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Telefon/Phone: +90 (530) 177 30 97

E-posta/E-mail: info@galenos.com.tr/yayin@galenos.com.tr

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AMAÇ VE KAPSAM

Türk Osteoporoz Dergisi, Türkiye Osteoporoz Derneği'nin süreli yayın organı olup, osteoporoz ve metabolik kemik hastalıkları içerikli, yayın dili Türkçe ve İngilizce olan, bağımsız ve önyargısız hakemlik (peer-review) ilkelerine dayanan uluslararası, periyodik bir dergidir. Türk Osteoporoz Dergisi, Nisan, Ağustos ve Aralık aylarında olmak üzere yılda 3 sayı çıkar.

Türk Osteoporoz Degisi'nin hedefi uluslararası düzeyde nitelikli, sürekli ve osteoporoz konusunda özgün bir periyodik olarak klinik ve bilimsel açıdan en üst düzeyde orijinal araştırmaları yayınlamaktır. Bununla birlikte eğitim ile ilgili temel yenilikleri kapsayan derlemeler, editöryel kısa yazılar, olgu sunumları, orijinal görüntüler ve geniş fiziksel tıp, romatoloji, rehabilitasyon ve jinekoloji kesimlerinin konular hakkındaki deneyimlerini ve eleştirilerini içeren mektuplar ve sosyal konulu yazılar yayınlamaktır.

Osteoporoz ve kemik hastalıklarına ilgi duyan birinci basamak tıp hizmeti veren pratisyen hekim, iç hastalıkları, jinekoloji, romatoloji ve fiziksel tıp ve rehabilitasyon uzmanlarının "bilmesi gerekli olanları" iyice saptayarak; bunları Türk Osteoporoz Dergisi'nde bulmaları için gerekli düzenlemeler yapılacaktır.

Türk Osteoporoz Dergisi, **Emerging Sources Citation Index (ESCI), DOAJ, EBSCO Database, Gale/Cengage Learning, CINAHL, CABI, Index Copernicus, Embase, Scopus, ProQuest, J-Gate, IdealOnline, TÜBİTAK/ULAKBİM, Hinari, GOALI, ARDI, OARE, AGORA, Türk Medline, Türkiye Atıf Dizini** tarafından indekslenmektedir.

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Derginin açık erişim politikası 'Budapest Open Access Initiative(BOAI) kuralları esas alınarak uygulanmaktadır.

Açık Erişim, "[hakem değerlendirmesinden geçmiş bilimsel literatürün], İnternet aracılığıyla; finansal, yasal ve teknik engeller olmaksızın, serbestçe erişilebilir, okunabilir, indirilebilir, kopyalanabilir, dağıtılabilir, basılabilir, taranabilir, tam metinlere bağlantı verilebilir, dizinlenebilir, yazılıma veri olarak aktarılabilir ve her türlü yasal amaç için kullanılabilir olması"dır. Çoğaltma ve dağıtım üzerindeki tek kısıtlama yetkisi ve bu alandaki tek telif hakkı rolü; kendi çalışmalarının bütünlüğü üzerinde kontrol sahibi olabilmeleri, gerektiği gibi tanınmalarının ve alıntılanmalarının sağlanması için, yazarlara verilmelidir.

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Türk Osteoporoz Dergisi, ülkemizde görev yapan fiziksel tıp ve rehabilitasyon uzmanlarına, akademisyenlerine ve osteoporoz'a ilgi duyan diğer tüm tıp branşlarına mensup uzmanlara ücretsiz olarak dağıtılmaktadır. Derginin tüm sayılarına ücretsiz olarak www.turkosteoporozdergisi.org adresinden tam metin ulaşılabilir. Dergiye abone olmak isteyen kişiler Türkiye Osteoporoz Derneği'ne başvurmalıdır.

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Web Sayfası: www.turkosteoporozdergisi.org
E-posta: yesim.kirazli@ege.edu.tr

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E-posta: yesim.kirazli@ege.edu.tr

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Materyal Sorumluluk Reddi

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AIMS AND SCOPE

Turkish Journal Of Osteoporosis is the regular publishing organ of the Turkish Osteoporosis Society. This periodical journal covers osteoporosis and metabolic bone diseases subjects. It is a periodic international journal, published in Turkish and English languages and is independent, being based on peer-review principles. The journal is published 3 times per year (April, August and December).

The aim of the journal "Turkish Journal Of Osteoporosis" is to continuously publish original research papers of the highest scientific and clinical values specifically on osteoporosis, on an international level. Additionally, reviews on basic developments in education, editorial short notes, case reports, original views, letters from the fields of physical medicine, rheumatology, rehabilitation, gynaecology containing experiences and comments as well as social subjects are published.

Thing that must be known' subjects for general practitioners giving first line medical service who are interested in osteoporosis and metabolic bone diseases, specialists in internal medicine, gynecology, rheumatology and physiotherapy will be determined It will then be possible to make the necessary adjustments to the journal "Turkish Journal Of Osteoporosis" according to their needs.

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Turkish Journal Of Osteoporosis is sent free to physiotherapy specialists, academicians in our country as well as other specialists in all branches of medicine interested in osteoporosis. All published volumes can be reached full text without fee through the web site www.turkosteoporozdergisi.org. Those who wish to subscribe to the journal should apply to the Turkish Osteoporosis Association.

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Fax: +90 212 560 40 79
Web Page: www.turkosteoporozdergisi.org
E-mail: yesim.kirazli@ege.edu.tr

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Address: Ataköy 4. Kısım O/121 Blokları Kat: 3 Daire: 6 Bakırköy-İstanbul, Turkey
Phone: +90 212 560 40 69 / +90 232 412 39 51
Fax: +90 212 560 40 79
Web Page: www.turkosteoporozdergisi.org
E-mail: yesim.kirazli@ege.edu.tr

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YAZARLARA BİLGİ

Türk Osteoporoz Dergisi, Türkiye Osteoporoz Derneği'nin resmi yayın organıdır.
Dergi, osteoporoz, metabolik kemik hastalıkları ve rehabilitasyon alanlarını ilgilendiren tüm konulardaki yazıları yayınlar. Dergide orijinal makalelerin dışında derleme yazıları, orijinal olgu sunumları, editöre mektuplar, bilimsel mektuplar, eğitim yazıları, yeni literatür özetleri ve gelecek kongre/toplantı duyuruları da yayınlanır.
Dergide yayınlanacak yazıların seçimine temel teşkil eden hakem heyeti, dergide belirtilen danışmanlar ve gerekirse yurt içi/dışı otörler arasından seçilir.
Yazılarda Türk Dil Kurumu'nun Türkçe Sözlüğü ve Yazım Kılavuzu temel alınmalıdır. İngilizce yazılan yazılar özellikle desteklenmektedir.
Makaleletin formatı 'Uniform reqıuirements for Manuscripts Submitted to Biomedical Journals' (http.//www.icmje.org) kurallarına göre düzenlenmelidir.
Editör tarafından, etik kurul onayı alınması zorunluluğu olan klinik araştırmalarda onay belgesi talep edilecektir. İnsan üzerinde yapılan deneysel araştırmaların bildirildiği yazıların metnin içerisinde, yazarların bu araştırmanın prosedürünün sorumlu olan etik kurulun insan üzerine deney yapılma etik standartlarına (kurumsal ve ulusal) ve 2013 yılında revize edilen1964 Helsinki Deklarasyonuna uyulduğunu ve hastaların onaylarının alındığını belirtilmelidir. Hayvan üzerinde yapılan deneysel araştırmalarda, yazarlar yapılan prosedürlerin hayvanlar haklarına uygun olduğunu belirtilip (Guide for the care and use of laboratory animals. www.nap.edu/catalog/5140html) ayrıca etik kurulu onayı'nı alınmalıdır.
Yazıların içeriğinden ve kaynakların doğruluğundan yazarlar sorumludur.
Yazarlar, gönderdikleri çalışmanın başka bir dergide yayınlanmadığı ve/veya yayınlanmak üzere incelemede olmadığı konusunda garanti vermelidir. Daha önceki bilimsel toplantılarda 200 kelimeyi geçmeyen özet sunumlarının yayınları, durumu belirtilmek koşulu ile kabul edilebilir.
Tüm yazarların çıkar çatışma olmadığını, bilimsel katkı ve sorumluluklarını bildiren toplu imza ile yayına katılmalıdır.
Tüm yazılar, editör ve ilgili editör yardımcıları ile en az üç danışman hakem tarafından incelenir. Yazarlar, yayına kabul edilen yazılarda, metinde temel değişiklik yapmamak kaydı ile editör ve yardımcılarının düzeltme yapmalarını kabul etmiş olmalıdırlar.

Genel Kurallar

Yazılar sadece "online" olarak kabul edilmektedir. Yazarların makale gönderebilmesi için Journal Agent web sayfasına (www.journalagent.com/osteoporoz) kayıt olup şifre almaları gereklidir. Bu sistem on-line yazı gönderilmesine ve değerlendirilmesine olanak tanımaktadır. Makale gönderimi yapılırken sorumlu yazarın ORCID (Open Researcher ve Contributor ID) numarası belirtilmelidir. http://orcid.org adresinden ücretsiz olarak kayıt oluşturabilir.
Bu sistem ile toplanan makaleler ICMJE-www.icmje.org, Index Medicus (Medline/PubMed) ve Ulakbim-Türk Tıp Dizini kurallarına uygun olarak sisteme alınmakta ve arşivlenmektedir. Yayına kabul edilmeyen yazılar, sanatsal resimler hariç geriye yollanmaz.
Yazının tümünün 5000 kelimeden az olması gerekmektedir. İlk sayfa hariç tüm yazıların sağ üst köşelerinde sayfa numaraları bulunmalıdır. Yazıda, konunun anlaşılmasında gerekli olan sayıda ve içerikte tablo ve şekil bulunmalıdır.
Başlık sayfası, kaynaklar, şekiller ve tablolar ile ilgili kurallar bu dergide basılan tüm yayın türleri için geçerlidir.

Orijinal Makaleler

1) Başlık Sayfası (Sayfa 1)
Yazı başlığının, yazar(lar)ın bilgilerinin, anahtar kelimelerin ve kısa başlıkların yer aldığı ilk sayfadır.
Türkçe yazılarda, yazının İngilizce başlığı da mutlaka yer almalıdır; yabancı dildeki yayınlarda ise yazının Türkçe başlığı da bulunmalıdır. Türkçe ve İngilizce anahtar sözcükler ve kısa başlık da başlık sayfasında yer almalıdır.
Yazarların isimleri, hangi kurumda çalıştıkları ve açık adresleri belirtilmelidir. Yazışmaların yapılacağı yazarın adresi de ayrıca açık olarak belirtilmelidir. Yazarlarla iletişimde öncelikle e-posta adresi kullanılacağından, yazışmaların yapılacağı yazara ait e-posta adresi belirtilmelidir. Buna ek olarak telefon ve faks numaraları da bildirilmelidir.
Çalışma herhangi bir bilimsel toplantıda önceden bildirilen koşullarda tebliğ edilmiş ya da özeti yayınlanmış ise bu sayfada konu ile ilgili açıklama yapılmalıdır.
Yine bu sayfada, dergiye gönderilen yazı ile ilgili herhangi bir kuruluşun desteği sağlanmışsa belirtilmelidir.
2) Özet (Sayfa 2)
İkinci sayfada yazının Türkçe ve İngilizce özetleri (her biri için en fazla 200 sözcük) ile anahtar sözcükler belirtilmelidir.
Özet bölümü; Amaç, Gereç ve Yöntem, Bulgular, Sonuç şeklinde alt başlıklarla düzenlenir. Derleme, vaka takdimi ve eğitim yazılarında özet bölümü alt başlıklara ayrılmaz. Bunlarda özet bölümü, 200 kelimeyi geçmeyecek şekilde amaçlar, bulgular ve sonuç cümlelerini içermelidir.
Özet bölümünde kaynaklar gösterilmemelidir. Özet bölümünde kısaltmalardan mümkün olduğunca kaçınılmalıdır. Yapılacak kısaltmalar metindekilerden bağımsız olarak ele alınmalıdır.
3) Metin (Özetin uzunluğuna göre Sayfa 3 veya 4'den başlayarak)
Genel Kurallar bölümüne uyunuz.
Metinde ana başlıklar şunlardır: Giriş, Gereç ve Yöntem, Bulgular, Tartışma.
Giriş bölümü çalışmanın mantığı ve konunun geçmişi ile ilgili bilgiler içermelidir. Çalışmanın sonuçları giriş bölümünde tartışılmamalıdır.
Gereç ve yöntem bölümü çalışmanın tekrar edilebilmesi için yeterli ayrıntılar içermelidir. Kullanılan istatistik yöntemler açık olarak belirtilmelidir.
Bulgular bölümü de çalışmanın tekrar edilebilmesine yetecek ayrıntıları içermelidir.
Tartışma bölümünde, elde edilen bulguların doğru ve ayrıntılı bir yorumu verilmelidir. Bu bölümde kullanılacak literatürün, yazarların bulguları ile direkt ilişkili olmasına dikkat edilmelidir.
Teşekkür mümkün olduğunca kısa tutulmalıdır. Çalışma için bir destek verilmişse bu bölümde söz edilmelidir.
Çalışmanın kısıtlılıkları başlığı altında çalışma sürecinde yapılamayanlar ile sınırları ifade edilmeli ve gelecek çalışmalara ilişkin öneriler sunulmalıdır.
Sonuç başlığı altında çalışmadan elde edilen sonuç vurgulanmalıdır.
Metinde fazla kısaltma kullanmaktan kaçınılmalıdır. Tüm kısaltılacak terimler metinde ilk geçtiği yerde parantez içinde belirtilmelidir. Özette ve metinde yapılan kısaltmalar birbirinden bağımsız olarak ele alınmalıdır. Özet bölümünde kısaltması yapılan kelimeler, metinde ilk geçtiği yerde tekrar uzun şekilleri ile yazılıp kısaltılmalıdırlar.
4) Kaynaklar
Kaynakların gerçekliğinden yazarlar sorumludur.
Kaynaklar metinde geçiş sırasına göre numaralandırılmalıdır. Kullanılan kaynaklar metinde parantez içinde belirtilmelidir.
Kişisel görüşmeler, yayınlanmamış veriler ve henüz yayınlanmamış çalışmalar bu bölümde değil, metin içinde şu şekilde verilmelidir: (isim(ler), yayınlanmamış veri, 19..).
Kaynaklar listesi makale metninin sonunda ayrı bir sayfaya yazılmalıdır. Altıdan fazla yazarın yer aldığı kaynaklarda 6. isimden sonraki yazarlar için "et al" ("ve ark") kısaltması kullanılmalıdır. Dergi isimlerinin kısaltmaları Index Medicus'taki stile uygun olarak yapılır. Tüm referanslar Vancouver sistemine göre aşağıdaki şekilde yazılmalıdır.
a) Standart makale:
Intiso D, Santilli V, Grasso MG, Rossi R, Caruso I. Rehabilitation of walking with electromyographic biofeedback in foot-drop after stroke. Stroke 1994;25:1189-92.
b) Kitap:
Getzen TE. Health economics: fundamentals of funds. New York: John Wiley & Sons; 1997.
c) Kitap Bölümü:
Porter RJ, Meldrum BS. Antiepileptic drugs. In: Katzung BG, editor. Basic and clinical pharmacology. 6th ed. Norwalk, CN: Appleton and Lange; 1995. p. 361-80.
Birden fazla editör varsa: editors.
d) Toplantıda sunulan makale:
Bengtsson S, Solheim BG. Enforcement of data protection, privacy and security in medical informatics. In: Lun KC, Degoulet P, Piemme TE, Reinhoff O, editors. MEDINFO 92. Proceedings of the 7th World Congress on Medical Informatics; 1992 Sep 6-10; Geneva, Switzerland. Amsterdam: North-Holland; 1992. p. 1561-5.
e) Elektronik formatta makale:
Morse SS. Factors in the emergence of infectious disease. Emerg Infect Dis [serial online] 1995 1(1):[24 screens]. Available from:s URL:http://www/cdc/gov/ncidoc/ EID/eid.htm. Accessed December 25, 1999.
f) Tez:
Kaplan SI. Post-hospital home health care: the elderly access and utilization (thesis). St. Louis (MO): Washington Univ; 1995.
5) Tablolar-grafikler-şekiller-resimler
Tüm tablolar, grafikler veya şekiller ayrı bir kağıda basılmalıdır. Her birine metinde geçiş sırasına göre numara verilmeli ve kısa birer başlık yazılmalıdır. Kullanılan kısaltmalar alt kısımda mutlaka açıklanmalıdır. Özellikle tablolar metni açıklayıcı ve kolay anlaşılır hale getirme amacı ile hazırlanmalı ve metnin tekrarı olmamalıdır. Başka bir yayından alıntı yapılıyorsa yazılı baskı izni birlikte yollanmalıdır. Fotoğraflar parlak kağıda basılmalıdır. Çizimler profesyonellerce yapılmalı ve gri renkler kullanılmamalıdır.

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2) Olgu Sunumları:
Nadir görülen ve önemli klinik deneyimler sunulmalıdır. Giriş, olgu ve tartışma bölümlerini içerir.
3) Editöre Mektuplar:
Bu dergide yayınlanmış makaleler hakkında yapılan değerlendirme yazılarıdır. Editör gönderilmiş mektuplara yanıt isteyebilir. Metnin bölümleri yoktur.
4) Bilimsel Mektuplar:
Bu yazılar orijinal araştırma yapısında olmayan bilimsel ilgi uyandırabilen yeni fikir, buluş ve verilerin sunulduğu ön bildirilerdir. Bu konuyla ilgili gelecekteki yayınlara merak uyandırmayı amaçlar. Metnin bölümleri yoktur.
5) Eğitim Yazıları:
Bu kategoride otörler osteoporoz, metabolik kemik hastalıkları ve rehabilitasyon konularındaki güncel bilgileri özetlerler.

Yazışma
Tüm yazışmalar dergi editörlüğünün aşağıda bulunan posta veya e-posta adresine yapılabilir.

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Türkiye Osteoporoz Derneği
Ataköy 4. Kısım O-121 Blokları, K: 3, D: 6 Bakırköy-İstanbul, Türkiye
Tel.: +90 212 560 40 69 - +90 232 412 39 51 Faks: +90 212 560 40 79
E-posta: yesim.kirazli@ege.edu.tr

Türk Osteoporoz Dergisi
TURKISH JOURNAL OF OSTEOPOROSIS

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Address:
Turkish Osteoporosis Society
Ataköy 4. Kısım O-121 Blokları, K: 3, D: 6 Bakırköy-İstanbul, Turkey
Phone: +90 212 560 40 69 - +90 232 412 39 51 Fax: +90 212 560 40 79
E-mail: yesim.kirazli@ege.edu.tr

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Türk Osteoporoz Dergisi
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Editörden / Editorial

Sevgili Meslektaşlarımız,

Değerli meslektaşlarımıza Emerging Sources Citation Index (ESCI) tarafından indekslenen dergimize araştırma makalesi ve olgu sunumları şeklinde çalışmalarını yayınlanmak üzere düzenli olarak ilettikleri için çok teşekkür ederiz.

Türkiye Osteoporoz Derneği tarafından düzenlenen; **OSTEOAKADEMİ 2023 Sempozyumu**'nun ana teması "Kas-İskelet Hastalıkları Önleme, Tanı ve Tedavilerindeki Stratejilere ve Seçeneklere Güncel Bakış" olarak belirlenmiştir. **OSTEOAKADEMİ 2023 12-14 Haziran 2023 tarihlerinde Crowne Plaza Otel-Kapadokya**'da gerçekleşecektir.

Sempozyumun içeriğinde gerek akademik çalışma ve araştırmalarda gerekse günlük hekimlik uygulamalarında sıklıkla karşılaşılan; "Osteoporozda karmaşık olgular-sorular ve yanıtlar, Kas iskelet ağrısında klinik yaklaşım nasıl olmalı? Nöropatik ağrıya klinik yaklaşımda yeni ne var? Sarkopenide güncelleme-tanım ve değerlendirme, COVID sonrası dönemin kas-iskelet sistemi boyutu, Osteoporoz tedavilerinde yenilikler, Fiziksel aktivite; ne kadarı çok? Düşmelerin öngörülmesi ve önlenmesi, Osteoporoz ve Osteoartritte yaşam kalitesi nasıl değerlendirilmeli? Osteoporoz ve Osteoartritte obezite ve kilo kaybı, D vitamini ile kas-iskelet sistemi hastalıkları ilişkisi, Osteoartrit tedavilerinde yenilikler, Osteoartritte PRP, Kök hücre tedavileri, Osteoporozda kişiselleştirilmiş yönetim, Osteoartritte kişiselleştirilmiş yönetim, Osteoporozda sürekli veya aralıklı tedaviler, Osteoporotik kırık sonrası yaklaşım nasıl olmalı?" konularına yönelik bir program hazırlanmış, osteoporoz ve osteoartrit yanında ağrıya, yaşam kalitesinde olumsuz etkilenmelere ve iş gücü kaybına neden olan farklı kas iskelet sistemi sorunlarına da yer verilmiştir.

Osteoporoz, osteoartrit ve kas iskelet sistemi ağrıları konularındaki bilgilerimizi güncellemek amacı ile 3 günlük fiziki katılımlı bir akademi ile sizlerle bilgi paylaşımında bulunmayı planladığımız; konularında önde gelen isimlerin konuşmacı olarak yer alacağı akademi sizlerin de katkıları ve destekleri ile gerçekleştirilecektir.

Siz değerli meslektaşlarımıza çalışmalarınızda kolaylıklar dileyerek, sevgi ve saygılarımı sunarım.

