REVIEW

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Morphological Changes and Pathological Findings in the Achilles Tendons of Diabetic Patients: A Meta-Analysis of Comparative Clinical Studies

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SUMMARY

Objective. There is a greater risk of tendon rupture requiring hospitalization in people with diabetes. Diabetes could induce substantial alteration in Achilles tendon (AT) that could affect its mechanical properties mainly in relation to gait and foot ulceration. Many studies reported AT morphological changes using diagnostic methods in clinical settings. However, there is no quantitative synthesis of the published data.

Methods. A systematic review was conducted using several electronic databases. Only comparative clinical studies comparing AT changes and findings between healthy people and patients with diabetes, with and without neuropathy were included. Studies using ultrasound or MRI were eligible for inclusion.

Results. Seventeen studies comprising 2,938 subjects (5,822 tendons) were analyzed. Increased AT thickness in patients with diabetes was found, but the difference did not reach significance. The weighted Odds Ratios (OR) were all significantly favoring changes in diabetes: 1) overall AT morphological changes (OR 3.5, CI 2.970-4.181); 2) AT fiber disorganization (OR 3.48, CI 2.291-12.1840); 3) tendinopathy (OR 3.5, CI 2.934-4.333), d) enthesopathy (OR 4.08, CI 1.130-14.723), and 4) calcifications (OR 2.38, CI 1.424-3.976).

Conclusions. A trend for increased Achilles tendon thickness was noticed in diabetic patients, especially those with peripheral neuropathy. When compared to healthy subjects, patients with diabetes expressed greater morphological changes in the form of tendon fiber disorganization, calcifications, and enthesopathies. Such anomalies could increase the risk of Achilles rupture, falls and the development of diabetic foot ulcers.

KEY WORDS

Achilles tendon; diabetes mellitus; diabetic neuropathies; ultrasound; magnetic resonance imaging.

INTRODUCTION

Diabetic foot, a major manifestation of diabetes mellitus, is characterized by peripheral neuropathy, and is at risk of diabetic foot ulceration (DFU) (1, 2). DFU is a major source of morbidity, and it is estimated that 50-70% of all lower limb amputations are due to DFU (3). Besides the presence of peripheral neuropathy, altered gait mechanics in patients with diabetes are known to be risk factors for DFU (4).

Patients with diabetes, especially diabetic neuropathy, experience altered range of movement at the joints, one of which is reduced motion at the ankle in dorsiflexion and plantar flexion, resulting in reduced walking speed, cadence and step length (4, 5). Possible explanations have been sought, and the current concepts range from central and autonomic dysfunction to motor neuropathy and soft tissue alterations (4-6).

In addition, during locomotion and propulsion in actions such as walking, running, and jumping, the gastrocnemius-soleus complex translates forces through the Achilles tendon (AT) to allow for plantar flexion of the foot (4, 7). Studies showed an altered leverage around the ankle during walking in people with diabetes due to a reduced AT length and moment arm length (8, 9). It has been demonstrated that tendons of patients with diabetes exhibited a significant inferior biomechanical profile over non-diabetic tendons (10, 11). In mouse models, diabetes induced substantial alteration in AT mechanical properties (12) and similarly following tenotomy (13).

In people living with diabetes, advanced glycation end products have deleterious effects on the biological and mechanical effects of the tendons and ligaments throughout the body, resulting in stiffness and chronic tendinopathy (14, 15). Hence, with such an important role in gait, AT function is of interest, and several studies throughout the literature attempted to characterize the change in AT function in diabetes. Biomechanical studies tend to show an increased stiffness and decreased elongation of the AT with increased plantar pressure during gait in people with diabetes (8, 16). In addition, a community-based case-control study showed that there was a 44% greater likelihood of hospitalization for any tendon rupture in subjects with Type 2 diabetes than in those without (17).

The aim of this meta-analysis is therefore to report evidence-based morphological differences of the AT between healthy patients and patients living with diabetes with or without peripheral neuropathy.

