ORİJİNAL ARAŞTIRMA ORIGINAL RESEARCH

DOI: 10.31609/jpmrs.2021-83980

Effect of Thyroid Dysfunctions on Pain and Physical Function in Patients with Gonarthrosis

Gonartrozlu Hastalarda Tiroid Fonksiyon Bozukluklarının Ağrı ve Fiziksel Fonksiyon Üzerine Etkisi

Ömer GEZGİNASLAN[a], Gökhan BAŞAR[b], Sevgi GÜMÜŞ ATALAY[c]

[a]Clinic of Physical Medicine and Rehabilitation, Giresun Physical Therapy and Rehabilitation Center, Giresun, TURKEY
[b]Department of Physical Medicine and Rehabilitation, University of Health Sciences Ümraniye Training and Research Hospital, İstanbul, TURKEY
[c]Clinic of Physical Medicine and Rehabilitation, Ankara City Hospital, Ankara, TURKEY

ABSTRACT Objective: This study aims to investigate the effects of thyroid dysfunction on pain and physical function in patients with gonarthrosis. **Material and Methods:** A total of 82 patients with the diagnosis of Grade 1-3 gonarthrosis according to the Kellgren-Lawrence (K/L) radiographic grading system were included. Patients were divided into 2 groups. Group 1 (n=41) included gonarthrosis patients with thyroid dysfunctions, Group 2 (n=41) included gonarthrosis patients with normal thyroid functions. Visual analog scale (VAS) and The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) subscale scores were compared between the groups. **Results:** There was no statistically significant difference in age, knee symptom duration, VAS, WOMAC-Pain, WOMAC-Stiffness and K/L scores between groups. The WOMAC-Physical Function score was significantly higher in Group 1 ($p<0.05$). **Conclusion:** Physical function level may be lower in gonarthrosis patients with thyroid dysfunction than in patients with gonarthrosis alone. It may be useful for physical function, to treat thyroid dysfunction in patients with gonarthrosis who apply to outpatient clinics.

Keywords: Gonarthrosis; pain; physical function; thyroid dysfunction

ÖZET Amaç: Bu çalışma, gonartrozlu hastalarda tiroid fonksiyon bozukluklarının ağrı ve fiziksel fonksiyon üzerindeki etkilerini araştırmayı amaçlamaktadır. **Gereç ve Yöntemler:** Kellgren-Lawrence (K/L) radyografik derecelendirme sistemine göre Grade 1-3 diz osteoartritli gonartroz tanısı alan toplam 82 hasta dâhil edildi. Hastalar 2 gruba ayrıldı. Grup 1 (n=41) tiroid disfonksiyonlu gonartroz hastası, Grup 2 (n=41) ise sadece gonartroz hastasıydı. Vizüel analog skala (VAS) ve "Western Ontario ve McMaster Universities Osteoartritis Index (WOMAC)" alt ölçek puanları gruplar arasında karşılaştırıldı. **Bulgular:** Gruplar arasında; yaş, diz semptom süresi VAS, WOMAC-Ağrı, WOMAC-Sertlik ve K/L skorlarında istatistiksel olarak anlamlı bir fark yoktu. WOMAC-Fiziksel Fonksiyon skorları Grup 1'de istatistiksel olarak anlamlı derecede yüksekti ($p<0,05$). **Sonuç:** Tiroid disfonksiyonunun eşlik ettiği gonartrozlu hastalarda, fiziksel fonksiyon düzeyi, tek başına gonartrozlu hastalara göre daha düşüktür. Polikliniklere başvuran gonartrozlu hastalarda tiroid fonksiyon bozukluklarının tedavi edilmesi fiziksel fonksiyon açısından yararlı olabilir.

Anahtar Kelimeler: Gonartroz; ağrı; fiziksel fonksiyon; tiroid disfonksiyonu

Osteoarthritis (OA) is a chronic, common disease that affects especially the elderly population and is accompanied by destruction and remodeling of the joint cartilage.[1] Symptomatic OA can affect any joint where the synovium is present, and it mostly affects large joints such as the knee, hip, hand, and spine.[2] The knee joint is the most affected joint among these.[3] Symptomatic OA of joints such as knee and hip leads to a decrease in quality of life and physical function.[4] In some studies, a correlation between mortality due to cardiovascular diseases and symptomatic OA was found.[5] Therefore, it is important to identify and treat predisposing factors alongside the OA treatment.

Correspondence: Ömer GEZGİNASLAN
Clinic of Physical Medicine and Rehabilitation, Giresun Physical Therapy and Rehabilitation Center, Giresun, TURKEY/TÜRKİYE
E-mail: omergezginaslan@hotmail.com

Peer review under responsibility of Journal of Physical Medicine and Rehabilitation Science.