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Osteoporoz Epigenetiği

Epigenetics of Osteoporosis

Şengül Tural, Esra Tekcan*, Ercan Tural**

Ondokuz Mayıs Üniversitesi Tıp Fakültesi, Tıbbi Biyoloji Anabilim Dalı, Samsun, Türkiye
*Ondokuz Mayıs Üniverstitesi Tıp Fakültesi, Merkez Laboratuvarı, Samsun, Türkiye
**Ondokuz Mayıs Üniversitesi Sağlık Bilimleri Fakültesi, Fizyoterapi ve Rehabilitasyon Anabilim Dalı, Samsun Türkiye

Öz

Osteoporoz (OP), düşük kemik kütlesi ve kemik dokusunun mikromimarisinin bozulması, bunun sonucunda kemik kırılganlığında ve kırılma eğiliminde artış ile karakterize sistemik bir hastalıktır. Prenatal dönem dahil olmak üzere yaşamın erken dönemindeki çevresel faktörler, yaşamın sonraki dönemlerinde kemik kütlesini ve dolayısıyla OP riskini etkileyebilir. Epigenetik esas olarak transkripsiyon sonrası düzenleyici bir rol oynar ve biyolojik sinyal düzenleyici yolakta önemli işlevlere sahiptir. Epigenetik mekanizmalar, kemik oluşumu ve kemik erimesinden sorumlu olan kemik hücrelerinin, osteoblastların ve osteoklastların farklılaşmasında önemli rol oynar. Birkaç çalışma, OP'lu hastalarda bazı farklı şekilde metillenmiş genler göstermiştir. Anormal epigenetik düzenleme, OP gibi bir dizi kemik metabolizması ile ilgili hastalığa yol açabilir. Bunlar, osteoblast farklılaşmasının önemli bir düzenleyicisi olan *Wnt* yoluna ait genleri ve iskeletin gelişiminde rol oynayan diğer genleri içerir. Benzer şekilde, bu hastalarda bazı MikroRNA'lar farklı şekilde eksprese edilebilir. Ancak, bu sonuçların diğer kohortlarda tekrarlanması önerilmektedir. Genomdan farklı olarak, epigenom hücreye özgüdür ve yaşlanma ve çevresel faktörlerle değişir. Bu nedenle, epigenetik epidemiyoloji çalışmalarının tasarımı ve yorumlanması birtakım pratik zorluklar doğurmaktadır. Epigenetik mekanizmalar, kemik oluşumu ve kemik erimesinden sorumlu olan kemik hücrelerinin, osteoblastların ve osteoklastların farklılaşmasında önemli rol oynamaktadır.
Anahtar kelimeler: Osteoporoz, epigenetik, menopoz sonrası kadınlar

Abstract

Osteoporosis (OP) is a systemic disease characterized by low bone mass and deterioration of the microarchitecture of bone tissue, resulting in increased bone fragility and fracture tendency. Environmental factors early in life, including the prenatal period, can affect bone mass later in life and thus the risk of OP. Epigenetics mainly plays a post-transcriptional regulatory role and has important functions in the biological signal-regulatory pathway. Epigenetic mechanisms play an important role in the differentiation of bone cells, osteoblasts, and osteoclasts, which are responsible for bone formation and bone resorption. Several studies have shown some differentially methylated genes in patients with OP. The abnormal epigenetic regulation can lead to a number of bone metabolism-related diseases such as OP. These include genes for the *Wnt* pathway, an important regulator of osteoblast differentiation, and other genes involved in skeletal development. Similarly, some MicroRNA's may be differentially expressed in these patients. However, it is recommended that these results should be replicated in other cohorts. Unlike the genome, the epigenome is cell-specific and changes with aging and environmental factors. Therefore, the design and interpretation of epigenetic epidemiology studies pose a number of practical challenges. Epigenetic mechanisms play an important role in the differentiation of bone cells, osteoblasts, and osteoclasts, which are responsible for bone formation and bone resorption.
Keywords: Osteoporosis, epigenetics, postmenopausal women

Giriş

Osteoporoz (OP), azalmış kemik kütlesi ve kemik dokusunun bozulması ile karakterizedir, bu da kemik gücünde azalmaya ve kırılma eğilimine yol açar. Menopoz sonrası kadınların üçte birinden fazlasını ve 60 yaş üstü erkeklerin %10-16'sını etkileyen yaygın bir hastalıktır (1,2). Kemik kütlesi birikimi intrauterin yaşamda başlar ve büyüme periyodu boyunca devam eder, böylece kemik kütlesi insanlarda yaşamın üçüncü on yılında zirveye ulaşır. Birkaç yıl stabil kaldıktan sonra, kemik kütlesi menopozu takip eden 5-10 yıl içinde kadınlarda hızlanan ilerleyici bir düşüşe başlar. Bu nedenle OP, büyüme periyodu sırasında yetersiz kemik birikiminden ve/veya doruk kemik kütlesine ulaşıldıktan sonra hızlanan kemik kaybından kaynaklanabilir (3,4). Kemik mineral yoğunluğunu (KMY) birçok çevresel faktör etkilemekle birlikte, çeşitli ikiz ve aile çalışmaları kemik oluşumunda genetik

Yazışma Adresi/Address for Correspondence: Doç. Dr. Şengül Tural, Ondokuz Mayıs Üniversitesi Tıp Fakültesi, Tıbbi Biyoloji Anabilim Dalı, Samsun, Türkiye
Tel.: +90 362 312 19 19-2846 **E-posta:** stural@omu.edu.tr **ORCID ID:** orcid.org/0000-0002-8946-8165
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faktörlerin etkisinin %50-80 olduğunu göstermektedir. Kemik kütlesini etkileyen birçok genin varlığı bildirilmiştir. Asosiyasyon çalışmaları, aday gen polimorfizmleri, meta-analizler ve daha yeni olan genom çaplı çalışmalar ile KMY ve OP fenotipiyle ilişkili diğer genler belirlenmiştir. Epigenetik mekanizmaların kemik metabolizmasının düzenlenmesindeki önemli rolü göz önüne alındığında, osteojenik farklılaşmadaki epigenetik mekanizmalar (DNA metilasyonu, histon modifikasyonu ve kodlayıcı olmayan RNA'lar) OP'nin patogenezi konusunda kemik metabolizması ile ilişkili hastalıkların tedavisi için yol gösterici olacaktır.

DNA Metilasyonu

DNA metilasyonu en çok çalışılan epigenetik mekanizmalardan biridir (5). Palindromik sitozin-fosfat-guanin (CpG) dinükleotitlerinde sitozinin 5' pozisyonuna kovalent olarak bağlı bir metil grubundan oluşur, 5mC olarak kısaltılır. CpG dinükleotitleri seyrek olarak meydana gelir, memeli genomunun sadece %2'si, esas olarak gen promotörleri ve düzenleyici bölgeler ile ilişkili olan CpG adacıkları olarak adlandırılan kısa yüksek frekanslı CpG uzantıları içerir (5). Metil gruplarının sitozine eklenmesi, DNA metiltransferazlar (DNMT) tarafından katalize edilir. Metilasyon sonucu, temel transkripsiyon faktörlerinin hedeflerine bağlanmasını doğrudan veya dolaylı olarak bloke ederek aracılık edebilen transkripsiyonel baskılamadır. Bununla birlikte, *in vivo* erken oluşturulan DNA metilasyon paterni genellikle dış çevreden etkilenir ve küçük farklılıklar, malign olmayan hastalıkların başlangıcıyla bağlantılı fenotip çeşitliliği üzerinde büyük bir etkiye sahip olabilir (5). DNMT'ler embriyogenez, gelişim ve metilasyon süreçlerinde önemli rol oynar. Hem prokaryotlarda hem de ökaryotlarda genom stabilitesi, gen ekspresyonu bireysel gelişimde önemlidir (6,7). DNA metilasyonunun modifikasyonları esas olarak DNMT ailesi proteinleri tarafından kontrol edilir ve CpG adalarındaki sitozin kalıntıları için metil donörü olarak S-adenosilmetiyonin kullanılır (8). Normalde genlerdeki CpG adaları metillenmemiş halde bulunur ve bu adalardaki sitozinlerin metilasyonu genin ekspresyonunu engelleyebilir (9). Belirli bir hipometilasyon durumu, ilgili genlerin ekspresyonuna elverişliyken, hipermetilasyon durumu, gen sessizleşmesine yol açabilir (8). Bu alanda giderek artan çalışmalar, DNA metilasyonunun, OP patomekanizmasında önemli bir rol oynadığı, osteoblastların ve osteoklastların farklılaşmasını ve apoptozunu düzenleyebileceğini göstermiştir (7). DNA metilasyon modifikasyonu ile düzenlenen osteojenik farklılaşma belirteçleri Tablo 1'de görülmektedir (Tablo 1).

Histon Modifikasyonu

Beş tipi (H1, H2A, H2B, H3 ve H4) bulunan histonlar, pozitif yüklü bazik amino asitler (arginin ve lisin) bakımından zengin ve DNA'daki negatif yüklü fosfat gruplarıyla etkileşime girebilen küçük moleküllü proteinlerdir. Histon kimyasal modifikasyonu, proteinin N-terminal kuyruğunda, özellikle H3 ve H4 bölgesinde meydana gelir ve kromatinde değişikliklere neden olur. Histon kuyruğu 20 amino asitten oluşur ve belirli bir hipometilasyon durumu, ilgili genlerin ekspresyonuna elverişliyken, bir hipermetilasyon durumu gen sessizleşmesine yol açabilir (8). Artan çalışmalar, DNA metilasyonunun, OP'nin patomekanizmasında önemli bir rol oynadığı ve osteoblastların ve osteoklastların farklılaşmasını ve apoptozunu düzenleyebileceğini göstermiştir (7). Nükleozom, birkaç histon alt biriminden oluşan bir kompleks olup, DNA'yı ve epigenetik bilgiyi korur. Histonların translasyon sonrası modifikasyonu önemli bir adımdır. Yeniden katlanan

Tablo 1. DNA metilasyon modifikasyonu ile düzenlenen osteogenik farklılaşma belirteçleri

Genler	Metilasyon seviyesi	Osteopgeneziste gen fonksiyonu	Referans
RUNX2	Düşük	TF, hedef genlerin ekspresyonunu ve osteojenik farklılaşmayı teşvik eder.	(10)
OSX	Düşük	TF, hedef genlerin ekspresyonunu ve osteojenik farklılaşmayı teşvik eder.	(10)
BMP2	Düşük	Kemik büyüme faktörü, osteojenik farklılaşmayı teşvik eder.	(11)
SOST	Yüksek	Glikoprotein, osteojenik farklılaşmayı inhibe eder.	(12)
ALP	Düşük	Hidroksiapatit birikimi için gerekli fosforik asidi sağlamak üzere fosfat esteri hidrolize edin ve aynı zamanda kemik tuzu oluşumu üzerindeki inhibitör etkisini ortadan kaldırmak için pirofosfatı hidrolize eder.	(13)
OCN	Düşük	Normal kemik mineralizasyonunu korur.	(13)
Frizzied1	Düşük	*Wnt* yolunu aktive eder ve osteojenik farklılaşmayı teşvik eder.	(14)
RANKL	Yüksek	Osteoklast farklılaşmasını uyarır ve kemik rezorpsiyonunu destekler.	(15)
OPG	Düşük	Osteoklast farklılaşmasını inhibe eder.	(16)
LOX	Düşük	Osteojenik farklılaşmayı teşvik eder.	(17)
ESR1	Düşük	Osteojenik farklılaşmayı teşvik eder.	(18)
DLX5	Düşük	Osteojenik farklılaşmayı teşvik eder.	(19)
Alu elements	Yüksek	Kemik oluşumu ile negatif korelasyon	(20)

RUNX2: Runt-related transcription factor 2, OSX: Osterix, BMP2: Kemik morfojenik proteini-2, SOST: Sklerostin, ALP: Alkalen fosfataz, OCN: Osteokalsin, RANKL: Nükleer faktör kappa-β ligandının reseptör aktivatörü, OPG: Osteoprotegerin, LOX: Lizil oksidaz, ESR1: Östrojen reseptörü 1, DLX5: Distal-Less homeobox 5

kovalent histon modifikasyonları, çoğunlukla kimyasal olarak kararsız amino asit kalıntılarının (örneğin; lizin, arginin, serin, treonin, tirozin ve histidin) amino ve karboksil uçlarında ve ayrıca histonun versiyonu sırasında veya nükleozomal çekirdeklerin kor alanlarında meydana gelir (21). Her modifiye edilmiş histon kalıntısı spesifik bilgi taşır ve genel olarak H3K3 bölgesindedir. Bilgi iletimi, histonların kendi aralarındaki veya histonlar ile DNA arasındaki etkileşimi değiştirmek dahil olmak üzere çeşitli mekanizmalar yoluyla olabilir (22). Histon deasetilazlar, hedef histonlar ve osteoblast farklılaşmasındaki rolleri Tablo 2'de görülmektedir. Histon deasetilazlar, hedef histonlar ve osteoblast farklılaşmasındaki rolleri Tablo 3'te görülmektedir.

Kodlamayan RNA'lar

Kodlamayan RNA, genomdan kopyalanan ancak bir proteini kodlamayan bir RNA türüdür (41). RNA'nın uzunluğuna göre, kodlama yapmayan RNA üç tipe ayrılır: Bunlardan ilki mikroRNA'lar dahil 50 nt'den az uzunluk mikroRNA'lar (miRNA), küçük enterferans yapan RNA'lar siRNA ve yeni kodlamayan küçük RNA'lar priRNA; ikincisi ribozomal RNA ve transfer RNA dahil olmak üzere 50 ila 500 nt arasında değişen uzunluktadırlar; ve üçüncüsü geleneksel lineer RNA'dan farklı olan uzun kodlayıcı olmayan RNA'lar lncRNA ve dairesel RNA'lar circRNA dahil olmak üzere çeşitlidir (42,43). Geçmişte, bilim adamları genellikle kodlamayan RNA'nın rolünü "önemsiz RNA" olarak gördüler. Bilimsel düşünce ve laboratuvar teknolojisinin ilerlemesiyle, artan sayıda çalışma, kodlamayan RNA'nın anormal ifadesi ile kemik metabolik hastalıklarının gelişimi arasında bir ilişki olduğunu bildirmiştir (7,43). Kodlamayan RNA'nın kemik metabolizması sürecindeki anahtar rolü belirlenirse, kemik metabolizmasıyla ilişkili hastalıkları temelde bloke etmesi ve tedavi etmesi beklenen hedefe yönelik tedavi için ilaçlar tasarlanabilineceği öne sürülmektedir. LncRNA'lar hedef genleri ve fonksiyonları Tablo 4'te görülmektedir.

Tablo 2. Histon deasetilazlar, hedef histonlar ve osteoblast farklılaşmasındaki rolleri

HDAC	Hedef histonlar	Fonksiyon	Referans
HDAC1	H2A, H2B, H3, H4		(23)
HDAC2	H2A, H2B, H3, H4	Osteoblast farklılaşmasını düzenler.	(23)
HDAC3	H2A, H2B, H3K27, H3, H4	Osteoblast gen ekspresyonunu inhibe eder.	(24)
HDAC4	H2A, H2B, H3K9, H3, H4	Kondrositlerin transkripsiyonunu, hipertrofisini ve kemikleşmesini düzenler.	(25)
HDAC5	H2A, H2B, H3K9, H3, H4	Kondrositlerin transkripsiyonunu, hipertrofisini ve kemikleşmesini düzenler.	(25)
HDAC6	H2A, H2B, H3K9, H3, H4	RUNX2 aktivitesini ve gen ekspresyonunu düzenler.	(26)
HDAC7	H2A, H2B, H3K9, H3, H4	Osteoblast gen ekspresyonunu inhibe eder.	(27)
HDAC8	H2A, H2B, H3K9, H3, H4	Maksillofasiyal kemik gelişimi	(28)
SIRT1	H3, H4	BMMSC'lerin çoğalmasını ve osteoblast farklılaşmasını düzenler.	(29)
SIRT6	H3, H4, H3K9, H3K56	Kondrosit proliferasyonunu düzenler.	(30)

BMMSC: Kemik iliği kaynaklı mezenkimal kök hücreler

Tablo 3. Histon deasetilazlar, hedef histonlar ve osteoblast farklılaşmasındaki rolleri

HDM	Hedef histonlar	Hedef genler	Fonksiyon	Referans
LSD1/KDM1A	H3K4me3	*Wnt7B, BMP2*	Osteoblast farklılaşmasını inhibe eder.	(31)
KDM2B	H3K4me3, H3K36me1/2	*AP-2a*	Erken ve geç ameloblast hücrelerinin proliferasyonu ve farklılaşmasının yanı sıra dentinin farklılaşmasında yer alır.	(32)
KDM4A	H3K9me3	*Sfrp4, C/EBPa*	Adipojenik farklılaşmayı teşvik eder ve kök hücrelerin osteoblastik farklılaşmasını inhibe eder.	(33)
KDM4B	H3K9me3, H3K27me3	*DLX*	Osteoblast farklılaşmasını teşvik eder.	(34)
KDM5A	H3K4me3	*BMP2, RUNX2*	Osteoblast farklılaşmasını inhibe eder.	(35)
JMJD3/KDM6B	H3K9me3, H3K27me3/2	*HOX*	Osteoblast farklılaşmasını teşvik eder.	(36)
KDM7A	H3K9me2, H3K27me2	*C/EBPa, Wnt pathway*	Adipojenik farklılaşmayı teşvik eder ve osteoblastik farklılaşmayı inhibe eder.	(37)
NO66	H3K4, H3K36	*OSX*	Osteoblast farklılaşmasını inhibe eder.	(38)
RBP2/JARID1A	H3K4me3/2	*RUNX2*	Osteoblast farklılaşmasını inhibe eder.	(39)
JMJD7	-	*c-fos, Dc-stamp, CtsK, Acp5 and Nfatc1*	Osteoblast farklılaşmasını inhibe eder.	(40)

Mikro RNA'lar

MiRNA'lar, yaklaşık 22 nükleotit uzunluğunda, kodlama yapmayan küçük, tek sarmallı bir RNA türüdür. Hedef gen mRNA'sına diziye özgü baz eşleştirmesi yoluyla bağlanır (7). miRNA'lar, osteojenik farklılaşma ile ilgili hedef genleri düzenleyerek kemik metabolizmasını düzenlediği yapılan çalışmalarla bildirilmiştir. Bazı önemli miRNA'lar ve etkileri Tablo 5'te görülmektedir.

Yetersiz Pik Kemik Kütlesi

OP genç bireylerde nadirdir. Aslında, yetersiz bir tepe kemik kütlesine sahip bireyler bile büyüme döneminde yetersiz kemik kütlesi birikimi nedeniyle nadiren OP'ye bağlı kırıklara maruz kalır. Bununla birlikte, bu bireyler daha sonraki yaşamlarında kırıklar için yüksek risk altındadır, çünkü zaten düşük bir kemik kütlesi üzerine bindirilmiş yaşa bağlı azalan kemik kütlesi kırık eşiğini düşürür (62). Doruk kemik kütlesinin güçlü bir genetik bileşene sahip olduğu bilinmektedir. Bu nedenle, çeşitli etnik kökenlere sahip ebeveynlerin kemik kütleleri ile çocukları arasında doğrudan korelasyonlar bildirilmiştir (63,64). Bununla birlikte, kemik kütlesi üzerindeki kalıtsal etkiyi açıklayan genler tam olarak aydınlatılamamıştır. *Wnt* ailesinin üyeleri de dahil olmak üzere bazı genlerin genç bireylerde kemik kütlesi ile ilişkili olduğu tutarlı bir şekilde tanımlanmıştır (65). Bir dizi edinilmiş faktörün büyüyen iskelet üzerinde derin etkileri vardır. Besin faktörlerini, egzersizi, komorbid bozuklukları vb. içerirler. Rahim içinde veya doğumdan sonra etki edebilirler. Aslında, daha sonraki yıllarda rahim içi büyüme ile kemik kütlesi arasında bir ilişki olduğuna dair kanıtlar vardır (66,67). Örneğin; gözlemsel bir meta-analiz çalışması, doğum ağırlığı ile yaşamın sonraki dönemlerindeki kemik kütlesi arasında bir ilişki bildirmiştir. Doğum ağırlığı, KMY'den daha çok kemik mineral içeriği ile ilişkili bulunmuştur (68). Bu, ilişkinin tercihen kemik yoğunluğundan ziyade doğum ağırlığının gelecekteki kemik boyutu ile bir korelasyonu

Tablo 4. LncRNA'lar hedef genleri ve fonksiyonları

LncRNA'lar	Hedef genler	Fonksiyonlar	Referans
H19	*miR-675, miR-141, miR-22,*	Osteoblastik farklılaşmayı teşvik eder.	(42)
	CTCF/H19/HDAC pathway	Adipojenik farklılaşmayı teşvik eder.	(43)
LncRNA	*p21 Wnt/β-actin pathway*	Osteoblastik farklılaşmayı teşvik eder.	(44)
Bmcob	*SBP2*	Osteoblastik farklılaşmayı teşvik eder.	(31)
HIF1α-AS1	*HOXD10, SIRT1*	İnhibisyon	(45)
LncRNA TUG1	*Wnt/β-actin pathway*	Osteoblastik farklılaşmayı teşvik eder.	(46)
XR-111050	*RUNX2*	Osteoblastik farklılaşmayı teşvik eder.	(47)
DNACR	*P38 MAPK pathway*	Osteoblastik farklılaşmayı inhibe eder.	(48)
AK-096529, uc003ups, AK05611	*Smurf1, RUNX2*	Osteoblastik farklılaşmayı teşvik eder.	(45)
HOTAIR	*BMP/TGF-β pathway*	Osteoblastik farklılaşmayı iteşvik eder.	(49)
lncRNA MALAT1	*RANK/RANKL/OPG pathway*	Osteoblastik farklılaşmayı teşvik eder.	(50)
MODR	*MiR-454/RUNX2*	Osteoblastik farklılaşmayı teşvik eder.	(51)
AK141205	*CXCL13*	Osteoblastik farklılaşmayı teşvik eder.	(52)
MEG3	*MiR-133a-3p*	Osteoblastik farklılaşmayı inhibe eder.	(53)
ANCR	*EZH2, RUNX2*	Osteoblastik farklılaşmayı inhibe eder.	(45)
BDNF-AS	*RUNX2*	Osteoblastik farklılaşmayı inhibe eder.	(54)
Plnc1	*PPAR-g2*	Adipojenik farklılaşmayı teşvik eder.	(45)
ADINR	*C/EBPα*	Adipojenik farklılaşmayı teşvik eder.	(55)
HoxA-AS3	*EZH2*	Adipojenik farklılaşmayı teşvik eder, osteoblastik farklılaşmayı inhibe eder.	(56)
ORLNC1	*ORLNC1-miR-296-PTEN*	Adipojenik farklılaşmayı teşvik eder, osteoblastik farklılaşmayı inhibe eder.	(57)
Bmncr	*BMP2, TAZ, RUNX2, PPARG*	Osteoblastik farklılaşmayı teşvik eder, adipojenik farklılaşmayı inhibe eder.	(58)
lncRNA	*RUNX2*	Osteoblastik farklılaşmayı teşvik eder, adipojenik farklılaşmayı inhibe eder.	(59)
LncRNA BDNF-AS	*miR-204-5p, miR-125a-3p*	Osteoblastik farklılaşmayı inhibe eder.	(54)
Linc-ROR	*miR-138, miR-145*	Osteoblastik farklılaşmayı teşvik eder.	(54)

tarafından yönlendirildiğini göstermektedir. Yavruların iskelet kütlesini etkileyen doğum öncesi çevresel faktörler arasında annenin D vitamini seviyeleri çok dikkat çekmiştir (69). Bu çalışmalar, intrauterin olayların iskelet fenotipini etkilediğini göstermektedir. Deney hayvanlarında bazı düşündürücü verilere rağmen (70), gerçek epigenetik mekanizmaların intrauterin çevresel faktörlerin insan iskeleti üzerindeki etkisini ne ölçüde açıkladığı açıklanamamıştır. Bununla birlikte, birkaç çalışma, doğumdaki DNA metilasyon modelinin iskelet homeostazını etkileyebileceğini öne sürmüştür. Bu nedenle, bazı çalışmalar kordon kanındaki eNOS (nitrik oksit sentezinden sorumlu bir enzim) ve retinoid-X reseptörü metilasyonunun çocukluk çağı kemik kütlesi ile ilişkilerini bildirmiştir (71,72).

