to undergo late treatment were assigned to group 2 (delayed ACLR). In the delayed reconstruction group, ACLR was preceded by a preoperative rehabilitation protocol aimed to recover full range of motion and muscle tone and trophism. The study was approved by the local Ethical Committee (Nr. 0031/2018). All patients provided informed consent prior to participating in the study in accordance with the Declaration of Helsinki (1964). The study meets the ethical standards of the journal (17).

Surgical technique

An arthroscopically assisted anatomic single-bundle 2-incision technique using doubled semitendinosus and gracilis tendons (DGST) autografts was used for all patients. A standard tibial guide at 60-65° was placed at the centre of the anatomic footprint of the ACL. The tunnel was drilled with the same diameter of the graft with an outside -in technique. On the femoral side, a 25-mm-long bone socket was drilled with retrodrill (Flipcutter, Arthrex, Naples, FL) using a femoral guide at 100°-110° that was placed midway between resident ridge and over the top position (18). The graft was passed through the tibial tunnel to the femoral socket and then fixed with the ACL TightRope (Arthrex, Naples, FL) on the femoral side and a bioabsorbable screw (Bio-Interference Screw; Arthrex, Naples, FL) on the tibia, sized 1 mm greater than the graft diameter and 28 or 35 mm in length.

Post-operative protocol

Pain relief after surgery was based on Paracetamol 1 g every 8 hours and NSAIDs (non steroidal anti-inflammatory drugs) as needed. In all patients the knee was placed in a full extension brace immediately after surgery, the first post-operative day partial weight-bearing was allowed as tolerated with crutches and the brace and daily isometric exercises were prescribed. The patients started physical therapy the day after surgery. After the hospital discharge, all the patients have done outpatient physiotherapy; they started progressive ROM exercises from the first postoperative day with the aim to maintain full extension and progressively recover flexion. At two weeks postoperatively, the patients come for a visit, medication of the surgical wound and suture removal. At this time the brace was unlocked to 0°-90°. All patients were focused on reaching a full range of motion and full weight-bearing within 4 weeks. The brace and the crutches were abandoned at 4 weeks postoperatively. From the second month post-operatively, a heavier muscle-strengthening program was prescribed. Patients began gradual noncontact athletic activity and sport-specific training at 3 months. Return to full sports activities was allowed if the neuromuscular function had recovered, which usually occurs within 5-6 months. Timing and objectives of the postoperative physical therapy protocols are reported in table I.
Follow-up evaluation
All patients were re-evaluated at 2, 4, 8, 12 and 24 weeks postoperatively by the same observer, a structured physiotherapist, who was independent and not involved in the initial surgery and blinded for the timing of the reconstruction. A standard physical knee examination with stability testing (Lachman and Pivot shift test) and passive ROM measurement, using a goniometer, were performed at each follow-up. Knee injury and osteoarthritis outcome score (KOOS) (19), Tegner Lysholm score (20), and International Knee Documentation Committee (IKDC 2000) (21) were obtained at final follow-up as well as manual maximum (MM) KT1000 evaluation (Medmetric, San Diego, USA). Single leg hop test and thigh circumference measurement (10 cm proximal to the proximal pole of the patella) were also performed at final follow up (22). The Limb Symmetry Index (LSI) was calculated for all hop tests by dividing the result for the injured leg by that of the uninjured leg and multiplying by 100 (LSI = injured leg / uninjured leg × 100) (22).

Statistical analysis
Data were analysed with IBM® SPSS® Statistics version 25 for MacOS, level of statistical significance was set at 0.05 (95% interval of confidence).

Table I. Rehabilitation protocol.

<table>
<thead>
<tr>
<th>Timing</th>
<th>Exercises</th>
<th>Goals</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-2 weeks</td>
<td>Brace locked in extension</td>
<td>Maintain full extension</td>
</tr>
<tr>
<td></td>
<td>Full weight-bearing using crutches and brace</td>
<td>90° of flexion</td>
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<tr>
<td></td>
<td>Static quadriceps exercises</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Gradual passive flexion up to 90°</td>
<td></td>
</tr>
<tr>
<td>3-4 weeks</td>
<td>Brace locked in extension</td>
<td>Brace discontinued at 4 weeks</td>
</tr>
<tr>
<td></td>
<td>Static and dynamic quadriceps and hamstrings exercises</td>
<td>Maintain full extension</td>
</tr>
<tr>
<td></td>
<td>Gradual passive flexion over 90°</td>
<td>Over 90° of flexion</td>
</tr>
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<td></td>
<td>Active muscle strengthening exercises</td>
<td></td>
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<tr>
<td></td>
<td>Patella mobilization if needed</td>
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<tr>
<td>4-8 weeks</td>
<td>Closed kinetic chain exercises for quadriceps and hamstrings</td>
<td>Full range of motion</td>
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<tr>
<td></td>
<td>Hamstrings training (isokinetic)</td>
<td>Full weight bearing</td>
</tr>
<tr>
<td></td>
<td>Proprioceptive and balance training</td>
<td></td>
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<tr>
<td></td>
<td>Stationary biking</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Full range of motion</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Full weight bearing without crutches and brace</td>
<td></td>
</tr>
<tr>
<td>8-12 weeks</td>
<td>Functional exercises</td>
<td>Muscle strengthening</td>
</tr>
<tr>
<td></td>
<td>Eccentric muscle contraction</td>
<td>Neuromuscular training</td>
</tr>
<tr>
<td></td>
<td>CKC (leg press, squat, step ups)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>OKC without weight</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Jogging straight ahead on a plain surface</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Swim</td>
<td></td>
</tr>
<tr>
<td></td>
<td>cycling</td>
<td></td>
</tr>
<tr>
<td>12-24 weeks</td>
<td>Increase OKC with weight</td>
<td>Return to sport</td>
</tr>
<tr>
<td></td>
<td>Concentric and eccentric training</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Jogging and running on an uneven surface</td>
<td></td>
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<tr>
<td></td>
<td>Jogging with turns 90°; 180°; 360°</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cutting with 45° changes of direction</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Acceleration and deceleration running</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Sport-specific exercises</td>
<td></td>
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</tbody>
</table>

CKC: closed kinetic chain; OKC: open kinetic chain.
Descriptive statistics were conducted considering the nature of the criteria examined. For quantitative data, we included the number of observations, means and standard deviations. For qualitative data, we described the number of observed values and the percentage of patients by category. Nominal variables were tested by Pearson’s χ² test. The distribution of values was assessed with the Kolmogorov-Smirnov test. The ordinal variables normally distributed data were compared using Student’s T-test while non-normally distributed data with the Mann-Whitney U Test.

We conducted a Relative Risk study to see if there was a risk of developing associated lesions over time injury-recon. A sample size calculation was performed using, as the primary outcome variable, the ROM in flexion. With a mean difference of 5° (corresponding to means of 130° versus 125°), the study will have a power of 90% to yield a statistically significant result with 5% risk of a type-one error, with a proposed sample size of 42 patients, 21 for each group (23).

RESULTS

At the end of the selection process, 52 patients were enrolled in the study; 26 were assigned to the acute group and 26 to the delayed group. Demographic data are displayed in table II. Mean time between injury and reconstruction was 7 days in group 1 and 271 days in group 2 (P < 0.001). Data regarding associated injuries are reported in table III. There were no differences in associated lesions between the two groups. The calculation of Relative Risk for the associated injuries between the two groups showed no differences. There were no cases of arthrofibrosis in both groups. No significative difference was detected between groups regarding the range of motion; mean flexion and extension values at each follow up are shown in (table IV). At 8 weeks, 78% of patients in the group 1 (acute surgery) reached full ROM while 64% of patients reached complete ROM in the group 2 (delayed surgery). Full range of motion was achieved at 12 weeks in both groups (figure 1).

At final follow up no statistically significant difference was found between the two groups concerning IKDC, KOOS and Tegner Lysholm Knee Scoring Scale evaluations as well as knee laxity clinical examinations and manual maximum side to side difference at KT1000 measurements. (table V) Results regarding muscle circumference and functional strength at the single leg hop test (OLH) showed no significative difference between groups. The mean LSI value was 92.8 in group 1 and 92.4 in group 2 (table VI).

<table>
<thead>
<tr>
<th>Table II. Demographic of the patient population.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age, mean ± SD</strong></td>
</tr>
<tr>
<td>Age, mean ± SD</td>
</tr>
<tr>
<td>female, n (%)</td>
</tr>
<tr>
<td>male, n (%)</td>
</tr>
<tr>
<td>BMI, mean ± SD</td>
</tr>
<tr>
<td>Smokers, n (%)</td>
</tr>
<tr>
<td>Occupation n (%)</td>
</tr>
<tr>
<td>Workers</td>
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<tr>
<td>Students</td>
</tr>
<tr>
<td>Type of Injury n (%)</td>
</tr>
<tr>
<td>Soccer</td>
</tr>
<tr>
<td>Rugby</td>
</tr>
<tr>
<td>Karate</td>
</tr>
<tr>
<td>Paragliding</td>
</tr>
<tr>
<td>Volleyball</td>
</tr>
<tr>
<td>Dance</td>
</tr>
<tr>
<td>Time injury - recon, ± SD</td>
</tr>
</tbody>
</table>

SD: standard deviation; ACLR: acute anterior cruciate reconstruction. Patient demographic are displayed as mean ± standard deviation (SD), number and percentage.
Quick Recovery and No Arthrofibrosis in Acute Anterior Cruciate Ligament Reconstruction

Table III. Associated injury.

<table>
<thead>
<tr>
<th>Associated injury</th>
<th>Acute ACLR (n = 26)</th>
<th>Delayed ACLR (n = 26)</th>
<th>Relative Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>MM bucket handle tear</td>
<td>1</td>
<td>2</td>
<td>0.5</td>
</tr>
<tr>
<td>LM radial tear</td>
<td>1</td>
<td>2</td>
<td>0.5</td>
</tr>
<tr>
<td>LMPHRT</td>
<td>1</td>
<td>0</td>
<td>n.s.</td>
</tr>
<tr>
<td>Chondral injuries</td>
<td>1</td>
<td>2</td>
<td>0.5</td>
</tr>
</tbody>
</table>

ACL: acute anterior cruciate ligament reconstruction; MM: medial meniscus; LM: lateral meniscus; LMPHRT: lateral meniscus posterior horn root tears. The relative risk for LMPHRT was not calculable because there were no cases of lesion in the delayed ACLR group.

Table IV. Mean ROM Degree at 2-4-8-12-24 Weeks.

<table>
<thead>
<tr>
<th></th>
<th>Acute ACLR (n = 26)</th>
<th>Delayed ACLR (n = 26)</th>
<th>Sign.</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 weeks</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Extension ± SD</td>
<td>0.4 ± 1.4</td>
<td>0.3 ± 2.8</td>
<td>n.s.</td>
</tr>
<tr>
<td>Flexion ± SD</td>
<td>72.2 ± 18.2</td>
<td>76.8 ± 18.9</td>
<td>n.s.</td>
</tr>
<tr>
<td>4 weeks</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Extension ± SD</td>
<td>0.6 ± 1.6</td>
<td>0.9 ± 1.8</td>
<td>n.s.</td>
</tr>
<tr>
<td>Flexion ± SD</td>
<td>103.6 ± 13.4</td>
<td>93.6 ± 15.8</td>
<td>n.s.</td>
</tr>
<tr>
<td>8 weeks</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Extension ± SD</td>
<td>0.4 ± 1.5</td>
<td>0 ± 0</td>
<td>n.s.</td>
</tr>
<tr>
<td>Flexion ± SD</td>
<td>127.3 ± 9.0</td>
<td>119.1 ± 12.2</td>
<td>n.s.</td>
</tr>
<tr>
<td>12 weeks</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Extension ± SD</td>
<td>0 ± 0</td>
<td>0 ± 0</td>
<td>n.s.</td>
</tr>
<tr>
<td>Flexion ± SD</td>
<td>130.0 ± 0</td>
<td>124.7 ± 1.3</td>
<td>n.s.</td>
</tr>
<tr>
<td>24 weeks</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Extension ± SD</td>
<td>0 ± 0</td>
<td>0 ± 0</td>
<td>n.s.</td>
</tr>
<tr>
<td>Flexion ± SD</td>
<td>130.0 ± 0</td>
<td>130.0 ± 0</td>
<td>n.s.</td>
</tr>
</tbody>
</table>

ROM: range of motion; ACLR: acute anterior cruciate ligament reconstruction; SD: standard deviation. Data regarding ROM are reported with mean ± SD.

Table V. Subjective and objective evaluations at 24 weeks

<table>
<thead>
<tr>
<th></th>
<th>Acute ACLR (n = 26)</th>
<th>Delayed ACLR (n = 26)</th>
<th>Sign.</th>
</tr>
</thead>
<tbody>
<tr>
<td>IKDC ± SD</td>
<td>98.7 ± 3.3</td>
<td>95.2 ± 3.8</td>
<td>n.s.</td>
</tr>
<tr>
<td>TEGNER LYSHOLM ± SD</td>
<td>100 ± 0.0</td>
<td>93.8 ± 7.0</td>
<td>n.s.</td>
</tr>
<tr>
<td>KOOS ± SD</td>
<td>99.0 ± 1.8</td>
<td>95.5 ± 4.1</td>
<td>n.s.</td>
</tr>
<tr>
<td>LACHMAN n (%)</td>
<td></td>
<td></td>
<td>n.s.</td>
</tr>
<tr>
<td>0</td>
<td>25 (100)</td>
<td>26 (100)</td>
<td></td>
</tr>
<tr>
<td>1 +</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>2 +</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>PIVOT SHIFT n (%)</td>
<td></td>
<td></td>
<td>n.s.</td>
</tr>
<tr>
<td>0</td>
<td>23 (92)</td>
<td>23 (89)</td>
<td></td>
</tr>
<tr>
<td>1 +</td>
<td>2 (8)</td>
<td>3 (11)</td>
<td></td>
</tr>
<tr>
<td>2 +</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>3 +</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>KT1000 MM ± SD</td>
<td>1.1 ± 1.3</td>
<td>1.8 ± 1.7</td>
<td>n.s.</td>
</tr>
</tbody>
</table>

SD: standard deviation; ACLR: anterior cruciate ligament reconstruction; IKDC: International Knee Documentation Committee; KOOS: Knee injury and Osteoarthritis Outcome Score. Data are displayed as mean ± SD.
DISCUSSION

The most important finding of this prospective study is that timing of ACLR does not influence postoperative ROM. Acute reconstruction ensures quick recovery with similar outcomes and functional strength at 6 months if compared to delayed reconstruction.