Received: 21 Apr 2021 ***Received in revised form:*** 18 Oct 2021 ***Accepted:*** 23 Oct 2021 ***Available online:*** 03 Nov 2021

The inflammatory process plays a major role in the pathogenesis of OA. Especially interleukin-1 (IL-1) and IL-6 have been shown to have a role in OA pathogenesis in patients with early and late OA.[6,7] In a study, increased intracellular 3'3'5-triiodothyronine (T3) levels have been shown to affect OA onset.[8] Levels of cytokines such as IL-6, interferon gamma, IL-8 and IL-12 correlate with levels of thyroid hormones.[9,10] In a study, it was reported that increased intracellular T3 level was predisposing to OA while decreased intracellular T3 level was protective against OA.[11]

In this study, we examined the effect of thyroid dysfunction on pain and physical function, which may be a predisposing factor for symptomatic OA, and a cause of serious morbidity and mortality.

MATERIAL AND METHODS

STUDY POPULATION

This comparative clinical study was conducted at the University of Health Science Ümraniye Training and Research Hospital Musculoskeletal Outpatient Clinic between July 2020 and October 2020. A total of 82 patients (20 males, 62 females; mean age: 55.75±5.36 years; range, 45 to 65 years) with Grade 1-3 knee OA according to the Kellgren-Lawrence (K/L) radiographic grading system were included in the study.[12] A written informed consent was obtained from each patient. The study protocol was approved by the University of Health Science Umraniye Training and Research Hospital Clinical Research Ethics Committee (25.06.2020, B.10.1.TKH.4.34.H.GP.0.01/263). The study was conducted in accordance with the principles of the Declaration of Helsinki. Inclusion criteria were as follows: Having a clinical diagnosis of gonarthrosis (Group 1-2), thyroid disease (Group 1) and having persistent pain for at least for 6 months that is assessed by visual analog scale (VAS).[13] Exclusion criteria were as follows: No prior treatment including steroid injection within the past 6 months; having a malignancy; patients who underwent total knee arthroplasty and other knee surgery; diabetes mellitus and other metabolic diseases; other inflammatory and autoimmune diseases; neuromuscular diseases; severe liver, cardiac and renal diseases. To rule out other diseases, all patients underwent a detailed physical examination, knee X-rays and laboratory testing.

OUTCOME MEASURES

The VAS was used to evaluate the intensity of knee pain. The score ranges from 0 to 10 (0: No pain and 10: Pain). The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) is a self-reported questionnaire. WOMAC is used to assess pain at 5 activities, stiffness at 2 situations, and physical function at 17 activities.[14] WOMAC-Pain (WOMAC-P) was used to assess pain; the WOMAC-Physical Function (WOMAC- PF).

RECENT THYROID FUNCTION

Thyroid function status of the patients in Group 1 in the last 3 months was evaluated with thyroid stimulating hormone (TSH), free T3 (fT3) and free T4 (fT4) tests. The patients were divided into 3 subgroups as euthyroid, hypothyroid and hyperthyroid. Subclinical hypothyroidism was included in the hypothyroidism subgroup, and subclinical hyperthyroidism was included in the hyperthyroid subgroup. While the diagnosis of hypothyroidism is defined by decreased fT3 and/or fT4 hormone levels together with increased TSH levels; the diagnosis of hyperthyroidism was defined by increased fT3 and/or fT4 levels with decreased TSH levels. The diagnosis of euthyroidism is defined by normal hormone levels. Subclinical hypothyroidism is defined by increased TSH and normal fT3 and fT4 hormone levels; subclinical hyperthyroidism is defined by decreased TSH and normal fT3 and fT4 hormone levels. The reference ranges of thyroid function tests are as follows: TSH, 0.35-4.94 mIU/mL; fT3, 1.71-3.71 pg/mL; f T4, 0.7-1.48 ng/dL.

STATISTICAL ANALYSIS

IBM SPSS Statistics 25 for statistical analysis (SPSS IBM, Turkey) program were used for statistical analysis. The Kolmogorov-Smirnov test is used to determine whether sample data are normally distributed. Student t-test was used to compare quantitative data as well as general characteristics including descriptive statistical methods (mean, standard deviation, frequency). Significance was evaluated at the $p<0.05$ level.

RESULTS

Of a total of 82 patients, 62 were females and 20 were males with a mean age of 55.75±5.36 (range, 45 to 65) years. There were 41 (50%) patients in Group 1 and 41 patients (50%) in Group 2. There were no statistically significant difference in general characteristics between the groups (p>0.05). General characteristics of the patients are shown in Table 1.