MATERIALS AND METHODS

Search strategy

A systematic electronic search was conducted through a number of databases such as PubMed, Scopus, Google Scholar and the Cochrane Library from 1997 to June 1st, 2021. The combination of keywords such as [Achilles AND Diabetes AND (ultrasound OR MRI)] were used. The references of the deemed relevant papers were checked. All included articles were citation-tracked using Google Scholar to ensure that all relevant articles were identified. Duplicates were deleted. The PRISMA guidelines were followed during the preparation of this meta-analysis (18).

Criteria for study selection

Articles that were deemed irrelevant to the study aim were excluded. Systematic reviews, case series, and all animal model studies were excluded. Included were only retrospective or prospective case-control or randomized control trials that compared AT changes between healthy people (control group) and people with diabetes mellitus (DM group) or with people having diabetic neuropathy (DN group). Methods of investigation were limited to ultrasound and MRI.

Quality appraisal

The Joanna Briggs Institute (JBI) critical appraisal checklist for case control studies was used to evaluate the quality of the included studies (19).

Study outcomes

The searched outcomes were set as follows: AT thickness, any pathological change in AT gross structure at any level (proximal, middle or distal) such as fiber disorganization, tendinopathy, calcifications or enthesopathy.

Data extraction

Data extraction included sample size, both according to individuals and number of tendons, grouped into healthy controls and diabetic subjects with and without peripheral neuropathy. Included as well were the patient demographics, type and duration of diabetes, HbA1C, average body mass index (BMI), as well as tendon morphological changes and pathological findings.

Data analysis

The software StatsDirect (Cambridge, UK) was used for statistical analysis. Continuous variables were expressed in means ± standard deviation (SD). Univariate and multivariate analysis tests were used to look for differences in pooled means between groups. Weighted proportions were yielded using proportion meta-analysis. Heterogeneity was assessed via the I^2 statistic; whenever the I^2 value was superior to 50%, the random-effect value was reported.

RESULTS

Search results

The search yielded 101 results and 4 duplicates were deleted. After title and abstract checking, 36 articles were scrutinized for eligibility. Seventeen papers were excluded: 11 biomechanical studies, 7 using x-rays and 1 study compar-

ing diabetic patients with and without ulcers. In total, 17 studies were retained for analysis (20-36). **Figure 1** shows the flowchart of study identification.

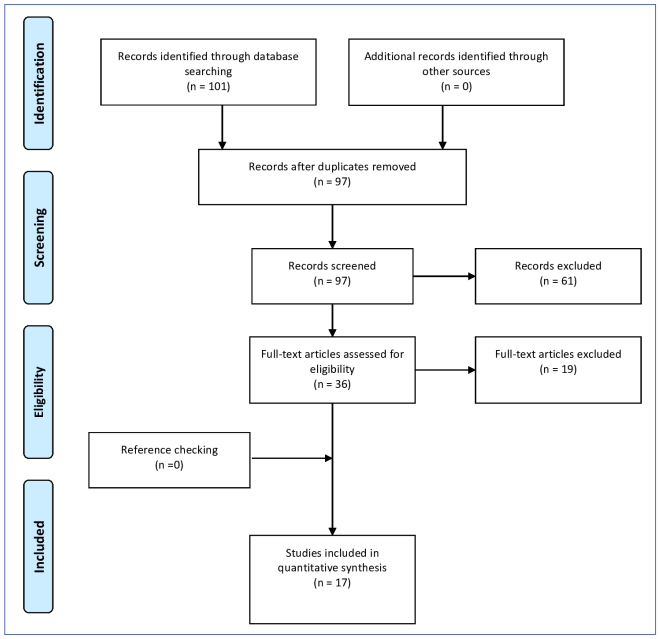

Figure 1. PRISMA flow diagram.

Modified from: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med. 2009;6(7):e1000097. doi: 10.1371/joumal.pmed1000097 (18).