Arthrofibrosis of the knee is the most common post-operative complication of ACLR, with rates between 4% and 38% (24). Several definitions have been proposed for arthrofibrosis. According to Wasilewski et al., arthrofibrosis was a total loss of motion greater than 25% at 6 months postoperatively or knees requiring lysis of adhesions and manipulation (5). A study conducted by Shelbourne et al., classified arthrofibrosis of the knee in 4 types based on loss motion and patellar tightness and contracture compared with the other knee. Type 1 was < 10° of extension loss and normal flexion. Type 2 was > 10° of extension loss and normal flexion. Type 3 was > 10° extension loss and > 25° of flexion loss with patellar tightness and no patella infera. Type 4 was > of 10° extension loss, 30° or more of flexion loss loss and objective patella infera with patellar tightness (25).

A systematic review conducted by Ektiari et al. analyzed 25 studies including 647 patients treated for arthrofibrosis after ACLR. They concluded that arthrofibrosis is poorly defined and outcomes measures varies widely (24).

The effect of the timing of ACLR on the development of post-operative arthrofibrosis has long been discussed. Older studies, supporting delayed reconstruction, reported a higher incidence of postoperative stiffness after acute ACLR, however most of these were retrospective studies that included patients with additional ligament injuries often operated with arthrotomy technique and more restrictive postoperative rehabilitation protocols (4, 5, 26).

In 1990s Ferretti et al. published a medium-term follow-up study on a series of 55 cases of acute ACL hamstrings reconstruction, performed within ten days since the initial injury (27). Besides the overall good subjective and objective outcomes, the authors reported a lower rate of meniscectomies as compared with a comparable series of patients operated in a chronic phase. However, they also reported ten cases

Table VI. Functional strength.

<table>
<thead>
<tr>
<th></th>
<th>Acute ACL-R</th>
<th>Delayed ACL-R</th>
<th>Sign.</th>
</tr>
</thead>
<tbody>
<tr>
<td>OLH - injured leg (cm)</td>
<td>91 (25.5)</td>
<td>82 (20.6)</td>
<td>n.s.</td>
</tr>
<tr>
<td>Mean (SD)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>OLH - uninjured leg (cm)</td>
<td>99.9 (24.8)</td>
<td>89.2 (18.8)</td>
<td>n.s.</td>
</tr>
<tr>
<td>Mean (SD)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>OLH inj. - uninj. difference (cm)</td>
<td>8.1 (18.7)</td>
<td>7.2 (15)</td>
<td>n.s.</td>
</tr>
<tr>
<td>Mean (SD)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LSI (%)</td>
<td>92.8 (14.4)</td>
<td>92.4 (18.2)</td>
<td>n.s.</td>
</tr>
<tr>
<td>Mean (SD)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thighs circumference inj. - uninj. difference (cm)</td>
<td>2.1 (1.3)</td>
<td>2.9 (2.3)</td>
<td>n.s.</td>
</tr>
<tr>
<td>Mean (SD)</td>
<td></td>
<td></td>
<td></td>
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</tbody>
</table>

SD: standard deviation; OLH: One Leg Hop; LSI: Limb Symmetry Index. Data are reported with mean ± SD, differences are displayed in cm, thigh circumference was measured 10 cm above the patella.
of manipulation under anesthesia performed within three months since surgery in due to a delay in recovery of ROM as a result of an up to six weeks postoperative cast immobilization. In the present series, as a more accelerated rehabilitation was used this procedure has never been required. The study by Shelbourne et al. was one of the first to recommend delaying an ACL reconstruction by at least 3 weeks (4). The authors reported a significantly increased incidence of arthrofibrosis in patients reconstructed within 8 days when compared with those reconstructed after 21 days. The authors also reported that patients treated between 8 and 21 days who underwent an aggressive rehabilitation program had better range of motion if compared to patients following conservative protocol. As a result, subsequent studies adopted a similar accelerated rehabilitation protocol (12, 13, 28). This, along with the use of modern surgery technique, may explain why recent studies reported no clinical difference between early versus chronic ACLR supporting our findings (6, 7, 29).

Debate et al. found no differences in terms of PROMs, risk of complications, ROM limitation, risk of re-tears, and residual laxity comparing early versus delayed ACLR (14). In the meta-analysis conducted by Ferguson et al., only statistically significant finding was for the Tegner activity scale, which demonstrated improved reported outcomes with early surgery (15).

No other findings reached significance, which was in keeping with other systematic reviews and meta-analysis reporting no differences in subjective and objective outcomes related to surgical timing of ACL reconstruction (3, 12-14).

A systematic review and meta-analysis conducted by Smith et al. examined six papers including 370 ACLR. Early reconstructions were performed within a mean of 3 weeks from injury; delayed reconstructions were performed with a minimum of six weeks from injury. They found that there were no difference in clinical outcome between early and delayed reconstructions (13).

On KT-1000 arthrometric evaluation, Li et al. found evidence of greater stability with early surgery (30), conversely Raviraj et al. showed no differences between the groups as well as to clinical examination by Lachman, Pivot shift, and anterior draw testing (31).

Different studies reported other advantages of early surgery such as less muscle atrophy and less risk of exposing the knee to subsequent injuries associated with recurring instability such as meniscal and chondral injuries (11, 32). In our cohort of patients, we reported no difference regarding functional strength and associated lesions. Otherwise, Von Essen et al. showed superior outcome in the acute ACLR group regarding strength and how patients felt their knee functioning at 24 months (7).

It has been reported that the odds for cartilage lesion occurrence increases by nearly 1% for each month that elapses from injury to surgery, and that a lesion of the cartilage is associated with a 2-fold increase in the risk of developing a meniscal tear (33). In our study, we didn’t detect a relevant greater number of associated lesions in the delayed ACLR group, but it might have existed if surgery had been delayed by months or years while in our group 2 (delayed surgery) the mean time injury surgery was 271 days (9 months). Conteduca et al. as matter of fact, reported a statistically significant difference regarding the percentage of chondromalacia when comparing patients who waited less and more than 30 months (34). Moreover, in the work conducted by Ferretti et al. the incidence of meniscal tears was directly correlated with the time between the first injury and operation (8).

According to Bottoni et al. we believe that delayed surgery represents a “second hit” for the knee, on the contrary, if the surgery is performed proximate to the injury, the body has just one “trauma” from which to heal and only one rehabilitation program to deal with (29). This, along with a shorter injury-surgery time, can guarantee a faster and easier return to sport. Moreover, although in the absence of statistical significance, our results showed a trend towards a faster ROM recovery in a greater percentage of patients undergoing acute versus delayed ACLR.

This study has several strengths, one of which is the prospective design, all of the ACLRs were performed with the same surgical technique and our results were obtained with the same accelerated rehabilitation protocol that was minimally supervised. Furthermore, acute ACLRs have been performed in a very early phase with a mean time injury surgery of 7 days. Potential limitations are the lack of randomization; the relative small number of patients and the relatively short postoperative follow-up; however, follow-up is not a major concern, as the primary outcome is return of range of motion.

CONCLUSIONS

Acute ACL reconstruction can be performed safely with no increased risk of arthrofibrosis and clinical outcomes are comparable to delayed ACLR.

Early reconstruction, if followed by an aggressive rehabilitation program, promotes a rapid recovery for motivated patients with only one rehabilitation protocol needed.

CONFLICT OF INTERESTS

The authors declare that they have no conflict of interests.
REFERENCES

SUMMARY

Introduction. The anterior cruciate ligament (ACL) is an important structure for knee stability. Transcutaneous electrical nerve stimulation (TENS) is an electrical current that significantly reduces pain.

Objective. To assess drug costs associated with high frequency TENS in the immediate postoperative period of ACL reconstruction.

Methods: A single-blind randomized clinical trial with 46 patients randomly assigned to a control group (CG = 23) and a TENS group (TG = 23). Individual and total drug costs were assessed in both intervention groups. The TENS intervention protocol started in the recovery room shortly after surgery, being maintained uninterruptedly for the first 48 hours after surgery. The parameters used were pulse width of 100 µs, frequency of 120 Hz, and intensity according to the patient’s tolerance.

Results. The average cost of drugs was US $ 3.12 in the TG and US $ 9.12 in the CG (p = 0.0001). Tramadol accounted for the biggest difference in costs: US $ 4.34 ± 1.36 in the CG and US $ 0.81 ± 0.95 in the TG (p = 0.0001). The total cost of drugs was US $ 13.48 in the TG and US $ 39.62 in the CG (p = 0.0001).

Conclusions. The treatment with high frequency TENS application was three times less expensive regarding drug costs, which makes it a promising resource for postoperative analgesia. Using this technique minimizes drug side effects and reduces costs for health systems.

KEY WORDS
Transcutaneous electrical nerve stimulation; anterior cruciate ligament; physical therapy specialty; knee; anterior cruciate ligament reconstruction.
INTRODUCTION
The anterior cruciate ligament (ACL) is an important knee stabilizer against tibial translational and rotational forces on the femoral condyle (1). Individuals who present ACL injury develop changes in motor control as this injury usually leads to a loss of sensory information, impairing proprioception and postural control (2). It is a very common sports injury, affecting approximately 1 in every 3,000 people in the USA (3). The ACL reconstruction surgery is one of the most frequent orthopedic surgical procedures and generally produces good results. However, development of postoperative complications may hamper the patient’s recovery (4). In the immediate postoperative period, this injury is usually accompanied by pain and functional limitation (5).

Transcutaneous electrical nerve stimulation (TENS) is a technique that transmits low voltage electrical impulses through electrodes applied to the painful area (6-8). This technique is effective in treating various musculoskeletal disorders as it influences and modulates nerve conduction of pain (6). In association with other physiotherapeutic approaches, TENS may increase the level of activity, reduce hospital stay, and improve function in the affected region (9). Moreover, it is a relatively low cost therapeutic resource (7, 9).

Transcutaneous electrical nerve stimulation (TENS) is a nonpharmacological method of analgesia (10) approved by the Food and Drug Administration (FDA). It is a fast, safe, noninvasive, and low cost physical therapy. In comparison to other analgesic methods, it also has the advantage of minor side effects (10). Due to this analgesic effect, TENS can be administered in the postoperative routine of several surgical conditions as an adjunct to conventional opioid analgesia (11).

This study evaluates the effects of using high frequency TENS on pain, function, and opioid analgesic consumption in the immediate postoperative period of ACL reconstruction.

METHODS
Study design
This is a randomized, single-blind clinical trial with 46 male patients who underwent reconstructive surgery (bone-tendon-bone graft). Outcome measures were evaluated prior to surgery, on the 1st and 2nd postoperative days. The study received ethical approval from the Ethics Committee of the Lutheran University of Brazil (2,175,301) and is registered in the Brazilian Registry of Clinical Trials (ReBEC) under the number RBR-9FZFYS. This study meets the ethical standards of Muscles, Ligaments and Tendons Journal (12).

Participants
Figure 1 shows the study flowchart. Initially, 47 male participants who were candidates for ACL reconstruction using arthroscopic bone-tendon-bone graft were referred for physical therapy. The same surgeon would perform the surgery for all these patients. All participants were assisted by the Brazilian Unified Health System (SUS). The participants were examined by the evaluating researcher, and were aware of the inclusion and exclusion criteria. Only one patient did not consent to participate in the study. Therefore, 46 consecutive patients were considered eligible for the study.

Eligibility criteria
The study included men aged between 18 and 40 years, with ACL rupture, who underwent surgery using arthroscopic bone-tendon-bone graft. All participants were assisted by the Unified Health System (SUS), and were admitted to a regional hospital that is a reference in Orthopedics and Traumatology.

The study excluded participants with previous meniscus rupture requiring intervention, with evidence of degenerative disease on radiological or magnetic resonance imaging (MRI), with superficial sensitivity deficit, with loss of consciousness and cognitive impairment that prevented understanding, with stroke sequelae, and those that developed infection in the surgical wound or died during the research period.

Sampling and randomization
The primary outcome of the study was the administered dose of dipyrone. Following the study by Silva et al. (13), we estimated the sample size through the differences between the mean and standard deviation of the initial and final dose of dipyrone of participants who received TENS application. In the first postoperative evaluation, the dipyrone dose in the TENS group was 1,000 ± 1,240.35 mg, and the final dipyrone dose was 500.00 ± 1,091.93 mg. In the control group, the initial dipyrone dose was 1,357.14 ± 744.95 mg, and the final dipyrone dose was 857.14 ± 534.52 mg. Using a study power of 80%, a significance level of 95%, and a sample size ratio of 1:1 (intervention group:control group), we reached the estimated number of 23 subjects for each group, totaling a sample of 46 participants.