There was no statistically significant difference between the groups in terms of VAS, age, knee symptom duration, K/L, WOMAC-P and WOMAC-Stiffness. The WOMAC-PF score was higher in Group 1 than in Group 2. VAS, WOMAC subscales, knee symptom duration and K/L scores in Group 1 and Group 2 are shown in Table 2.

DISCUSSION

Gonarthrosis decreases the quality of life and physical function due to pain and limitation. The decrease in the physical functioning state predisposes to cardiovascular diseases. Therefore, it is very important to treat factors that predispose to gonarthrosis. Previous studies have shown that the increase in intracellular T3 level leads to the initiation and progression of joint degeneration, while its decrease is protective against the development of OA.[8,11] Similarly, in our study, physical function level was found to be lower in gonarthrosis patients with thyroid dysfunction compared to patients with only gonarthrosis. This situation highlights the importance of treating thyroid dysfunctions.

In a study, a relationship between musculoskeletal ultrasound abnormalities, knee pain and thyroid

TABLE 1: General characteristics of patients.

		n	%
Age Minimum-maximum±SD (range)		45-65	55.75±5.36
Sex	Man	20	24.4
	Woman	62	75.6
Group	Group 1	41	50
	Group 2	41	50
Current thyroid status (Group 1)	Euthyroid	22	53.7
	Hypohyroid	13	31.7
	Hyperthyroid	614.6	
Disease symptom duration (Thyroid dysfunction) Minimum-maximum±SD (range)	Group 1 (n=41)	41	9.02±2.72
Current thyroid treatment (Group 1)	Group 1 (n=41)	37	90.2

SD: Standard deviation.

TABLE 2: Evaluation of VAS, WOMAC, knee symptom duration and K/L scores between groups.

		Group 1 Mean±SD (median)	Group 2 Mean±SD (median)	p[1]
VAS		5.09±1.67	4.68±1.52	0.244
Age		53.68±5.36	55.75±5.62	0.092
Knee symptom duration		8.51±3.42	8.73±3.56	0.777
K/L		1.63±0.69	1.60±0.7	0.875
WOMAC	P	9.48±3.32	8.41±2.98	0.128
	S	3.73±1.56	3.12±1.41	0.068
	PF	33.02±11.14	28.21±10.41	0.047*
	Total	47.60±16.29	45.84±28.64	0.733

[1]Student t-test; *p<0.05; SD: Standard deviation; VAS: Visual analog scale; K-L: Kellgren-Lawrence; WOMAC-P: Western Ontario and McMaster Universities Osteoarthritis Index-Pain; WOMAC-S: Western Ontario and McMaster Universities Osteoarthritis Index-Stiffness; WOMAC-PF: Western Ontario and McMaster Universities Osteoarthritis Index-Physical Function.

dysfunction was found.[15] Similar to our study, this study shows that thyroid function disorders worsen OA symptoms. In some studies, high TSH levels have been shown to increase the synovial fluid amount and viscosity by increasing the synthesis of hyaluronic acid and proteoglycans.[16-19] Increase in intra-articular fluid may lead to limitation of movement in the joint and as a result limitation of physical activity may occur. In our study, the decrease in the physical activity level of the patients in Group 1 may occur due to the limitation in the joint movements as well.

In hypothyroidism, impaired bone formation and resorption lead to a decrease in bone turnover and the prolonged bone remodeling cycle leads to an increase in secondary mineralization.[20,21] Conversely, in thyrotoxicosis, increased bone turnover shortens the remodeling and as a result bone mineralization decreases due to osteoblast and osteoclast activity disruption.[21]

Thyroid dysfunctions lead to disruption of cartilage and bone turnover. This deterioration may play a role in the formation of OA. Therefore, similarly to our study, symptoms related to OA can be seen more frequently in patients with hypothyroidism.

Cakir et al. reported that musculoskeletal diseases often accompany thyroid dysfunctions in patients with both hypothyroidism and thyrotoxicosis.[22] In a study conducted in 2016, the femoral cartilage thickness of hypothyroid patients was compared with that of the healthy control group. The thickness of the femoral cartilage in hypothyroid patients was found to be thinner than in healthy individuals. They stated that thinning of the femoral cartilage may be useful for the early diagnosis of knee OA.[23] In another study, they reported that in OA patients over 50 years of age with a high chance of comorbidity, thyroid examination is important for early diagnosis and treatment of hypothyroidism.[24] In a case report, the heterozygous LAMA5 mutation has shown to be associated with many diseases such as OA, muscle weakness, and hypothyroidism. All these studies show that there is a relationship between thyroid dysfunctions and musculoskeletal diseases and OA.[25] In a study conducted in a very large patient population in 2021, hypothyroidism was seen at a higher rate in patients with knee OA than in normal healthy individuals.[26] Similar to these studies, our study shows that there is a relationship between thyroid dysfunctions and a decrease in physical function. Therefore, it may be useful to refer the patients with thyroid dysfunctions to the musculoskeletal outpatient clinic.