Study characteristics results

The 17 studies comprised 2,938 subjects including 1,791 controls, 940 with DM and 211 with DN. The total number of studied tendons in the sample was 5,822. The mean age of the whole pooled sample was 59.7 ± 8.6 years with no statistical difference between the 3 groups. The population sum was divided almost equally based on sex, with 48% males and 52% females with no statistical difference between the 3 groups.

All studies but Papanas *et al.* (20) used ultrasound imaging for AT evaluation. Thirteen studies (22-30, 33-35) reported the mean BMI of their samples with pooled values of 25.8 ± 2 .3, 27.5 ± 2 and 27.5 ± 2.1 kg/m^2 for healthy and DM and DN groups, respectively. The mean duration of DM was of 8.5 ± 4.2 and 12.7 ± 3.7 years for the DM and DN groups, respectively. The mean values of HbA1c were of 7.6 ± 0.7 and 8.1 ± 1.6 years for the DM and DN groups, respectively. **Table I** summarizes patients' characteristics.

Study quality results

Out of a maximum of 10, the mean JBI score for the included studies was 8.6 ± 0.9.

Outcomes

AT thickness

The results of AT thickness are shown in **table II**. Ten studies showed the increasing trend of AT thickness in DM and DN patients, 6 studies reported statistically significant differences between DM and DN with the respective controls, and 3 studies stated no statistical significance between DM and control groups. One study (20) used MRI for Achilles thickness measurements with a significant difference only between DM and control groups ($p = 0.01$). For the remaining "ultrasound studies", there was a trend towards higher thickness in patients of DM group and particularly DN group when compared to healthy subjects, but the difference did not reach significance (**table III**).

AT morphological changes and pathological findings

Based on 8 studies (3,038 tendons in control group and 1,396 tendons in DM group), the weighted proportions of the overall AT morphological changes were 19.5% (95%CI 0.126-0.275, $I^2 = 93.5\%$) and 45.8% (95%CI 0.287-0.633, $I^2 = 97.7\%$) for the control and DM groups, respectively, with an OR of 3.5 (95%CI 2.970-4.181, $I^2 = 37\%$, $p < 0.0001$).

Six studies reported AT fiber disorganization comprising 384 and 584 tendons in control and diabetic groups respectively. The weighted proportions were 12.2% (95%CI 0.091-0.156, $I^2 = 31\%$) and 42.5% (95%CI 0.163-0.712, $I^2 = 98\%$) with an OR of 3.48 (95%CI 2.291-12.184, $I^2 = 75\%$, $p < 0.0001$).

Six studies reported the frequency of tendinopathy if hypo or hyperechoic foci were present, totalizing 2,930 control tendons and 1,160 diabetic tendons. The weighted proportions were 8% (95%CI 0.049-0.119, $I^2 = 84.5\%$) and 25.5% (95%CI 0.195-0.320, $I^2 = 82.3\%$) with an OR of 3.5 (95%CI 2.934-4.333, $I^2 = 0\%$, $p < 0.0001$).

Two studies reported the presence of enthesopathy, totalizing 626 control tendons and 358 diabetic tendons. The weighted proportions were 22.5% (95%CI 0.047-0.873, $I^2 = 99\%$) and 40.8% (95%CI 0.0004-0.958, $I^2 = 99\%$) with an OR of 4.08 (95%CI 1.130-14.723, $I^2 = 84.8\%$, $p = 0.03$).

Four studies reported the presence of calcifications, totalizing 382 control tendons and 540 diabetic tendons. The weighted proportions were 6.4% (95%CI 0.006-0.175, $I^2 = 91\%$) and 13.4% (95%CI 0.043-0.2367, $I^2 = 93.7\%$) with an OR of 2.38 (95%CI 1.424-3.976, $I^2 = 48.5\%$, $p = 0.0008$).