Participants were randomly assigned to two groups according to a list of random numbers provided by the EPI-INFO® software, with 23 patients in the TENS group (TG) and 23 patients in the control group (CG). An external researcher, not involved neither in the recruitment nor in the evaluation of patients, performed the allocation.
Intervention protocol
The intervention protocol was carried out by an independent researcher previously trained in TENS administration and who had not participated in the evaluation step. Both study groups received the standard postoperative rehabilitation protocol for ACL reconstruction. The protocol consisted of continuous passive motion (CPM) exercises, isometric exercises, and active assisted exercises for knee flexion and extension according to the patient’s tolerance. The TENS intervention started in the surgical recovery room, after approval by the nurse in charge. Intervention was maintained 24 hours a day, and ended 48 hours after surgery. The researchers turned off the equipment only for personal hygiene purposes. The patients underwent the application of continuous high frequency TENS (conventional mode) from two channels with 3 × 5 cm self-adhesive electrodes surrounding the surgical wound. The parameters used were: frequency of 120 Hz, pulse width of 100 µs, and intensity of stimulation at the highest comfortable level reported by the patient so as to promote intense paresthesias without, however, causing discomfort.

The patient’s companion was instructed to observe and control the positioning of the electrodes during the absence of any team member or researchers. In case of any disconnection of the device, the companion should immediately contact the nurse in charge, who would contact the intervening researcher to make the necessary adjustments.

Following the orientations of the Hospital Infection Control Commission (CCIH) of Santa Luzia Hospital, the electrodes were cleaned in running water after the end of each application. Moreover, for greater infection control, the device and cables were disinfected with a cloth moistened with Incidin®.

Outcomes and evaluation
The primary outcome was drug intake. Evaluations were carried out by a blind evaluator, that is, a researcher who did not know which group the participant belonged to. All results were measured before surgery, on the 1st and 2nd postoperative days.
Drug Intake
The analgesic routine adopted by the attending physician remained unaltered. The analgesic protocol adopted by the entire medical team in the Department of Orthopedics and Traumatology of the institution included ketoprofen (100 mg) every 12 hours, sodium dipyrone (2 mg) in case of pain or fever, tramadol (100 mg) in case of pain, morphine (3 mg) every 3 hours in case of pain, and diazepam (10 mg). We recorded the daily and total consumption of drugs on each of the first three postoperative days in each study group on a registration form. Afterwards, we calculated the total dose administered to each study participant in both groups.

Data analysis
Data were presented as mean ± standard deviation or mean (95% confidence interval) and median (interquartile range). Initially, the data were tested for normal distribution using the Shapiro-Wilk test. Proportion comparisons were made using \( \chi^2 \) square tests. One-way ANOVA was used to compare baseline characteristics between groups. Parametric data were analyzed statistically by one-way analysis of variance (ANOVA) for repeated measures, followed by the Bonferroni post hoc test for intragroup analyses. The Student t test was used for intergroup analyses. Nonparametric data were analyzed using the Kruskal-Wallis test. A value of \( p < 0.05 \) was required for statistical significance. All statistical analyses were performed using commercial software (Statistical Package for the Social Sciences, version 23, SPSS Inc., Chicago, IL, USA).

RESULTS
A total of 46 patients underwent arthroscopic ACL reconstruction using bone-tendon-bone graft. All subjects who started the intervention completed the study and there were no losses or exclusions (figure 1). Table I shows demographic characteristics and outcome measures prior to the intervention and in both groups (TG and CG). Participants in the TG had more right knee injuries than participants in the CG.

Drug Costs
The TG showed a significant cost reduction (US $) for all drugs administered in the postoperative protocol (\( p < 0.05 \)) (table II).

Table I. Demographic characteristics of the sample (n = 46).

<table>
<thead>
<tr>
<th></th>
<th>Intervention Group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>TG (n = 23)</td>
</tr>
<tr>
<td>Age, years (± sd)</td>
<td>26.52 ± 6.27</td>
</tr>
<tr>
<td>Gender, n (%)</td>
<td>1.000$</td>
</tr>
<tr>
<td>Male</td>
<td>23 (100.0)</td>
</tr>
<tr>
<td>Female</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Time of injury, months (± sd)</td>
<td>19.61 ± 22.82</td>
</tr>
<tr>
<td>Smoking, n (%)</td>
<td>0.524^</td>
</tr>
<tr>
<td>Yes</td>
<td>1 (4.3)</td>
</tr>
<tr>
<td>No</td>
<td>22 (95.7)</td>
</tr>
<tr>
<td>Skin color, n (%)</td>
<td>1.000^</td>
</tr>
<tr>
<td>White</td>
<td>23 (100.0)</td>
</tr>
<tr>
<td>Black</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Affected knee, n (%)</td>
<td>0.023^</td>
</tr>
<tr>
<td>Right</td>
<td>18 (78.3)</td>
</tr>
<tr>
<td>Left</td>
<td>5 (21.7)</td>
</tr>
<tr>
<td>Dominant limb</td>
<td>0.963^</td>
</tr>
<tr>
<td>Right</td>
<td>21 (91.3)</td>
</tr>
<tr>
<td>Left</td>
<td>2 (8.7)</td>
</tr>
</tbody>
</table>

^Student t, $Chi-square.
Total Costs in the Intervention Groups
The total drug cost (US $) for the TG was about 1/3 of the total drug cost for the CG (p < 0.05) (table III).

DISCUSSION
This randomized clinical trial evaluated the costs of adding TENS to the exercise protocol applied in the first 48 hours after ACL reconstruction. Few studies have evaluated the effect of using TENS on drug costs in the postoperative period of orthopedic trauma.

The standard analgesic drugs used in surgical procedures in the Department of Orthopedics and Traumatology of the hospital where the study was carried out are ketoprofen, dipyrone, tramadol, and morphine. The CG had a higher drug intake than the TG (P < 0.0001). Such findings are parallel to previous studies that analyzed analgesic consumption associated with TENS after several types of surgical procedures (13-15).

The results of this clinical trial showed that continuous use of TENS in the first 48 hours after anterior cruciate ligament (ACL) reconstruction significantly reduced the costs of all drugs included in the postoperative protocol, reducing about 1/3 of the total cost for the TG in comparison to the CG (p < 0.0001). Corroborating the findings of this study, Pivec et al. (8) observed that TENS was a noninvasive option that provided clinical and economic advantages in comparison with not using TENS. Several variables can interfere so that TENS may not achieve the desired analgesic effect. Variation in the intensity and frequency used, as well as the stimulation time, may not be sufficient to achieve significant analgesia in the acute phase, thus not closing the pain gate.

Silva et al. (13) approached 42 patients with proximal femoral fractures divided into a TENS group, a placebo TENS group, and a control group. All groups received the same exercise protocol in the postoperative period (13). As in the present study, transcutaneous electrical nerve stimulation (TENS) was applied uninterruptedly (13). The authors observed a significant reduction in pain and drug intake, the latter decreasing by 62.96% (tramadol), 45.61% (tenoxicam), 24% (dipyrone), and 87.5% (morphine) in groups of patients in the postoperative period of proximal femoral fractures who used continuous high frequency TENS (13). The costs decreased by US $ 3,975.34 for every 1,000 patients with proximal femoral fracture treated with TENS in the first three days after surgery (13).

Pivec et al. (8) demonstrated that patients with chronic low back pain, without neurological impairment, and who were treated with TENS had significantly less hospitalizations and medical visits than those who did not receive TENS. The analysis of total annual costs showed that patients who received TENS had significantly lower total costs, although the difference was modest (US $ 17,957 for patients treated with TENS versus US $ 17,986 for patients who were not treated with TENS) (8). In addition, patients who used TENS had significantly lower hospital costs (US $ 4,074 vs US $ 4,772, respectively), but significantly higher outpatient costs (US $ 10,489 vs US $ 9,643, respectively; P < 0.0001) (8).

<table>
<thead>
<tr>
<th>Table II. Average cost (US $) of each drug per participant in the intervention groups during the study period.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Drug</strong></td>
</tr>
<tr>
<td>-----------------------</td>
</tr>
<tr>
<td>Ketoprofen</td>
</tr>
<tr>
<td>Dipyrone</td>
</tr>
<tr>
<td>Tramadol</td>
</tr>
<tr>
<td>Morphine</td>
</tr>
<tr>
<td>Diazepam</td>
</tr>
<tr>
<td><strong>Total</strong></td>
</tr>
</tbody>
</table>

Bold values are statistically significant. CI: Confidence interval; sd: standard deviation. a: Student t test for intragroup comparisons.

<table>
<thead>
<tr>
<th>Table III. Total drug costs in the study groups (US $).</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Intervention Group</strong></td>
</tr>
<tr>
<td>-------------------------</td>
</tr>
<tr>
<td>TG</td>
</tr>
<tr>
<td>CG</td>
</tr>
</tbody>
</table>
A study analyzed the use of opioids after thoracic surgery and demonstrated a lower opioid intake for patients receiving TENS in comparison to the control group. (11). Silva et al. (15) demonstrated that continuous use of TENS (24 hours a day, ending 72 hours after surgery) for proximal femoral fracture significantly decreased drug intake (15). According to the authors, the tramadol dose was significantly higher in the control group than in the TENS group at forty-eight hours after surgery (15). Kara et al. (13) evaluated the effect of TENS on analgesic consumption in the immediate postoperative period of spinal surgery. The application started when the patients arrived at the postsurgical ward (two to three hours after surgery) (13). The researchers administered TENS twice a day, 30 to 40 minutes each time, with a rest interval of three to four hours between applications (13). The TENS group showed lower analgesic consumption in the first 24 hours and throughout the experiment (13). Even with a small reduction in opioid use in patients treated with TENS, its application can be an important general public health measure to reduce the exposure of patients with musculoskeletal pain to chronic use of opioids and related sequelae (8).

Gore et al. (16) evaluated the use and direct medical costs of pharmacological and alternative treatments for patients with osteoarthritis (OA) and chronic low back pain. Opioids were the most prescribed drugs (above 70%), followed by nonsteroidal anti-inflammatory drugs (above 50%). Transcutaneous electrical nerve stimulation was used in 14% of the OA cases. Opioids represented an average cost of US $ 287.4 in the treatment of OA, and 364.5 in chronic low back pain. Tramadol represented an average cost of 137.6 and 119.4, respectively (16). Notwithstanding, TENS represented an average cost of US $ 155.9 in OA and US $ 115.20 in chronic low back pain (16). It is noteworthy that a substantial proportion of patients had baseline comorbidities associated or contraindicated with drugs, NSAIDs, and medications used during the study period, which have been documented to increase the risk of NSAID-related events (16). These side effects can technically increase the total economic burden of patient management, although their contribution to total costs is difficult to assess.

Finally, the results of the present study demonstrate that TENS application in the immediate postoperative period of several traumatic orthopedic surgeries can significantly reduce drug consumption and costs in health systems. However, success with the use of TENS depends both on appropriate selection of parameters and on understanding the application principles. The current intensity for effective postoperative analgesia should be strong but comfortable for the patient, and the electrodes should be positioned around the surgical area or at corresponding acupuncture points.

Study limitations
The main limitation of the present study is the small number of patients. Another limitation is the absence of a placebo TENS group. Furthermore, the study did not analyze neither the side effects presented in the groups that received drugs, nor the cost generated by addressing these effects.

CONCLUSIONS
Drug costs were about three times lower in the group that used continuous high frequency TENS than in the control group. High frequency TENS can be a promising resource for postoperative analgesia, minimizing drug side effects and reducing costs for health systems in the postoperative period of musculoskeletal conditions.

ACKNOWLEDGEMENTS
To the Group of Studies and Research in Sports Rehabilitation and Orthopedic Trauma (GEPRETO) of the Lutheran University of Brazil, Torres/RS, Brazil.

CONFLICT OF INTERESTS
The authors declare that they have no conflict of interests.

REFERENCES
SUMMARY

Objective. To evaluate the effectiveness of two antifibrinolytic drugs (tranexamic acid and epsilon-aminocaproic acid) in reducing postoperative hemarthrosis after anterior cruciate ligament reconstruction.

Methods. 45 patients diagnosed with primary anterior cruciate ligament tears were randomly placed into 3 groups: control, tranexamic acid (TXA) and epsilon-aminocaproic acid (EAC). The first group was operated on without the use of the drugs, and for the other two, the dose was adjusted by weight. The evaluation was conducted for 1 and 7 postoperative days to assess the degree of hemarthrosis, assess the visual pain scale and measure the range of motion (ROM) in degrees. The patients were then assigned a subjective functional score at 14 and 28 postoperative days.

Results. The TXA group showed improvement on the postoperative pain scale after 7 days compared to the control group. When evaluated with the Lysholm functional score, the TXA group showed improvement compared to the control group. No significant statistical difference emerged in the parameter evaluated for the EAC group.

Conclusions. The tranexamic acid group showed reduced pain and improved function after arthroscopic reconstruction of the ACL. Up to this point, the use of epsilon-aminocaproic acid yielded no benefit. A follow-up study with more participants may confirm our findings or present new relevant findings.

KEY WORDS
Knee; anterior cruciate ligament reconstruction; hemarthrosis; antifibrinolytics; arthroscopy.

INTRODUCTION

Arthroscopic reconstruction is a reliable procedure with good outcomes for the treatment of lesions of the anterior cruciate ligament (ACL). Despite the great advances in the development of techniques, improvement of implants and graft-related studies, management of the intra-articular bleeding inherent to the procedure remains a point of discussion (1, 3-5, 11).

