ORIGINAL ARTICLE

Nr 2022;12 (4):537-541

Evaluation of Serum Calcium, Phosphorus and Vitamin D Levels and History of Calcium and Vitamin D Supplementation in Patients with Calcified Shoulder Tendinopathy

H. Saremi[1], M. H. Bagheri[2], H. Naderifar[3], M. A. Seifrabiei[4]

[1] *Department of Orthopedic Surgery, Faculty of Medicine, Hamadan University of Medical Sciences, Hamadan, Iran*
[2] *Medical School, Hamadan University of Medical Sciences, Hamadan, Iran*
[3] *Hearing Disorders Research Center, Hamadan University of Medical Sciences, Hamadan, Iran*
[4] *Department of Community and Preventive Medicine, School of Medicine, Hamadan University of Medical Sciences, Hamadan, Iran*

CORRESPONDING AUTHOR:
Homa Naderifar
Hearing Disorders Research Center
Hamadan University of Medical Sciences
Building No. 4, Shariati Crossroad
Hamadan, Iran
E-mail: Hnaderifar121@gmail.com

DOI:
10.32098/mltj.04.2022.09

LEVEL OF EVIDENCE: 3

SUMMARY

Introduction. Calcific Tendinopathy (CT) of the shoulder is a common painful disorder. Due to the unknown etiology of CT, the present study aimed to evaluate possible relationship of serum calcium, phosphorus and vitamin D levels, history of calcium and vitamin D supplementation and incidence of CT.

Methods. The present study is a case-control study which was performed on 38 patients with CT of the shoulder (n = 17) and the control group (n = 21). Data were recorded using a checklist including demographic information and serum levels of calcium, phosphorus and vitamin D and history of calcium and vitamin D supplementation. Data were analyzed by SPSS software version 21.

Results. There was no significant difference between the two groups in terms of age and sex, history of calcium and vitamin D supplementation, serum calcium level, serum phosphorus level. There was a significant difference between the mean serum levels of vitamin D in patients with CT (P-value = 0.042).

Conclusions. The results of the present study show a higher level of vitamin D in people with CT than the control group who were selected from normal people in the community.

KEY WORDS

Calcific tendinopathy; rotator cuff; calcium; vitamin D supplement; shoulder pain.

INTRODUCTION

Calcific shoulder tendinopathy is caused by calcium deposits inside or around the rotator cuff tendons. It is an acute or chronic painful disease, especially due to the deposition of calcium hydroxyapatite crystals, usually inside the supraspinatus and infraspinatus muscle tendons (1). Clinical manifestations of the calcification process in the tendons include chronic pain associated with activity, tenderness, local edema, and varying degrees of reduced range of motion (ROM) (2).

The cause of calcific tendonitis has not yet been determined. The pathogenesis of CT is largely unknown, as it is difficult to identify the stages that cause crystal deposition in the tendon and biopsy is also done when patients are symptomatic (3).

This disease is more common in women than men (4). The onset of CT in adults is 2.7% to 10.3%, which is usually seen in people between 30 and 60 years of age and can occur in up to 10% of cases. It is bilateral and in 15% of cases it can be accompanied by rupture of the rotator cuff (5) Vari-

ous theories have been proposed about the pathology of this disease including degenerative calcification, reactive calcification, endochondral ossification and chondral metaplasia (6). Codman *et al.* (7) (1931) stated that degenerative changes in tendons increase with age, leading to a decrease in the distribution of blood vessels and a decrease in oxygen supply, followed by thinning and rupture of tendons, and eventually necrosis and subsequent calcification of tendons (8). The most common site is the supraspinatus muscle tendon, 1.5 to 2 cm from the junction of the supraspinatus tendon with the large tuberosity of the humerus. Calcified tendonitis are diagnosed through patient history, physical examination and imaging (9). Many endocrine and metabolic diseases may impair tendon homeostasis. Several factors play a role in the development of tendonitis (3, 10). One of these factors is the role of thyroid hormone in changing the homeostasis of tendons and its failure to repair after injury (11). In studies of inter genes in the disease, the results of the Oliva's study showed a significant increase in the expression of tissue transglutaminase (tTG) 2 and its substrate, osteopontin, in calcified areas compared to the levels observed in normal tissue of the same subject. Calcific tendinopathy was observed (12). Significant increase in the expression of tissue transglutaminase (tTG) 2 and its substrate, osteopontin, was observed in calcified areas compared to normal tissue levels in a person with calcific tendinopathy. In contrast, a moderate increase was observed for cathepsin K (2). There was also a significant decrease in mRNA expression. Bone morphogenetic protein (BMP) 4 and BMP6, BMP-2, collagen V and vascular endothelial growth factor (VEGF) did not show significant differences in calcific region (12). Regarding the effect of hyperglycemia on bone differentiation of mesenchymal stem cells, studies showed that the expression of collagen genes type I, type II, alkaline phosphatase and osteopontin was significantly increased in high glucose complement mesenchymal stem cells. CT may be due to incorrect differentiation of mesenchymal stem cells in the presence of high serum glucose levels (13).