Table IV shows details of ultrasound findings in relation with AT morphological changes and pathological findings. **Figure 2** shows the Odds Ratio forest plots of the AT morphological changes and pathological findings.

Table I. Characteristics of the included studies.

Study	Sample patients	Sample tendons	Groups (patients)			Groups (tendons)			Average age (years)			Gender (Males, %)			Average BMI (kg/m²)			Diabetes type	Mean duration of diabetes (years)	
			C	DM	DPN	C	DM	DPN	C	DM	DPN	C	DM	DPN	C	DM	DPN		DM	DPN
Giacomozzi *et al.* 2005	82	164	21	27	34	42	54	68	56.6	52.7	55.5	13 (62%)	19 (70%)	20 (58%)	25	25.3	27.25	1 and 2	15.1	18.2
Akturk *et al.* 2007	89	178	34	55	-	68	110	-	52.24	55	-	21 (61.7%)	29 (52%)	-	27.5	28.5	-	2	10.3	-
Batista *et al.* 2008	80	160	10	70	-	20	140	-	67	65	-	-	29 (41.4%)	-	-	-	-	2	11	
Papanas *et al.* 2009	54	54	16	19	19	16	19	19	61.6	63.6	63.9	8 (50%)	9 (47%)	9 (47%)	-	-	-	2	12.1	10.7
Abate *et al.* 2012a	1186	2372	993	193		1986	386	-	69.1	68.6	-	95 (43%)	48 (46%)	-	23.6	24.7	-	2	-	-
Abate *et al.* 2012b	69	138	18	51	-	36	102	-	68.5	69.1	-	9 (50%)	24 (47%)	-	23	27.9	-	2	0.58	-
Chieng *et al.* 2013	64	128	32	23	9	64	46	18	59.8	63.9	65.3	9 (28%)	5 (26%)	5 (55%)	23.7	24.6	28	2	10.4	10.7
Abate *et al.* 2014	409	818	273	136	-	546	272	-	63.9	64.6	-	124 (45%)	61 (44%)	-	23.9	25.7	-	1 and 2		-
Evranos *et al.* 2015	111	222	33	43	35	66	86	70	57.1	55.7	59.3	10 (30%)	19 (44%)	18 (51%)	26.6	26.5	25.7	2	6	15
de Jonge *et al.* 2015	92	184	44	48	-	88	96	-	35.4	36.5	-	22 (50%)	24 (50%)	-	24.9	28.1	-	1 and 2	9.4	-
Ursini *et al.* 2017	83	166	40	43	-	80	86	-	58.4	60.8	-	21 (52.5%)	25 (58.1%)	-	28.6	29.2	-	2	11	-
Afolabi *et al.* 2019	160	320	80	23	57	160	46	114	61	60.9	-	30 (42.5%)	34 (37.5%)	-	25.92	25.1	-	2	3.5	-
Lyldir *et al.* 2018	75	150	30	23	22	60	46	44	58.4	59.9	63.3	9 (30%)	10 (43.5%)	6 (27%)	30.3	31.7	31.5	2	8	9
Coombes *et al.* 2019	40	80	7	33	-	14	66	-	55.6	58.6	-	1 (14.3%)	19 (57.6%)	-	27	33.4	-	2	12.5	-
Afolabi *et al.* 2020	160	320	80	80	-	160	160	-	61	60.9	-	34 (42.5%)	30 (37.5%)	-	-	-	-	2	3.5	-
Harish *et al.* 2020	142	284	61	50	31	122	99	55	30-77	30-88	-	35 (57.8%)	41 (50.62%)		-	-	-	2	5.76	
Kuo *et al.* 2020	42	84	19	23	-	38	46	-	65	65	-	10 (53%)	12 (52%)	-	-	-	-	2	9.5	-

C: control; DM: diabetes mellitus ; DN diabetic neuropathy.

Table II. Results of characteristics of Achilles tendon.