The use of antifibrinolytic drugs has helped control bleeding in several surgical areas, including orthopedics (2, 6-10, 16). Tranexamic acid and epsilon-aminocaproic acid are two of the most used drugs in this context and are commonly available in tertiary-care service in the public health-care system (PHCS) (16). The current study aims to assess the reproducibility of good results with the use of these drugs in the reduction of hemarthrosis after ACL arthroscopic reconstruction (ACLR) and to evaluate improvement in rehabilitation in the short and long term. Thus, we can verify the possibility of a faster dehospitalization with the administration of these drugs.
MATERIALS AND METHODS

The current study is characterized as a randomized prospective clinical trial. To date, 43 patients diagnosed with anterior cruciate ligament lesions employed our service between April and October 2017 and were included in the study. Furthermore, we intend to increase the number of participants to increase our study’s impact. This study was approved by the hospital ethical committee under number 2.045.499 in May 2017.

As inclusion criteria, we selected patients older than 18 with indication of ACLR. As exclusion criteria, we considered patients presenting with any of the following features: coagulation disorders, currently attending anticoagulant therapy, altered preoperative coagulation tests, vasculopathies, pregnant or lactating woman, renal disease or renal insufficiency (15), sickle cell anemia, allergy to anesthetics, allergy to epsilon-aminocaproic acid, important preoperative pain (Visual Analog Scale for Pain > 5) (13) and large preoperative edema (grade 3 or 4) (12). Patients submitted to meniscal suture or review cases of previous surgeries were also excluded from the study along with those who did not agree to sign the free informed term of consent (FITC). An examiner, who was not the surgeon in each case, randomly assigned patients to 3 groups.

The same team operated on all patients. We utilized the anatomical reconstruction technique of the ACL with flexor tendons, with an endobutton for the fixation in the femur and an interference screw in the tibia. We applied the tourniquet in all the groups. All the cases were operated on by group members with similar numbers of years of experience (> 5 years). An aspiration drain was not employed (3-5). All patients executed the same physiotherapy rehabilitation protocol.

One group was operated on without using the studied drugs. This group was classified as the control group. In another group, 1 dose of 10 mg/kg of tranexamic acid (Transamin R) was used during the anesthetic induction, adding 10 mg/kg/h in the 3 hours after the initial dose (Bula Transamin. Lab Nikkho 2012). This group was the TXA group.

Finally, in the last group, epsilon-minocaproic acid (Ipsilon R) was used at a dosage of 100 mg/kg in 250 ml of sodium chloride 0.9% running for 2 hours, starting at the induction. These participants also received 1 g/h in the 2 hours after the loading dose (Bula IPSILON. Lab Nikkho 2012). This group was the EAC group.

As variables in the study, we evaluated gender, age, score on the pain scale, hemarthrosis graduation on the Coupens and Yates scale, degrees of range of motion at 1 and 7 days postoperation, and score on the Lysholm scale at 14 and 28 postoperative days.

Results analysis

Patients were seen during their visits on the first postoperative day (with a similar time interval from the end of procedure to the time of visit). They underwent an assessment of their knees’ range of motion in degrees of total flexion and extension using a digital goniometer (figure 1; iGaging R, San Clemente, CA). Joint effusion was assessed and stratified according to the classification proposed by Coupens et al. (12) (table I), and pain degree to the passive ROM by visual analogue scale (VAS). The evaluation was repeated in outpatient care 7 days after surgery. Patients underwent subjective evaluation of functionality with the Lysholm questionnaire (11, 15) at the 14th and 28th postoperative days.

Statistical analysis

To analyze the partial results, we used the Kruskal-Wallis Test to verify the difference between the three groups in the studied variables. The groups were then compared pairwise with the Mann-Whitney Test adjusted by Bonferroni’s Correction. A P value of 0.05 (5%) was used as the level of significance.

Table I. Clinical Scale of hemartosis (12).

<table>
<thead>
<tr>
<th>Degree</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>No palpable effusion</td>
</tr>
<tr>
<td>1</td>
<td>Palpable effusion with fluid</td>
</tr>
<tr>
<td>2</td>
<td>Palpable effusion in the suprapatellar space</td>
</tr>
<tr>
<td>3</td>
<td>Evident patellar rejection</td>
</tr>
<tr>
<td>4</td>
<td>Strained hemartosis</td>
</tr>
</tbody>
</table>
RESULTS

Two of the 45 initially included patients in the study were excluded due to a failure to follow-up in the 4 weeks of postoperative analysis. To date, 15 patients have been evaluated in the control group, 14 in the TXA group, and 14 in the EAC group. All three studied groups were statistically similar for the age and gender variables.

The control and TXA groups presented a significant difference in the Visual Analog Scale for Pain on the 7th postoperative day (0.011). Regarding the Lysholm score variable, the TXA and EAC groups and control groups presented significant differences on the 14th postoperative day (0.012 and 0.025, respectively) (Table II).

Despite not being statistically significant, comparison of the control group with the TXA group and then the EAC group showed statistically significant differences in the Lysholm analysis at 2 weeks postoperation (0.021 and 0.028, respectively). The remaining results have shown no statistically relevant differences.

DISCUSSION

Tranexamic acid and epsilon-aminocaproic acid are antifibrinolytic drugs that block the lysine binding site on plasmin and plasminogen molecules, thereby preventing clot dissolution (2). The use of these drugs for peri and postoperative bleeding control has been shown to reduce blood loss in cardiac surgeries, digestive tract surgeries, and transplants and in patients presenting with coagulation disorders (6, 7, 9).

Some studies in our survey show these drugs’ effectiveness in reducing blood loss and the need for hematotransfusion in the primary knee arthroplasty (7, 9, 10). However, these drugs do not show a difference between one another regarding control of bleeding in the primary knee arthroplasty (2).

Karaaslan et al. (1) demonstrated the existence of good outcomes in the arthroscopic reconstruction of the ACL by using a tranexamic acid dose of 10 mg/kg/h for 3 hours in 105 operated knees. He also noted hemarthrosis reduction (better bow of early movement in rehabilitation, less need for relief punctures) postoperation (1); however, that study compared the use of an antifibrinolytic with the use of a suction drain.

Even though the hemarthrosis content aspirated through the drain would be an objective value to evaluate the studied drugs’ efficacy, we have not made use of this artifice. The use of a drain was evaluated in several studies regarding its efficacy in the ACLR postoperation, with most of the studies showing the benefit of its nonuse (3-5). As our goal is to evaluate the drugs’ clinical outcomes, we chose not to use the aspiration drain.

We did not find in the literature studies comparing tranexamic acid with epsilon-aminocaproic acid in ACLR reconstruction, which motivated us to start our trial. We also believe most of surgeons don’t use drugs to minimize hemarthrosis for two main reasons: usually it’s not a major complication and unfamiliarity on the part of many surgeons.

Although we plan to include a larger number of participants in a follow-up study, the use of TXA was shown to be effective in reducing patients’ pain one-week post-operation and improving knee function in the same period.

We believe that a larger number of studied cases is needed along with a follow-up on our study to increase the current findings’ reliability and confirm other trends, as well as other studies on this topic.

The use of TXA and EAC in the management of postoperative ACLR hemarthrosis is a viable option with low economic and morbidity impact. These results will allow us to evaluate, in a forthcoming study, these drugs’ applicability to the earliest safe dehospitalization in the ACLR.

We had some limitations in this present study more than one surgeon was performing the surgeries, follow up was limited to the first month and despite of finding some significant statistical differences between the groups the number of patients could be higher.

Table II. Comparison among groups.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Pairs of Groups</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CONTROL X TXA</td>
</tr>
<tr>
<td>VAS 7 PO</td>
<td>0.011*</td>
</tr>
<tr>
<td>LYSOLM 14 PO</td>
<td>0.012*</td>
</tr>
</tbody>
</table>

Bonferroni’s alpha = 0.016952; *: statistically relevant.

CONCLUSIONS

According to the parameters evaluated in the present study, the use of TXA in the ACLR proved to be more effective than the administration of EAC and the control group in the first postoperative weeks. The study meets the ethical standards of the journal (17).
CONFLICT OF INTERESTS
The authors declare that they have no conflict of interests.

REFERENCES
Low Back Pain and Associated Factors among Italian Equestrian Athletes: a Cross-Sectional Study

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INTRODUCTION

LBP is defined as pain and discomfort, localized below the costal margin and above the inferior gluteal folds, with or without referred leg pain. LBP is considered chronic if it is present for most of the days in the previous 3 months (1). The relationship between low back pain (LBP) and physical activity has been largely investigated and the role of physical activity in the treatment of low back pain is generally accepted (1, 2). However, physical activity has been suggested to be both a preventive factor and a possible risk factor for LBP (3).
There is, furthermore, evidence of an association between high physical work-loads and back injury (4). LBP is a widespread condition in sport as for the general population and, as reported in literature, lifetime prevalence in athletes ranges from 1 to 94% (5, 6). As for the general population, LBP in athletes can lead to high treatment costs, dropping out of training and competition, decreased quality of life, and limitations to performance (6, 7). In this context, LBP is a relevant topic for sports medicine professionals as well as for athletes, coaches, and physiotherapists (6). Moreover, a large number of sport athletes suffer from chronic low back pain (CLBP) (8). According to published data, equestrian athletes have a significantly higher incidence of LBP compared to the general population, and this is generally accepted as a physiological consequence of sport (9).

A previous study reported that the highest forces during riding are absorbed through the rider’s ischial tuberosities, pelvis, sacrum, and lumbar spine. That could contribute to the development of LBP (10). In addition, using an inappropriate saddle can be a risk factor for LBP (10, 11). However, in 3 equestrian disciplines (dressage, show jumping and vaulting) significant correlation between the intensity of riding or the riding discipline and frequency or severity of back pain was not observed. (9) This data has been confirmed in another study on a small group of elite riders (12). To the best of our knowledge no data was available for the Italian rider population.

The purpose of this study is to investigate, through a self-reported questionnaire, the prevalence of LBP among Italian equestrian athletes; which disciplines in equestrian sports are associated with a higher prevalence of LBP; how the training and competition levels affect the prevalence.

Furthermore, we investigate the prevalence of the CLBP and the correlation between training and equestrian disciplines. This information would facilitate identification of associated factors and the development of preventive strategies in special-risk sport groups.

MATERIALS AND METHODS

Study design, setting and participants
A cross-sectional survey among athletes members of the Italian National Equestrian Federation (FISE) was conducted from 1st November 2018 to 31st January 2019. The study conforms to the Reporting of Observational Studies in Epidemiology (STROBE statement) for reporting cross-sectional studies and to the Checklist for Reporting Results of Internet E-Surveys (CHERRIES).

All the athletes were asked to complete an online questionnaire on LBP through SurveyMonkey website (13). To complete the questionnaire all the participants had to accept the consent form describing purposes and procedures of the study and privacy policy. Athletes were informed about the survey through the official (FISE) website and the related social network pages, such as Facebook, Instagram, and WhatsApp. Furthermore, equestrian centers were informed through email sent by FISE.

Exclusion criteria were the presence of neurological disease, thus, paralympic riders were excluded.

All the athletes aged 18 or more, members of the FISE, were invited to answer the questionnaire. According to the FISE database there were 40932 athletes eligible for the questionnaire, 37.68% were male and 62.32% female. 20704 (50.58%) were competitive athletes (8192 males, 12512 females). 20228 (49.42%) were recreational athletes (7232 males, 12996 females). The minimum sample size to reach was 655; it was calculated with a confidence level of 99% and a confidence interval of 5 by Creative Research Systems survey software. Ethical approval was obtained from the Committee for the Authorization of Departmental Research (CARD) of the University of Rome “Foro Italico” (case CAR.2018/19). The study meets the ethical standards of the journal (14).

Survey monkey
We used the online survey cloud-based software “SurveyMonkey” (Palo Alto, California, USA, www.surveymonkey.com), that is a software commonly used in cross-sectional studies. All questionnaires were anonymous and voluntary. The Survey was released in November 2018 and remained open for twelve weeks. If the survey link was accessed, it contained an opening message relaying the survey’s intent, privacy policy, and investigator details. Skip logic was programmed into the survey so that respondents did not have to answer not applicable questions. Because of this, not all respondents received every question. Ten minutes was the expected time calculated by SurveyMonkey to complete the survey. The software does not permit a double access.

For the extraction data, answers were reported on an Excel file for the Statistician, who was not aware of participants’ IP address. No randomization was used.

Questionnaire
The questionnaire was made up by 28 question based on the standardized Nordic questionnaires that have been developed and validated in order to study the prevalence of occupational musculoskeletal symptoms (13). It has been vali-
Low back pain

LBP is defined as pain and discomfort, localized below the costal margin and above the inferior gluteal folds, with or without referred leg pain. We classified LBP as chronic if it was present for most of the days in the last 3 months (1).

Self-efficacy

Pain-related self-efficacy is a person’s confidence in his or her ability to minimize the impact of pain on physical and psychological functioning, activities and participation.

Competitive athletes

Athletes were considered competitive if having sport license as Grade 1 (G1), Grade 2 (G2) or any of B license (B) (18).

Disciplines

Briefly, show jumping is an equestrian discipline in which a rider’s horse is jumped over an array of obstacles. The predominant pace of the horse is the canter. In Dressage, riders use their seat and pressure from knees and reins as communication to control the horse to such an extent that they can perform a set of complex figures in the paces of walk, trot, and canter. Eventing is a combination of Dressage, Cross-country, and Jumping, riders use the same horse for each phase of competition. Show jumping, dressage and eventing are also called Olympic Disciplines. Endurance is a long-distance competition against the clock. Vaulting is the sport of gymnastics and dance routines performed on horseback and on the longe line. Driving involves a carriage pulled by one to four horses. Reining is a judged event designed to show the athletic ability of a ranch type horse. These are called Non-Olympic Disciplines. All the recreational activities conducted in the country are defined Country Horse Riding.

Weekly training volume

We identified 6 groups according to the hours of training:
Group 1: 1-2 hours/week.
Group 2: 3-4 hours/week.
Group 3: 5-6 hours/week.
Group 4: 7-12 hours/week.
Group 5: 13-18 hours/week.
Group 6: more than 19 hours/week.