It has been shown in previous studies that thyrotoxicosis causes osteoporosis and muscle weakness.[27-29] Some previous studies have shown that quadriceps/hamstring muscle strengthening exercises have positive effects on knee OA symptoms.[30-32] Since muscle weakness caused by thyrotoxicosis contributes to the progression and development of OA, it would be appropriate to refer patients with thyrotoxicosis to a physiatrist

Relatively small sample size and retrospective aspect of the study are the limitations of this study. Also it should have been investigated how thyroid dysfunction treatment could affect symptoms in patients with gonarthrosis with thyroid dysfunction. Comparative studies can be conducted in patients with hypothyroid, euthyroid and hyperthyroid gonarthrosis. Thyroid dysfunction can also independently affect physical activity. This may have affected the results of this study. Further large-scale, long-term studies are needed to confirm these findings.

CONCLUSION

In conclusion, the lower level of physical function in gonarthrosis patients with thyroid dysfunction may increase cardiovascular risk in patients with gonarthrosis and requires effective treatment. It may be useful to treat thyroid dysfunction in patients with gonarthrosis. Demonstrating the effect of thyroid hormone function values on the physical functions of patients with OA may pave the way for new studies in this field.

Source of Finance

During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

REFERENCES

1. Hootman JM, Helmick CG. Projections of US prevalence of arthritis and associated activity limitations. Arthritis Rheum. 2006;54:226-9. [Crossref] [Pubmed]
2. Dieppe PA, Lohmander LS. Pathogenesis and management of pain in osteoarthritis. Lancet. 2005;365:965-73. [Crossref] [Pubmed]
3. Guccione AA, Felson DT, Anderson JJ, et al. The effects of specific medical conditions on the functional limitations of elders in the Framingham Study. Am J Public Health. 1994;84:351-8. [Crossref] [Pubmed] [PMC]
4. Samuels J, Krasnokutsky S, Abramson SB. Osteoarthritis: A tale of three tissues. Bull NYU Hosp Jt Dis. 2008;66:244-50. [Pubmed]
5. Haara MM, Manninen P, Kröger H, et al. Osteoarthritis of finger joints in Finns aged 30 or over: prevalence, determinants, and association with mortality. Ann Rheum Dis. 2003;62:151-8. [Crossref] [Pubmed] [PMC]
6. Goldring MB. The role of cytokines as inflammatory mediators in osteoarthritis: Lessons from animal models. Connect Tissue Res. 1999;40:1-11. [Crossref] [Pubmed]
7. Kaneko S, Satoh T, Chiba J, et al. Interleukin-6 and interleukin-8 levels in serum and synovial fluid of patients with osteoarthritis. Cytokines Cell Mol Ther. 2000;6:71-9. [Crossref] [Pubmed]
8. Meulenbelt I, Bos SD, Chapman K, et al. Meta-analyses of genes modulating intracellular T3 bio-availability reveal a possible role for the DIO3 gene in osteoarthritis susceptibility. Ann Rheum Dis. 2011;70:164-7. [Crossref] [Pubmed]
9. De Vito P, Incerpi S, Pedersen JZ, et al. Thyroid hormones as modulators of immune activities at the cellular level. Thyroid. 2011;21:879-90. [Crossref] [Pubmed]
10. Jara EL, Mu-oz-Durango N, Llanos C, et al. Modulating the function of the immune system by thyroid hormones and thyrotropin. Immunol Lett. 2017;184:76-83. [Crossref] [Pubmed]
11. Waung JA, Bassett JH, Williams GR. Adult mice lacking the type 2 iodothyronine deiodinase have increased subchondral bone but normal articular cartilage. Thyroid. 2015;25:269-77. [Crossref] [Pubmed] [PMC]
12. Kellgren JH, Lawrence JS. Radiological assessment of osteo-arthrosis. Ann Rheum Dis. 1957;16:494-502. [Crossref] [Pubmed] [PMC]
13. Collins SL, Moore RA, McQuay HJ. The visual analogue pain intensity scale: What is moderate pain in millimetres? Pain. 1997;72:95-7. [Crossref] [Pubmed]