Study	Imaging	Portion of AT examined	AT Thickness (mm)			% of AT morphological changes on US*	
			Control	DM	DN	Control	DM
Giacomozzi *et al.* 2005	US	Distal	4 ± 0.5	4.6 ± 1.0	5.05 ± 1.7	-	-
Akturk *et al.* 2007	US	Middle	4.65 ± 0.67	5.16 ± 0.67	-	-	-
Batista *et al.* 2008	US	Middle	5.9	5 ±0.8	-	24.30%	88.60%
Papanas *et al.* 2009	MRI	Middle	6.7 ± 1.4	7.4 ± 1	7 ± 1.1		
Abate *et al.* 2012	US	-	-	-	-	26.80%	68.30%
Abate *et al.* 2012	US	Middle	4.0 ± 0.3	5.23 ± 0.8	-	13.80%	34.30%
Chieng *et al.* 2013	US	Distal	6.1 ± 0.8	6.9 ± 1.0	8.3 ±1.3	-	-
Abate *et al.* 2014	US	Middle	-	-	-	11.70%	25.70%
Evranos *et al.* 2015	US	Proximal	1.8 ± 0.2	1.9 ± 0.3	2.1 ± 0.8	-	-
		Middle	4.5 ± 0.7	4.7 ± 0.6	5.2 ± 0.6		
		Distal	4.2 ± 0.6	4.6 ± 0.7	5.2 ± 0.7		
de Jonge *et al.* 2015	US	Middle	-	-	-	7.25%	11.80%
Ursini *et al.* 2017	US	Distal	4.2 ± 0.8	4.4 ± 1.1	-	57.50%	74.40%
Afolabi *et al.* 2018	US	Middle	4.6 ± 0.56	5.04 ± 0.55	6.1 ± 0.65	-	-
Lyldir *et al.* 2018	US	Middle	4.6 ± 0.75	5 ± 0.75	5.1 ± 0.8	-	-
Coombes *et al.* 2019	US	Middle	4.6 ± 0.15	5.3 ± 0.3	-	-	-
		Distal	3.8 ± 0.07	4.3 ± 0.2	-	-	-
Afolabi *et al.* 2020	US	Distal	-	-	-	15%	43%
Harish *et al.* 2020	US	Proximal	2.89 ± 0.6	3.29 ± 0.71	3.12 ± 0.79	17.9%	44%
		Middle	4.41 ± 0.61	4.72 ± 0.77	4.81 ± 0.7		
		Distal	3.91 ± 0.58	4.60 ± 0.98	4.52 ± 0.98		
Kuo *et al.* 2020	US	Middle	5.1 ± 0.8	4.9 ± 0.9	-	-	-

DM: diabetes mellitus group; DN: diabetic neuropathy group; US: ultrasound; AT: Achilles tendon.

Table III. Thickness outcome pooled results (in mm).

Achilles level	n of studies	n of tendons	Mean thickness control	Mean thickness DM	Mean thickness DN	P-values*
Proximal	2	498	2.34 ± 0.8	2.6 ± 1	2.6 ± 0.7	0.8/0.7**
Middle	9	3,842	4.9 ± 0.8	5.3 ± 0.8	5.3 ± 0.5	0.18/0.1**
Distal	6	1,040	4.3 ± 0.9	4.9 ± 1	5.7 ± 1.7	0.17/0.18**

*P-values of univariate regression analysis; **value between control and DM groups/value between control and DN groups.

Table IV. Details of Ultrasound Abnormalities.