Radiography, sonography and magnetic resonance imaging (MRI) can be used to view calcium deposits (1, 3, 14, 15). Limited studies have been performed on the cause and treatment of this disease. It is most often seen in people whose job requires keeping their arms in internal rotation and brief abduction, such as cashiers, tailors, and production line workers. Limited studies have been performed on the etiology of this disease. In a communication study, a history of calcium supplementation with more pain and decreased functional ability has been concluded (16). Another study also showed low levels of vitamin D and high levels of parathyroid hormone (PTH) and a link between secondary hyperparathyroidism to vitamin D deficiency and calcified tendonitis (17). The study of Rouhani *et al.* showed that vitamin D supplementation was high in people with shoulder tendonitis (16). The aim of this study was to investigate the relationship between calcium and vitamin D and phosphorus levels and the history of calcium and vitamin D supplementation with CT.

METHODS

This study was a case-control study. All patients included with a diagnosis of symptomatic calcified tendonitis in our shoulder clinic from April 2020 to May 2021 in our study.

Inclusion criteria were shoulder pain and presence of calcium in the rotator cuff tendons based on a conventional anteroposterior, lateral, or axillary view. Exclusion criteria were lack of cooperation for performing laboratory tests. The control group includes people from the normal population who did not history of any diseases that may affect calcium, phosphorus and vitamin D levels. The control group did not have any injuries in the shoulder area and in order to measure the variables of this study, the control group was selected from a healthy population (18). And these people were matched with the experimental group in terms of age and sex.

The study was approved by Hamadan University of Medical Sciences with protocol number IR.UMSHA.REC.1399.891 (Date of approval: January 16, 2021). Written consent was obtained from all controls and patients in the study. Levels of vitamin D, calcium and phosphorus, alkaline phosphatase of all cases including patients and control group evaluated in the same laboratory. We decided to check serum albumin level if the patient's calcium level was less than 5.8, but no case had the same level of calcium. At the same time, the demographic information of patients with a history of taking calcium and vitamin D supplements during the last two years were included in the checklist.

Data analysis

After collecting the research data, it was entered into SPSS 21 software and using independent sample t test to compare the average of quantitative data between the two groups and chi square test. It was analyzed for qualitative comparisons between the two groups.

RESULTS

In this study, 17 patients with CT based on clinical signs and shoulder X-ray examination compared to 21 patients without history of diseases that had any effect on serum levels of calcium, phosphorus and vitamin D were included as control group. The results of **table I** showed that there was

Table I. Demographic characteristics of in two groups of patients with calcific tendonitis and control group.

		Case group		Control group		P-value
		Mean	SD	Mean	SD	
Age (year)		53.4	8.9	52.5	14.5	0.788*
		Frequency	Percent	Frequency	Percent	
Gender	Men	4	23.5	9	42.9	0.212**
	Female	13	76.5	12	57.1	

*t-test; **chi square test.

no significant difference between the two groups in terms of age (P-value = 0.788). There was no significant difference between the two groups in terms of gender (P-value = 0.212).

Table II. Frequency of history of calcium and vitamin D supplementation in two groups of patients with calcific tendonitis and control group.