Hızlı Kemik Kayıbı

Epigenetik mekanizmalar kemik hücrelerinin farklılaşması ve aktivitesinde önemli rollere sahiptir. Bununla birlikte, epigenetik mekanizmaların OP riskini ve diğer iskelet bozukluklarını nasıl etkilediği hakkında çok az bilgi bulunmaktadır. Kemik kütlesinde zıt yönde değişiklik gösteren iki bozukluk olan OP ve osteoartrit arasındaki DNA metilasyonundaki farklılıklar araştırılmış, bu bozuklukların gelişimsel bir bileşeni olduğu hipotezi doğrultusunda, farklı şekilde metillenmiş genler arasında, iskeletin gelişiminde rol oynayan birkaç yolak üyesi bulunmuştur (73). Ayrıca, bu konsepte uygun olarak, sklerostin promotörlerinin ve *Wnt* yolunun diğer genlerinin metilasyon durumunun OP riskini etkilediği öne sürülmüştür (74,75). Ancak, kesin sonuçlara varmadan önce bu sonuçların diğer gruplarda tekrarlanması gerekir. Kodlamayan RNA'lar ayrıca kemiğin yeniden şekillenmesinin ana etkenleri olan osteoblastların ve osteoklastların farklılaşmasının düzenlenmesinde rol oynar (76,77). Aslında, insan doku örneklerinde miRNA'ların miktarını analiz eden çalışmalarda, birkaç miRNA'nın OP'de farklı şekilde eksprese edildiği bulunmuştur (78,79). OP'nin patogenezinde hangi miRNA'ların gerçekte rol oynadığını belirlemek için ilave araştırmalara ihtiyaç vardır.

Epigenetik Epidemiyoloji Çalışmalarının Yorumlanması

Mevcut teknolojiler, aday ve epigenom çapında çalışmaların verimli bir şekilde gerçekleştirilmesine olanak tanır. Bu nedenle, beklenmedik bir şekilde, epigenetik epidemiyoloji üzerine yayınlanmış çalışmaların sayısı katlanarak artmaktadır (80).

Çalışma Konuları

İlk olarak, bireylerin fenotipi açıkça belirlenmelidir. Çalışma hastalıklı denekleri içeriyorsa hastaların fenotipinin tüm hastalık spektrumunu veya sadece bozukluğun belirli bir evresini veya varyantını temsil edip etmediğini incelememiz gerekir. Genomdan farklı olarak epigenomun yaşla ve çevresel etkilerle değişebileceğini belirtmek önemlidir. Bu nedenle, bireylerin yaşı ve önceki tedaviler de dahil olmak üzere diğer olası karıştırıcı etkenlerin dikkate alınması gerekir. Diğer yandan, çalışma hastaları ve kontrolleri karşılaştırdıysa kontrol grubunun çalışılan hasta grubu için yeterli olup olmadığını kontrol etmek önemlidir. Yaş, cinsiyet, etnik köken ve beslenme gibi özellikler ve diğer çevresel etkiler her iki grup arasında karşılaştırılabilir olmalıdır.

Örnek Konular

Epigenomun hücreye özgü olması, epigenomik çalışmalara özgü bir zorluktur. Diğer bir deyişle, genetik dizilerden farklı olarak, epigenetik değişimler hücreler arasında farklılık gösterir. Bu nedenle, ilgili dokularda hastalığın epigenetik değişimlerini belirlemeye yönelik çalışmalar yapılmalıdır. Ancak uygun doku örneklerinin alınması etik ve pratik problemler doğurabilir. Bu nedenle, bazı durumlarda, keşif analizlerinde vekil olarak erişilebilir doku veya sıvıların (kan, tükürük, idrar) kullanılması faydalı olabilir. Ek olarak, bu yaklaşım, epigenetik işaretlerin biyobelirteçler olarak kullanılması için yararlı bilgiler sağlayabilir. Bununla birlikte, patofizyolojik bir perspektiften, iskelet bozuklukları çalışılırken sonuçların kemik gibi ilgili doku örneklerinde doğrulanması gerekir. Farklı bireylerden alınan numuneler karşılaştırılacaksa hücre kompozisyonundaki farklılıklara dikkat etmek önemlidir ve bu faktörün potansiyel etkisi dikkate alınmalıdır (81). Kan örneklerinin DNA metilasyonu çalışmalarında hücre kompozisyonu ayarlamaları yapmaya uygun algoritmalar vardır (82). Bununla birlikte, katı numuneler analiz edildiğinde benzer ayarlamalar daha zordur. Lazer destekli mikrodiseksiyon ve ardından az sayıda hücrenin CpG metilasyonunun analizi için optimize edilmiş yöntemler bir alternatif olabilir (83). Son olarak, aynı bireyin hastalıklı ve kontrol dokularının eşleştirilmiş çalışmalarında, kontrol dokusu, çalışma amaçlarına bağlı olarak dikkatli bir şekilde seçilmelidir. Yalnızca

Tablo 5. Bazı önemli miRNA'lar ve etkileri

miRNA	Hedef gen	Sonuç	Referans
miR-2861	*RUNX2* *HDAC5*	Mutasyon genç bireylerde osteoporoza neden olur.	(19)
miR-214	*ATF-4*	Osteoporoza yatkınlık	(59)
miR-21 miR-23ª-24 miR-100 miR-125b	*PDCD4* *RUNX2* *BMPR2*	Osteoporozda ifadesi farklıdır.	(60)
miR-518 miR-187	*WISP1* *CTNBP1* *IL6, TNF*	Osteoporozda ifadesi farklıdır.	(61)

hastalığın değil, aynı zamanda konakçı yanıtlarının da doku kompozisyonunda ve epigenetik işaretlerde değişikliklere neden olabileceğini düşünmek önemlidir. Örneğin; tümör dokusunun epigenetik imzası, sıklıkla bitişik tümörsüz dokununkiyle karşılaştırılır. Bununla birlikte, sonuncusu, konakçı bağışıklık tepkisi nedeniyle değiştirilmiş bir hücre bileşimine sahip olabilir ve sonuç olarak, gerçek normal dokunun iyi bir temsili olmayabilir.

Teknoloji ve Veri Analizi

Tüm araştırma makalelerinde olduğu gibi, metodoloji/detaylar ve kullanılan teknolojinin tam olarak açıklanması gerekir. Özellikle epigenom çapındaki çalışmalarda kapsamın dikkate alınması önemlidir. Genomda yaklaşık 25 milyon CpG vardır. Metilasyon seviyelerini keşfetmek, maliyetli tam bisülfitom dizilimi gerektirebilir. Sık kullanılan alternatif prosedürler, yaklaşık 5 milyon CpG'yi (84) inceleyebilen popüler 450K array'dir. DNA metilom oluşturmak için nispeten daha ucuz ve uygun metottur. Ancak, bu dizilerin yaklaşık 485.000 CpG bölgesini sorguladığını bilmek önemlidir (85); bu, potansiyel olarak metillenmiş CpG'lerin sadece yaklaşık %2'sini keşfeder. Bu nedenle, birçok bölge keşfedilmemiş durumdadır. Bu bilgi, özellikle olumsuz sonuçları olan çalışmalarda dikkate alınmalıdır. Sonuçların teyit edilmesi için, aynı teknikle tekrar çalışılabilir ya da başka tekniklerle doğrulanabilir. Örneğin; metilasyon dizileriyle elde edilen veriler, piro-sıralama veya MALDI-TOF MS (matrix assisted laser desorption ionization time of flight mass spectrometry) verileriyle teyit edilebilir. Diğer çalışmalarda olduğu gibi örneklem büyüklüğü önemli bir konudur. Çalışmanın istatistiksel gücü ve buna bağlı olarak tip II hata olasılığı (yani, çalışılan gruplar arasında gerçek farklılıklar olduğunda olumsuz bir sonuç elde edilmesi) dikkate alınmalıdır. Numune boyutu ve ölçümün değişkenliği (yani, CpG metilasyon seviyesi, miRNA bolluğu vb.) istatistiksel gücü etkileyen başlıca faktörlerdir. Epigenom çapındaki çalışmalar, birçok lokusta (birkaç milyona kadar) potansiyel gruplar arası farklılıkları araştırır. Bu nedenle, tip I hatanın şişirilmesi (yani, tesadüfen bulunan bir farkın istatistiksel olarak anlamlı kabul edilmesi) bir sorundur. Bunu en aza indirmek için istatistiksel olarak anlamlılık için olağan 0,05 eşiği artık uygun değildir. Yapılan karşılaştırma sayısına göre ayarlanan yeni bir eşiğe indirilmelidir.

Bu tür bir ayarlamayı gerçekleştirmek için Bonferroni prosedürü ve daha az katı olan yanlış keşif oranı hesaplaması dahil olmak üzere çeşitli yöntemler mevcuttur.

Tek Lokus, Genomik Bölgeler ve Ağlar

İlk adım olarak, veri analizi genellikle tekli CpG'lerin metilasyon düzeyi veya bireysel miRNA'ların miktarı gibi tekli analiz birimine odaklanır. Gruplandırma prosedürleriyle daha derin bir sonuç elde edilebilir. DNA metilasyonu için bireysel CpG'lerin analizinden sonra, diğer yaygın prosedürler, gen gövdeleri, promotör bölgeleri, CpG adaları, transkripsiyon faktörü bağlanma bölgeleri vb. gibi ilgili genomik bölgelerde gruplandırılmış CpG'lerin analizini içerir. Bu verilerin ardından, genellikle bir tür ağ analizi yapılmalıdır. Basit yol analizi, özel bir özellik gösteren genlerin (örneğin; çalışılan gruplar arasındaki diferansiyel metilasyon), genel genomla karşılaştırıldığında belirli bir "yolda" fazla temsil edilip edilmediğini bulmaya çalışır. Diğer çalışmalar, bireysel analizde önemli olarak tanımlanan genler veya genomik bölgeler arasındaki ilişkileri bulmaya çalışır. Bir dizi ticari yazılım paketinin yanı sıra internette ücretsiz olarak bulunan diğer araçlar (DAVID, GESEA, WebGestalt, EnrichNet, NetworkAnalyst, vb.), yolların ve ağ analizlerinin gerçekleştirilmesine yardımcı olur (86).

Fonksiyonel Çalışmalar

Fonksiyonel deneyler, çalışmanın sonuçlarını geliştirir. Örneğin; bir gen promotörünün bir hastalığı olan hastalarda kontrollere göre daha fazla metillendiğini gösteren bir çalışmada, hasta grubunda gen ekspresyonunda azalma veya baskılayıcı histon kuyruk işaretleri gösterilirse bu bulgunun geçerliliği ve ilgisi artacaktır. Bazı durumlarda, hipotezi doğrulayan veriler aranarak mevcut veri tabanları araştırılabileceğinden, in silico doğrulama uygundur.

Ancak, çalışmanın amaçlarına bağlı olarak fonksiyonel veriler elde etmek için *in vitro* deneyler gerekebilir (87).

Sonuçların Önemi ve Genelleştirilmesi

Bireylerin bağımsız kohortlarında tekrar önemlidir. Bir yandan, ilk sonuçların teknik geçerliliğini destekler; diğer yandan, sonuçların keşif kohortunda temsil edilenlerin dışındaki popülasyonlara uygulanabileceğini doğrular. Yine de tekrar olmamasının, çalışılan kohorttaki sonucun sahte olduğu anlamına gelmediğini belirtmek önemlidir. Genetik arka plan ve çevresel koşullar dahil olmak üzere bir dizi faktörün epigenom üzerinde güçlü etkileri vardır. Bu nedenle bazı durumlarda epigenetik farklılıklar ancak bireyler belirli çevresel faktörlere maruz kaldıklarında veya belirli bir etnik kökene sahip olduklarında gözlemlenebilir.

Doğrudan ve Ters Nedensellik

Genom gebelikten itibaren stabildir. Bu nedenle, genetik çalışmalarda ters nedensellik sorunu önemli değildir. Bununla birlikte, epigenetik çalışmaların yorumlanması için kesinlikle bir endişe nedenidir. Bir grup hasta ile bir grup kontrol arasındaki farklı epigenetik işaretleri gösteren bir çalışmada, hastalığa epigenetik farklılıkların mı neden olduğu yoksa tersi mi sorusunu sormalıyız. İnsan çalışmalarında bu, çözülmesi çok zor bir soru olabilir. Ancak bazı durumlarda, hastalığın erken ve geç evrelerindeki epigenetik imzaların karşılaştırılması bazı yararlı ipuçları sağlayabilir (88,89).

Bilimsel ve Klinik Uygunluk

Epigenetik çalışmalar, hücre farklılaşmasını ve işlevini düzenleyen moleküler mekanizmalara daha iyi bir bakış açısı sağladığı için bilimsel açıdan çok önemli olan yeni verileri ortaya çıkarıyor. Çalışmalar hastalığın patogenezini aydınlatmak, hastalığın tanısını veya prognozunu belirlemek için yeni biyobelirteçleri kullanmak ve özellikle terapötik hedefler bulmak için yeni pencereler açarsa biyomedikal açıdan önemi daha da artar bu durumda daha etkili ve güvenli tedavilere yol açabilir (88,89).

Etik

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Neuropathic Pain in Females with Fibromyalgia Syndrome: The Role of Obesity

Fibromiyalji Sendromlu Kadın Hastalarda Nöropatik Ağrı Değerlendirmelerinde Obezitenin Rolü

Meltem Yener Mankır, Özge Ardıçoğlu*, Berat Meryem Alkan*, Fatma Fidan*

Ankara Gölbaşı Şehit Ahmet Özsoy Public Hospital, Clinic of Physical Medicine and Rehabilitation, Ankara, Turkey
*Ankara Bilkent City Hospital, Clinic of Physical Medicine and Rehabilitation, Ankara, Turkey

Abstract

Objective: This study aimed to assess the impact of obesity on neuropathic pain, fibromyalgia symptoms, and quality of life in female patients diagnosed with fibromyalgia syndrome.
Materials and Methods: This study enrolled 40 normal-weight and 40 obese female patients who were diagnosed with fibromyalgia syndrome. The patients enrolled in this study satisfied all of the American Collage of Rheumatology (ACR) 1990 and 2010 classification criteria. For fibromyalgia syndrome. The Leeds Assessment of Neuropathic Symptoms and Signs (LANSS) scale and douleur neuropathique 4 questions (DN4) scale was used to assess the extent of neuropathic pain experienced by the patients enrolled in this study. The assesment of patient health status was conducted using the Fibromyalgia Impact Questionnaire (FIQ) scale.
Results: Based on the results obtained from the LANSS scale, neuropathic pain was identified in 56.3% patients, while according to the DN4 scale, it was present in 78% of the patients. The analysis of data from the LANSS scale revealed that 42.5% of the patients in the normal weight group and 70% of the patients in the obese group had neuropathic pain. Furthermore, the prevalence of neuropathic pain was significantly higher among the patients in the obese group. The comparison of quality of life scores using the FIQ scale between the two groups did not reveal any statistically significant variation.
Conclusion: Neuropathic pain is high in female patients with fibromyalgia syndrome (FMS). Neuropathic pain was significantly higher in the obese group. Therefore, obese women with FMS would benefit from an increased focus on managing their neuropathic pain.
Keywords: LANSS, fibromyalgia, neuropathic pain, obesity, pain

Öz

Amaç: Bu çalışmada fibromiyalji sendromlu (FMS) kadın hastalarda nöropatik ağrının değerlendirilmesi ve obezitenin fibromiyalji semptomları, yaşam kalitesi ve nöropatik ağrı üzerine etkisinin değerlendirilmesi amaçlandı.
Gereç ve Yöntem: Bu çalışma fibromiyalji teşhisi konulan 40 normal kilolu ve 40 obez hastayı içermiştir. Çalışmaya dahil edilen hastalar Amerikan Romatoloji Koleji (*American College of Rheumatology*) 1990 ve 2010 sınıflama kriterlerinin tümünü karşılamışlardır. Hastaların nöropatik ağrı düzeyini değerlendirmek için Leeds Nöropatik Semptom ve Bulgu Değerlendirme (LANSS) ve Douleur Nöropatik 4 sorgulama (DN4) ölçekleri kullanıldı. Hastaların yaşam kalitesini değerlendirmek için Fibromiyalji Etki Anketi (FIQ) ölçeği kullanıldı.
Bulgular: Nöropatik ağrı LANSS skalasına göre %56,3, DN4 skalasına göre %78 hastada saptandı. Nöropatik ağrı oranı normal kilolu FMS'li grupta %42,5, obez FMS'li grupta %70 oranındaydı ve obez grupta istatistiksel olarak anlamlı olarak daha yüksekti. FIQ skorları iki grup arasında anlamlı farklı saptanmadı.
Sonuç: Nöropatik ağrı obez kadın FMS hastalarında normal kilolu kadın FMS hastalarına göre anlamlı daha yüksek çıkmıştır, bu nedenle FMS'li kadın hastalarda obez olanlarda nöropatik ağrı açısından daha dikkatli olunmalıdır.
Anahtar kelimeler: LANSS, fibromiyalji, nöropatik ağrı, obezite, ağrı

Address for Correspondence/Yazışma Adresi: Meltem Yener Mankır MD, Ankara Gölbaşı Şehit Ahmet Özsoy Public Hospital, Clinic of Physical Medicine and Rehabilitation, Ankara, Turkey
Phone: +90 312 484 03 22 **E-mail:** meltemyener06@gmail.com **ORCID ID:** orcid.org/0000-0001-9266-6077
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Introduction

Fibromyalgia syndrome (FMS) is a chronic condition causing wide-spread pain, fatigue, sleep disturbance and many somatic symptoms (1). Although its pathophysiology is not clear, in the light of scientific research that reveals neuropsychological and neurophysiological mechanisms in FMS, it has begun to be accepted that the disease should be classified as a central sensitization syndrome in recent years (2). Pain that arises following a lesion or dysfunction in the somatosensory system is known as neuropathic pain (3). Many of the mechanisms involved in neuropathic pain are shared with those implicated in the pathogenesis of FMS, as evidenced by studies on its etiology (4). Research conducted on individuals with FMS has shown alterations in the activation of sympathic system, central sensitization, the wind-up phenomenon, and rearrangement in the central nervous system (5). FMS is a suitable disorder to be considered in the neuropathic pain group because of the similarity of hyperalgesia, allodynia and paresthesia in the clinic as well as similar approaches in the pathogenesis (6).

Research has shown that FMS is more frequently observed in females and is often comorbid with obesity (7). The relationship between obesity and chronic pain is multifactorial (8). The two main mechanisms, mechanical loading and proinflammatory process, are held responsible for this (8). It has been shown that in obesity, insulin growth factor levels, adipokines such as resitin, adiponectin and leptin levels are altered (9) and neuropathic pain could linked to them and depression (7). In some studies, it has been shown that the increase in pain perception in obese patients is not only due to mechanical reasons, but that the central mechanisms can be activated and obesity can increase neuropathic pain (10). Together with studies showing that the symptoms associated with FMS are more severe in obese FMS patients (11), but there is a lack of literature on the examination of how obesity affects neuropathic pain in individuals with FMS. The purpose of the study was twofold: firstly, to assess the evaluation of neuropthic pain and secondly to explore how neuropathic pain and obesity affects their quality of life.

Materials and Methods

This study enrolled patients who were diagnosed with FMS and admitted to Ankara Yıldırım Beyazıt University Atatürk Training and Research Hospital Physical Medicine and Rehabilitation Clinic Outpatients Division between October 2015 and November 2016 and fullfilled the classification criteria of both American College of Rheumatology (ACR) 1990 (12) and 2012 (13). Those who have been receiving medical treatment for FMS for the last 1 year, those with neuropathic pain due to other causes (diabetes mellitus, nevre injury etc.), the study excluded cases of acute pain.

Approval for the study was granted by the Clinical Research Ethics Committee at Ankara Yıldırım Beyazıt University Faculty of Medicine (decision no: 232, date: 18.11.2015).

Patients aged 25-55 years, meeting the ACR 1990 classification criteria and 2010 new diagnostic criteria, female, normal weight or obese participated in our study.

Consent form was obtained from all patients participating in the study. Patient symptom duration, occupation, smoking, alcohol use, systemic diseases were asked. Patients were measured for height and weight. Body mass indexes (BMIs) calculated. Two groups were created among the patients based on the obesity classification established by the World Health Organization (WHO), with patients being classified as either normal weight or obese.

Patients were grouped into two groups as normal weight and obese according to the obesity classification of the WHO. As per the WHO, indivduals with a BMI falling within the range of 18.5 to 24.9 kg/m^2 were classified as having normal weight, while those with a BMI of 30 kg/m^2 or higher were classified obese (14).

Assesments

Physical examination was done to determine the number of tender point and tender point distributions. The Wide-Spread Pain index (WPI) and Symptom Severity score (SSS) were calculated for the 2012 ACR criteria. Patient's resting and moving visual analogue scale (VAS) (15) values were questioned. In the scale 0 mean no pain, 10 show the highest intensity. In order to evaluate the presence of neuropathic pain, the scale Leeds Asseessment of Neuropathic Symptoms and Signs (LANSS) was applied (16). Seven questions were asked about the neuropathic pain components. After which two examinations were carried out in terms of sensory evaluation. Allodynia, hyperalgesia, paresthesia, hyperesthesia, hypoesthesia was interrogated with parameters such as tingling, burning, feeling of warmth, feeling of pain with light touching, color change, electric shock. Allodynia was tested by touching with cotton. A pin prick test was performed with a needle to evaluate the change in sensory threshold between painful and non-painful areas. A score of 12 and above is reported to have a high likelihood of neuropathic pain. Douleur Neuropathique 4 questions (DN4) test was employed to evaluate the neuropathic pain (17). In this test, 7 questions and 3 examinations were questioned for a total of 10 items of neuropathic pain parameters. A score of 4 or grater is indicative of a strong likelihood of neuropathic pain.

The LANSS scale and DN4 questionnaires are validated scales with established reliability and avaliable in Turkish (18,19). FIQ was utilized to assess the quality of life (20,21). Depression, anxiety and daily life tasks such as shopping, cooking, walking, washing dishes were questioned. It is considered as mild impact between 0-38 points, moderate impact between 39-58 points and severe impact 59 point and over.

Statistical Analysis

The results of the patients were analyzed statistically. Descriptive variables were presented. Analytical methods thods (Kolmogorov-Smirnov/Shapiro-Wilks) were employed to evaluate whether the variables exhibited normal distribution. Numerical variables

with normal distribution were compared with t-test. The Mann-Whitney U test was used to compare numerical variables that followed normal distribution.