Table I. Questions regarding LBP and its characteristics.

<table>
<thead>
<tr>
<th>Question</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>The time frame of prevalence of LBP*</td>
<td>(in life, the last year, the last 6 months, the last three months, the last month).</td>
</tr>
<tr>
<td>The site of low back pain.</td>
<td></td>
</tr>
<tr>
<td>The duration of symptoms.</td>
<td></td>
</tr>
<tr>
<td>The frequency of symptoms.</td>
<td></td>
</tr>
<tr>
<td>The severity of low back pain measured by NRS**</td>
<td></td>
</tr>
<tr>
<td>Secondary disabilities and/or limitation in participation</td>
<td>(limitation of ADL*** and suspension from training).</td>
</tr>
<tr>
<td>Consultation with Health Care Professionals</td>
<td>(physician, physical therapist, osteopath).</td>
</tr>
<tr>
<td>The use of drugs to control low back pain.</td>
<td></td>
</tr>
</tbody>
</table>

LBP* = low back pain; NRS** = numeric rating scale; ADL*** = daily living activity.
Statistical analysis
The mean with standard deviation (SD) was used, while median and 25th-75th percentile were used for other continuous variables. Count and percentages were reported for categorical factors.

Association between LBP and binary characteristics were investigated with Pearson chi square test. A p-value of 0.05 was considered statistically significant. The univariate impact of baseline characteristics of equestrian athletes on LBP was assessed by means of a univariate and multivariate logistic model. Odds ratio (OR) and 95% CI were estimated. A p-value of 0.05 was considered statistically significant. Statistical analyses were carried out using software STATA (StataCorp. 2019. *Stata Statistical Software: Release 16*. College Station, TX: StataCorp LLC.).

**RESULTS**

Population
886 Italian equestrian athletes fulfill the survey. The average time to complete the survey was 3 minutes and 39 seconds. Participant characteristics are presented in table II.

The mean age of the athletes who completed the questionnaire was 33.2 years ± 13.3.

Considering years of practice, the median value was 16 (10-25) years while the median weekly hours of training was 5.5 hours (3.5-9).

35% of athletes follow a physical training plan for equestrian sport. The prevalence of LBP is reported in table III. The athletes declaring at least one episode of LBP were 812 (91.6%), while 658 athletes (74.2%) suffered from

<table>
<thead>
<tr>
<th>Table II. Descriptive data of the participants (n = 886).</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Variables</strong></td>
</tr>
<tr>
<td>Gender</td>
</tr>
<tr>
<td>Women: 78.1% Man: 21.9%</td>
</tr>
<tr>
<td>Age (years), mean (SD)</td>
</tr>
<tr>
<td>30.6 ± 11.9 40.6 ± 13.8</td>
</tr>
<tr>
<td>Height (cm), mean (SD)</td>
</tr>
<tr>
<td>166 ± 6.4 177 ± 6.8</td>
</tr>
<tr>
<td>Weight (Kg), mean (SD)</td>
</tr>
<tr>
<td>60.1 ± 9.3 76.5 ± 10.7</td>
</tr>
<tr>
<td>Discipline*</td>
</tr>
<tr>
<td>S.J. 65.01% Dr 15.01% Eve 8.01% Co 3.49% Rei 2.48% End 1.24% Vau 1.02% Dri 0.68% Oth 3.06%</td>
</tr>
<tr>
<td>Sport license**</td>
</tr>
<tr>
<td>B: 31.50% G1: 41.14% G2: 11.88% N.C.: 15.47%</td>
</tr>
<tr>
<td>WTV (hours), median (25%-75% percentile)</td>
</tr>
<tr>
<td>5.5 (3.5-9)</td>
</tr>
<tr>
<td>Years of sport practice (years), mean (SD)</td>
</tr>
<tr>
<td>18.70 ± 11.59</td>
</tr>
<tr>
<td>Athletic training</td>
</tr>
<tr>
<td>Yes: 35.35% No: 64.65%</td>
</tr>
<tr>
<td>Musculoskeletal disorders (n = 701)**</td>
</tr>
<tr>
<td>Sco: 30.24% Fract: 19.40% Foot: 17.12% Knee: 10.13% DLL: 6.13% Other: 52.64%</td>
</tr>
</tbody>
</table>

*Discipline: S.J. = Show jumping, Dr = Dressage, Eve = Eventing, Co = Country Horse Riding, Rei = Reining, End = Endurance, Vau = Vaulting, Dri = Driving, Oth = Other. **Sport License: B, G1, G2 = Competitive, N.C. = Non-Competitive. ***Musculoskeletal disorders: Sco = Scoliosis, Fract = Previous Fractures, Foot = Flat Foot/Pes Cavus, Knee = Varum/Valgus Knee, DLL= Lower Limb Dismetria WTV = Weekly training volume.
LBP over the last year and 212 (23.9%) during the last three months.

In **Figure 1** are showed frequency and duration of episodes of LBP. The mean intensity of pain during the last event was 5.75 ± 2 on NRS.

**Table III** shows disorders and remedies among patients with LBP. Particularly, 214 athletes (26.40%) suffered physical disability during the last event of LBP. Among the athletes (62.80%) who sought care or treatment, 61.69% consulted a physical therapist, 44.01% an osteopath and 36.74% a medical doctor. Several athletes recurred to more than one specialist and 510 athletes (62.80%) used drugs to control LBP.

**Table IV** reports prevalence of LBP among disciplines. **Table V** shows results of univariate and multivariate logistic regression.

Weight is a strong risk factor (O.R. 1.05) for LBP (p < 0.05), while age (O.R. 0.95) is a protective factor (p < 0.05).

---

**Figure 1.** Number and durations of episodes of LBP.

**Table III.** Prevalence and disorders for athletes with low back pain.

<table>
<thead>
<tr>
<th>Prevalence, disorders and remedies</th>
<th>N (percentage)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lifetime Prevalence</td>
<td>812 (91.6%)</td>
</tr>
<tr>
<td>1 year prevalence</td>
<td>658 (74.2%)</td>
</tr>
<tr>
<td>6 months prevalence</td>
<td>575 (64.8%)</td>
</tr>
<tr>
<td>Last month prevalence</td>
<td>409 (46.2%)</td>
</tr>
<tr>
<td>CLBP prevalence*</td>
<td>212 (23.9%)</td>
</tr>
<tr>
<td>Pain Intensity (measured by NRS)**</td>
<td>5.75 ± 2</td>
</tr>
<tr>
<td>Disability in ADL***</td>
<td>812</td>
</tr>
<tr>
<td>No</td>
<td>598 (73.6%)</td>
</tr>
<tr>
<td>Yes</td>
<td>214 (26.4%)</td>
</tr>
<tr>
<td>Break of practice</td>
<td>812</td>
</tr>
<tr>
<td>No</td>
<td>581 (71.5%)</td>
</tr>
<tr>
<td>Yes</td>
<td>231 (28.5%)</td>
</tr>
<tr>
<td>Recourse to cures</td>
<td>812</td>
</tr>
<tr>
<td>No</td>
<td>297 (36.6%)</td>
</tr>
<tr>
<td>Yes</td>
<td>515 (63.4%)</td>
</tr>
<tr>
<td>Drugs</td>
<td>812</td>
</tr>
<tr>
<td>No</td>
<td>510 (62.8%)</td>
</tr>
<tr>
<td>Yes</td>
<td>302 (37.2%)</td>
</tr>
</tbody>
</table>

CLBP* = Chronic Low Back Pain; NRS** = Numeric Rating Scale; ADL*** = Daily Living.
Table IV. Results of univariate and multivariate logistic regression.

<table>
<thead>
<tr>
<th>Disciplines</th>
<th>N*</th>
<th>Absence of LBP</th>
<th>N*</th>
<th>Presence of LBP</th>
<th>Total</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Showjumping</td>
<td>35</td>
<td>(6.08%)</td>
<td>541</td>
<td>(93.92%)</td>
<td>576</td>
<td>P &lt; 0.001</td>
</tr>
<tr>
<td>Dressage</td>
<td>12</td>
<td>(9.02%)</td>
<td>121</td>
<td>(90.98%)</td>
<td>133</td>
<td>P &lt; 0.001</td>
</tr>
<tr>
<td>Eventing</td>
<td>15</td>
<td>(21.13%)</td>
<td>56</td>
<td>(78.87%)</td>
<td>71</td>
<td>P &lt; 0.001</td>
</tr>
<tr>
<td>Country</td>
<td>5</td>
<td>(16.13%)</td>
<td>26</td>
<td>(83.87%)</td>
<td>31</td>
<td>P &lt; 0.001</td>
</tr>
<tr>
<td>Reining</td>
<td>2</td>
<td>(9.09%)</td>
<td>20</td>
<td>(90.91%)</td>
<td>22</td>
<td>P &lt; 0.001</td>
</tr>
<tr>
<td>Endurance</td>
<td>2</td>
<td>(18.18%)</td>
<td>9</td>
<td>(81.82%)</td>
<td>11</td>
<td></td>
</tr>
<tr>
<td>Vaulting</td>
<td>0</td>
<td>(0%)</td>
<td>9</td>
<td>(100%)</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>Driving</td>
<td>1</td>
<td>(16.67%)</td>
<td>5</td>
<td>(83.33%)</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>2</td>
<td>(7.41%)</td>
<td>25</td>
<td>(92.59%)</td>
<td>27</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>74</td>
<td></td>
<td>812</td>
<td></td>
<td>886</td>
<td></td>
</tr>
</tbody>
</table>

*N = absolute frequencies; in parentheses = percentage on discipline; in bracket = percentage on total of athletes. LBP=Low Back Pain.

Table IV. Prevalence of LBP among disciplines.

| LBP Life         | Odds Ratio | Std. Err. | z     | P > |z| | [95% Conf. Interval] |
|------------------|------------|-----------|-------|-----|---|---------------------|
| Gender           | 1.423758   | .4779299  | 1.05  | 0.29| | .7374001  2.748965 |
| Training Volume  | .9862864   | .0197851  | - 0.69| 0.49| | .9482608  1.025837 |
| Height           | .9962784   | .0183325  | - 0.20| 0.83| | .9609876  1.032865 |
| Age              | .9574858   | .0082729  | - 5.03| 0.00| | .9414077  .9738385|
| Weight           | 1.000583   | .0123024  | 0.05  | 0.962| | .9767586  1.024988 |
| Other Phy.Act.*  | .6603239   | .1408023  | - 1.95| 0.052| | .4347639  1.002907 |

| LBP 1 Year       | Odds Ratio | Std. Err. | z     | P > |z| | [95% Conf. Interval] |
|------------------|------------|-----------|-------|-----|---|---------------------|
| Gender           | 1.423758   | .4779299  | 1.05  | 0.29| | .7374001  2.748965 |
| Training Volume  | .9862864   | .0197851  | - 0.69| 0.49| | .9482608  1.025837 |
| Height           | .9962784   | .0183325  | - 0.20| 0.83| | .9609876  1.032865 |
| Age              | .9574858   | .0082729  | - 5.03| 0.00| | .9414077  .9738385|
| Weight           | 1.000583   | .0123024  | 0.05  | 0.962| | .9767586  1.024988 |
| Other Phy.Act.*  | .6603239   | .1408023  | - 1.95| 0.052| | .4347639  1.002907 |

| Chronic LBP     | Odds Ratio | Std. Err. | z     | P > |z| | [95% Conf. Interval] |
|-----------------|------------|-----------|-------|-----|---|---------------------|
| Gender          | .859537    | .2567001  | - 0.51| 0.612| | .4787041  1.543401 |
| Age             | .9241299   | .2286571  | - 0.32| 0.750| | .5690108  1.500878 |
| Training Volume:|            |           |       |     |   |                      |
| 3-4 hours       | 1.137759   | .5068456  | 0.29  | 0.772| | .4751814  2.724213 |
| 5-6 hours       | 2.883225   | 1.273646  | 2.40  | 0.017| | 1.213014  6.853167 |
| 7-12 hours      | 2.275042   | 1.013908  | 1.84  | 0.065| | .949813  5.449302 |
| 13-18 hours     | 3.269185   | 1.747812  | 2.22  | 0.027| | 1.146462  9.322218 |
| > 19 hours      | 2.864249   | 1.488436  | 2.02  | 0.043| | 1.034368  7.931334 |
| Sport License   | .6378679   | .2127536  | - 1.35| 0.178| | .3317585  1.226421 |

Other physical activities*.
Gender, hours of training or height were not identified as risk factors for LBP. Analyzing sport license, competitive and non-competitive athletes did not show a significative association with presence of LBP. With regard to CLBP, we found a weakly significative association with training volume. Investigating associated factors, we found that female, such as younger athletes, are more prone to CLBP; nevertheless, associations were not significative (p > 0.05). Relating to weekly training volume, athletes who ride 5-6 hours (O.R. 2.88), 13-18 hours (O.R. 3.27) or more than 19 hours per week (O.R. 2.86) have a risk to develop CLBP higher than 1-2 hours per week. CLBP is associated with interrupted activity (p < 0.001), drugs consumption (p < 0.001) and restriction in participation (p < 0.001). Moreover, athletes with CLBP believe that LBP has affected their performance and that LBP is a significative condition among equestrian athletes (p < 0.05). The athletes reporting CLBP over the last three months were asked to complete the Pain Self Efficacy questionnaire (PSE). The mean value of the questionaire was 37.6 ± 13.5. Correlation between NPRS and PSE questionaire was -0.28 while Scale reliability coefficient was 0.9458. In figure 2 correlations between NPRS and each question of PSE questionaire are shown.