Study	AT abnormality on US		Disorganization of AT fibers		Tendinopathy/hypo-hyperechoic foci		Enthesopathy		Calcifications	
	Control	DM	Control	DM	Control	DM	Control	DM	Control	DM
Batista *et al.* 2008	8/20 (40%)	124/170 (88.6%)	2/20 (10%)	124/170 (88.6%)	-	-	-	-	6/20 (30%)	32/170 (24.3%)
Abate *et al.* 2012	262/993 (26.8%)	132/193 (68.3%)	-	-	262/993 (26.8%)	132/193 (68.3%)	-	-	-	-
Abate *et al.* 2012	5/36 (13.8%)	35/102 (34.3%)	5/36 (13.8%)	35/102 (34.3%)	5/36 (13.8%)	35/102 (34.3%)	-	-	-	-
Abate *et al.* 2014	45/546 (8.2%)	60/272 (22%)	-	-	45/546 (8.2%)	60/272 (22%)	9/546 (1.6%)	32/272 (11.7%)	-	-
de Jonge *et al.* 2015	6/88 (6.8%)	12/96 (12.5%)	6/88 (6.8%)	12/96 (12.5%)	-	-	-	-	-	-
Ursini *et al.* 2017	46/80 (57.5%)	64/86 (74.4%)	7/80 (8.8%)	21/86 (24.4%)	2/80 (2.5%)	23/86 (26.7%)	46/80 (57.5%)	64/86 (74.4%)	0/80 (0%)	3/86 (3.5%)
Afolabi *et al.* 2020	30/160 (18.7%)	86/160 (53.75%)	26/160 (16.25%)	84/160 (52.5%)	10/160 (6.2%)	31/160 (19.4%)	-	-	2/160 (1.2%)	9/160 (5.6%)
Harish *et al.* 2020	19/123 (15.4%)	68/166 (41%)	-	-	6 (4.9%)	27 (17.5%)	-	-	13 (10.6%)	41 (26.6%)

DISCUSSION

Main findings

The AT tendon seems to be thicker among people with diabetes. Many morphological and pathological changes were significantly higher than in healthy patients, namely fiber disorganization, tendinopathy, enthesopathy and calcifications.

AT thickness

The general trend was an increase in average AT thickness between diabetic patients with or without neuropathy and healthy controls. This trend however was not observed in one study (21) in which the control group had higher AT thickness than the DM group. However, this article could be criticized for selection bias, in which the DM group had 70 patients while the control group had only 10. Another study (22) revealed statistical significance only in DN *vs* controls.

AT thickness has been hypothesized to alter gait mechanics by increasing energy expenditure during gait (9), as well as decreasing calf muscle endurance and increasing patient-related symptoms during gait in patients with Achilles Tendinopathy (37). Therefore, further studies are definitely in need to better quantify this outcome.

Despite the difference in location measurement, the AT thickness remained trending towards an increase in DM and particularly in DN group. Perhaps different measures at different locations, including proximal, middle and distal AT should be taken into consideration in future studies to maximize the efficacy of the results. The introduction of the MRI could have an added value as well for its excellent modality of structure delineation (20). It might be more relevant for future research to measure the maximal thickness of AT for better accuracy of this anatomical change. Using this method, Papanas *et al.* (20) found significant thickness difference between both groups via MRI measurements.

Clinical relevance of morphological and pathological changes

The overall AT morphological changes and in particular fiber disorganization were 3.5 and 5.3 times higher, respectively, in DM group compared to healthy people. Tendinopathy (OR 3.5), enthesopathy (OR 4.08), and calcifications (OR 2.38) were also significantly higher. An epidemiological study reported that AT calcification and insertional AT radiological calcifications were significantly higher in people with DM compared to those without DM, with an OR of 3 (38). Another study found that DM can strongly affect post-operative outcomes following surgical repair of acute Achilles tendon tears (39).