14. Tüzün EH, Eker L, Aytar A, et al. Acceptability, reliability, validity and responsiveness of the Turkish version of WOMAC osteoarthritis index. Osteoarthritis Cartilage. 2005;13:28-33. [Crossref] [Pubmed]
15. Kim BY, Kim SS, Park HK, et al. Assessment of the relationship between knee ultrasound and clinical symptoms in patients with thyroid dysfunction. J Int Med Res. 2020;48:300060519897701. [Crossref] [Pubmed] [PMC]
16. Bland JH, Frymoyer JW, Newberg AH, et al. Rheumatic syndromes in endocrine disease. Semin Arthritis Rheum. 1979;9:23-65. [Crossref] [Pubmed]
17. Dorwart BB, Schumacher HR. Joint effusions, chondrocalcinosis and other rheumatic manifestations in hypothyroidism. A clinicopathologic study. Am J Med. 1975;59:780-90. [Crossref] [Pubmed]
18. Newcombe DS, Ortel RW, Levey GS. Activation of human synovial membrane adenylate cyclase by thyroid stimulating hormone (TSH). Biochem Biophys Res Commun. 1972;48:201-4. [Crossref] [Pubmed]
19. Kloppenburg M, Dijkmans BA, Rasker JJ. Effect of therapy for thyroid dysfunction on musculoskeletal symptoms. Clin Rheumatol. 1993;12:341-5. [Crossref] [Pubmed]
20. Eriksen EF, Mosekilde L, Melsen F. Kinetics of trabecular bone resorption and formation in hypothyroidism: Evidence for a positive balance per remodeling cycle. Bone. 1986;7:101-8. [Crossref] [Pubmed]
21. Mosekilde L, Eriksen EF, Charles P. Effects of thyroid hormones on bone and mineral metabolism. Endocrinol Metab Clin North Am. 1990;19:35-63. [Crossref] [Pubmed]
22. Cakir M, Samanci N, Balci N, et al. Musculoskeletal manifestations in patients with thyroid disease. Clin Endocrinol (Oxf). 2003;59:162-7. [Crossref] [Pubmed]
23. Devrimsel G, Beyazal MS, Turkyilmaz AK, et al. Ultrasonographic evaluation of the femoral cartilage thickness in patients with hypothyroidism. J Phys Ther Sci. 2016;28:2249-52. [Crossref] [Pubmed] [PMC]
24. Voloshyna L, Doholich O, Sithinska I. Hypothyroidism - a special comorbidity factor in patients with osteoarthrosis: Clinical, pathophysiological and prognostic aspects. Georgian Med News. 2017;53-9. [Pubmed]
25. Sampaolo S, Napolitano F, Tirozzi A, et al. Identification of the first dominant mutation of LAMA5 gene causing a complex multisystem syndrome due to dysfunction of the extracellular matrix. J Med Genet. 2017;54:710-20. [Crossref] [Pubmed]
26. Lentz TA, Hellkamp AS, Bhavsar NA, et al. Assessment of common comorbidity phenotypes among older adults with knee osteoarthritis to inform integrated care models. Mayo Clin Proc Innov Qual Outcomes. 2021;5:253-64. [Crossref] [Pubmed] [PMC]
27. Yasoda A. [Secondary osteoporosis. Hyperthyroidism.]. Clin Calcium. 2018;28:1619-25. Japanese. [Pubmed]
28. Patel K, McCoy JV, Davis PM. Recognizing thyrotoxic hypokalemic periodic paralysis. JAAPA. 2018;31:31-4. [Crossref] [Pubmed]
29. Correia M, Darocki M, Hirashima ET. Changing management guidelines in thyrotoxic hypokalemic periodic paralysis. J Emerg Med. 2018;55:252-6. [Crossref] [Pubmed]
30. Gezginaslan Ö, Öztürk EA, Cengiz M, et al. Effects of isokinetic muscle strengthening on balance, proprioception, and physical function in bilateral knee osteoarthritis patients with moderate fall risk. Turk J Phys Med Rehabil. 2018;64:353-61. [Crossref] [Pubmed] [PMC]
31. Benli Küçük E, Özyemişci Taşkıran Ö, Tokgöz N, et al. Effects of isokinetic, isometric, and aerobic exercises on clinical variables and knee cartilage volume using magnetic resonance imaging in patients with osteoarthritis. Turk J Phys Med Rehabil. 2017;64:8-16. [Crossref] [Pubmed] [PMC]
32. Ay S, Koldaş Doğan Ş, Evcik D. Is there an effective way to prescribe a home-based exercise program in patients with knee osteoarthritis? A randomized controlled study. Turk J Phys Med Rehab. 2013;59:1-6. [Link]