		Case group		Control group		P-value
		Yes	No	Yes	No	
Vit D	Numb	9	8	6	15	0.126
	Present	52.9	47.1	28.6	71.4	
Ca	Numb	5	12	11	10	0.154
	Present	29.4	70.6	52.4	47.6	

Table II demonstrates the frequency of history of calcium and vitamin D supplementation in two groups. There was no significant difference in the history of calcium supplementation (P-value = 0.154) and vitamin D (P-value = 0.126) between the two groups in the study.

Table III demonstrates results of comparing serum levels of calcium, vitamin D and phosphorus in the two groups. There was no significant difference in serum calcium levels between the two groups (P-value = 0.132). Also, there was no significant difference in serum phosphorus levels between the two groups (P-value = 0.950). Serum vitamin D levels were significantly different between patients with CT and the control group (P-value = 0.0420), the mean level of vitamin D was 38.8 ng/ml in the group with CT and 27.4 ng/ml in the control group.

DISCUSSION

The present study was a case-control study aimed to assess and compare the serum levels of calcium, phosphorus and vitamin D and also history of calcium and vitamin D supplementation in patients with CT and a control group

Table III. Evaluation of the relationship and comparison of serum levels of calcium, vitamin D and phosphorus in the two groups of patients with calcific tendonitis and the control group.

		Case group	Control group	P-value
Serum level Ca	Mean (mg/dl)	9.5	9.2	0.132
	SD	0.5	0.56	
Serum level Vit D	Mean (ng/ml)	38.8	27.4	0.042
	SD	17.5	15.6	
Serum level P	Mean (mg/dl)	3.8	3.7	0.950
	SD	0.58	0.75	

of normal individuals. There was no significant difference between the two groups of patients in terms of gender, age and history of calcium and vitamin D supplements intake. This view of the two groups had an acceptable similarity to have a valid comparison. Limited studies have been done in this regard. Rouhani *et al*., in a descriptive-analytical study, examined the history of calcium supplementation and CT in patients with shoulder pain (16). The results showed that calcium supplementation was associated with CT and was associated with more pain (P-value = 0.01) and decreased functional ability (P-value = 0.03) in patients with CT (16). In our study there is no significant relationship between serum calcium and phosphorus levels and history of calcium consumption; and also, there was no difference of calcium or vitamin D consumption between the two groups of patients with CT and the control group. In a study by Cavalli *et al*., a group of 30 people including people with CT treated with two needles through the skin underwent an ultrasound guide. Blood calcium, phosphorus and vitamin D levels, urinary calcium and phosphorus levels (PTH) were measured (19). Vitamin D levels in patients with calcific tendinitis were in the lower normal range the level (PTH) was in the upper normal range (20). Finally, the researchers suggested that calcification in the rotator cuff tendons may occur due to a secondary hyperparathyroidism due to vitamin D deficiency (8, 20). In our study, the level of vitamin D in patients with CT was significantly different and higher the level of vitamin D in the control group (P-value = 0.042) which is not consistent with their study. Based on recent studies, the relationship between calcium levels of vitamin D and calcite tendonitis has been proposed. It was caused by an overdose of vitamin D and calcium supplements.

Various studies have been performed on the role of vitamin D in rotor cuff repair, and studies have shown a reduction in vitamin D and the risk of rupture of the rotator cuff (21, 22), although other studies have rejected these results (23). Kinoshita *et al*. demonstrated that increased levels of vitamin D inhibit production (PTH) in primary hyperparathyroidism (17). Martins *et al*. found a significant negative correlation between serum levels (PTH) and vitamin D, meaning that people with low levels of vitamin D had higher levels of serum (PTH) and people with high levels of vitamin D had lower levels (24).

Dimich *et al*., in a 10-year study of 34 patients with hypoparathyroidism, stated that there were four patients with calcific tendinitis among the patients (25). The ambiguous mechanism by which intracranial calcification occurs in lenses in hypoparathyroidism may also be present in other tissues (26). Although we did not evaluate PTH level, according to what was said at the beginning of the discussion about the possibility of low levels (PTH) following higher levels of vitamin D in patients with calcified tendonitis, our study is consistent with and reinforce the results of Dimich's research that high level of vitamin D and hypothyroidism can have a role in incidence of calcific tendinitis (25). Since several studies have been performed on the effect of PTH on calcification tendonitis, people with a history of PTH have been excluded from the study due to the prevention of confounding factor.