Categorical variables were assessed by chi-square Pearson and Fisher Exact test. Correlation tests between variables were performed by Pearson and Spearman correlation test. Quantitative variables was defined using measures of centralization and variation (mean ± standard deviation). Statistical significance was established $p<0.05$ for all cases. In this study, the strength of the relationship was evaluated based on the correlation coefficient (r-values), which were classified as very high (>0.90), high (0.7 to 0.9), moderate (0.5 to 0.7) or low (0.3 to 0.5).

Results

Within this study, a total of 80 female patients were recruited, with 40 being of normal weight and the other 40 classified as obese. The mean age of the patients with normal weight FMS was 42.43±8.3. Patients who had obese weight in this study had an average age of 45.23±6.6 years. The cases in this study are compared and their demographic characteristics are presented in Table 1. The demographic characteristics of fibromyalgia patients, both those with normal weight and those who were obese, did not exhibit any notable statistical variance.

The mean value of the LANSS scale of whole group was 13.2, the mean value of the DN4 scale was 5.6, and the mean value of the FIQ score was 63.8. Neuropathic pain was present in 56.2% of the patients according to the LANSS scale and 78.7% in the DN4 scale (Table 2).

The LANSS scores for neuropathic pain assesment differed significantly between the two groups. Scoring over 12 had been rated as having neuropathic pain. The mean of the LANSS score of the normal weight group was 11.78±5.85 and the mean of the LANSS score of the obese group was 14.7±5.82. 42.5% of normal weight group had neuropathic pain on LANSS scale whereas 70% of obese fibromyalgia patients had neuropathic pain. When we look at the results of the DN4 scale, 85% of the obese group had neuropathic pain while 72.5% of normal weight patients had neuropathic pain. However, both groups had comparable DN4 scores and the difference was not statistically significant. There was no significant difference between the two groups in FIQ scores. In total, 67.5% of the patients had severe FIQ scores. Comparison of the variables between the two groups are presented in Table 3.

Correlation analyses were presented on Table 4, $r>0.3$, $r<-0.3$ and $p<0.05$ were considered significant. The value of the correlation coefficient was interpreted as very high (>0.90), high (0.7 to 0.9), moderate (0.5 to 0.7) or low (0.3 to 0.5). Significant correlations between LANSS and DN4 scales were established. Significant correlation was found between tender point scores and the WPI scores that available in the 2012 classification criteria. In addition, VAS moving scores and tender point counts, VAS resting scores and FIQ score, SSS and the study found a correlation between FIQ scores.

Discussion

The study assessed neuropathic pain in female patients with FMS using LANSS and DN4 scales, additionally, the study aimed to examine the impact of obesity on neuropathic pain, fibromyalgia symptoms and quality of life in these patients. In the assessment of neuropathic pain among patients with FMSs, scales such as LANSS, Pain Detect (22) and Melzack (23) and DN4 are commonly utilized. Within the context of this study, the findings revealed that 56.2% of the patients had neuropathic pain according to the LANSS scale, whereas the DN4 scale diagnosed neuropathic pain in 78.7% of the patients. In a

Table 1. Comparison of demographic characteristics of normal weight and obese patients with fibromyalgia syndrome

	Normal weight group	Obese group	p-value
n	40	40	
Age (mean ± SD/median) (min-max)	42.43±8.3/42.20 (25-55)	45.23±6.6/46.50 (30-55)	0.101
Occupation, %			**0.068**
Not working	62.5	85	
Non-exhausting work	22.5	7.5	
Hard work	15	7.5	
Systemic disease, %			**0.444**
No	80	67.5	
1 chronic illness	15	25	
>1 chronic illness	5	7.5	
Smoking/not smoking, %	15/85	12.5/37.5	0.745
Alcohol yes/no, %	2.5/97.5	0/100	0.237

SD: Standard deviation, min-max: Minimum-maximum
*p<0.05

Table 2. The fibromyalgia and neuropathic pain scale scores and percentages of scales of the whole study group		
All patients n=80		
Wide-spread pain index (mean ± SD)		12.8±3.8
Symptom severity scale (mean ± SD)		8.6±2.3
LANSS (mean ± SD)		13.2±5.9
LANSS	Neuropathic pain, n (%)	45 (56.3)
	No neuropathic pain, n (%)	35 (43.8)
DN4 (mean ± SD) (min-max)		5.6±2.6
DN4	Neuropathic pain, n (%)	63 (78.8)
	No neuropathic pain, n (%)	17 (21.3)
FIQ (mean ± SD)		63.8±12.4
FIQ	Mild, n (%)	2 (2.5)
	Moderate, n (%)	24 (30)
	Severe, n (%)	54 (67.5)

SD: Standard deviation, min-max: Minimum-maximum, LANSS: Leeds Asseessment of Neuropathic Symptoms and Signs, DN4: Douleur Neuropathique 4 questions, FIQ: Fibromyalgia Impact Questionnaire

study by Martínez-Lavin et al. (24), 20 patients with FMS and rheumatoid arthritis (RA) were compared with the LANSS scale. The percentage of sensory symptoms, including dysesthesia, thermal, paroxysmal, and autonomic symptoms, was found to be greater among patients with FMS when compared to those with RA (24). It was reported that tender points may be allodynia areas due to the presence of too many sympathetic ganglia in the neck region. We found that FMS patients had an average of 13.24 scores in the LANSS scales and 5.6 scores in the DN4 scales. The study by Giske et al. (25) included 98 patients with localized and wide-spread muscle pain, and the LANSS score was substantially elevated (9.5) in the sample of 39 patients who met the criteria for FMS compared to other painful groups. Additionally, pain intensity, duration, and depression were found to be correlated with LANSS scores in this study (25). However, in contrast to this previous study, the current study found no relevant dependence between LANSS and DN4 scores and pain severity or quality of life scores.

In a study comparing 150 patients with FMS and 42 patients with chronic wide-spread pain in Turkey, the mean of the LANSS score

Table 3. Comparison of symptom, findings and scale outcomes and categorization of evaluations of patients with normal weight fibromyalgia syndrome and patients with obese fibromyalgia syndrome			
	Normal weight group n=40 Mean ± SD/median	**Obese group n=40 Mean ± SD/median**	**p-value**
	(Min-max)	**(Min-max)**	
Number of tender points	13.83±2.74/14.00 (11-18)	13.18±2.51/12.00 (11-18)	0.249
Wide-spread pain index	12.55±3.88/12.00 (5-19)	13.05±3.86/14.00 (6-22)	0.566
Symptom severity scale	8.9±2.56/9.00 (3-12)	8.30±2.21/8.00 (3-12)	0.178
VAS resting	6.53±1.97/7.00 (1-10)	6.53±1.55/6.00 (3-9)	0.965
VAS moving	6.23±1.91/6.00 (2-9)	6.38±2.19/7.00 (1-10)	0.539
LANSS score	11.78±5.85/11.00 (0-24)	14.7±5.82/16.00 (0-24)	0.032*
FIQ score	64.83±15.77/64.50 (21-96)	62.84±8.05/63.50 (48-78)	0.479
DN4 score	5.2±2.92/5.50 (0-10)	6.13±2.31/6.00 (1-10)	0.121
Number of lower extremity tender points	3.78±1.92/4.00 (0-6)	4.35±1.67/4.00 (0-6)	0.178
Lower extremity wide-spread pain index	4.18±1.59/4.00 (0-6)	4.63±1.69/5.00 (0-6)	0.178
FIQ classification, n (%)			**0.338**
Mild	2 (5)	0 (0)	
Moderate	11 (27.5)	13 (32.5)	
Severe	27 (67.5)	27 (67.5)	
DN4 classification, n (%)			**0.172**
Neuropathic pain	29 (72.5)	34 (85)	
No neuropathic pain	11 (27.5)	6 (15)	
LANSS classification, n (%)			**0.013***
Neuropathic pain	17 (42.5)	28 (70)	
No neuropathic pain	23 (57.5)	12 (30)	
Back pain, n (%)			**0.775**
Yes	32 (80)	33 (82.5)	
No	8 (20)	7 (17.5)	

SD: Standard deviation, min-max: Minimum-maximum, LANSS: Leeds Asseessment of Neuropathic Symptoms and Signs, DN4: Douleur Neuropathique 4 questions, FIQ: Fibromyalgia Impact Questionnaire, VAS: Visual analogue scale
*p<0.05

Table 4. Correlation of variables with each other

	r/p-value	LANSS	DN4	FIQ	VAS resting	VAS moving	WPI
LANSS	r	1	0.661***	0.282	0.098	0.216	0.268
	p	0.00	0.00**	0.011	0.388	0.054	0.016
DN4	r	0.661***	1	0.189	0.073	0.054	0.255
	p	0.00**	0.00	0.093	0.52	0.633	0.02
FIQ	r	0.282	0.189	1	0.302*	0.198	0.271
	p	0.011	0.093	0	0.006**	0.078	0.015
VAS resting	r	0.098	0.073	0.302*	1	0.144	0.131
	p	0.388	0.52	0.006**	0	0.204	0.247
VAS moving	r	0.216	0.054	0.198	0.144	1	0.163
	p	0.054	0.633	0.078	0.204	0	0.148
Symptom duration	r	0.132	0.154	0.2	0.082	0.205	0.407*
	p	0.242	0.172	0.075	0.471	0.068	0.00**
Number of tender point	r	0.228	0.231	0.297	0.089	0.405*	0.445*
	p	0.042	0.039	0.007	0.435	0.00**	0.00**
Symptom severity scale	r	0.134	0.192	0.308*	0.073	0.04	0.248
	p	0.236	0.087	0.005**	0.52	0.722	0.027

LANSS: Leeds Asseessment of Neuropathic Symptoms and Signs, DN4: Douleur Neuropathique 4 questions, FIQ: Fibromyalgia Impact Questionnaire, VAS: Visual analogue scale, WPI: Wide-Spread Pain index
*r 0.3 to 0.5, **p<0.05, ***r 0.5 to 0.7

in the FMS group was 6.34±4.3 and substantially elevated than the chronic wide-spread pain group (2.13±2.6) (26). In addition, the increase in the number of tender points correlated with the severity of pain and the rate of neuropathic pain (26). We found that the number of tender points and neuropathic pain is not related.

Gauffin et al. (27) conducted a study on 158 patients with FMS, which involved dividing them into two groups based on the presence or absence of neuropathic pain using electrophysiological tests. The results showed that the Pain Detect scores were sunstantially higher in the group with neuropathic pain in comparison to the other group (27). Neuropathic pain was detected in 34% of 158 patients. In addition, Pain Detect and FIQ scores were found to be correlated (27).

The study also evaluated the potential impact of obesity on neuropathic pain in female individuals diagnosed with FMS. As stated by the LANSS the mean score of obese FMS patients was 14.7 and 70% had neuropathic pain. The mean LANSS score of FMS patients with normal weight was 11.7 and 42.5% had neuropathic pain. In our study, in obese FMS patients, neuropathic pain was statistically significantly higher than normal weight FMS patients. When it was compared the neuropathic pain level in obese and normal weight FMS patients with the DN4 scale, the results of the study did not reveal any notable variations between the two groups. However, there was no remarkably disparity in the severity of rest and moving pain assessed by VAS scale among patients with obese FMS and patients with normal weight FMS.

Quality of life scores in FMS patients was very low in this study. Similarly, in studies conducted with FMS, the quality of life scores were reported to be lower than normal population (28,29) and lower than some other musculoskeletal system diseases (30,31). According to the FIQ scale, the quality of life of 67.5% of our patients were affected severely. In the literature, although there were link between FIQ scores and number of tender points, pain severity and obesity (32), there was no strong connection between FIQ and other clinical parameters in our study. Several studies have shown that obesity in FMS patients affects quality of life negatively (33,34). Our study did not uncover any significant distinctions in the well-being scores of patients with FMS who were obese compared to those with a normal weight. In our study, we did not observe any significant association between BMI and clinical parameters such as number of tender points, WPI, SSS, number of lower extremity tender points and lower extremity WPI. In studies in the literature, there is a significant relationship between BMI and the number of sensitive points (35,36); in the current investigation there was no link between BMI and the number of tender points.

In summary of the above; more than half of the FMS patients had neuropathic pain according to the LANSS scale in this study. In obese women patients with FMS, neuropathic pain was significantly more frequent than normal weight women patients with FMS. Also according to the DN4 scale, neuropathic pain was seen at high rates in patients with FMS. However, no significant difference was found between obese FMS patients and normal weight FMS patients in the DN4 questionnaire.

Conclusion

Neuropathic pain assessments in women with FMS were thought to be very important. Different pain scales can affect

treatment choice, especially in obese patients. In patients with FMS there is a need for further study of the relationship among obesity and neuropathic pain.

*"Comparison of Neuropathic Pain Assesment in Obese and Normal Weight Female Patients with Fibromyalgia Syndrome" The thesis named belongs to Meltem Yener Mankır.

Ethics

Ethics Committee Approval: Approval for the study was granted by the Clinical Research Ethics Committee at Ankara Yıldırım Beyazıt University Faculty of Medicine (decision no: 232, date: 18.11.2015).

Informed Consent: Consent form was obtained from all patients participating in the study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: M.Y.M., Ö.A., B.M.A., F.F., Design: M.Y.M., Ö.A., B.M.A., F.F., Data Collection or Processing: M.Y.M., B.M.A., Analysis or Interpretation: M.Y.M., Ö.A., B.M.A., F.F., Literature Search: M.Y.M., Ö.A., B.M.A., F.F., Writing: M.Y.M., Ö.A., B.M.A.

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Change of Vitamin D Levels According to Age, Gender and Seasons in Şırnak Province

Şırnak İlinde D Vitamini Seviyesinin Yaş, Cinsiyet ve Mevsimlere Göre Değişimi

Veysel Tahiroğlu, Naci Ömer Alayunt*

Şırnak University Faculty of Health Sciences, Department of Nursing, Şırnak, Turkey
*Siirt University Faculty of Medicine, Department of Medical Biochemistry, Siirt, Turkey

Abstract

Objective: This study determines the 25-hydroxy vitamin D [25(OH)D] profile according to season, age, and gender by examining the vitamin D levels of the patients who applied to Cizre State Hospital, which is the warmest district of Turkey, in 2021.
Materials and Methods: 13,387 patients admitted to Cizre State Hospital were included in the study, and their [25(OH)D] levels were analyzed retrospectively. In the study, [25(OH)D] levels were evaluated according to the age, gender and seasonal differences of the patients. [25(OH)D] levels in serum are <12 ng/mL, severe deficiency, 12-20 ng/mL mild-moderate deficiency, 21-30 ng/mL insufficient, >30 ng/mL conditions were accepted as qualifications.
Results: The findings of 9,800 women and 3,587 men were evaluated in the study. The mean serum level of [25 (OH)D] was 12.31±0.08 ng/mL in women and 17.58±0.15 ng/mL in men. Amongst the age groups, vitamin D levels in both male and female patients were statistically significant (p<0.01). Statistically significant changes were identified across seasons, with [25(OH)D] levels in both women and men being lowest in winter and greatest in summer (p<0.01).The mean [25(OH)D] level was 18.51±0.17 ng/mL in patients aged 0-15 years (n=3,219), 11.86±0.12 ng/mL in patients aged 16-30 years (n=4,093), between 31-45 years old 12.12±0.14 ng/mL in patients (n=3,008), 12.39±0.18 ng/mL in patients aged 46-60 years (n=1,817), and 13.40±0.28ng/mL in patients aged 61-75 years (n=962).
Conclusion: In this study, very serious vitamin D deficiency was detected in patients admitted to Cizre State Hospital.
It is thought that low vitamin D levels may be related to the absence of vitamin D synthesis because of insufficient sunlight in winter, the closed dressing habits of the region, or foods deficient in vitamin D. Because of this study, the need for supportive treatment gained more importance.
Keywords: Osteoporosis, gender, vitamin D, seasons, age

Öz

Amaç: Bu çalışma, 2021 yılında Türkiye'nin en sıcak ilçesi olan Cizre Devlet Hastanesi'ne başvuran hastaların D vitamini düzeylerini inceleyerek mevsim, yaş ve cinsiyete göre 25-hidroksi vitamin D [25(OH)D] profilini belirlemeyi amaçlamaktadır.
Gereç ve Yöntem: Cizre Devlet Hastanesi'ne başvuran 13.387 hasta çalışmaya dahil edilmiştir ve [25(OH)D] düzeyleri retrospektif olarak incelenmiştir. Çalışmada [25(OH)D] düzeyleri, hastaların yaş, cinsiyet ve mevsimlerdeki farklılık durumlarına göre değerlendirilmiştir. [25(OH)D] düzeyinin serumdaki düzeyleri <12 ng/mL olduğu durumlar ciddi eksiklik, 12-20 ng/mL olduğu durumlar hafif-orta düzeyde eksiklik, 21-30 ng/mL olduğu durumlar yetersizlik, >30 ng/mL olduğu durumlar ise yeterlilik olarak kabul edilmiştir.
Bulgular: Çalışmada 9.800 kadın ve 3.587 erkeğe ait bulgular değerlendirilmiştir. Kadınlarda [25(OH)D] serum düzeyi ortalaması 12,31±0,08 ng/mL, erkeklerde 17,58±0,15 ng/mL olarak tespit edilmiştir. Yaş grupları arasında hem erkek hem de kadın hastalarda D vitamini düzeyleri istatistiksel olarak anlamlıydı (p<0,01). [25 (OH)D] düzeylerinin hem kadınlarda hem de erkeklerde kışın en düşük ve yazın en yüksek olduğu mevsimler boyunca istatistiksel olarak anlamlı değişiklikler belirlendi (p<0,01). 0-15 yaş arası hastalarda (n=3.219) ortalama [25(OH)D] düzeyi 18,51±0,17 ng/mL, 16-30 yaş arası hastalarda (n=4.093) 11,86±0,12 ng/mL, 31-45 yaş arası hastalarda (n=3.008) 12,12±0,14 ng/mL, 46-60 yaş arası hastalarda (n=1.817), 12,39±0,18 ng/mL ve 61-75 yaş arası hastalarda (n=962) 13,40±0,28 ng/mL bulunmuştur.
Sonuç: Bu çalışmada Cizre Devlet Hastanesi'ne başvuran hastalarda çok ciddi D vitamini yetersizliği tespit edilmiştir. Düşük D vitamini seviyelerinin, kışın güneş ışığının yetersizliği sonucunda hemen hemen hiç D vitamini sentezinin olmaması, bölgenin kapalı giyinme alışkanlıkları veya D vitamininden yetersiz yiyecekler ile ilişkili olabileceği düşünülmektedir. Bu çalışma sonucunda, destek tedaviye olan ihtiyaç daha fazla önem kazanmaktadır.
Anahtar kelimeler: Osteoporoz, cinsiyet, D vitamini, mevsimler, yaş

Address for Correspondence/Yazışma Adresi: Lect. Veysel Tahiroğlu MD, Şırnak University Faculty of Health Sciences, Department of Nursing, Şırnak, Turkey
Phone: +90 486 216 82 40-1182 **E-mail:** veysel0793@hotmail.com **ORCID ID:** orcid.org/0000-0003-3516-5561
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Introduction

Although some of the vitamin D is obtained from the diet, its main source is ultraviolet exposure. Vitamin D is also defined as a steroid-formed vitamin that occurs in the skin with sunlight (1). Vitamin D; It is available in form of vitamin D2 and vitamin D3. Vitamin D2 is dietary ergocalciferol. Vitamin D3 is cholecalciferol, which is synthesized in the skin of the human body. First these two inactive forms it is hydroxylated by 25 hydroxylases and 25 dihydroxy vitamin D (25-OH D) in the liver and then in the kidneys. Its active form, 1.25 dihydroxy vitamin D, is hydroxylated by 1 α-hydroxylase (2). Apart from calcium homeostasis, vitamin D has versatile functions for bone and muscle (3). Rickets or osteomalacia, characterized by impaired bone mineralization, occurs in vitamin D deficiency. Apart from bone, vitamin D has potential benefits on diabetes mellitus, cardiovascular diseases, cancer, multiple sclerosis, allergies, asthma, infections, depression, psychiatric disorders and pain (4). Vitamin D is very important for our immune system, especially in winter, it is not easy to replenish vitamin D stores. Vitamin D reduces vitamin D stores for various reasons, such as the reduce in vitamin D synthesis by tropospheric ozone in the skin after malnutrition and environmental pollution (5). Today, [25(OH)D] levels below 50 nmol/L (<20 ng/mL) are defined as deficiency, and 50-75 nmol/L (20-30 ng/mL) as deficiency (subclinical deficiency) (6). The preference of [25(OH)D] in serum is explained the long half-life, an indicator of the storage of vitamin D in the body, which is taken in the diet and synthesized in the skin (7). Vitamin D insufficiency is a problem that significantly effects health costs, morbidity and mortality, especially among the elderly and closed communities. The goal of this study was to assess the district's [25(OH)D] profile by gender, age, and season by looking at the vitamin D levels of patients admitted to Cizre State Hospital.

Materials And Methods

The Şırnak University Scientific Research and Publication Ethics Committee authorized the study protocol (decision no: 2022/71, dated no: 20/04/2022). The study looked back at desired [25(OH)D] levels in patients admitted to Cizre State Hospital between January 2021 and January 2022. The data obtained from the electronic health records of the patients in the hospital database were analyzed retrospectively. As a result, patients were unable to sign an informed consent form. This study included 13,387 participants who applied to the hospital. The patients' [25(OH)D] levels were calculated based on their gender, age, and season. Patient names were kept anonymous during data analysis, and ethical guidelines were observed. In age group comparisons, patients above the age of 75 were omitted. The electrochemiluminescence technique was used using the Roche cobas device and Immunoassay equipment considered serum [25(OH)D] levels. Severe adequate was described as serum [25(OH)D] level of 12 ng/mL, mild-moderate adequate as 12-20 ng/mL, deficiency as 21-30 ng/mL, and sufficiency >30 ng/mL.

Statistical Analysis

To detect the link among vitamin D and gender, age and seasons, the compatibility of the variables with the normal distribution was examined by the skewness-kurtosis test using the Statistical Package for the Social Sciences 21.0 package program. Distanced samples t-test was applied to identify whether there was a important variation between vitamin D averages according to gender. One-way ANOVA test was used to determine whether there was a significant different between the mean vitamin D levels of age, month and season. Tukey test was applied in multiple comparison (post-hoc) tests to find out the significance of the difference within the groups. Mean and standard error values are given in descriptive statistics. A value of $p<0.05$ was considered important.