**DISCUSSION**

Low back pain

The findings of this study clearly show that LBP is very common among Italian equestrian athletes with a life-time and 1 year prevalence of 91.6% and 74.2% respectively. Prevalence of LBP among equestrian athletes appear to be higher than in general population. According with literature 65-80% and 22-65% are the life and 1-year rates for general population, while 24-66% was the 1 year rates found in athletes (6, 19). However, these data come from studies which adopted different definition of LBP and investigated population samples of different age. For this reason, these data should be compared with care. It is not possible to compare prevalence data between equestrian sport and other sports. This is due to methodological heterogeneity of the studies present in literature, as reported in a systematic review by Trumpeter et al. (6). Compared to previous studies on equestrian athletes, we found higher rates of LBP. These findings should be considered with caution (9, 11). Nevertheless, the prevalence of LBP in younger athletes is rising, it remains lower than in adults. Conversely, we found that age is a protective factor against LBP, young athletes are more at risk compared to the older. Our hypothesis is that training sessions of younger athletes are more intense compared to that of older athletes; moreover, older athletes

![Figure 2. NPRS and PSE questionnaire correlation](image-url)
could have a better technical competence compared to younger and that can decrease spinal loads while riding. This hypothesis needs to be confirmed in prospective studies. Male athletes reporting LBP were about 20% but statistical analysis have not found significant association with gender and this is in agreement with previous study on equestrian sport (9). Investigating disciplines, we found a strong association with LBP: in Show Jumping it appeared to be more frequent (94% of athletes) compared to other disciplines, while in eventing it was less frequent (79% of athletes). Our results differ from data reported by Kraft et al., but this finding could be explained by the different sample size (9). As found by Kraft et al., we confirm that gender and training volume were not associated with LBP (9). Previous studies found a correlation between weekly training volume and LBP (2, 5). For example, in speed skaters and rowers training volume is a risk factor for back pain. On the other hand other studies on rowers or soccer players did not found this correlation (6).

In our study training volume was not found to be related to LBP, this indicate that sport-specific differences might lead to different loads on the spine, but in literature there is not a consensus on this topic (20). As previously reported, training volume, years of sport and practicing other physical activity have not significative association with LBP (6, 21). The association between weight or Body mass index (BMI) and LBP in general population and in athletes is well known (21, 22). It is confirmed that weight is a strong risk factor in equestrian athletes but it was not found a correlation with height or BMI.

Chronic low back pain

CLBP prevalence was 23.9%, this value is similar compared to 23% found in general population (1). Despite CLBP was more frequent in female and younger athletes, we did not find correlation with gender, age, weight, disciplines, or sport license.

Considering weekly training volume, we found that practicing equestrian sport 5-6 hours/week or more has a weak association with CLBP. CLBP might be related to alterations of neuromuscular control as reported by Català et al. but this is only an aspect of the multifactorial etiology of CLBP, comprising psycho-social factors (23).

Analyzing psycho-social aspects, the athletes with CLBP showed more disability in ADL and they tend to suspend sports activity more frequently. Moreover, they habitually use painkillers and non-steroid anti-inflammatory drugs to manage LBP, however it is known, according to international guidelines, that excessive use of drugs does not provide adequate clinical benefit in CLBP (1). Athletes with CLBP reported limitations in performance, and they believed that LBP is a widespread condition among riders. To summarize, the impact of psycho-social aspects is distinctly associated with CLBP among equestrian athletes and this is in accordance with Hasenbring et al. (24). The most important aspect considered in CLBP is self-efficacy, notwithstanding, we did not find any correlations between the severity of pain and self-efficacy (25).

Strengths and limits

This is the first study on the Italian equestrian population and the sample size reached is the largest compared to similar previous study in equestrian sport.

Since it is not possible to have knowledge of how many athletes were aware of the questionnaire, we cannot establish the response rate. We did not analyze by logistic regression some disciplines, considering the little sample size. Additionally, athletes with LBP could have been more likely to fulfill questionnaire; for this reason, responder bias must be taken into consideration.

It should be taken in consideration that a large part of the sample practiced physical training for equestrian sport, and this can lead to a change in the results found.

Granted that this is a cross-sectional study, the results show only correlations and not causations.

CONCLUSIONS

LBP and CLBP are very common conditions in equestrian athletes and their prevalence is higher compared to general population. LBP is more frequent in show-jumping compared to other disciplines. Age and weight are associated with lifetime LBP, with, respectively, a negative and a positive association. One fourth of Italian riders suffer from CLBP and psycho-social aspects related to CLBP need to be further investigated. Equestrian athletes with CLBP showed more disability in ADLs and tendency to suspend sports more frequently. Further studies are needed to identify risk factors for LBP and CLBP to realize prevention strategies in equestrian sport.

ACKNOWLEDGEMENTS

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CONFLICT OF INTERESTS

The authors declare that they have no conflict of interests.
REFERENCES


Most Impacting Injuries in Football: a Possible Association?

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INTRODUCTION

Anterior cruciate ligament (ACL) injury, groin pain syndrome (GPS) and hamstring injury (HI) are heavily impacting availability in sprinting and cutting sports activity, particularly in soccer, when time loss value is considered (1-4). In soccer, HI is the most frequent muscle injury and accounts for 39.5% of all muscle injuries, followed by GPS that represents 25.6% of all injuries (4), whereas ACL injuries count 0.66 events per 1000 hours of total exposure time (i.e., 0.5 ACL per team per season) (5). In Australian football, the most common and prevalent injury proved to be HI followed by ACL and GPS (6) with these three injuries causing a total percentage of missed games equal to 21.2% for HI, 12.8% for ACL injuries and 11.9% for GPS (6). Furthermore, found that, in Australian football (7), HI causes a loss of 21 games per team per season (i.e., 6.1 injuries per team per season) followed by GPS with 16 games lost per team per season (i.e., 3.9 injuries per team per season) and ACL injury with 12 games lost per team per season (i.e., 0.7 injuries per team per season). Despite the fact that the majority of studies in literature consider the etiopathogenesis of these three injuries to be independent, recent studies consider a possible association between them (7-10). However, the results of these studies are conflicting. Indeed, several studies show that HI could be a risk factor for ACL injury (9); ACL injuries and GPS could be risk factors for HI (11) and GPS could be a risk factor for HI (8). On the contrary, Toohey et al. (10) affirmed no association between GPS and HI. This lack of consensus in literature prevents us
from being able to answer two fundamental questions with certainty: is there a connection between these three injuries? Do these three injuries have a common intrinsic risk factor? In this study, we present 4 cases where there is an association of these three injuries. The data, obtained from professional football players playing both in the Qatar first division (Star League) and in the Qatar National Team, were collected by medical and physiotherapeutic staff through an informatics recording system and confirmed. All the interested subjects were informed of the purpose of the research and signed an informed consent. The aim of this study is to describe the possible association between these three injuries and to discuss their possible logical association. The research is ethically according to international standards and as required by the journal (12). Furthermore, the study was conducted following the I.S.MuL.T. Guidelines for muscle injuries (13).

Case 1
BM, a 30-year-old professional football player, suffered from GPS due to posterior abdominal wall weakness (September 2007) and twice (October 2009 and March 2010) from adductor-related GPS. The posterior abdominal wall weakness was treated surgically by the “minimal repair technique” (14), while the first episode of adductor-related GPS was conservatively treated and the second was surgically treated by a bilateral tenotomy of the adductor longus. The player resumed sports activity after 8 weeks following minimal repair surgery, after 4 weeks following the adductor-related GPS conservative treatment, and after 24 weeks following tenotomy (15). Furthermore, this player suffered from grade III right HI in February 2011 which was treated with physiotherapy and sports activity was resumed after 8 weeks. Finally, the player suffered two ACL injuries (right knee in August 2014 and left knee in September 2018); both injuries occurred during a contact situation and were treated with a patellar autograft (April 2009) respectively and consequently, return to full sports activity was possible after 20 months and 36 weeks respectively. Later, the player experienced a grade II right HI in February 2012. The injury was dealt with conservative treatment and after 3 weeks the player returned to sports activity. After the first ACL injury, the player returned to play after 28 weeks, whereas after the second ACL injury, return to play occurred after 36 weeks.

Case 2
LP, a 35-year-old professional football player suffered an ACL right knee injury during a non-contact situation in December 2009: surgical reconstruction (hamstring autograft) was carried out and the player returned to full sports activity after 28 weeks. Later, LP suffered GPS due to posterior inguinal wall weakness for which laparoscopic mesh placement was undergone (October 2014). Sports activity was resumed 12 weeks after surgery. In March 2015, LP suffered a bilateral adductor-related GPS that underwent conservative treatment and return to play was possible after 2 weeks. Finally, LP suffered grade II right HI in October 2018 and in September 2018, both injuries were treated conservatively and, in both cases, return to play was possible after 6 weeks.

Case 3
MJ, a 32-year-old professional football player, suffered a right ACL non-contact injury in January 2008 which was surgically treated (hamstring autograft) and a second ipsilateral non-contact ACL injury in November 2008, which also treated with surgery (patellar tendon autograft). After the first ACL reconstruction, the player returned to full sports activity after 24 weeks, whereas after the revision ACL reconstruction, he resumed full sports activity after 40 weeks. Later, MJ suffered a bilateral GPS in July 2012 due to a posterior inguinal wall weakness and underwent bilateral minimal repair surgery (14): return to full sports activity was possible after 8 weeks. Finally, MJ suffered two HI, initially in the right leg in April 2015, and then in the contralateral limb in March 2017. Both the injuries were grade II and were conservatively treated: return to the sports activity was possible after 4 and 3 weeks respectively.

Case 4
BK, a 31-year-old professional football player, experienced a non-contact right ACL injury in April 2007. The player later experienced a second ipsilateral non-contact ACL injury in April 2009. Both injuries were treated surgically with a patellar autograft (April 2007) and a hamstring autograft (April 2009) respectively and consequently, return to play was possible after 20 months and 36 weeks respectively. Later, the player experienced a grade II right HI in February 2012. The injury was dealt with conservative treatment and after 3 weeks the player returned to sports activity. In July 2015, the player then experienced GPS due to posterior inguinal wall weakness and underwent minimal repair surgery (14): the player returned to sports activity after 12 weeks. In January 2017, the player experienced another grade II HI, resolved with conservative treatment and return to sports activity was possible after 3 weeks. The chronology and the kind of injuries are resumed in table I.

DISCUSSION
This study provides a concrete example of how, within the context of a career in soccer, ACL injury, HI and GPS may be
linked. It is difficult, based on actual evidence, if not impossible, to try to explain this connection in terms of a cause-effect relationship. Indeed, even though a certain number of studies have shown that a correlation exists between some injuries and a previous injury, our understanding of pathophysiology and the factors that predispose to injury are still limited (9). However, based on current literature, we can try to explain a rationale underlying the association between these three types of injury and anticipate future hypotheses.

### Previous ACL injuries and HI

Several authors (7) reported that, in Australian football, a history of ACL lesion triggered an odds ratio of 5.6 (95% CI, 1.1-28.1) for experiencing a future HI. Other studies (10) showed that athletes who had suffered an ACL injury during their career had more than twice the chance of incurring a HI compared to athletes without a history of ACL injury (RR: 2.25, 95% CI 1.34 to 3.76). Moreover, it is worth noting that several authors (11) demonstrate that the chance of incurring HI a second time increases almost four-fold if an athlete has already suffered an ACL injury. In two studies (8, 11) the graft technique employed in the consequent reconstruction (patellar tendon autograft or hamstring autograft) was not associated with subsequent HI. This concept contradicts the hypothesis formulated by other authors (16) in which HI, subsequent to ACL reconstruction, was seen to depend on the type of graft used, the harvesting procedure used for the hamstring autograft (17) and the residual hamstring weakness following hamstring autograft (16). The most plausible hypothesis seems to be that harvesting hamstrings for ACL reconstruction lays them open to risk subsequent injury due to iatrogenic damage per se and the consequent imbalance between lateral (biceps femoris) and medial (semitendinosus) hamstrings (16, 17). Even when a patellar tendon autograft is used for ACL reconstruction, this association may be explained by the fact that ACL injury and the subsequent rehabilitation programme alter the biomechanics of the lower limb causing an increased risk of HI (8, 9).