In another study by Harvie *et al*., due to the high prevalence of endocrine and autoimmune diseases among patients with calcific tendinitis, they concluded that CT can be divided into idiopathic and secondary categories (27). Our patients did not have history of any endocrine or autoimmune disease. According to the results of this study and review of literature, this hypothesis can be proposed that higher level of serum vitamin D may have a role of inducing hypoparathyroidism. Hypoparathyroidism may increase calcium deposition in tendons with suitable background as it increases calcium deposition in bones, although this hypothesis should be carefully examined in the future researches with large number of cases and evaluating PTH level in patients and control group, which can be a big step in identifying the etiology of the disease. On the other hand, due to the higher level of vitamin D in the patients according to our study, vitamin D supplements should be prescribed more carefully and by controlling serum vitamin D level, at least in those who are in the common age of calcific tendinitis. One of the limitations of this study was the small number of patients based on inclusion criteria, due to need to eliminate study confounders and that only symptomatic patients with a history of shoulder pain were included in the study. However, due to the small number of these valuable results, it could be a basic study to conduct studies in a larger sample size. According to the results obtained in this study, it can be recommended to perform the study in a wider population in people with and without a history of PTH.

CONCLUSIONS

The results of the present study show higher levels of vitamin D in people with CT than the control group who people were selected from normal people in the community. This may have a role in calcium deposition in tendon by influencing PTH level. Extensive studies are suggested to confirm this finding. Besides that, vitamin D supplements should be prescribed carefully and by controlling vitamin D level in whose who are in common age of the disease.

FUNDINGS

The study was funded by Vice-chancellor for Research and Technology, Hamadan University of Medical Sciences (No. 14000110129).

DATA AVAILABILITY

Data are available under reasonable request to the corresponding author.

CONTRIBUTIONS

HS: study design. MHB: data collection. HN, HS: writing. HN: editing and revision. MASR: data analysis and discussion section improvement.

ACKNOWLEDGEMENTS

This study has been adapted from Thesis for the Degree of Professional Doctorate in Medicine at Hamadan University of Medical Sciences.

CONFLICT OF INTERESTS

The authors declare that they have no conflict of interests.