Results

The age and gender status of the patients who came to Cizre state hospital were divided into groups according to months and seasons, and descriptive statistics, mean and standard deviation values were given in the tables. Demographic information and mean vitamin D levels of the patients are given in Table 1. Considering the gender of the patients; It is seen that this study consisted of 9,800 women and 3,587 men. When the mean vitamin D level of the patients was evaluated as a total, it was found that the mean was 12.31±0.08 ng/mL in women and 17.58±0.15 ng/mL in men. D vitamin levels in females were found to be significantly lower than those in men $p<0.01$ significance level (Table 1).

Vitamin D levels based on the patients' ages are given in Table 2. In patients aged 0-15 years, the mean vitamin D level (n=3,219)

Table 1. Demographic information of patients and average 25-OH Vitamin D levels

Gender	n	Average (ng/mL)	p
Woman	9,800	12.31±0.08	p<0.01
Man	3,587	17.58±0.15	

Data are given as mean and standard error

Table 2. 25-OH D change according to the age of the patients

Age group	n	Average (ng/mL)	p
Group 1	3,219	18.51±0.17	Group 1-2, p<0.01 Group 1-3, p<0.01 Group 1-4, p<0.01 Group 1-5, p<0.01 Group 2-3, NS Group 2-4, NS Group 2-5, p<0.01 Group 3-4, NS Group 3-5, s<0.01 Group 4-5, s<0.05
Group 2	4,093	11.86±0.12	
Group 3	3,008	12.12±0.14	
Group 4	1,817	12.39±0.18	
Group 5	962	13.40±0.28	

Data are given as mean and standard error,
NS: Not significant, Group 1: 0-15 years, Group 2: 16-30 years, Group 3: 31-45 years, Group 4: 46-60 years, Group 5: 61-75 years

was found to be 18.51±0.17 ng/mL. Mean vitamin D level in patients aged 16-30 years (n=4,093) 11.86±0.12. The mean vitamin D level in patients aged 31-45 years (n=3,008) was 12.12±0.14 ng/mL, In patients aged 46-60 years, the mean vitamin D level (n=1,817) was 12.39±0.18 ng/mL, The mean vitamin D level in patients aged 61-75 years was 13.40±0.28 (n=0,962). As a variable of age, consequently the regression analysis, it can be said that the p value is statistically significant ($p<0.05$) and the vitamin D value changes at the highest level, especially in the 0-15 age group. (Table 2). Tukey test was applied between 4 groups for seasonal differences. As a result of the test, statistical differences were observed between the seasons (Table 3). One-Way ANOVA test was used to test whether there is a relationship between vitamin D and month. Since the variances assume homogeneity, the Tukey test was applied to determine in which months the difference was experienced and the average values of the months were given. All groups except Eylul group had a significant difference within themselves ($p<0.01$) (Table 4).

Discussion

Vitamin D absence is a global public health problem. This problem effects 92% of the world. It is the most common among the diseases seen in Northern Europe. In Turkey, on the other hand, this rate is between 57-64% (8,9). Reports from many different countries show that; Vitamin D levels show insufficiency and deficiency depending on defined threshold values (10). Asians do not have adequate vitamin D levels despite living in an area with sufficient sun (11,12). Apart from external factors such as exposure to direct sunlight, location of the place of residence, air pollution, seasonal changes, and clothing style, vitamin D taken with food also directly affects vitamin D level (13-17). The vitamin D levels of patients hospitalized to Cizre State Hospital were examined retrospectively in this study. Vitamin D levels in women were found to be statistically significantly lower than in men (Table 1). On the other hand, Öğüş et al (18) in a study conducted in Ankara, they reported the mean vitamin D level of 3,242 patients as 22.80±13.27 ng/mL. In the same study, 50% of women and 38% of men had vitamin D levels below 20 ng/mL. Similarly, in our results, we found that women's vitamin D levels were significantly lower than men. Bolland et al (19) in 1,606 healthy postmenopausal women and 378 middle-aged and elderly men. He studied vitamin D levels. They reported that 73% of women and 39% of men were vitamin D deficient. Hekimsoy et al. (5) investigated the vitamin D levels of 391 patients over the age of 20 living in rural and rural areas. They found the mean of vitamin D levels to be 16.9±13.09 ng/mL. They found that the deficiency was 66.4% and 78.7% higher in women than in men. In a recent study that included 21,555 women and 9,596 men in the Siirt region, women found lower levels of vitamin D than men (20). This study, which was conducted in Siirt, was found to be remarkable both in terms of being a region close to Cizre and the similarity of social habits, customs and traditions. Studies have mentioned the presence of vitamin D levels similar to our results, and the data obtained show that women have lower vitamin D levels than men. Vitamin D levels were also observed to be lower in women than in males in our research ($p<0.01$). The fact that we think it is related to high fertility, wearing traditional and covered clothes in Şırnak province, and the fact that women have a lower vitamin D profile than men will support the literature. This study is important both in terms of clarifying the profile of the region and the measures that can be taken.

Rabenberg et al. (21) found that serum 25-OH D levels of the adult population between the ages of 18-79 were below 50 nmol/L (<20 ng/mL) especially in winter and spring. Brustad and colleagues measured vitamin D levels in Norwegian people living in the northern part of the country. Those who spent the previous summer in the south of the country found higher levels of vitamin D in winter measurements than those in the north of the country (22). The highest vitamin D levels are reached especially in the summer months, and very little vitamin D is synthesized in the November-March period as the parallels increase in northern spherical countries (23,24). In addition, vitamin D levels were found to be below the normal value (22.5 nmol/L) in 80% of those who wore closed clothes in Australia (25). In a study conducted in Adana province, [25(OH)D] levels in

Table 3. Seasonal variation of patients' mean 25-OH Vitamin D levels

Season	n	Average (ng/mL)	p
Group 1	2,064	13.07±0.18	Group 1-2, p<0.01 Group 1-3, p<0.01 Group 1-4, p<0.01 Group 2-3, p<0.01 Group 2-4, p<0.01 Group 3-4, p<0.01
Group 2	3,835	11.32±0.12	
Group 3	4,173	14.77±0.14	
Group 4	3,315	15.59±0.15	

Data are given as mean and standard error,
NS: Not significant, Group 1: Autumn, Group 2: Winter, Group 3: Spring, Group 4: Summer, NS: Not Significant

Table 4. Average 25-OH Vitamin D levels by month

Months	n	Average (ng/mL)
January	1,190	12.33±0.23
February	1,565	11.49±0.19
March	1,810	13.98±0.23
April	1,219	15.30±0.25
May	1,144	15.46±0.27
June	1,675	16.36±0.22
July	843	15.43±0.30
August	797	14.12±0.29
September	65	13.17±1.11
October	947	13.81±0.28
November	1,052	12.40±0.23
December	1,080	9.96±0.20

Data are given as mean and standard error

the extremities were dimensions as 53.9 ng/mL and 33.1 ng/mL in women with uncovered heads and hands and face covered, respectively, in August-September (26). A study conducted in Canada displayed that 25-OH D levels were especially in black people and older people (<30 ng/mL). Particularly in the winter and spring seasons, approximately 25-OH D levels have been shown to be low with a seasonal variation between 60% and 120% (<20 ng/mL) (27). In a study conducted in young adults in India, it was reported that vitamin D was found to be 38.7 nmol/L in women with open arms and forearms, and 47.5 nmol/L in women with open body parts living in villages and living in rural areas (28). Telo et al. (29) In a study conducted by the Turkish side in Elazığ, they found that 25-OH vitamin D levels were highest in summer and autumn, and lowest in winter and spring. Given the information from our investigation, it is clear that [25(OH)D] levels are low. It has been determined that [25(OH)D], which is low in the fall and winter and high in the summer and spring when exposed to the sun's potent rays, is below the necessary levels in all four seasons. This low vitamin D level may be brought on by inadequate vitamin D consumption and nearly nonexistent winter vitamin D production. Considering the social diet, it should not be forgotten that the people of Cizre are actually engaged in small cattle breeding and are fed rich in animal fats. Considering the high vitamin D content of animal fats, a new hypothesis emerges about why vitamin D is low in Cizre. In addition, when the distribution table according to months is examined, it is quite interesting (Table 4). Namely; while an increase in vitamin D was observed in April, May and June, vitamin D levels showed a decreasing trend in July, August and September, respectively (Figure 1). What we knew was the assumption that vitamin D stores would increase rather than decrease in these months when we are mostly faulted by the sun's rays in summer. In the studies of Telo et al. (29) and Alayunt et al. (20), vitamin D levels exceeded 20 ng/mL in summer months, while our graphs remained at 16 ng/mL levels. While interpreting the data obtained in our study, it is clear that low vitamin D levels cannot be explained only by the living conditions of a closed-knit community. Large-scale studies are needed to explain this profile with other hypotheses. I wonder if it's too much fertility that keeps vitamin D or whether a social

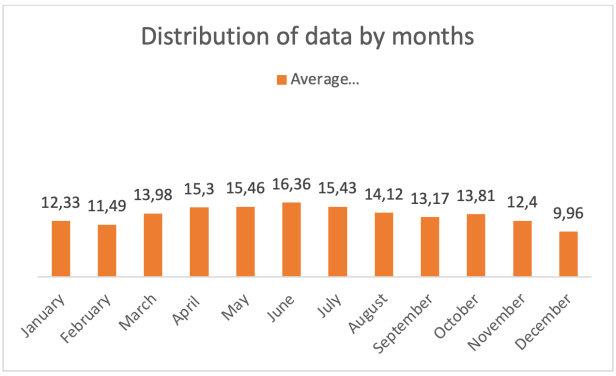

Figure 1. 25-OH vitamin D levels by month

bone disease related to vitamin D or a chain of diseases related to regional metabolic predisposition have an effect on vitamin D, we will try to reveal this in our future studies. In the first place and urgently, it will be to inform the society and recommend vitamin D supplements with plenty of sun and nutrients.

Study Limitations

The most important limitation of this study is that more comprehensive studies are needed to establish a relationship between vitamin D levels and metabolic bone disorders. Furthermore, the relationship between the region's fertility rates and bone mineralization has yet to be discovered. There is a need for new studies that will take into account the average age of menopause, including the osteoporosis rates of women, and there are limitations in this regard.

Conclusion

Because the Cizre district of Şırnak Province is Turkey's hottest and most sun-drenched location, vitamin D deficiency is unlikely to be detected. However, this study revealed that people living in Cizre have serious levels of vitamin D deficiency in all seasons, especially in winter, and in both sexes, especially in women. It is not surprising that vitamin D insufficiency is detected in this district during the summer, considering that women wear clothing that covers all regions save the face and hands, and that males wear clothing that is somewhat covered compared to western provinces. In late years, the importance of vitamin D has been growing day by day. This is due to osteoporotic fracture studies, vitamin D and calcium meta-analyses and their relationship. The data obtained in this study will require new and more comprehensive studies on the relationship between the low vitamin D profile of the region and metabolic bone diseases such as osteomalacia and osteoporosis, as well as cancer, diabetes, multiple sclerosis and cardiovascular diseases.

Ethics

Ethics Committee Approval: The present study is retrospective and its permission was obtained from Şırnak University Ethics Committee on (decision no: 2022/71, date: 20/04/2022).
Informed Consent: Retrospective study.
Peer-review: Externally peer-reviewed.

Authorship Contributions

Design: Ö.N.A., Data Collection or Processing: V.T., Ö.N.A., Analysis or Interpretation: V.T., Literature Search: V.T., Ö.N.A., Writing: V.T., Ö.N.A.
Conflict of Interest: No conflict of interest was declared by the authors.
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Association of PPAR-α Gene Polymorphism (rs4253778) with Osteoporosis in Postmenopausal Turkish Women

Postmenopozal Türk Kadınlarında PPAR-α Gen Polimorfizminin (rs4253778) Osteoporoz ile İlişkisi

Şengül Tural, Amir Saghafian, Gamze Alaylı*, Ercan Tural, Esra Tekcan*****

Ondokuz Mayıs University Faculty of Medicine, Department of Medical Biology, Samsun, Turkey
*Ondokuz Mayıs University Faculty of Medicine, Department of Physical Medicine and Rehabilitation, Samsun, Turkey
**Ondokuz Mayıs University Faculty of Health Sciences, Samsun, Turkey
***Ondokuz Mayıs University Faculty of Medicine, Central Laboratory, Samsun, Turkey

Abstract

Objective: Osteoporosis is a multifactorial disease characterized by decreased bone mineral density and deterioration of the microstructure of bone tissue. The existence of various candidate genes affecting bone mass has been reported. In this study, we examined the relationship between *PPAR-α* gene intron 7 G>C (rs4253778) polymorphism and osteoporosis.
Materials and Methods: The stud included 250 postmenopausal women (150 cases with osteoporosis and 100 postmenopausal healthy controls) mostly from the Central Black Sea Region. Peripheral blood samples were taken from the patient and control groups, and deoxyribonucleic acid isolation was performed using the kit methodology. Genotyping was performed by polymerase chain reaction - restriction fragment length polymorphism method. Statistical Package for the Social Sciences 20 program and chi-square analyzes were performed for statistical analysis.
Results: Because of the study, while there was no statistical significant association between genotype distribution and osteoporosis, the C allele frequency was higher in the patient group and it was statistically significant (p=0.017).
Conclusion: To our knowledge, this is the first study conducted in the Central Black Sea Region, Turkey. By expanding the study population and combining the results, more descriptive results regarding the susceptibility of polymorphic regions to osteoporosis can be obtained.
Keywords: Osteoporosis, gene polymorphism, postmenopausal woman

Öz

Amaç: Osteoporoz, kemik mineral yoğunluğunun azalması ve kemik dokusunun mikro yapısının bozulması ile karakterize multifaktöriyel bir hastalıktır. Kemik kütlesini etkileyen çeşitli aday genlerin varlığı bildirilmiştir. Bu çalışmada *PPAR-α* geni intron 7 G>C (rs4253778) polimorfizmi ile osteoporoz arasındaki ilişkiyi incelemeyi amaçladık.
Gereç ve Yöntem: Çalışmaya çoğunlukla Orta Karadeniz Bölgesi'nden 250 postmenopozal kadın (osteoporozlu 150 olgu ve 100 postmenopozal sağlıklı kontrol) dahil edildi. Hasta ve kontrol gruplarından periferik kan örnekleri alındı ve kit metodolojisi kullanılarak DNA izolasyonu yapıldı. Genotiplendirme polimeraz zincir reaksiyonu-kısıtlama parçası uzunluk polimorfizmi yöntemi ile gerçekleştirildi. İstatistiksel analiz için Statistical Package for the Social Sciences 20 programı ve ki-kare analizi yapıldı.
Bulgular: Çalışma sonucunda genotip dağılımı ile osteoporoz arasında istatistiksel olarak anlamlı bir ilişki bulunmazken, C allel sıklığı hasta grubunda daha yüksekti ve istatistiksel olarak anlamlıydı (p=0,017).
Sonuç: Bildiğimiz kadarıyla bu, Türkiye'de Orta Karadeniz Bölgesi'nde yapılan ilk çalışmadır. Çalışma popülasyonunun genişletilmesi ve sonuçların birleştirilmesiyle polimorfik bölgelerin osteoporoza duyarlılığı ile ilgili daha açıklayıcı sonuçlar elde edilebilir.
Anahtar kelimeler: Osteoporoz, gen polimorfizmi, postmenopozal kadın

Address for Correspondence/Yazışma Adresi: Şengül Tural Assoc. Prof., Ondokuz Mayıs University Faculty of Medicine, Department of Medical Biology, Samsun, Turkey
Phone: +90 362 312 19 19-2846 **E-mail:** stural@omu.edu.tr **ORCID ID:** orcid.org/0000-0002-8946-8165
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Introduction

Osteoporosis (OP) (Online Mendelian Inheritance in Man: OMIM 166710) is a skeletal disorder in which the risk of fracture increases due to the decrease in bone strength, which reflects the composition of bone quality and quantity (1,2). The most important health problem of OP is fracture formation. With the prolongation of human life and the aging of the world population, OP and OP-related fractures have become an important health problem due to their negative effects on morbidity and quality of life (3). OP is included in the group of multifactorial diseases in which genetic and environmental factors play important roles together (4). Therefore, we aimed to examine *PPAR-α* gene that may cause OP development. The *PPAR-α* gene is a transcription factor and coactivator gene that controls lipid, glucose and energy homeostasis, *PPAR-α* is particularly highly expressed in tissues that catabolize fatty acids such as liver, skeletal and cardiac muscle, and its association with OP and bone loss has been reported. PPARs are members of the nuclear receptor family and have three isoforms as PPARα, PPARβ/δ and PPARγ. PPARs play an important role in lipid, glucose homeostasis, metabolic control and related to osteoblasts and adipocytes (5-8). Especially PPARγ important for bone and bone related diseases interms of effects of activation on bone turnover, fat-bone connection, adipocyte differentiation and effects on osteoblasts. PPAR-α and PPAR-β/γ has been reported to promote osteoblastogenesis. Regarding their effects on osteoclast formation and activity in PPARα and PPARβ/δ, both PPARα and PPARβ/δ agonists inhibited osteoclast formation in differentiated cells, whereas the PPARα agonist failed to reduce resorption (9-12). There are many polymorphic regions, the (G>C rs4253778) polymorphic region is located in intron 7 and its relationship with physical activity has been reported in previous studies. In the light of this information, our study aimed to examine the relationship between *PPAR-α* gene polymorphisms and OP in postmenopausal Turkish women.

Materials and Methods

Subjects

This study included 250 postmenopausal women mostly from the Central Black Sea Region from Turkey. Among them, a total of 150 had osteoporotic bone mineral density (BMD) (T-score <-2.5) and 100 had normal BMD (T-score >-1). The mean age of the patients was 62.8±8.485 (standard deviation) (the minimum was 47, the maximum was 87), and the mean age of the controls was 58.91±7.910 (the minimum was 44, the maximum was 78). Participants were asked to fill in the information form asking for information such as body mass index (BMI), height, weight, age at menarche, age of menopause, number of children and births, smoking/alcohol use, and an informed consent form was signed. In addition, Ondokuz Mayıs University Clinical Research Ethics Committee approved the study (decision no: OMÜ-KAEK 2022/17, date: 26.01.2022). The Power Analysis was made with the Open Epi program, and the minimum number of individuals required in each group was calculated as n=56 in the power analysis performed by taking power =80% and it was decided to include at least n=100 individuals in each group. We do not have financial support from any source for his research.

Bone Mineral Density Measurements

The dual-energy X-ray absorptiometry (DEXA) method is the most widely used method for bone density measurement. We used DEXA (Norland EXCELL, USA) to define OP according to the World Health Organization. In this method, while the patient is lying still on a table, measurements are made with a moving camera and a beam source, and the results are evaluated with the help of a computer. Processing time is about 10 minutes.

DNA Isolation and Genotyping *PPAR-α* gene Polymorphism

Peripheral blood samples were taken from the patient and control groups and DNA isolation was performed using the kit methodology (Gene Jet, Lithuanian). Genotyping was performed by polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) methods. The polymorphic region of the *PPAR-α* gene (rs4253778) identified according to the PCR-RFLP method of Eynon et al. (8). The 266-bp segment containing the C/T substitution of the *PPAR-α* gene was amplified by PCR method. Primers were F - 5′-TAAAGATGTCTCCTCTGATT -3′ and (R) 5′-GGGACACATTGAACAATGAATAGGATTG -3′. Amplification reaction in 50 µL total volume by adding 100-200 ng genomic DNA, 200 µM dNTP, 1x reaction buffer (1.5 mM $MgCl_2$), 1.5 mM $MgCl_2$, 0.25 units Taq polymerase and 2-6 pm of each primer for each reaction carried out. Then, in the (Techne Gradient) thermal cycling device, 30 cycles of initial denaturation at 94 °C for 8 minutes, 30 cycles at 94 °C for 30 seconds, at 59 °C for 30 seconds, and at 72 °C for 60 seconds applied. Final elongation applied at 72 °C for 10 minutes. PCR products cut with Taq E restriction enzyme for 3 hours at 37 °C. In case of a recognition site when cut with Taq E restriction enzyme, 216 bp and 50 bp fragments obtained. The resulting products run on a 3% agarose gel. 266 bp fragments considered as AA genotype; Fragments of 253 bp, 216 bp, and 50 bp considered as CA genotype and fragments of 232bc and 21bp considered as CC genotype.

Statistical Analysis

For the statistical analysis we used SPSS15 (SPSS, Chicago, IL, US) program and OpenEpi Info Software program. Chi-square analysis was used to calculate genotype distribution and allele frequencies.

Results

The mean age was 62.87±8.48 years in patients and 59.37±7.91 years in control group. Table 1 represents demographic and clinical findings of patients and controls. Table 2 represents the *PPAR-α* gene genotype distribution and allele frequency findings of the patients and controls. As a result of the study a statistically significant difference found between the

groups with respect to *PPAR-α* allelic frequency (p=0.017). As a result of the study, while there was no statistical significant association between genotype distribution and OP, C-allele frequency was higher in patient group and it was statistically significant (p=0.017). *PPAR-α* gene C-allele frequency was indicated as 58.57% in the patients and 32.85% in the control group (Table 2). *PPAR-α* gene genotype correlation with fracture history and BMI presented in Table 3. There was no statistically significant difference between fracture history and genoype correlation (p=0.69). There is also no statistically significant difference between BMI and genoype correlation (p=0.41). There was also no statistical significant difference between the study and control groups in terms of fracture history and BMI (Table 4).