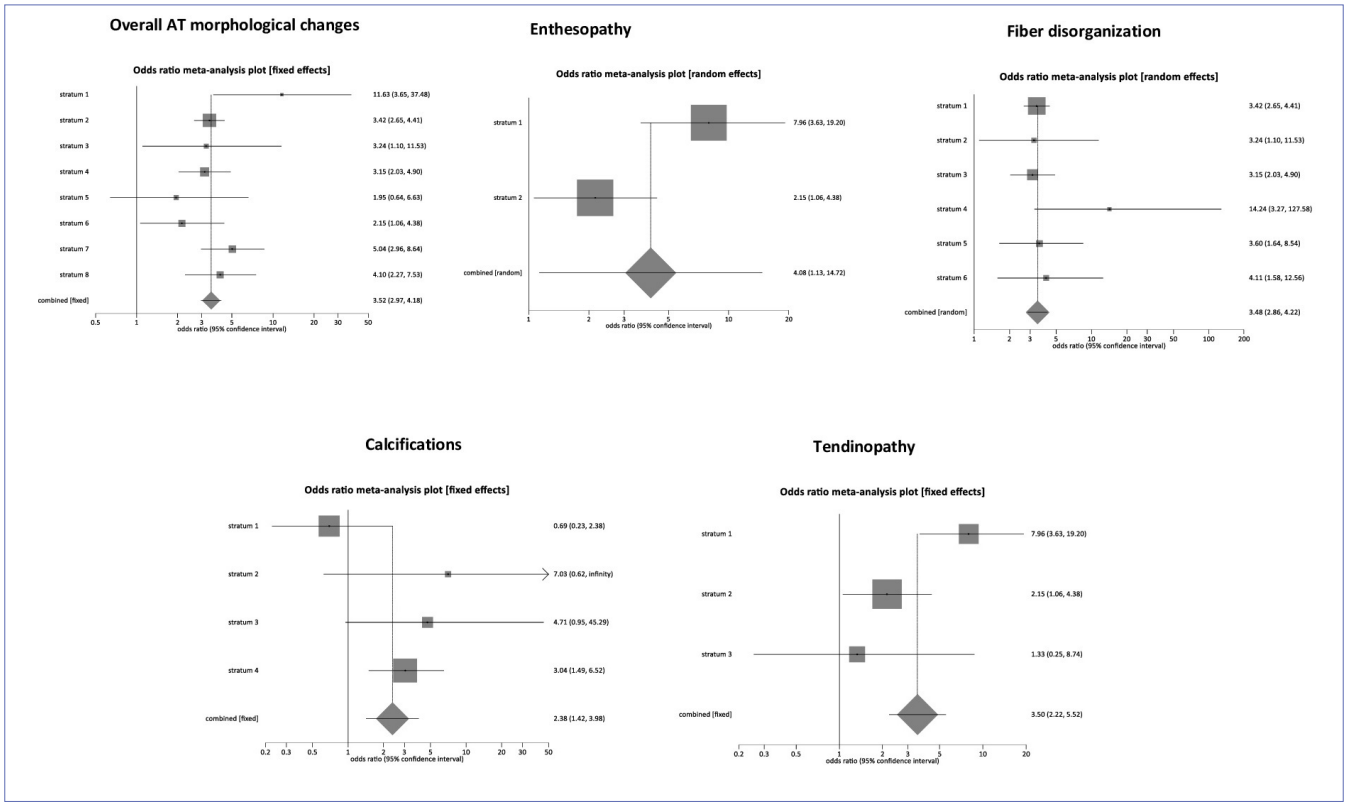

Figure 2. Odds ratio plots.

Additionally, tendon's mechanical properties are determined by the collagen fiber organization which is extremely important for the tendon's ability to adapt to the loading environment (40). Any disruption of these mechanical properties through disorganization of the collagen fibers or disruption by materials such as calcifications can be detrimental to the function of the tendon (40). It has been demonstrated that a persistent state of hyperglycemia could affect the crosslink reaction between collagens and advanced glycosylation end-products, inducing disruption of tendon homeostasis and rupture (41). Therefore, our findings would imply that the AT could be at a higher risk of rupture in this population.