### Previous HI and ACL injuries

ACL injury classically occurs when the foot locks to the ground with concurrent low knee flexion angle, knee joint rotation, and excessive valgus stress (18). In this biomechanical situation, the femoral shear forces above the tibia increase, resulting in an anterior tibial translation which, in turn, causes ACL elongation (19). During non-contact ACL injuries, this situation typically occurs when changing direction or during sidestep cutting maneuvers (18, 20, 21). Several studies show that, in such situations, the hamstring and quadriceps electromyographic activity increases significantly (20, 22). The correct balance between hamstring- and quadriceps- activation plays a paramount role in the correct kinematics of these situations (20, 22). Indeed, a reduction in hamstring activity compared to the quadriceps, reduces the knee flexion angle and increases the ground reaction force on the knee-joint (18). For this reason, correct hamstring neuromuscular function is a critical aspect of ACL injury prevention (18). When changes in direction or sidestep cutting occur during running, it is interesting to note that the three muscles composing the hamstring group act differently: the semitendinosus and the semimembranosus control internal rotation and the varus stress, whilst the biceps femoris control external rotation and the valgus stress (18, 20, 21). Therefore, functionality impairment of the lateral- (semitendinosus and the semimembranosus muscles) or medial- hamstring (biceps femoris) represents a risk factor for ACL injury (9). In other words, optimal hamstring functionality

### Table I. The chronology and type of injuries in the four cases considered.

<table>
<thead>
<tr>
<th>PLAYER 1</th>
<th>PLAYER 2</th>
<th>PLAYER 3</th>
<th>PLAYER 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>GPS (September 2007)</td>
<td>ACL (December 2009- right)</td>
<td>ACL (January 2008- right)</td>
<td>ACL (April 2007- right)</td>
</tr>
<tr>
<td>GPS (October 2009)</td>
<td>GPS (October 2014)</td>
<td>ACL (November 2008 right)</td>
<td>ACL (April 2009- right)</td>
</tr>
<tr>
<td>GPS (March 2010)</td>
<td>GPS (March 2015)</td>
<td>GPS (July 2012)</td>
<td>Hamstring (February 2012)</td>
</tr>
<tr>
<td>ACL (September 2018-left)</td>
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In this study, correlation between previous ACL injuries and HI can be found in cases 2, 3 and 4. The athlete described in case 2 underwent an initial ACL reconstruction with hamstring autograft. The case 3 athlete underwent an initial ACL reconstruction with hamstring autograft and a revision ACL reconstruction with patellar tendon autograft, whereas the athlete described in case 4 first underwent ACL reconstruction with patellar tendon autograft and then a revision ACL reconstruction with hamstring autograft.
is an important prevention factor for ACL injury. It clearly emerges from current literature that a past HI causes an alteration in lower limb muscular functionality compared with the contralateral uninjured limb. Several studies show the following neuromuscular mal-adaptation after HI:

1. lower eccentric knee flexor strength (10%-24%) (23, 24);
2. lower voluntary myoelectric activity during a maximal knee flexor eccentric contraction (18%-20%) (25, 26);
3. lower knee flexor eccentric rate of torque development (39% 40%) (27);
4. lower voluntary myoelectric activity during the initial part of eccentric contraction (19%-25%) (23, 26);
5. lower hamstrings/quadriceps ratio (19%) (23).

These data show that a past episode of HI involves impairment of muscular functionality in the injured limb compared to the contralateral uninjured limb.

Furthermore, it is worth noting that uninjured female hamstrings, compared to uninjured male hamstrings, show:

1. lower hamstring /quadriceps strength ratios (23, 28);
2. lower knee flexor rate of force development during eccentric isokinetic contractions (27);
3. lower knee flexor rate of force development during isometric contraction (29);
4. lower electromyographic hamstring activity during isokinetic eccentric knee flexion (25, 26);
5. lower electromyographic hamstring activity during a sidestep cutting maneuver (30).

These data clearly appear to overlap with those previously reported concerning the alteration of the hamstring neuromuscular function following injury: since the above data explain the elevated risk of ACL injury in women (19, 31, 33), it is reasonable to advance the hypothesis that, in the same way, an early episode of HI and the neuromuscular deficit arising, may represent a risk factor for ACL injury. However, it is important to note that the majority of these data are recorded by a single joint isokinetic test. For this reason, further studies assessing the impact of previous HI in knee kinematics, during movement of greater degrees of freedom, are needed to confirm the aforementioned hypothesis. Moreover, further studies concerning the different role of lateral and medial hamstrings during change in direction and cutting maneuvers are needed.

In this study, the association between earlier episodes of HI and ACL injuries can be found in the subject case 1.

**Previous GPS and HI**

In literature, several studies show the association between GPS and HI (7-9). A possible explanation for this association is that, after GPS, the biomechanical properties of the core muscles (i.e., the major muscles that stabilize and controls the pressure inside the trunk) and lower limb muscles are perturbed and the possibility of the athlete incurring HI is increased (9). As in the association between previous ACL injuries and subsequent HI, either the GPS clinical framework or the subsequent rehabilitation programme (especially post-surgical rehabilitation) or, a combination of both, may cause this increased risk for HI. However, it should be pointed out that in literature two studies (34, 35) did not find a significant correlation between GPS and subsequent HI. It is anyway important to note that in both these studies, an exact definition of GPS was not given and only the generic term of “chronic groin pain” was offered, omitting any concept of etiopathogenesis. This obviously may lead to bias in the authors’ conclusions.

Furthermore, in the scientific literature the definition of GPS in athletes is ambiguous and controversial (36, 37). For this reason, the hypothesis between the association of a previous GPS clinical framework and subsequent HI must be considered with care.

In this study, the association between previous GPS and HI can be found in cases 1, 2 and 3.

**Previous HI and GPS**

Since the top five causes of GPS are (38): femoroacetabular impingement (~ 32% of the cases), posterior wall inguinal canal weakness (~ 24% of the cases), adductor-related pathologies (~ 12% of the cases), inguinal-related pathologies (~ 10% of the cases) and hip labral pathologies (~ 5% of the cases), it is possible to hypothesize that previous episodes of HI may perturb running biomechanics and unmask the onset of the clinical frameworks causing GPS as reported . However, as already mentioned, the controversy in defining GPS (36, 37) must always be kept in mind as it represents a source of confusion in determining the factors that can influence the onset of this condition.

In this study, the association between previous HI and GPS can be found in subject case 4.

**Previous GPS and ACL injuries**

Several authors showed the association between GPS and ACL injuries (7). It is important to note that a decreased range of motion of the hip joint, particularly internal rotation of the hip due to a cam-FAI deformity, is a risk factor for developing GPS (36, 39, 40). by causing biomechanical stress on the posterior wall inguinal canal (36, 38, 39). Moreover, it is known that an increased tibial internal rotation of the knee joint is considered a risk factor for ACL injuries (41). Hence,
it is reasonable to hypothesize that, with a reduction of the hip range of motion leading to an excessive posterior wall inguinal canal stress, the knee joint also undergoes additional stress to compensate for this biomechanical situation and thus increases the tibial internal rotation (7). These changes in biomechanical stress, leading to an increased risk of ACL injury, may also exacerbate under particular conditions such as fatigue (42).

In this study, an association between previous GPS and ACL injuries can be found in the players described in in cases 2, 3 and 4.

### Previous ACL injury and GPS
The same hypothesis formulated for the association between previous HI and GPS, may also be extended to the association between previous ACL injury and GPS onset. In other words, the perturbation in running biomechanics caused by a previous ACL injury, could favor the onset of the clinical framework underlying GPS (7). Furthermore, we must also consider the influence of iatrogenic damage, resulting from autograft harvesting, on the biomechanics of the pelvis in general and in particular dynamic situations such as the change in direction and cutting maneuvers (16, 17, 30).

In this study, the association between previous ACL injury and GPS can be found in the case study 1.

### Limitations of the study
The major limitation of this study is that it is based on anecdotal examples, which obviously cannot be generalized. Although, a physiological connection between these pathologies are conceivable. For this reason, one of the messages that this study wants to promote is that of a “call for action” so further studies of greater evidence can confirm or confute the advanced hypotheses.

### CONCLUSIONS
Most of the epidemiological studies have often disregarded the full picture of the athlete’s history of injury. Thus, the consequences of previous injury on the athlete’s overall injury risk profile have probably been underestimated or improperly understood (10, 43). In other words, a possible association between previous injuries, apparently unrelated both in nature and in anatomical location, can rarely be found in the literature. Despite this, some studies have recently suggested a complex interaction between what seem to be extremely distinct types of injuries. This represents an important aspect of research for the identification of causal risk factors aimed at developing effective tertiary prevention strategies. The present study, based on anecdotal data, does not claim to explain the association between the three pathologies described above but it highlights some logical hypotheses that should be confirmed by further studies. Furthermore, this study allows us to underline the fact that our understanding of the pathophysiology and factors predisposing athletes to muscle, tendon and articular injury is still limited. Therefore, above all, this study aspires to be a “call for action” for studies able to clarify the possible association between the sport injuries described herein. In the light of our own current knowledge, the most probable hypothesis is not a pathophysiology based on some common risk factors to these three types of injuries (7) but rather the hypothesis relating these injuries to each other through a cause-effect mechanism.

Given the importance of injury prevention programmes implementation, we hope for the future development of studies focusing on the correlation between the distinct types of sport injuries occurring throughout the history of an athlete.

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### CONFLICT OF INTERESTS
The authors declare that they have no conflict of interests.

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Most Impacting Injuries in Football: a Possible Association?

The Relationship between Active and Passive Flexibility of the Knee Flexors

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SUMMARY

Background. Hamstrings flexibility measurements are of both, research and clinical relevance for evaluation of the training progression, prognosis of acute hamstrings injuries and monitoring recovery from such injuries. The active knee extension test and the passive knee extension test are widely used for hamstrings flexibility evaluation. However, they are based on different neurophysiological mechanisms.

Objective. The aim of this study was to assess the relationship between results of both tests: active knee extension test and passive knee extension test.

Methods. 314 generally healthy and physically active subjects (204 women and 110 men), aged 18-45, participated in this study. Each subject performed 3 trials of the active knee extension test and the passive knee extension test for both lower extremities and the range of motion was measured. To make the passive knee extension test more objective the force gauge was used for ensuring constant force in each repetition. The correlations between both tests were assessed using the Pearson coefficient (r). Additionally, the ICCs for intra-rater reliability were calculated.

Results. All of the outcomes revealed a significant (p < 0.01) positive, moderately high correlation (r values ranged from 0.67 to 0.73). Presented versions of both tests yield excellent intra-rater reliability – the ICCs (3.1) ranged from 0.98 to 0.99. Although moderately high levels of correlation, in our opinion, both tests can be used interchangeably only for general hamstring flexibility evaluation, but in more specific assessment the suitable test should be chosen, considering passive versus active nature of the movement.

Conclusions. The PKET and the AKET are useful and reliable tools for evaluation the flexibility of hamstrings. There is a significant positive, moderately high correlation between results of both tests. In our opinion, AKET is a sufficient test for a simple clinical evaluation in everyday practice and it’s recommended special for people with little experience. Additionally, in more specific clinical assessment due to the different neurophysiological mechanisms, they are based on, the choice of the tests should take into account whether the purpose of the analysis is passive versus active form of the movement.

KEY WORDS

Muscles; hamstrings; reliability; knee extension test; flexibility.
INTRODUCTION

Flexibility is an important physical parameter often related to athletes’ performance (1) and also to muscle injuries (2, 3). Poor flexibility, specifically affecting the hamstrings muscle group, has been linked not only to muscle strains (4, 5), but also to other conditions such as patellofemoral pain (6). Moreover, there is evidence that increased stiffness of hamstrings is likely to be associated with insufficient core stabilization (7). Therefore, hamstrings flexibility measurements are of both, research and clinical relevance for evaluation of the training progression, prognosis of acute hamstrings injuries and monitoring recovery from such injuries (8, 9).

There are many functional tests for assessing flexibility, extensibility, tightness and stiffness of hamstrings (in this study they are referred to as muscle flexibility tests), which validity and reliability has been confirmed (2, 8, 10-15). Common methods to evaluate hamstrings flexibility are active knee extension test (AKET) and passive knee extension test (PKET). In the AKET, the patient actively extends the knee until reaching maximal stretch of the hamstrings while the ipsilateral hip is kept at a fixed angle, usually 90° or 120° of flexion (2, 8, 15). The PKET is performed identically except that the knee is extended passively by the rater (8, 10, 15). The advantage of these tests is the lack of any significant movement of the hip, sacroiliac joint or lumbar spine during the test performance (2, 14, 16).

One of the difficulties in interpretation and comparing the results of these tests lies in the fact, that passive and active flexibility are based on different neurophysiological mechanisms. The passive flexibility of muscles is influenced by the size and length of muscle fibres (series elastic components) and by the amount and arrangement of connective tissues (parallel elastic components) of the muscle belly (17, 18), while the result of active test is not only a function of the resistance offered by the passive properties of tissues, but it also depends on reciprocal inhibition an example of which is the ability to simultaneously contract quadriceps and relax hamstrings (13).

Another issue is to determine the end point at which the measurement of range of motion is taken. Both tests are mainly based on subjective feelings of the participant, it could be especially problematic in the PKET (8). To make the passive tests more objective, some researches (13, 19), instead of listening subject’s indication of reaching the maximal tolerable stretch of the hamstring muscles, establish the standardized, constant force, which is applied to perform knee extension – the force values are monitored with special tools like force gauges or dynamometers.

Although the AKET and the PKET are proved to be reliable tools in assessing hamstring flexibility (8, 10, 13-15). We have only found one study, which compare results of both tests (15). It might be important to assess the correlation between both tests, because they are commonly used for general flexibility examination, but they refer to different kinds of flexibility – passive, which is influenced by mechanical properties of the tissue and active, which connects the mechanical properties with the nervous system control – it was assumed that, this fact might cause the divergent results of both test in single subject. The researcher has shown that there is a significant sex-related difference in the accuracy of knee joint proprioception (20), influenced by the receptors functioning, which are also responsible for stretching sensations. Due to that fact, it was hypothesised, that sex-related differences might be found in correlation coefficients too. Because of commonly confirmed human body asymmetry, it was assumed, that body site-related difference might also appear.

MATERIALS AND METHODS

Study design

The aim of this study was to assess the relationship between results of both tests: active knee extension test and passive knee extension test. Therefore, is there a strong enough correlation between them to use these tests interchangeably.

Participants

314 subjects (204 women and 110 men), aged 18-45, volunteered to participate in this study. Their mean ± SD age, height, and weight were 24.58 ± 4.86 years, 171.97 ± 8.85 cm, 67.34 ± 11.99 kg, respectively. All subjects were physically active, but without engaging in competition-level sports. Participants had no history of lower limb injury that required surgery, and no history of acute lower limb injury within the last year that required a missed day of work or requirement to seek medical treatment. All participants were healthy, with no known metabolic or neuromuscular disease, and no musculoskeletal abnormalities. Other exclusion criteria were BMI > 29.9, pregnancy and menopause. The research project obtained approval number KNW/0022/KB46-7/15 of the Bioethics Committee of the University. All participants had given written informed consent before data collection began. The study meets the ethical standards of the journal (21).