Discussion

OP is a complex disease that occurs with the interaction of many genetic and environmental factors. Twin and family studies have shown that genetic factors have a significant effect on bone formation. In diseases with complex pathophysiology such as OP, it is important to investigate whether there is a relationship between a polymorphic genetic marker and the phenotype of the disease in the identification of related genes. It is hoped that understanding the complex interactions between genetic

Table 1. Clinical and laboratory Findings

Characteristics	Patients (n=150) (mean ± SD)	Median (min-max)	Controls (n=100)	Median (min-max)
BMI (kg/m^2)	27.52±4.777	28.00 (12-45)	29.38±4.177	29 (27-41)
Age at menapause (yr)	48.24±5.525	48.60 (34-60)	45.66±4.7243	46 (33-59)
Age at menarche (yr)	13.32±1.481	13.0 (9-18)	13.26±1.41	13 (11-17)
Number of birth (n)	3.66±1.938	3.0 (0-10)	3.0±1.528	3 (0-6)
Serum calcium (mg/dL)	9.75±0.550	9.55 (8.30-11.5)	9.65±0.4992	9.85 (8.6-11)
Serum phosphorus (mg/dL)	3.83±2.65	3.73 (2.2-26.30)	3.84±0.67825	4 (2.05-5.29)
Serum PTH (pg/mL)	78.02±52.94	78.2 (11.80-453)	74.22±28.553	73.6 (31-178)
Serum ALP (U/L)	188.03±62.93	189.325 (2.32-420)	188.55±46.156	187.7 (97-301)

SD: Standard deviation, BMI: Body mass index, yr: Year, PTH: Parathyroid hormone, ALP: Alkaline phosphatase, min-max: Minimum-maximum

Table 2. Genotype and allele frequencies of *PPAR-α* gene intron 7 G>C (rs4253778) polymorphism

Genotype/allele	Patients (n=150)		Controls (n=100)		χ^2	p-value	OR (95 %CI)
Genotype	n	%	n	%			
CC	97	60.6	71	71			
CG	11	6.9	4	4	χ^2=3.076	p=0.215	
GG	52	32.5	25	25			
Total	150		100				
Allele	n	%	n	%			
C	205	58.57	146	47.71	χ^2=4.481	p=0.017*	0.65 (0.45-0.97)
G	115	32.85	54	15.42			

*p<0.05 is statistically significant, OR: Odds ratio, CI: Confidence interval

Table 3. *PPAR-α* gene genotype correlation with fracture history and BMI

	Patients, n (%)			c^2	p-value	Controls/n (%)			c^2	p-value
	G/G	G/C	C/C			G/G	G/C	C/C		
Fracture history										
+	12 (8)	2 (1.3)	11 (7.3)	0.422	0.83	2 (2)	1 (1)	2 (2)	0.723	0.69
-	81 (54)	9 (6)	35 (23.4)	5.191	0.27	65 (65)	6 (6)	24 (24)		
BMI										
<25	12 (8)	3 (2)	13 (8.6)	7.341	0.12	10 (10)	2 (2)	4 (4)	1.402	0.41
≥25	81 (54)	6 (4)	35 (23.4)			56 (56)	5 (5)	23 (23)		

*p<0.05 is statistically significant, BMI: Body mass index, +: Patients have fracture, -: Patients have no fracture

Table 4. PPAR-α gene genotype correlation with fracture history and BMI between groups

	Patients (n=150)		Controls (n=100)		c^2	p-value
	G-allele	C-allele	G-allele	C-allele		
Fracture history						
+	26 (17)	24 (16)	5 (5)	5 (5)	0.013	0.90
-	171 (114)	79 (53)	136 (136)	54 (54)	0.517	0.47
BMI						
<25	27 (18)	29 (20)	22 (22)	10 (10)	3.48	0.06
≥25	168 (112)	76 (51)	117 (117)	51 (51)	0.02	0.08

*p<0.05 is statistically significant, BMI: Body mass index, +: Patients have fracture, -: Patients have no fracture

factors and environmental factors will contribute to the clarification of disease pathogenesis and to the development of future genetic-based risk regulation and disease prevention and treatment. In order to contribute to the studies showing the relationship between the *PPAR-α* gene and OP, we aimed to examine *PPAR-α* gene in postmenopausal Turkish women. Our study showed that, the C-allele of the *PPAR-α* gene may be a risk factor for the development of OP. In terms of fracture history and BMI there was no statistically significant difference between genotype correlations in the present study. There was also no statistical significant difference between the study and control groups in terms of fracture history and BMI. Our study revealed that *PPAR-α* gene is not associated with fracture risk in our study population. Harsløf et al. (13) examined *PPARγ* gene in Danish osteopotic patients and they suggested an association with *PPARγ* gene and fracture risk. They also indicated that the effect may be modifiable by environmental factors (13). In a study conducted on postmenopausal Turkish women, the *PPARα L162V* gene polymorphism was examined and it was found that the CC genotype was at a higher frequency in the patient group and was statistically associated with the development of OP (p<0.05) (14). In a study conducted on Turkish elite athletes, the effect of *PPAR-α* gene polymorphism on performance was examined and it was determined that this gene, which affects the skeletal and muscular system, is highly correlated with performance (8). An animal study examined the positive effects of *PAR-α* activation on the skeleton (5). Studies on the relationship between the *PPAR-α* gene and OP or bone-related diseases are very limited. In a recent review published in 2019, it was reported that *PPAR-α* gene polymorphism is associated with atherosclerosis and metabolic diseases (15). The relationship of *PPAR-α* gene with metabolic diseases has been revealed (16). It is known that OP is also considered as a metabolic disease (16,17), so we wanted to reveal its relationship with *PPAR-α* in our study. And our results confirmed these data, with the *P* gene C-allele being higher in the patient group. In our previous study we examined relationship between OP and *BGLAP, ESR1, COL1-A1* and *CALCR* genes in Turkish postmenopausal women and our results showed that, while there was no statistical significant difference in terms of allelic and genotype frequency, *ER1* gene CC genotype was detected 2-fold increased risk for OP (p=0.039) (18). In our different previous study we examined *IL-10* and *TGF-beta* genes in postmenopausal osteoporotic Turkish women and there was a statistical significant difference in terms of *IL-10* genotype distribution (p=0.001) and allele frequencies (p<0.0002) (19).

Conclusion

In conclusion, polimorphic C-allele of *PPAR-α* gene is found to be associated with development of OP in postmenopausal osteoporotic Turkish women. However, to confirmation our results larger and further studies should be done.

Ethics

Ethics Committee Approval: In addition, Ondokuz Mayıs University Clinical Research Ethics Committee approved the study (decision no: OMÜ-KAEK 2022/17, date: 26.01.2022).

Informed Consent: Participants were asked to fill in the information form asking for information such as body mass index, height, weight, age at menarche, age of menopause, number of children and births, smoking/alcohol use, and an informed consent form was signed.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: A.S., E.T., Design: Ş.T., Data Collection or Processing: A.S., G.A., Analysis or Interpretation: G.A., Es.T., Literature Search: Ş.T., E.T., Es.T., Writing: Ş.T.

Conflict of Interest: No conflict of interest was declared by the authors.

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Kinesiophobia and Related Factors in Fibromyalgia Syndrome

Fibromiyalji Sendromunda Kinezyofobi ve İlişkili Faktörler

Uğur Ertem, Alev Alp

Bursa Uludağ University Faculty of Medicine, Department of Physical Medicine and Rehabilitation, Bursa, Turkey

Abstract

Objective: This study aimed to determine the kinesiophobia levels in female patients with fibromyalgia (FMS). In addition, we intended to search the factors associated with kinesiophobia in patients with FMS and to evaluate the effect of kinesiophobia on work outcomes in this patient population.
Materials and Methods: Between January 2021 and May 2021, 50 female patients with FMS and 44 female patients with musculoskeletal pain but not meeting the diagnostic criteria for FMS were included in the study. Pain was evaluated using the numeric scale, kinesiophobia levels with the Tampa Scale for Kinesiophobia (TSK), and the work outcomes with a questionnaire form prepared by us.
Results: The median TSK scores were 41,50 (21-61) in the FMS group and 37 (23-61) in the control group. TSK score was significantly higher in the FMS group (p=0.030). Pain scores (p<0.001), and symptom duration (p<0.001) were significantly associated with high levels of kinesiophobia. When multiple linear regression analysis was performed, it was found that body mass index (p=0.411) was not associated with kinesiophobia levels, whereas age (p<0.001) was associated with kinesiophobia levels. Increased levels of kinesiophobia in patients with FMS patients have been associated with worse work outcomes.
Conclusion: Evaluating the level of kinesiophobia in patients with FMS and developing preventive strategies in the presence of kinesiophobia can provide useful information when creating a treatment program.
Keywords: Fibromyalgia, kinesiophobia, work outcomes

Öz

Amaç: Bu çalışmanın amacı fibromiyaljili (FMS) kadın hastalarda kinezyofobi düzeylerini belirlemektir. Ayrıca, FMS'li hastalarda kinezyofobi ile ilişkili faktörleri araştırmayı ve bu hasta popülasyonunda kinezyofobinin iş sonuçlarına etkisini değerlendirmeyi amaçladık.
Gereç ve Yöntem: Ocak 2021-Mayıs 2021 tarihleri arasında FMS'li 50 kadın hasta ve kas-iskelet ağrısı olan ancak FMS tanı kriterlerini karşılamayan 44 kadın hasta çalışmaya dahil edildi. Ağrı sayısal skala, kinezyofobi düzeyleri Tampa Kinezyofobi Skalası (TSK) ile, çalışma çıktıları tarafımızca hazırlanan anket formu ile değerlendirildi.
Bulgular: TSK ortanca puanları FMS grubunda 41,50 (21-61), kontrol grubunda 37 (23-61) idi. TSK puanı FMS grubunda anlamlı olarak yüksekti (p=0,030). Ağrı skorları (p<0,001) ve semptom süresi (p<0,001) yüksek düzeyde kinezyofobi ile anlamlı şekilde ilişkiliydi. Çoklu lineer regresyon analizi yapıldığında, vücut kitle indeksinin (p=0,411) kinezyofobi düzeyleri ile ilişkili olmadığı, yaşın (p<0,001) ise kinezyofobi düzeyleri ile ilişkili olduğu bulundu. FMS hastalarında artan kinezyofobi seviyeleri, daha kötü iş sonuçlarıyla ilişkilendirilmiştir.
Sonuç: FMS'li hastalarda kinezyofobi düzeyinin değerlendirilmesi ve kinezyofobi varlığında koruyucu stratejiler geliştirilmesi tedavi programı oluşturulurken faydalı bilgiler sağlayabilir.
Anahtar kelimeler: Fibromiyalji, kinezyofobi, iş sonuçları

Introduction

Fibromyalgia syndrome (FMS) is a chronic musculoskeletal pain disease, characterized by sleep disturbances, debility and cognitive symptoms (1,2). FMS is more frequent in females, and its incidence makes a peak in the ages of 40 and 60 years (3,4). The prevalence of FMS varies between 1.3-8% and is the second most common rheumatological disease after osteoarthritis (5). Although many theories have been put forward regarding the pathogenesis of FMS, it has not been clearly explained. Because women in general have lower pain thresholds than men and their symptoms are more clinically exacerbated, the majority of scientific studies have been conducted on women (6). FMS is a chronic health problem presenting with pain all over the body,

Address for Correspondence/Yazışma Adresi: Uğur Ertem MD, Bursa Uludağ University Faculty of Medicine, Department of Physical Medicine and Rehabilitation, Bursa, Turkey
Phone: +90 224 294 00 00-16240 **E-mail:** ugurertem@uludag.edu.tr **ORCID ID:** orcid.org/0000-0003-2142-2264
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tenderness to touch or pressure of the effected parts of the body, fatigue, sleeping and memory problems or clear thinking. Apart from these problems, kinesiophobia, which means the fear of movement, can also be observed in patients with FMS (7).

Kinesiophobia has been defined as an excessive and irrational fear to perform a physical act as a result of a painful injury or a sense of helplessness in the face of the injury (8). Kinesiophobia is present in around 79% of subjects with musculoskeletal pain, and it is associated with greater disability with the indication of a worse prognosis (9,10). Kinesiophobia is a barrier to initiating physical activity in patients or individuals and is an important moderator of response to treatment after physiotherapy and surgery (11). Therefore, determining the kinesiophobia level of the patients and developing preventive strategies, if any, are important for the treatment response.

The aim of this study was to determine the kinesiophobia levels in female patients with FMS. Also, we intended to search the factors associated with kinesiophobia in patients with FMS and to reveal the effect of kinesiophobia on work outcomes in this patient population.

Materials and Methods

This case control study was carried out in Bursa Uludağ University Physical Therapy and Rehabilitation Polyclinic between January 2021 and May 2021. Fifty consecutive female patients who met the 2016 FMS diagnostic criteria were included. As the control group, 44 female patients who did not meet the criteria for the diagnosis of FMS and had musculoskeletal pain were included. Participants in both of the groups were the members of the working population. Patients who have been operated for the musculoskeletal system in the last year, having inflammatory joint disease, having a job for less than 3 months time, and unemployed were not included. An informed consent form was signed by each patient. Permission for the study was obtained from the Bursa Uludağ University Faculty of Medicine is Clinical Research Ethics Committee and the study was approved (decision no: 2020-23/14, date: 23/12/2020). Our study was carried out in accordance with the principles of the Declaration of Helsinki.

Participants' age, body mass index (BMI), and duration of symptoms were recorded. A numeric scale was used to assess the participants' pain level. The patients were informed about the procedure of pain scale. The participants were told that the absence of pain was 0 points and the most severe pain they had experienced in their life was 10 points. Accordingly, the participants were asked to indicate their pain levels.

Tampa Kinesiophobia Scale (TSK), which includes 17 questions, was used for the assessment of kinesiophobia. Each question in the TSK is a minimum of 1 point and a maximum of 4 points. Using this scale, a maximum of 68 points and a minimum of 17 points can be obtained. Higher scores on this scale refers higher levels of kinesiophobia. According to this scale, scores higher than 37 points refer "high level of kinesiophobia", and scores less than or equal to 37 points refer "low level of kinesiophobia" (12-14).

We prepared a 6-question questionnaire to evaluate the work outcomes of patients with FMS. In Question 1, patients were asked how FMS negatively affected their general working life. The "A" option indicated the least affected, and the "D" option was the most affected. In the second question, patients were asked how FMS effected their working performance. The "A" option indicated the least negatively affected, and the "D" option was the most adversely affected. In the third question, the patients were asked how much official permission they took in 1 year due to FMS. The "A" option indicated the least frequent resting permission and the "D" option was the most frequent resting permission. In the 4th question, the patients were asked whether they had any problems in their professional life due to FMS. The "A" option indicated the least problem and the "D" option was the most problematic situation. In the 5th question, the patients were asked whether they had problems with their co-workers due to FMS. The "A" option indicated the least problem and the "D" option was the most problematic situation. In the 6th question, patients were asked whether their social activities at work were affected by FMS. The "A" option was the situation where social activities were least affected, and the "D" option was the situation where social activities were most negatively affected.

Statistical Analysis

Shapiro-Wilk test was used for assessing whether the variables follow normal distribution or not. Continuous variables were presented as median (minimum-maximum) and mean±standard deviation values. Categorical variables were expressed as n (%). Comparisons between the two groups according to the normality test results were made using the Independent sample t test or the Mann-Whitney U test. Pearson chi-square was used to compare categorical variables. Correlations between continuous variables were examined by correlation analysis. Pearson correlation coefficients and Spearman correlation coefficients were determined. Multiple linear regression analysis was used to estimate Tampa Scale for Kinesiophobia score. Variables were included in the multiple linear regression model using the Enter method. Variables that were found to be significant in the model were determined as independent variables. Multiple linear regression model was found to be significant ($p<0.001$). Statistical Package for the Social Sciences (SPSS) (IBM Corp. Released 2012. IBM SPSS Statistics for Windows, Version 21.0, Armonk, NY: IBM Corp.) was used for statistical analysis the level of significance was determined as $p<0.05$.

Results

The distribution of the participants according to their demographic characteristics and clinical variables is given in Table 1. There was no statistically significant difference in age between

patients with FMS and controls (p>0.05). But, the pain scores, symptom duration, TSK scores and BMI were significantly higher in the FMS group (p<0.05).

We separated the FMS group into two groups according to their TSK scores as low kinesiophobia level (n=18) and high kinesiophobia level group (n=32). Pain scores, symptom duration, and BMI were significantly higher in the high-level kinesiophobia group (p<0.05) (Table 2).

The correlations of demographic characteristics and clinical parameters with TSK scores in patients with FMS are given in Table 3. There was no statistically significant correlation between TSK scores and the age of the patients (p=0.989). A positive and significant correlation was found between TSK scores and pain levels, symptom duration and BMI (p<0.001).

Multiple linear regression analysis was performed to identify factors related to kinesiophobia in FMS group. The established logistic regression model was significant (p<0.001). According to the results of the analysis, pain scores, age, and symptom duration were significantly associated with TSK scores (p<0.001) (Table 4).

We divided the FMS group into low kinesiophobia group (n=18) and high kinesiophobia group (n=32) according to TSK scores. The distribution of the responses of these 2 groups to the questionnaire is given in Table 5. To analyze the internal reliability of the questionnaire, the Cronbach's alpha coefficient of the questions answered by the patients about their work life and their social relationships in work life was used. The internal reliability of the study was found to be excellent (α=0.914). According to the answers given to the questionnaire, it was determined that FMS patients with high kinesiophobia marked "C" and "D" options, which represent worse work results, more than patients with low kinesiophobia (Table 5).

Discussion

Psychological factors such as thinking things will get worse or fear that movement will increase pain are among the poor prognostic factors for FMS (15). In this case, it shows us that fibromyalgia and kinesiophobia are conditions that effect each other. In a study by Koçyiğit et al. (13) in which they compared the kinesiophobia levels of participants with FMS and healthy volunteers, kinesiophobia scores were higher in the FMS group. In a study examining kinesiophobia and related factors in patients with systemic lupus erythematosus; a significant relationship was found between kinesiophobia and depression and some subscales of quality of life (16). FMS related pain and functional disability may increase depression and anxiety (17). Considering

Table 3. Correlation between kinesiophobia scores and demographic and clinical characteristics in fibromyalgia patients

n=50	Tampa scale for kinesiophobia scores	
	r	p
Age	0.002[d]	0.989
Numeric scale	0.788[e]	<0.001
Symptom duration	0.496[e]	<0.001
Body mass index	0.519[d]	<0.001

[d]: Pearson correlation coefficient, [e]: Spearman correlation coefficient

Table 1. Demographic and clinical variables of fibromyalgia and control groups

n=94	FMS group (n=50)	Control group (n=44)	p
Age (year)	38.04±7.98	35.32±7.34	0.090[a]
Numeric scale (pain)	6.00 (3-9)	5.00 (2-8)	0.007[b]
Body mass index (kg/m^2)	25.20 (17-35)	23.20 (17-35)	0.049[b]
TSK scores	41.50 (21-61)	37 (23-61)	0.030[b]
Symptom duration (year)	6 (1-10)	4 (1-10)	0.025[b]

FMS: Fibromyalgia syndrome, TSK: Tampa Scale for Kinesiophobia
Data are expressed as mean±standard deviation and median (minimum-maximum).
[a]: Independent Sample t-test, [b]: Mann-Whitney U Test

Table 2. Comparison of demographic characteristics and clinical variables between low- and high-level kinesiophobia groups in patients with fibromyalgia

n=50	Low levels of kinesiophobia (n=18)	High levels of kinesiophobia (n=32)	p
Age (year)	37.67±9.06	38.25±7.46	0.807[a]
Numeric scale (pain)	4.50 (3-6)	7 (4-9)	<0.001[b]
Symptom duration (year)	3 (1-10)	7 (1-10)	<0.001[b]
Body mass index (kg/m^2)	22.72±3.67	26.71±4.52	0.002[a]

Data are expressed as mean±standard deviation and median (minimum-maximum).
[a]: Independent Sample t-test [b]: Mann-Whitney U Test

Table 4. Factors related kinesiophobia levels in fibromyalgia patients

				95% Confidence interval for B		
	Unstd. B	**Standart error**	**t**	**Lower bound**	**Upper bound**	**p**
Constant	25,386	5,224	4.86	14,864	35,907	**<0.001**
Numeric scale (pain)	5,044	0.642	7,852	3.75	6,338	**<0.001**
Body mass index (kg/m^2)	-0.187	0.225	-0.831	-0.64	0,266	0.411
Age (year)	-0.466	0.108	-4,297	-0.684	-0,247	**<0.001**
Symptom duration (year)	1,558	0.303	5,146	0.948	2,167	**<0.001**
n=50, R^2=0.783, Adj. R^2=0.763 (F=40,508, **p<0.001**)						

Unstd. B: Unstandardized beta coefficients

Table 5. Comparison of answers to survey questions between low and high kinesiophobia levels groups in patients with fibromyalgia

		Low levels of kinesiophobia (n=18)	**High levels of kinesiophobia (n=32)**
First question	A	4 (22.22%)	0
	B	11 (61.11%)	12 (37.50%)
	C	**3 (16.67%)**	20 (62.50%)
	D	**0**	0 (0.00%)
Second question	A	5 (27.78%)	1 (3.12%)
	B	10 (55.56%)	8 (25.00%)
	C	**2 (11.11%)**	**14 (43.75%)**
	D	**1 (5.56%)**	**9 (28.12%)**
Third question	A	16 (88.89%)	21 (65.62%)
	B	2 (11.11%)	9 (28.12%)
	C	0	**2 (6.25%)**
	D	0	0
Fourth question	A	4 (22.22%)	0
	B	7 (38.89%)	8 (25.00%)
	C	6 (33.33%)	**18 (56.25%)**
	D	1 (5.56%)	**6 (18.75%)**
Fifth question	A	9 (50.00%)	5 (15.62%)
	B	6 (33.33%)	14 (43.75%)
	C	3 (16.67%)	**9 (28.12%)**
	D	0	**4 (12.50%)**
Sixth question	A	4 (22.22%)	2 (6.25%)
	B	9 (50.00%)	12 (37.50%)
	C	5 (27.78%)	**10 (31.25%)**
	D	0	**8 (25.00%)**

Data are expressed as n (%)

the connection between depression and kinesiophobia, we can say that this situation may increase kinesiophobia scores in patients with FMS. The results of our study support the results of previous studies in patients with FMS, and it was found that kinesiophobia levels with FMS was higher than the control group.

Exacerbation of symptoms following physical activity is characteristic for FMS. These exacerbations make it understandable for people with FMS to develop kinesiophobia (18). In a study conducted in our country, Koçyiğit and Akaltun (13) found that 75.1% of the participants with FMS had high kinesiophobia levels. In another study, 72.9% of patients with FMS were found to have high levels of kinesiophobia (19). According to the literature, we can say that pain and fear of activity are common in FMS patients (20-22). The current study, high levels of kinesiophobia were detected in 64% of patients with FMS (TSK scores >37). High levels of kinesiophobia in more than half of the FMS patients (64%) in the results of our study supports the results in the literature.

In a study, pain levels and psychological state were found to be effective on fear of movement and therefore on functional status and quality of life in patients with ankylosing spondylitis (14). Vlaeyen et al. (23) showed that kinesiophobia was associated with gender, compensation status, and depression, but to a much lesser degree with pain intensity in patients with chronic low back pain. Another study in the literature, BMI levels, FMS disease activity levels and vitamin D levels were found to be associated with kinesiophobia levels in patients with FMS (13). In a systematic review, it was concluded that pain levels were associated with the levels of kinesiophobia in participants with chronic musculoskeletal pain (8). Our study, a positive correlation was detected between pain levels, symptom duration and high kinesiophobia levels. We consider that an increase in the duration of symptoms in patients with FMS increases depression and deterioration in functionality, and therefore may be related to kinesiophobia. In addition, we think that the increase in pain scores may have increased the level of kinesiophobia by causing the feeling that the severity of pain will increase more with movement and thus causing the behavior of avoiding movement. When BMI was taken alone, it was found to be associated with kinesiophobia levels in FMS group, but when multiple linear regression analysis performed, it was found not to be associated with kinesiophobia levels. On the contrary, the age variable was found to be unrelated to the level

of kinesiophobia when the correlation analysis was performed alone, while it was found related with kinesiophobia levels when the multiple linear regression analysis was performed.