On the other hand, Couppé *et al.* demonstrated that AT modulus, which represents the material stiffness after accounting for tendon dimensions, was higher in diabetic patients compared with controls (17). Petrovic *et al.* reported that AT in people with diabetes and particularly people with diabetic peripheral neuropathy was stiffer and less elongated (9). The degree to which a tendon stretches depends upon many factors such as tendon's tensile stiffness (42). Stiffness in the triceps surae muscle and tendon is thought to be largely responsible for equinus in patients with diabetes which could induce a reduction of its stretching ability thus, restricting dorsiflexion of the ankle joint (43). These changes would lead to a less flexible AT and thought to play a role in the development of plantar ulcers, stress fractures, and even Charcot foot in patients with diabetic neuropathy (17, 44). An increased stiffness and shorter length of the tendon placing the ankle in plantar flexion and resulting in excessive pressure over the metatarsal heads might worsen the deleterious effect of diabetic neuropathy of the foot. Such combination of local hyper-pressure and consequences of peripheral neuropathy would increase the risk of diabetic ulcers in this population.

Limitations

A number of limitations could be noted in this study. Ultrasound values are operator dependent, entailing risk of publication bias. Furthermore, levels for measurements, be it proximal, middle or distal, were rarely defined with no report of reference point. Therefore, the reported values might be affected by the lack of a standard method. Fiber disorganization was not quantified with a scoring system based on the severity of the disorganization. Furthermore, the diagnostic criteria for tendinopathy were not always defined. However, Ranger *et al.* demonstrated greater prevalence of tendinopathy in people with diabetes than

controls (OR 3.84) where many tendons were included in their meta-analysis (45). Few studies did not report diabetes duration. However, the mean duration of those reporting this variable was between 8 and 12 years, and that is in line with other studies which found greater duration of diabetes in participants with both diabetes and tendinopathy (of AT and other tendons) compared to those with diabetes but not tendinopathy (45). Four studies did not report the BMI of their samples with the remaining 11 studies showing a pooled men BMI of 27 and 28 kg/m^2 for the DM and DN groups, respectively. Knowing that tendinopathy could be associated with adiposity, BMI may be a possible confounder that could have impacted our result (46-48).

Implication for practice

Our findings would have implications in the management of diabetic foot. A stiff AT mediated by the pathological changes would shorten the tendon and consequently place the foot in equinus position. The resulted great pressure on the metatarsal heads would favor the development of plantar ulcers. Thus, our findings could add support to the rationale behind the use of some specific techniques when treating DFUs. Restoring tendon length, and consequently rectifying ankle equinus, would relieve the pressure and favor wound healing. In fact, it has been demonstrated that AT lengthening or gastrocnemius recession are effective surgical treatments when treating diabetic forefoot plantar wounds (48). Additionally, and since the risk of rupture could be higher with the presence of tendinopathy, our findings would suggest the need for careful monitoring during sport activity or rehabilitation of lower limbs in patients with diabetes.

Implication for research

A reference structure, such AT insertion onto the calcaneal tuberosity, is needed for a standardization of the measurement method for AT thickness. Therefore, the different levels could be better defined. Creating a scoring system for fiber disorganization would be of importance to better assess the severity of this outcome. Additionally, it is of interest to investigate in the future any correlation between the presence of those morphological/pathological changes and the development of ankle equinus, which reflects a higher stiffness induced by these changes.

CONCLUSIONS

Diabetes mellitus induces alteration of the structure of the Achilles tendon. Our review shows a trend for increased thickness of the tendon especially in those with peripheral neuropathy. Furthermore, a significant increase of morphological changes was demonstrated, mainly in the form of fiber disorganization, calcifications, and enthesopathies. These morphological changes could generate higher stiffness and may play an important role in the development of plantar foot ulceration, altered gait with risk of falls along with higher risk of tendon rupture.

FUNDINGS

None.

DATA AVAILABILITY

All data used in this review is appropriately cited.

CONTRIBUTIONS

KY: formulation of research idea. KY, ED: data extraction. KY: data analysis. KY, ED, CA: manuscript writing and reviewing.

CONFLICT OF INTERESTS

The authors declare that they have no conflict of interests.

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