REFERENCES

1. Albano D, Coppola A, Gitto S, Rapisarda S, Messina C, Sconfienza LM. Imaging of calcific tendinopathy around the shoulder: usual and unusual presentations and common pitfalls. Radiol Med 2021;126(4):608-19.
2. Oliva F, Via AG, Maffulli N. Physiopathology of intratendinous calcific deposition. BMC Med 2012;10:95.
3. Oliva F, Via AG, Maffulli N. Calcific tendinopathy of the rotator cuff tendons. Sports Med Arthrosc Rev 2011;19(3):237-43.
4. De Carli A, Pulcinelli F, Rose GD, Pitino D, Ferretti A. Calcific tendinitis of the shoulder. Joints 2014;2(3):130-6.
5. Sansone V, Maiorano E, Galluzzo A, Pascale V. Calcific tendinopathy of the shoulder: clinical perspectives into the mechanisms, pathogenesis, and treatment. Orthop Res Rev 2018;10:63-72.
6. Cvetanovich GL, Saltzman BM. B. Management of Calcific Tendonitis. Disorders of the Rotator Cuff and Biceps Tendon E-Book: The Surgeon's Guide to Comprehensive Management. 2019:197.
7. Codman EA, Akerson IB. The pathology associated with rupture of the supraspinatus tendon. Ann Surg 1931;93(1):348-59.
8. Brinkman JC, Zaw TM, Fox MG, et al. Calcific Tendonitis of the Shoulder: Protector or Predictor of Cuff Pathology? A Magnetic Resonance Imaging-Based Study. Arthroscopy 2020;36(4):983-90.
9. Kim MS, Kim IW, Lee S, Shin SJ. Diagnosis and treatment of calcific tendinitis of the shoulder. Clin Shoulder Elb 2020;23(4):210-6.
10. Ackermann PW, Hart DA. General Overview and Summary of Concepts Regarding Tendon Disease Topics Addressed Related to Metabolic Disorders. Adv Exp Med Biol 2016;920:293-8.
11. Oliva F, Piccirilli E, Berardi AC, Tarantino U, Maffulli N. Influence of Thyroid Hormones on Tendon Homeostasis. Adv Exp Med Biol 2016;920:133-8.
12. Oliva F, Barisani D, Grasso A, Maffulli N. Gene expression analysis in calcific tendinopathy of the rotator cuff. Eur Cell Mater 2011;21:548-57.
13. Via AG, McCarthy MB, Francke M, Oliva F, Mazzocca AD, Maffulli N. Hyperglycemia induces osteogenic differentiation of bone marrow derived stem cells: an in vitro study. Muscles Ligaments Tendons J 2018;8(1).
14. Yoo Y-S, Park J-Y, Kim M-s, et al. Calcific tendinitis of the shoulder in the Korean population: demographics and its relation with coexisting rotator cuff tear. Clin Shoulder Elb 2021;24(1):21-6.
15. Morsy MG, Taha Waly AH, Galal MA, Mohamed Ayman EH, Gawish HM. Arthroscopic Excision of Infraspinatus Calcific Tendinitis With Double-Row Margin Convergence Repair. Arthrosc Tech. 2021;10(6):e1455-e67.
16. Rouhani A, Soleimanpour J, Sadeghilar A, Tabrizi A. The Relation between Calcium Supplement Consumption and Calcific Shoulder Tendonitis. Adv Biosci Clin Med 2015;3(4):11-6.
17. Kinoshita Y, Taguchi M, Takeshita A, Miura D, Tomikawa S, Takeuchi Y. 1,25-dihydroxyvitamin D suppresses circulating levels of parathyroid hormone in a patient with primary hyperparathyroidism and coexistent sarcoidosis. J Clin Endocrinol Metab 2005;90(12):6727-31.
18. Naderifar H, Mohammad Khani Gangeh M, Mehri F, Shamloo Kazemi S. Effects of High Intensity Interval Training and Consumption of Matcha Green Tea on Malondialdehyde and Glutathione Peroxidase Levels in women. J Mazandaran University Med Sci 2022;32(212):42-53.
19. Cavalli L, D'Elia G, Caracchini G, et al. P28 - Calcific Tendinopathy and Vitamin D Status: A Potential Aetiopathogenetic Factor and Therapeutic Approach Clinical Cases in Mineral and Bone Metabolism 2010;7(3):234.
20. Oh JH, Kim SH, Kim JH, Shin YH, Yoon JP, Oh CH. The level of vitamin D in the serum correlates with fatty degeneration of the muscles of the rotator cuff. J Bone Joint Surg Br 2009;91(12):1587-93.
21. Lee JH, Kim JY, Kim JY, Mun JW, Yeo JH. Prevalence of and Risk Factors for Hypovitaminosis D in Patients with Rotator Cuff Tears. Clin Orthop Surg 2021;13(2):237-42.
22. Angeline ME, Ma R, Pascual-Garrido C, et al. Effect of diet-induced vitamin D deficiency on rotator cuff healing in a rat model. Am J Sports Med 2014;42(1):27-34.
23. Ryu KJ, Kim BH, Lee Y, Dan J, Kim JH. Low Serum Vitamin D Is Not Correlated With the Severity of a Rotator Cuff Tear or Retear After Arthroscopic Repair. Am J Sports Med 2015;43(7):1743-50.
24. Martins JS, Palhares MO, Teixeira OC, Gontijo Ramos M. Vitamin D Status and Its Association with Parathyroid Hormone Concentration in Brazilians. J Nutr Metab 2017;2017:9056470.
25. Dimich A, Bedrossian PB, Wallach S. Hypoparathyroidism. Clinical observations in 34 patients. Arch Intern Med 1967;120(4):449-58.
26. Fujita T. [Mechanism of intracerebral calcification in hypoparathyroidism]. Clin Calcium. 2004 Jun;14(6):55-7. Japanese.
27. Harvie P, Pollard TC, Carr AJ. Calcific tendinitis: natural history and association with endocrine disorders. J Shoulder Elbow Surg 2007;16(2):169-73.