In a study examining relationship between work outcomes and kinesiophobia, decreasing the level of kinesiophobia increased the level of work ability (24). Macías-Toronjo et al. (25) reported that kinesiophobia and catastrophizing were associated with sick leave duration in patients with work-related neck and low back pain. The study of Sugano et al. (26) showed that long or increased working hours may be a risk factor for chronic musculoskeletal pain. It showed that this was related with stronger fear-avoidance beliefs and reduced work outcomes. In general, previous studies showed that high kinesiophobia levels are related with reduced work outcomes. According to the answers given to the questionnaire, FMS patients with high kinesiophobia levels marked "C" and "D" options, which represent worse work results, more than patients with low kinesiophobia levels. Conversely, FMS patients with low kinesiophobia levels marked "A" and "B" options, which represent better work outcomes, more than patients with high kinesiophobia levels.

Study Limitations

The current study had some limitations. This was a single-center study with a small number of female-only subjects; this situation limits the generalization of our results. In addition, the participants among the groups were heterogeneously distributed. Moreover results obtained do not provide clear information, since the questionnaire form we use to evaluate the work outcomes is not a valid questionnaire created by us.

Conclusion

In conclusion, kinesiophobia levels of FMS group were significantly higher. The kinesiophobia levels in people with FMS can affect many areas, including work outcomes of individuals. Exercise therapy, especially aerobic exercises, are among the most important treatment methods in the treatment of FMS, and the presence of kinesiophobia limits the exercise of FMS patients. For this reason, evaluation of the kinesiophobia levels and the development of preventive strategies in the presence of kinesiophobia can provide useful information when creating a treatment prescriptions.

Ethics

Ethics Committee Approval: Bursa Uludağ University Faculty of Medicine is Clinical Research Ethics Committee approval was obtained for the study with the number of 2020-23/14 (date: 23/12/2020). This study adheres to the ethical rules reported in the 1964 Helsinki Declaration, which were revised in 2013.

Informed Consent: A written acceptance certificate was requested from the patients included in the study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: U.E., A.A., Concept: U.E., A.A., Design: U.E., A.A., Data Collection or Processing: U.E., A.A., Analysis or Interpretation: U.E., A.A., Literature Search: U.E., A.A., Writing: U.E., A.A.

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A Cross-sectional Study on Vitamin D Levels, Body Mass Index, Physical Activity Level and Life-style Factors in Postmenopausal Women

Postmenopozal Kadınlarda Vitamin D Seviyeleri, Vücut Kitle İndeksi, Fiziksel Aktivite Düzeyi ve Yaşam Tarzı Faktörleri Üzerine Kesitsel Bir Çalışma

Emine Esra Ergül, Gonca Sağlam*

Erzincan Binali Yıldırım University Mengücek Gazi Training and Research Hospital, Clinic of Physical Medicine and Rehabilitation, Erzincan, Turkey
*Karadeniz Technical University Faculty of Medicine, Department of Physical Medicine and Rehabilitation, Trabzon, Turkey

Abstract

Objective: The aim of this study was to evaluate the vitamin D levels, body mass index (BMI), physical activity levels and life-style factors in postmenopausal women and investigate the correlation between vitamin D levels, BMI and physical activity.
Materials and Methods: A total of 100 postmenopausal women were included in this cross-sectional study. Sociodemographic features, life-style factors such as calcium and vitamin D supplementation and sun exposure, and BMI, and 25 hydroxyvitamin vitamin D [25(OH)D3] levels of the participants were recorded. The [International Physical Activity Questionnaire (IPAQ) Short Form (SF)] was applied to all participants. The correlation between 25(OH)D3, BMI, and IPAQ scores has been investigated. Forty postmenopausal healthy individuals were included in the study for the comparison of physical activity level with the patient group.
Results: The mean 25(OH)D3 level of the postmenopausal participants was 18.97±10.0 ng/mL, the mean BMI was 27.93±5.19, and the IPAQ score was 316.15±370.42. Compared with the IPAQ-SF score of the control group, the activity level of the postmenopausal patients was lower ($p<0.001$). A negative significant correlation between 25(OH)D3 levels and BMI ($p<0.001$) and a positive significant correlation was observed between 25(OH)D3 levels and IPAQ-SF scores in postmenopausal women ($p<0.001$).
Conclusion: BMI and physical activity levels seem to be associated with vitamin D levels in the postmenopausal period. The importance of vitamin D deficiency, weight control, life-style factors, and physical activity in the postmenopausal period should be emphasized in patients.
Keywords: Vitamin D, body mass index, physical activity

Öz

Amaç: Bu çalışmanın amacı postmenopozal kadınlarda D vitamini düzeylerini, vücut kitle indeksini (VKİ), fiziksel aktiviteyi ve yaşam tarzı faktörlerini değerlendirmek ve D vitamini düzeyleri ile VKİ ve fiziksel aktivite arasındaki korelasyonu araştırmaktır.
Gereç ve Yöntem: Bu kesitsel çalışmaya toplam 100 postmenopozal kadın dahil edildi. Katılımcıların sosyodemografik özellikleri, kalsiyum ve D vitamini takviyesi ve güneş maruziyeti gibi yaşam tarzı faktörleri, VKİ'leri ve 25 hidroksivitamin D [25(OH)D3] düzeyleri kaydedildi. Katılımcılara ayrıca [Uluslararası Fiziksel Aktivite Anketi (IPAQ) Kısa Formu (SF)] uygulandı. 25(OH)D3 düzeyleri ile VKİ ve IPAQ skorları korelasyonu araştırıldı. Postmenopozal hasta grubunun fiziksel aktivite düzeyini karşılaştırmak için 40 postmenopozal sağlıklı birey çalışmaya dahil edildi.
Bulgular: Postmenopozal kadınların ortalama 25(OH)D3 düzeyi 18,97±10,0 ng/mL, ortalama VKİ 27,93±5,19 ve IPAQ skoru 316,15±370,42 idi. Kontrol grubunun IPAQ skoruyla karşılaştırıldığında postmenopozal hastaların aktivite düzeyi daha düşüktü ($p<0,001$). Postmenopozal kadınlarda, 25(OH)D3 düzeyleri ile VKİ arasında negatif anlamlı korelasyon vardı ($p<0,001$), 25(OH)D3 düzeyleri ile IPAQ-SF skorları arasında ise pozitif yönde anlamlı bir ilişki gözlendi ($p<0,001$).
Sonuç: VKİ ve fiziksel aktivite seviyeleri postmenopozal dönemde D vitamini düzeyleri ile ilişkili görünmektedir. Postmenopozal dönemde vitamin D eksikliğinin, kilo kontrolünün, yaşam tarzı faktörlerinin ve fiziksel aktivitenin önemi hastalara vurgulanmalıdır.
Anahtar kelimeler: Vitamin D, vücut kitle indeksi, fiziksel aktivite

Address for Correspondence/Yazışma Adresi: Gonca Sağlam MD, Karadeniz Technical University Faculty of Medicine, Department of Physical Medicine and Rehabilitation, Trabzon, Turkey
Phone: +90 505 452 56 88 **E-mail:** goncasaglam@hotmail.com **ORCID ID:** orcid.org/0000-0001-7713-4435
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Introduction

Vitamin D is included in the group of fat-soluble vitamins while it is also biologically synthesized in the human body. It performs an active role in calcium phosphorus metabolism and contributes to bone mineralization. Vitamin D deficiency and insufficiency, as an important global health problem, is predicted as a possible risk factor for many acute and chronic diseases with a broad spectrum (1).

Vitamin D3 (cholecalciferol) is synthesized endogenously in the human body from 7 dehydrocholesterols in the skin by ultraviolet B (UVB) rays. Vitamin D can be taken externally as ergocalciferol (vitamin D2) from plants and as cholecalciferol (Vitamin D3) from animal sources (2,3). The main sources of vitamin D are; milk, yogurt, kefir, cheese, beef liver, fatty fish such as mackerel-trout-tuna-herring and egg yolk (4). Vitamin D is first converted to 25 hydroxyvitamin D [25(OH)D] with the enzyme 25 hydroxylase in the liver, and then to 1.25 dihydroxy vitamin D [1.25(OH)2D], known as calcitriol, with the enzyme 1 alpha hydroxylase in the kidneys (2, 3). Calcitriol preserves the blood calcium level by increasing calcium absorption from the small intestine and reducing calcium loss from the kidneys, which is the overall function (3,5). The half-life of calcitriol is short and its level in the blood is much lower than 25(OH)D3. Therefore, 25(OH)D3 levels, which show both endogenous production and exogenous intake, are used to evaluate vitamin D levels (2,5).

Vitamin D deficiency increases dramatically in older age (6). It is more prevalent, especially in the postmenopausal period. This situation may be due to thinning of the skin structure during menopause, decreased vitamin D absorption, and decreased hydroxylation of vitamin D in the liver and kidney. Furthermore, decrease in estrogen levels and other hormone changes in postmenopausal women also contribute to the development of low vitamin D levels. In light of researches conducted during the menopausal period, vitamin D deficiency was associated with an increased risk of fractures and decreased bone mass. In addition, osteoporosis rates were found to be greater in postmenopausal women with vitamin D deficiency (7).

Some of the previous researches have documented a negative correlation between body mass index (BMI) and vitamin D in postmenopausal women (8). The aim of our study was to evaluate the association between vitamin D levels, BMI and many other factors including physical activity levels, sun exposure and consumption of foods containing vitamin D and calcium.

Materials and Methods

This cross-sectional study was conducted between September 2021 and November 2021. A hundred postmenopausal women who admitted to the physical medicine and rehabilitation outpatient clinic for musculoskeletal pain were included in the study. The exclusion criteria were as follows: history of malignancy, presence of alcohol use, drug or substance abuse, dementia, cognitive dysfunction that interferes with the normal function of the central and peripheral nervous system. Age, gender, occupation, educational status, BMI, calcium and vitamin D supplementation, consumption amount of foods containing calcium and vitamin D, sun exposure hours and intervals (March-September), and smoking status of all participants were recorded.

[International Physical Activity Questionnaire-Short Form (IPAQ-SF)] was used to determine the physical activity levels of the participants. A control group of 40 healthy postmenopausal women without musculoskeletal pain has been included to compare IPAQ scores with postmenopausal patients. The IPAQ-SF is a widely used questionnaire to determine physical activity levels in various populations. It not only classifies physical activity levels in the last 7 days as vigorous activity, moderate activity and walking, but also records the sitting times of individuals (9). According to the formula proposed by Ainsworth et al. (10) the data were converted to Metabolic Equivalent minutes per week (MET-min/week). MET values are calculated as 3.3 METs for walking, 4.0 METs for moderate physical activity and 8.0 METs for vigorous physical activity The participants were classified as inactive, minimally active and sufficiently active according to the total values of all results (11).

Serum 25(OH)D3 levels of all participants were analyzed and vitamin D status was classified as <10 ng/mL: vitamin D deficiency, 10-20 ng/mL: vitamin D insufficiency, >20 ng/mL: sufficient level for bone health, and 30-50 ng/mL: sufficient level for extra-bone activity (12).

The study was initiated after ethical approval and a written informed consent was obtained from all participants. It was conducted in accordance with the principles of the Declaration of Helsinki.

Statistical Analysis

All statistical analyses were performed by using IBM SPSS 22 (IBM Corp., Armonk, N.Y., USA). Data were presented as mean±standard deviation for continuous variables and count (n) and percentage (%) for categorical variables. Normality of variables was confirmed with the Kolmogorov-Smirnov test. Vitamin D and IPAQ values were compared with Student's t-test between two groups. For the variables which were not normally distributed, Mann-Whitney U test was used. For comparison of three or more groups Kruskal Wallis-H test was used and Dunn's test was applied as a post-hoc test. While determining the relations between Vitamin D and IPAQ or BMI, Spearman correlation coefficient was used. For graphical presentations box-plot and scatter plots were used. A p-value<0.05 was considered to be statistically significant for all tests.

Results

A hundred postmenopausal patients (mean age: 61.6±9.5, age range, 45-92 years) and 40 healthy individual were included in the analysis. The demographic and clinical data of the participants are summarized in Table 1. The mean 25(OH) D3 level of the postmenopausal patients was determined as 18.9+10.0. The mean values of BMI and IPAQ score were

Table 1. Demographic and clinical characteristics of postmenopausal and premenopausal women					
		Postmenopausal patients (n=100)		**Control group (n=40)**	**p**
Age (Mean ± SD)		61.6±9.5		60.5±8.8	0.52
BMI (Mean ± SD)		27.9±5.2		26.2±4.9	0.07
IPAQ score (Mean ± SD)		316.1±370.4		545.304.2	<0.001
		n	**%**	**n**	**%**
Marital status	Married	90	90	32	80
	Single	10	10	8	20
Occupation	Out of home, indoor activity	5	5	8	5
	Field gardening (outdoor)	3	3	1	2.5
	Housewife	87	87	32	80
	Retired	5	5	5	8
	Unemployed	0	0	0	0
Way to work	On foot	4	50	1	2.5
	Special vehicle	0	0	0	0
	Public transport	4	50	4	10
	Sometimes by car, sometimes on foot	0	0	5	8
Education	Illiterate	14	14	10	25
	Primary school	73	73	14	35
	Secondary school	5	5	16	40
	High school	5	5	0	0
	University	3	3	0	0

BMI: Body mass index, IPAQ: International Physical Activity Questionnaire Short Form, SD: Standard deviation

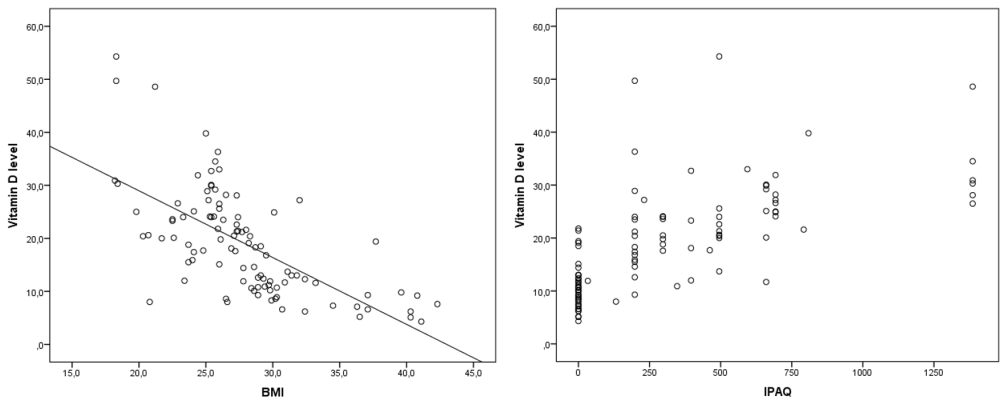

Figure 1. The correlation between 25(OH)D3 levels, BMI and IPAQ scores in postmenopausal patients
BMI: Body mass index, IPAQ: International Physical Activity Questionnaire Short Form

27.9±5.2 and 316.1±370.4 respectively. The postmenopausal patients' activity level was lower (p<0.001) when compared to the premenopausal control group's IPAQ score. The correlation between the postmenopausal patients' vitamin D levels and BMI, and IPAQ scores was statistically significant (Figure 1). Although BMI and vitamin D levels were negatively correlated, IPAQ scores and vitamin D levels were positively correlated (r: -0.698, p<0.001 for BMI; r: 0.777, p<0.001 for IPAQ). Additionally, multiple comparisons of BMI subgroups were found statistically significant and the results are summarized in Table 2.

There was no significant correlation between marital status, occupation and education level, and both vitamin D levels and IPAQ scores. Vitamin D levels were greater in those who used calcium or vitamin D supplements, as was expected. Additionally, individuals who took calcium or vitamin D supplements had statistically significantly higher IPAQ scores. Similarly, the amount of consumption of foods containing vitamin D contributed positively to vitamin D levels and IPAQ scores. The association of vitamin D and IPAQ scores with sunlight exposure time, exposure intervals to sunlight, and sunlight exposure were investigated. The results are shown in Table 3.

Table 2. Comparisons of BMI subgroups in terms of 25(OH)D3 levels and IPAQ scores in postmenopausal patients

		Mean 25(OH)D3±SD	p	Mean IPAQ±SD	p
BMI	<18.5: Weak	41.3±12.4	**<0.001**	866±612	**<0.001**
	18.5-24.9: Normal weight	22.1±8.9		485±307	
	25-29.9: Overweight	20.2±7.9		326±362	
	30-39.9: Obese	11.6±5.9		114±229	
	>40: Morbid obese	6.4±1.9		0	

BMI: Body mass index, IPAQ: International Physical Activity Questionnaire Short Form, SD: Standard deviation

Table 3. The association between 25(OH)D3 levels, IPAQ scores and other factors in postmenopausal patients

Mean		25(OH)D3		p Mean	IPAQ		p
		SD			SD		
Marital status	Married	18.8	10.2	0.418	310.6	367.9	0.546
	Single	20.6	8.3		366.3	409.7	
Occupation	Out of home (indoor)	13.9	9.4	0.192	346.6	600.2	0.179
	Field gardening (outdoor)	23.8	3.6		495.0	198.0	
	Housewife	19.4	10.2		321.9	367.8	
	Retired	14.2	9.1		79.2	108.4	
Education	İlliterate	18.3	8.7	0.694	310	294.3	0.753
	Primary school	19.6	10.3		327.5	379.3	
	Secondary school	13.1	9.2		198	305.1	
	High school	18	12		158.4	258.2	
	Bachelor's degree	19.3	10		528	749.6	
Calcium supplement intake	Yes	35.1	12	**<0.001**	630	520.2	**<0.001**
	No	17.0	7.7		277.4	331.3	
Vitamin D supplement intake	Yes	39.0	8,7	**<0.001**	823.4	515.5	**<0.001**
	No	16.8	7.3		259.8	306.0	
Daily vitamin D consumption	Little	16.8	7.3	**<0.001**	233.2	249.7	**<0.001**
	Moderate	31.6	12.8		685.4	537.4	
	Very	33.6	6.7		1193.7	333.1	
Sunlight exposure hours	Less than 15 minutes	14.6	6.6	**<0.001**	191.6	274.4	**<0.001**
	15 minutes-60 minutes	24.7	10.8		492.4	416.3	
	Over 60 minutes	25.0	11.0		465.7	430.2	
Sunlight exposure intervals	06:00-09:00	18.6	10.3	**<0.001**	240.9	240.4	**0.012**
	09:00-12:00	28.5	10		553.8	468.9	
	12:00-15:00	22.9	9.4		419.8	440,0	
	15:00-18:00	14.3	6.8		225.6	309.5	

25(OH)D3: 25 hydroxyvitamin vitamin D, IPAQ: International Physical Activity Questionnaire, SD: Standard deviation

Discussion

Previous studies have demonstrated that vitamin D deficiency increases in the postmenopausal period and hormonal changes, and BMI can affect vitamin D levels in the postmenopausal women (7). This study aimed to raise awareness of patients in the early period by investigating the factors affecting vitamin D levels in postmenopausal women. BMI, physical activity levels, sunlight exposure hours, and sunlight exposure intervals all affect vitamin D levels in postmenopausal women, according to the results of this study. Vitamin D insufficiency has been linked to several chronic conditions including obesity and low plasma 25(OH)D3 concentrations have been shown as a modest mediator of obesity. An inverse connection has been reported between vitamin D and BMI >30 kg/m^2 (13). However, the role of vitamin D metabolites in regulating obesity-related disorders remains unclear (14). The ability of vitamin D to modulate gene

expression linked to the adipogenesis process, inflammation, oxidative stress, and metabolism in adult adipocytes might be one proposed molecular explanation for the association between obesity and vitamin D deficiency (15). Moreover, Weishaar et al. (16) stated that a probable effect of dilution owing to body size has been proposed to explain the link between low vitamin D status and obesity. As a result, it's been hypothesized that oral vitamin D may be able to treat vitamin D insufficiency in obese subjects, but that greater dosages may be needed Wortsman et al. (17) Conducted a study to assess the bioavailability of vitamin D in obese individuals and found that obese people exhibited considerably lower basal 25(OH)D3 levels and significantly higher parathyroid hormone levels than age-matched healthy controls. They also revealed that 24 hours after exposure to ultraviolet-B irradiation, obese participants had a 57% lower increase in vitamin D levels than non-obese people. On the other hand, another study found that obese people with hypovitaminosis D benefit more from vitamin D replacement than normal weight controls, implying that obese people with vitamin D insufficiency may benefit more from vitamin D replacement than normal weight controls (18).

Physical exercise is defined as a practical way to elevate vitamin D levels, especially when performed outside. The combination of ultraviolet light with 7-dehydrocholesterol in the skin enhances vitamin D production during regular outdoor physical exercises. The indoor physical activity may also increase vitamin D levels through other biological pathways. There is evidence that regular exercise can increase vitamin D's anti-inflammatory action and its low status in postmenopausal women. Based on the available data, regular exercise can improve anti-inflammatory effects of vitamin D and its deficiency in postmenopausal women (19,20). Several studies have found that higher levels of physical activity are linked to higher levels of serum 25(OH)D3 in line with our results (21,22). Tanabe et al. (23) examined the relationship between 25(OH)D3 status and activities of daily living in the elderly hospitalized patients at a regional care hospital. Low 25(OH)D3 levels were linked to lower daily living activity scores, suggesting that vitamin D insufficiency may have an impact on physical activity. The majority of hospitalized elderly patients were vitamin D deficient. Similarly, a prospective long-term study of Scott et al. (24) and colleagues demonstrated a favorable relationship between changes in serum 25(OH)D3 and physical activity measured by accelerometry-irrespective of sun exposure. This observed association was attributed to beneficial changes in body composition such as adiposity and skeletal muscle mass as a result of physical exercise. Hansen et al. (25) used the Physical Activity Rating Questionnaire to evaluate physical activity in forensic inpatients and showed that individuals with a vitamin D level over 75 nmol/L engaged in considerably more physical activity than those with a vitamin D level below 46.7 nmol/L. In contrast, another relevant study showed no relationship with serum 25(OH)D3 concentration and weekly physical activity assessed by IPAQ (26). Similarly, in the study of Sun et al. (27) serum 25(OH)D concentrations were not significantly associated with vitamin D intake.

Osteoporosis risk can be reduced by adopting a healthy lifestyle that includes adequate levels of dietary calcium, vitamin D and physical activity (28). This study has confirmed that vitamin D deficiency is common and associated with BMI, sunlight exposure hours, sunlight exposure intervals and physical activity in postmenopausal women. The results of this study may have important clinical implications for postmenopausal women with inadequate vitamin D levels. Vitamin D intake should be emphasized for those with limited sun exposure, which remains an important determinant of vitamin D status in postmenopausal women as well as dietary factors.

Study Limitations

A limitation of this study could be explained by the cross-sectional study design and numerous factors that may influence physical activity levels. Furthermore, another limitation is that due to the study design and no cause-effect relationship could be determined between physical activity and vitamin D status. Studies with larger sample sizes will be required in future studies.