Procedures

Two physiotherapists with many years of clinical experience were involved in the study as raters, one as the primary rater (PR) and one as the assistant (AT). Their roles did not change throughout the whole study. It was assumed that
The Relationship between Active and Passive Flexibility of the Knee Flexors

for unequivocally assessment of the correlation between the results of both tests, high precision will be required during the measurements, therefore experienced researchers were engaged to ensure that all tests will be characterized by adequate repeatability.

Before joining the research, each subject’s medical history was evaluated. On the day of measurements, the demonstration of testing procedures took place. All data were collected in a single testing session. Before measurements, the participants performed a short 10-minute warm-up at average intensity using a stationary bike (5 min) and elliptical bike (5 min) with a low load to standardize the amount of activity. Then, the PKET and the AKET were performed consecutively. The passive test was performed prior to the active one assuming that the AKET would cause reciprocal inhibition in the hamstrings (22), which was noticed and analysed at the stage of the pilot study. The digital inclinometer (Saunders Group Inc., Chaska, USA) was used to record the knee motion degree during both tests (figure 1). The larger the angle indicated by inclinometer, the greater flexibility. Tested accuracy of the device proved to be ± 1°. Additionally, in the PKET, we used the Advanced Force Gauge (Mecmesin, Slinfold, West Sussex, UK) to determine the end point, at which the measurement was taken - it helped to make the procedures more objective.

Each measurement was taken 3 times for right and left side in random order to test its reliability. Subsequent statistical analyses were based on the mean value of these three repetitions. Prior to the main study, the researchers carried out a pilot study, which included 5 randomly selected individuals, to validate measurement procedures and to eliminate potential errors.

Passive knee extension test
The PKET (figure 2) was performed according to the methodology described by Gnat et al. (10) and Kuszewski et al. (19). The whole test was carried out with the subject’s maximum relaxation. Participant was positioned supine with the hip of the tested leg in 90° of flexion, stabilized with the stool that was placed under the posterior aspect of the tested thigh and held with the help of the subject’s hands (figure 2 a). Before testing, the force gauge was attached to the tested extremity, exactly on the line joining the 2 malleoli. From this position, the PR firstly placed the extremity in a 90° of knee flexion so that the shank did not lean on the stool. Then,

Figure 1. The digital inclinometer Saunders Group.

Figure 2. The passive knee extension test.
the force gauge was reset to eliminate the specific weight of
the shank from the measurement (figure 2 b). Next, the PR
passively extended the subject’s knee (maintaining the posi-
tion of the device perpendicular to the long axis of the shin)
until the force gauge indicated 2.5 kg (figure 2 c). This value
is very similar to the parameters presented by Kuszewski et
al. (19) and had been checked during our pilot study. It does
not trigger nociceptive effects and therefore, the stretch reflex
does not occur; it also does not require a lot of strength from
the researcher and allows for proper distinguishing levels of
passive stiffness, especially referring to very flexible subjects –
it helps to avoid situations in which the researcher reaches the
full range of passive motion before the dynamometer indicates
the assumed force value. The AT’s task during the passive
movement was to stabilize the thigh of tested and to visual-
ly control the maintaining position of contralateral extremity
without knee flexion.
At the end point, when the force gauge indicated assumed
value of applied force, the angle between anterior surface of
shin and horizontal plane was registered by the AT with the
digital inclinometer positioned at the anterior tibial border,
halfway between apex of the patella and the line between
the 2 malleolus. Both, the subject and the PR were blinded
to the readings.

Active knee extension test
The initial position for the AKET (figure 3) was the same
as for the PKET (figure 3 a). The subject was instructed to
perform active knee extension by himself/herself, until reach-
ing the maximal tolerable stretch of the hamstrings and main-
tain the position (this time the force gauge was not used).
During the whole movement the contralateral extremity was
stabilized by means of firm manual pressure applied by the
PR in the middle-anterior aspect of the thigh (figure 3 b). At
the end point the AT placed the inclinometer at the anterior
surface of the shin and registered the angle between horizon-
tal plane, once again both, the subject and the PR were blind-
ed (figure 3 c).

Statistical analysis
The correlations between both tests were assessed using the
Pearson coefficient (r) with regard to all subjects, as well
as women and men separately (concerning right and left
extremity). The independent t-test was used to compare
results obtained by females to males and in the right extrem-
ity to the left. The level of significance was set at p ≤ 0.05.
Additionally, the ICCs (3.1) for intra-rater reliability of both
tests (for each extremity) were calculated.
All statistical analyses were performed using the Statistica
13 software.

RESULTS
The angular results of the PKET and the AKET are present-
ed in table I. The outcomes obtained by females differ
significantly in comparison to males (p < 0.01). We found
no significant differences in the mean values of both tests
between the right and the left side (p > 0.05).
The Pearson coefficients are presented in table II. All of the outcomes revealed a significant \( p < 0.01 \) positive, moderately high correlation. The intra-rater ICCs \( (3.1) \) were \( 0.99 \) in the AKET for each extremity and in the PKET for right lower extremity; and \( 0.98 \) in the PKET for left lower extremity.

**DISCUSSION**

The angular values of the PKET obtained in this study are similar to those presented by Kuszewski et al. (19) in healthy subjects - mean value was \( 144.7^\circ \pm 17.8^\circ \) (without sex differentiation), including \( 90^\circ \) of initial flexion. Based on our formula it would be \( 54.7^\circ \), which is a little bit higher result than ours. It could be the effect of greater force applied during the test (\( 30N \) to \( 2.5 \) kg in our study). The mean results of the AKET presented by Yıldırım et al. (22), according to our formula of measuring, would be \( 84.9^\circ \pm 8.2^\circ \) for the right leg and \( 83.9^\circ \pm 8.5^\circ \) for the left. These values are also slightly higher than our outcomes, but the research was conducted on younger subjects. Moreover, in both cited studies the research groups were smaller than in ours.

However, the main purpose of presented study was to assess the relationship between the AKET and the PKET in healthy, generally active adults. The results we have obtained, revealed a significant positive, moderately high correlation between both tests, regarding men, women and subjects of both sexes taken together (concerning right, as well as left extremity). Our outcomes are consistent with research of Gajdosik et al. (15) \( (r = 0.64) \) - the only publication we have found, which had previously compared passive and active knee extension tests. However, the research group in that study included only 30 male subjects with right extremity tested. In our study we have rated many more participants of both sexes and the tests were performed for right and left side to catch the asymmetry, if any appear (afterwards, our results did not reveal any significant differences in the mean values of both tests between the right and the left extremity). Despite the fact that women were significantly more flexible in both tests than men, the correlation coefficients between the results of PKET and AKET were very similar. In the literature there are also studies, which show correlation between the AKET and another passive test for hamstring flexibility evaluation (straight leg rise (SLR)), but

### Table I. The angular values (°) of the passive and active knee extension tests.

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<tr>
<th></th>
<th>Female (n = 204)</th>
<th>Male (n = 110)</th>
<th>Total (n = 314)</th>
<th>Sex-related difference p-value</th>
<th>Body site-related difference p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PKET right</td>
<td>Mean ± SD</td>
<td>51.6 ± 11.6</td>
<td>45.7 ± 12.5</td>
<td>49.5 ± 12.2</td>
<td>0.000</td>
</tr>
<tr>
<td></td>
<td>Min-Max</td>
<td>23.3-85.0</td>
<td>15.0-78.3</td>
<td>15.0-85.0</td>
<td>0.304</td>
</tr>
<tr>
<td></td>
<td>Lower quartile</td>
<td>45.2</td>
<td>38.3</td>
<td>41.7</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Upper quartile</td>
<td>58.7</td>
<td>53.0</td>
<td>56.3</td>
<td></td>
</tr>
<tr>
<td>PKET left</td>
<td>Mean ± SD</td>
<td>50.4 ± 12.0</td>
<td>45.0 ± 13.2</td>
<td>48.5 ± 12.7</td>
<td>0.000</td>
</tr>
<tr>
<td></td>
<td>Min-Max</td>
<td>21.7-83.7</td>
<td>16.0-76.7</td>
<td>16.0-83.7</td>
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</tr>
<tr>
<td></td>
<td>Lower quartile</td>
<td>43.0</td>
<td>37.0</td>
<td>40.8</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Upper quartile</td>
<td>57.3</td>
<td>53.3</td>
<td>55.7</td>
<td></td>
</tr>
<tr>
<td>AKET right</td>
<td>Mean ± SD</td>
<td>72.9 ± 11.0</td>
<td>68.5 ± 12.3</td>
<td>71.3 ± 11.6</td>
<td>0.001</td>
</tr>
<tr>
<td></td>
<td>Min-Max</td>
<td>45.0-92.0</td>
<td>45.0-90.0</td>
<td>45.0-92.0</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Lower quartile</td>
<td>65.7</td>
<td>58.7</td>
<td>62.7</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Upper quartile</td>
<td>81.8</td>
<td>79.0</td>
<td>80.7</td>
<td></td>
</tr>
<tr>
<td>AKET left</td>
<td>Mean ± SD</td>
<td>71.9 ± 11.3</td>
<td>67.4 ± 12.5</td>
<td>70.3 ± 11.9</td>
<td>0.001</td>
</tr>
<tr>
<td></td>
<td>Min-Max</td>
<td>44.7-92.0</td>
<td>39.5-89.3</td>
<td>39.5-92.0</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Lower quartile</td>
<td>64.2</td>
<td>56.3</td>
<td>60.5</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Upper quartile</td>
<td>81.3</td>
<td>77.7</td>
<td>80.0</td>
<td></td>
</tr>
</tbody>
</table>

### Table II. The Pearson coefficients (r) between the AKET and PKET.

<table>
<thead>
<tr>
<th></th>
<th>Right leg</th>
<th>Left leg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>0.73</td>
<td>0.69</td>
</tr>
<tr>
<td>Women</td>
<td>0.72</td>
<td>0.67</td>
</tr>
<tr>
<td>Men</td>
<td>0.73</td>
<td>0.69</td>
</tr>
</tbody>
</table>
the outcomes are not patchy. Neto et al. (2) obtained $r = 0.71$ and $r = 0.67$ (depending on the side), while Gajdosik et al. (15) revealed $r = 0.43$ and $r = 0.37$ (depending on the modification of the SLR). Considering this, although our results show moderately high levels of correlation, we suggest being very precise in choosing the test variant, because they are based on different neurophysiological mechanisms, which could cause the difference in the outcome of both tests. The resistance to passive lengthening is influenced by the readily adaptable amount of muscle tissue, including the contractile proteins and the non-contractile proteins of the sarcomere cytoskeletons (17); while the active flexibility is associated not only with passive tissue properties, but also with the excitability of the motoneuron pool and the level of muscle activation (23).

In addition to the main purpose of the study, we have also evaluated the intra-rater reliability of the PKET and the AKET. Presented versions of both tests yield excellent reliability. Other studies showed high values of test-retest ICCs too, but not as perfect as ours (2, 15). The researchers also found high inter-tester reliability regarding both tests (8, 10, 12, 13). What is more, the tests turned out to be very reliable in acute hamstring injuries, without including any sophisticated tools, except for inclinometers (8). Performing the tests, some issues could appear with the indication of “a strong but tolerable stretch” feeling. According to the references, it seems that patients could better indicate the point of maximal tolerable stretch while actively extending the knee, compared with passive extension of the knee by the rater (8). Although the nature of this sensation is entirely subjective, we attempted to make this more “objective” during the PKET by using the force gauge in consecutive repetitions. This probably was one of the reasons of obtaining such highly values of ICC. Moreover, in our study all the measurements were performed by the same two physiotherapists, so they gained a lot of experience during testing so many subjects, which also may be reflected in ICC values. From a clinical point of view, the high intra-rater reliability values obtained in this study lead us to believe that the PKET and the AKET can be useful in physiotherapist’s/trainer’s daily work to measure length of the hamstrings. Both tests are easily to perform and, as researches show, even raters with not much experience in clinical practice can do it well (10, 12). The moderately high levels of correlations, that we presented in the study, in our opinion, allow to use both tests interchangeably, but only for general hamstring flexibility evaluation. For the precise muscle tissue properties assessment, especially in research work, the suitable test should be chosen, considering passive versus active nature of the movement and the specific purpose of the assessment. The presented study has some limitations. We assessed only healthy, quite young, asymptomatic subjects, so we do not know how other clinical populations might respond. Due to the main purpose of the study was to assess correlations between the PKET and the AKET, we wanted to obtain very precise results of measurement, which is why we only involved one PR – in that case we were not able to evaluate the inter-tester reliability, but it is well documented in the literature. Another issue is that although both tests are commonly used for hamstring flexibility evaluation, changes to neural structures, for example the sciatic nerve, are also likely to occur during the tests (12, 24). The neural mechano-sensitivity may play a significant role in the end point feeling of “a strong but tolerable stretch” (24). We think that future studies should compare the functional tests for hamstring flexibility assessment with the results of measurements, like myotonometry (25), which would not involve neural structures during muscle tone evaluation.

CONCLUSIONS
The PKET and the AKET are useful and reliable tools for evaluation the flexibility of hamstrings. There is a significant positive, moderately high correlation between results of both tests.

In our opinion, AKET is a sufficient test for a simple clinical evaluation in everyday practice and it’s recommended special for people with little experience. Additionally, in more specific clinical assessment due to the different neurophysiological mechanisms, they are based on, the choice of the tests should take into account whether the purpose of the analysis is passive versus active form of the movement.

CONFLICT OF INTERESTS
The authors declare that they have no conflict of interests.

REFERENCES
3. Witvrouw E, Danneels L, Asselman P, et al. Muscle flexibility as a risk factor for developing muscle injuries in male profes-