Conclusion

Adequate vitamin D levels and lifestyle factors may positively affect functions, muscle and bone mass in postmenopausal women. To this regard, vitamin D and calcium supplementation combined with regular physical activity should be included in the treatment of postmenopausal women. There is also a need to educate postmenopausal women about the optimal sun exposure hours and duration.

Ethics

Ethics Committee Approval: Approval for the study was granted by the Erzincan Binali Yıldırım University Clinical Research Ethics Committee (decision no: 10, date: 27.09.2021).

Informed Consent: Consent form was obtained from all patients participating in the study.

Peer-review: Internally peer-reviewed.

Authorship Contributions

Concept: E.E.E., Design: E.E.E., Data Collection or Processing: E.E.E., Analysis or Interpretation: E.E.E., G.S., Literature Search: E.E.E., G.S., Writing: E.E.E., G.S.

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Assessment of the Relationship Between Osteoporosis, Metabolic Syndrome and Physical Activity Level in Postmenopausal Women

Postmenopozal Kadınlarda Osteoporoz, Metabolik Sendrom ve Fiziksel Aktivite Düzeyleri Arasındaki İlişkinin Değerlendirilmesi

Zeynep Tuba Bahtiyarca, Azize Serçe*

University of Health Sciences Turkey, Dışkapı Yıldırım Beyazıt Training and Research Hospital, Clinic of Physical Medicine and Rehabilitation, Ankara, Turkey

*University of Health Sciences Turkey, Ankara Training and Research Hospital, Clinic of Algology, Ankara, Turkey

Abstract

Objective: This study aimed to investigate the relationship between osteoporosis, metabolic syndrome (MetS), and physical activity (PA) levels in postmenopausal women. The secondary aim was to evaluate the quality of life in postmenopausal women who were diagnosed with and without MetS.

Materials and Methods: One hundred fifteen postmenopausal women participated in this study. Biochemical parametersand bone mineral density (BMD) at the femoral neck and lumbar spine were measured. The MetS was diagnosed using the definitions of the Adult Treatment Panel III and the National Cholesterol Education Program. The PA level was determined using the International Physical Activity Questionnaire-Short Form (IPAQ-SF). The Questionnaire of the European Osteoporosis Foundation for the Quality of Life (QUALEFFO-41) was used to assess health-related quality of life (HRQoL).

Results: With respect to the classification of the World Health Organization, 66 (57.3%) women had osteoporosis and 49 (43.7%) women had osteopenia. MetS was present in 32 women (27.8%). According to IPAQ-SF, 27 (23.5%) women were inactive, 74 (64.3%) women were minimally active, and 14 (12.2%) women were highly active. There was no statistically significant relationship between MetS and PA levels in postmenopausal women ($p>0.05$). A statistically significant difference in BMD measurements was found between groups with and without MetS ($p<0.05$). Additionally, QUALEFFO-41 scores were similar between the two groups ($p>0.05$).

Conclusion: MetS was associated with greater BMD at the spine and hip in postmenopausal women, indicating that MetS has a bone-protective impact. Notwithstanding, PA level and HRQoL were similar between postmenopausal women with and without MetS.

Keywords: Postmenopausal osteoporosis, physical activity, metabolic syndrome

Öz

Amaç: Bu çalışmanın amacı, postmenopozal kadınlarda osteoporoz, metabolik sendrom (MetS) ve fiziksel aktivite (PA) düzeyi arasındaki ilişkiyi araştırmaktır. Sekonder amacı ise MetS tanısı olan ve olmayan postmenopozal kadınların yaşam kalitesini değerlendirmektir.

Gereç ve Yöntem: Bu çalışmaya 115 postmenopozal kadın katılmıştır. Femur boynu ve lomber omurga kemik mineral yoğunluğu (KMY) ve biyokimyasal parametreler ölçülmüştür. MetS, Yetişkin Tedavi Paneli III ve Ulusal Kolesterol Eğitim Programı tarafından belirlenen kriterler kullanılarak teşhis edilmiştir. PA seviyesi, Uluslararası Fiziksel Aktivite Anketi Kısa Formu (IPAQ-SF) kullanılarak belirlenmiştir. Avrupa Osteoporoz Vakfı Yaşam Kalitesi Anketi (QUALEFFO-41) sağlıkla ilgili yaşam kalitesini (HRQoL) değerlendirmek için kullanılmıştır.

Bulgular: Dünya Sağlık Örgütü sınıflamasına göre 66 (%57,3) kadında osteoporoz, 49 (%43,7) kadında osteopeni vardır. Otuz iki kadında (%27,8) MetS mevcuttur. IPAQ-SF'ye göre 27 (%23,5) kadın inaktif, 74 (%64,3) kadın minimal aktif, 14 (%12,2) kadın oldukça aktiftir. Postmenopozal kadınlarda MetS ile PA düzeyi arasında istatistiksel olarak anlamlı bir ilişki saptanmamıştır ($p>0,05$). MetS grubu ile non-MetS grubu arasında kemik mineral yoğunluğu (KMY) ölçümlerinde istatistiksel olarak anlamlı fark bulunmuştur ($p<0,05$). Ayrıca QUALEFFO-41 skorları iki grup arasında benzerdir ($p>0,05$).

Sonuç: Postmenopozal kadınlarda MetS'nin omurga ve kalçada daha fazla KMY ile ilişkili olması MetS'nin kemik üzerine koruyucu etkisi olduğunu göstermektedir. Bununla birlikte, MetS olan ve olmayan postmenopozal kadınlar arasında PA düzeyi ve HRQoL benzerdir.

Anahtar kelimeler: Postmenopozal osteoporoz, fiziksel aktivite, metabolik sendrom

Address for Correspondence/Yazışma Adresi: Zeynep Tuba Bahtiyarca MD, University of Health Sciences Turkey, Dışkapı Yıldırım Beyazıt Training and Research Hospital, Clinic of Physical Medicine and Rehabilitation, Ankara, Turkey
Phone: +90 312 596 29 94 **E-mail:** drztb@hotmail.com **ORCID ID:** orcid.org/0000-0002-3630-2524
Received/Geliş Tarihi: 31.05.2022 **Accepted/Kabul Tarihi:** 11.08.2022

Introduction

Osteoporosis is a systemic skeletal disease characterized by tissue degeneration and loss of bone mass, resulting in increased fracture risk and bone fragility (1). More than 200 million people worldwide are thought to be affected by this disease (2). Osteoporosis is becoming more common as people get older all over the world, including Turkey. The prevalence of osteoporosis in Turkish women over the age of 50 is 12.9 percent (3). Fragility fractures with low-energy trauma are the most important clinical outcome of osteoporosis (4). More than 40% of postmenopausal women are expected to experience a fracture at some time in their lives (5).

A healthy and balanced diet and regular physical activity (PA) are important contributors to bone health (6). External factors such as exercise help increase bone mass during adolescence and childhood, peaking in the third decade of life. After menopause, women's bone mass normally reduces by 2.5 percent and 0.5 percent respectively, each year. In elderly people, bone mass cannot be acquired with PA, however, bone loss can be avoided (7,8). On the other hand, continuous PA is beneficial to bone tissue and helps prevent bone loss (9). Falls may increase due to decreased mobility and physical ability as people get older, especially if they have osteoporosis. Exercise is a good way to reduce osteoporosis and fractures caused by aging (10).

Metabolic syndrome (MetS) is a serious health problem that affects 41.5 percent of postmenopausal women, according to studies from different nations (11). High insulin levels in the blood, excessive blood pressure, increased triglyceride levels, excessive fat levels around the waist, and poor high density lipoprotein (HDL) cholesterol are all symptoms of MetS (12). Observational data from systematic reviews and meta-analysis demonstrated a close relation between prolonged inactivity, lower PA levels, and an increased risk of developing MetS (13,14). The relationship between MetS and PA level in adults has been evaluated in many studies. However, the number of studies investigating this relationship in postmenopausal women is limited. Thus, the aim of this research is to assess the relationship between osteoporosis, PA level and MetS in postmenopausal women.

Materials and Methods

Subjects and Study Design

This cross-sectional study was carried out in the physical medicine and rehabilitation department of a state hospital between March 2019 and March 2020. A total of 115 postmenopausal women who were applied to the outpatient clinic for initial osteoporosis evaluation or annual check-ups were involved in the study. All participants gave their informed consent. Inclusion criteria accepted as all postmenopausal women with at least one year of menopausal experience who were referred to outpatient clinic for bone mineral density (BMD) test and agreed to participate in this study. Subjects were ruled out of the study if they (1) were significantly cognitively disabled and unable to follow instructions, (2) were terminally sick, or (3) refused to take part. MetS criteria were used to separate the participants into two groups. The MetS group (n=32) comprised individuals who had been diagnosed with MetS, whereas the non-MetS group (n=83) included those who had not been diagnosed with MetS. We followed the Declaration of Helsinki for the protocols of the researh, and the Local Ethics Committee of Malatya Clinical Research (decision no: 2019/124, date: 03.07.2019) confirmed the study.

Descriptive Data and Demographic Variables

The following variables were recorded: age, educational and marital status, parity, time since menopause (years), menopause (natural/surgical) type, body mass index (BMI), height, weight, smoking habits (yes/no), alcohol intake 3 or more units/day (yes/no), osteoporosis treatment (yes/no), systemic glucocorticoid use >3 months and ≥5 mg/day (yes/no), previous peripheral fracture (yes/no),previous spinal fracture (yes/no), history of hip fracture in parents (yes/no), rheumatoid arthritis (yes/no), secondary osteoporosis (yes/no), pain level last week by score between 0 and 10 on visual analog scale and comorbidities. Fragility fracture risks of the subjects were assessed using the Fracture Risk Assessment Tool (FRAX) which is a software that computes a ten-year risk of major osteoporotic fracture (wrist, humerus, spine, or hip fracture) and a ten-year risk of hip fracture.

Anthropometric Assessments and Laboratory Testing

Blood biochemical tests including fasting blood glucose, HDL cholesterol, triglycerides, 25-hydroxyvitamin D (3), serum electrolytes, parathormone, thyroid-stimulating hormone were requested from all subjects. The waist circumference of the participants was measured with a flexible tape measure while the subjects were standing in an upright stance with feet together, wearing minimal clothing. The blood pressure of the participants was measured by a nurse in the clinic while the patient was in a sitting position after resting. Body weights and heights of the participants were measured in light indoor attire without shoes. BMI was calculated by dividing weight in kilograms by the square of the height in meters.

Assessment of Osteoporosis

Osteoporosis was defined on the basis of BMD assessments. BMD was examined at the femoral neck and lumbar spine utilising X-ray absorptiometry with dual-energy (Discovery A series, Hologic QDR). The BMD results were categorized using World Health Organization (WHO) standards. Women with a T-score of -2.5 or less at the femoral neck or lumbar spine were classified as having osteoporosis according to WHO criteria. Women with a T-score between -1 and -2.5 were classified as having osteopenia and more than -1 were classified as healthy (15).

Assessment of MetS

Adult Treatment Panel III (ATP III) of the National Cholesterol Education Program (NCEP) was used to diagnose MetS.

Patients were diagnosed with MetS if they had three or more of abnormalities listed below: abdominal obesity (waist circumference >88 cm), high blood pressure: (systolic blood pressure ≥135 mmHg and/or diastolic blood pressure ≥85 mmHg, or if they were on anti-hypertensive medications), hypertriglyceridemia: (serum triglyceride level ≥150 mg/dL), low HDL-cholesterol <50 mg/dL, high fasting blood glucose (≥110 mg/dL, or if they were on anti-diabetic medications) (16).

Assessment of PA Level

PA level was measured using the International Physical Activity Questionnaire-Short Form (IPAQ-SF). This self-report questionnaire evaluates PA in the last seven days. This seven-question survey examines how much walking you did in the previous week, as well as how much moderate and severe PA you did at work, in transportation, at home, in the garden, and in leisure activities. On weekdays and weekends, sitting times are recorded individually. When PA is classified, it is divided into three categories: "inactive", "minimally active", and "highly active". The IPAQ-SF is mostly used as a measure of PA and is reported to have excellent reliability, its validity against objective measures of PA is questioned by Lee et al. (17,18). Saglam et al. (19) conducted validity and reliability studies on the Turkish version of the questionnaire.

Assessment of Health Related Quality of Life (HRQoL)

The Questionnaire of the European Foundation for Osteoporosis Quality of Life (QUALEFFO-41) was used to assess HRQoL. It is a self-reported, disease-specific, quality of life questionnaire with 41 items/questions separated into 5 parts: mental function, perception of general health, social function, physical function, and pain. Those five parts can be evaluated either individually or as part of a total result that includes all of the 41 questions (20).

Statistical Analysis

Using the G* Power (V3.1.7) tool, a total of 32 patients were identified as the minimum size for each group, with d=0.72, 80 percent power, and α =0.05. The sample size was also in line with past research (12). SPSS 20.0 was used to conduct the statistical analysis which is developed by IBM Corporation (Chicago, IL). Categorical variables, as well as, other discrete and continuous variables were represented in percentage and number, and median (min-max) respectively, while variables with normal distribution were represented in mean ± standard deviation. Kolmogorov-Smirnov test was used for data distribution analysis. Continuous and non-parametric variables were compared using the Mann-Whitney U test. Fisher's exact test and chi-square tests were used for comparison of categorical variables. With a type-I and type-II error of 5% and 20%, respectively, a p-value of less than 0.05 was found to be significant statistically.

Results

A total of 115 postmenopausal women included in this study. There were 66 (57.3%) women with osteoporosis and 49 (42.7%) women with osteopenia among them. Thirty-two (27.8%) women had MetS determined by the NCEP-ATP III. The mean age of the participants was 68±8.59, with a range of 46 to 90 years. On average, the participants were overweight, with a mean BMI of 31.2±6.09. According to IPAQ-SF, 27 (23.5%) women were inactive, 74 (64.3%) women were minimally active, and 14 (12.2%) women were highly active. Table 1 and Table 2 compare results from anthropometric data and cardiometabolic variables between women with and without MetS, respectively. Variables including BMD lumbar spine (L1-L4) T-scores, diastolic blood pressure, systolic blood pressure, waist circumference, BMI, mean body weight, and femoral neck T-scores were significantly lower in the non-MetS group than the MetS group ($p<0.05$) as shown in Table 1 and 2. When the FRAX values of the two groups were analyzed, the non-MetS group had a greater 10-year risk of major osteoporotic fracture ($p<0.05$). The 10-year risk of hip fracture was similar between the two groups ($p>0.05$). The non-MetS group also had a greater ratio of previous peripheral fractures ($p<0.05$). With regard to blood biochemical values, as summarized in Table 2, uric acid, fasting blood glucose, triglyceride levels were significantly higher and HDL cholesterol was significantly lower in the MetS group compared to the non-MetS group ($p<0.05$). For both disease-specific and general HRQoL instruments, there was no statistically significant difference between the groups across all subscales ($p>0.05$), as shown in Table 3. Furthermore, according to IPAQ-SF, there was no difference in PA levels between the MetS and non-MetS groups, as shown in Table 4 ($p>0.05$).

Discussion

The aim of this study was to determine the link between osteoporosis, MetS, and PA levels in postmenopausal women, as well as their impact on quality of life. Postmenopausal women with MetS had increased BMD at the spine and hip, according to the findings of this study. However, postmenopausal women with and without MetS had similar PA levels and HRQoL scores. In this research, the prevalence of MetS was determined to be 27.8%, which was lower than the prevalence of MetS reported in a Turkish survey in 2004 (percentage 41.1), but closer to the MetS prevalence in the overall population (percentage 33.8) (21). Obesity, determined as a BMI of 25 to 39.9 kg/m², is frequent in postmenopausal women. According to Silva et al. (22), roughly half of postmenopausal women are overweight or obese. BMI and body fat tissue mass are higher in postmenopausal women than in perimenopausal women, according to previous research (23). In this study, the mean BMI was over 30 kg/m² in both groups (34.3±6.63 vs. 30.05±5.47). Obesity is on the rise for a variety of reasons, including unhealthy nutrition habits and a sedentary lifestyle (24).

Studies have shown that the frequency of low PA levels in the people aged 15 and over ranges from 2.6 percent to 62.3 percent (25). According to IPAQ-SF, 23.5 percent of the individuals in this study had low PA levels, whereas 64.3 percent of the subjects

Table 1. Comparison of demographic and anthropometric characteristics between MetS and non-MetS group

Variables	MetS group (n=32)	Non-MetS group (n=83)	p-value
Age (years), mean ± SD	67.61±8.39	68.06±8.92	0.243
Weight (kg), mean ± SD	82.97±14.98	70.53±13.89	**<0.001***
Height (cm), mean ± SD	156.66±6.8	154.34±6.2	0.083
BMI (kg/cm²), mean ± SD	34.3±6.63	30.05±5.47	**0.001***
Marital status, N (%)			
Single	1 (33.3)	2 (66.7)	
Married	31 (27.7)	81 (72.3)	0.999#
Education level, N (%)	21 (34.4)	40 (65.6)	
Unschooled	11 (23.9)	35 (76.1)	0.190
Primary school			
High school	-	6 (100)	
University	-	2 (100)	
Number of pregnancies, median (min-max)	5 (1-11)	5 (0-10)	0.770
Type of menopause, N (%)			
Natural	28 (29.2)	68 (70.8)	0.583#
Surgical	4 (21.1)	15 (78.9)	
Duration of menopause (years), median (min-max)	22 (10-49)	21 (1-42)	0.651
Chronic diseases**, N (%)			
Yes	26 (32.1)	55 (67.9)	
No	6 (17.6)	28 (82.4)	0.171#
Rheumatoid arthritis, N (%)			
Yes	-	3 (100)	
No	32 (28.6)	80 (71.4)	0.559#
Secondary osteoporosis, N (%)			
Yes	-	5 (100)	
No	32 (29.1)	78 (70.9)	0.320#
History of spinal fracture, N (%)			
Yes	4 (25)	12 (75)	
No	28 (28.3)	71 (71.7)	0.999#
History of peripheral fracture, N (%)			
Yes	4 (13.3)	26 (86.7)	
No	28 (32.9)	57 (67.1)	**0.039#***
History of hip fracture in parents, N (%)			
Yes	2 (28.6)	5 (71.4)	
No	30 (27.8)	78 (72.2)	0.999#
Previous or current osteoporosis medication, N (%)			
Yes	14 (23)	36 (66.7)	
No	18 (33.3)	36 (66.7)	0.302#
Smoking, N (%)			
Yes	-	5 (100)	
No	32 (29.1)	78 (70.9)	0.320#
Alcohol intake (3 or more units/day), N (%)			
Yes	-	-	
No	32 (100)	83 (100)	-
Steroid use >3 months and ≥5 mg/day, N (%)			
Yes	1 (33.3)	2 (66.7)	
No	31 (27.7)	81 (72.3)	0.999#
Visual analog scale, median (min-max)	30 (0-80)	40 (0-70)	0.070
Bone mineral density, median (min-max)			
Lumbar spine (L1-L4) T-score	-2.05 (-3.7-1.2)	-2.7 (-4.8-0.2)	**0.014***
Femoral neck T-score	-2.20 (-4.50-0.20)	-1.50 (-2.40-0.10)	**0.030***
FRAX, median (min-max)			
10-year risk of major osteoporotic fracture	9.75 (3.1-42)	13 (4.2-42)	**0.041***
10-year risk of hip fracture	1.6 (0.2-29)	2.2 (0.8-33)	0.206

BMI: Body mass index, FRAX: Fracture risk assessment tool, MetS: Metabolic syndrome, SD: Standard deviation
Values are mean ± SD, median (min-max) or percentage (n, %)
*p-values are statistically significant (p<0.05) are shown in bold
**Chronic diseases include hypertension, diabetes mellitus, hypotyroidism, coronary heart disease

Table 2. Comparison results from cardiometabolic variables and biochemical blood tests between MetS and non-MetS group

Variables	MetS group (n=32)	Non-MetS group (n=83)	p-value
Waist circumference (cm)	100 (70-135)	83 (60-151)	**<0.001***
SBP (mm/hg)	140 (110-160)	120 (110-150)	**<0.001***
DBP (mm/hg)	80 (70-95)	75 (60-90)	**<0.001***
Fasting blood glucose (mg/dL)	106 (87-435)	93 (61-329)	**<0.001***
HDL-C (mg/dL)	43 (29.32-71)	51 (33-77)	**<0.001***
Triglyceride (mg/dL)	172 (74-750)	110 (57-312)	**<0.001***
25(OH)D3 (ng/mL)	13.8 (3-38)	16.4 (3-42)	0.079
Calcium (mg/dL)	9.40 (8.50-10.48)	9.51 (8.00-11.32)	0.263
Phosphate (mg/dL)	3.425 (2.5-4.91)	3.4 (2.05-5.37)	0.446
TSH (mlU/L)	1.4 (0.015-6.29)	1.5 (0.02-34.66)	0.769
PTH (pg/mL)	55.5 (18-95)	52.3 (22.7-209)	0.753
Uric acid (mg/dL)	5.1 (2.2-10.6)	4.2 (0.6-10.1)	**<0.001***

SBP: Systolic blood pressure, DBP: Diastolic blood pressure, HDL-C: High-density lipoprotein cholesterol, TSH: Thyroid-stimulating hormone, PTH: Parathormone, 25(OH) D3: 25-hydroxyvitamin D3, MetS: Metabolic syndrome
Values are median (min-max) *p-values with statistical significance (p<0.05) are shown in bold

Table 3. Comparison of physical activity distribution between MetS and non-MetS group

IPAQ-SF	MetS group (n=32)	Non-MetS group (n=83)	p-value
Inactive	8 (29,6)	19 (70,4)	0.483
Minimally active	22 (29.7)	52 (70.3)	
Highly active	2 (14.3)	12 (85.7)	

IPAQ-SF: International physical activity questionnaire short form, MetS: Metabolic syndrome
Values are percentage (n, %)

had moderate PA levels. In terms of PA levels, subjects with and without MetS both had a similar phenotype. MetS and PA levels in postmenopausal women were not found to have a significant relationship in this study (p>0.05). These results also showed that postmenopausal women with and without MetS had low-to-moderate PA levels. The link between PA level and MetS in adults has been studied extensively in the literature. In a study by Kazaz I et al. (26), PA level was evaluated in adults, and it was found that almost 81 percent of people with MetS were inactive. Frugé et al. (27) found in their study that patients with MetS were less active than patients without MetS. In a different research by Petersen et al. (28), it was found that when compared to active persons, those who were inactive in their leisure time had a greater risk of MetS. In this study, most of the subjects lived in rural areas. They were mostly occupied with farming and agriculture. As a result, the percentage of physically inactive people was found to be less than in previous studies. MetS is more likely in people stressed, having insufficient PA, and with unhealthy nutrition habits (26). In this study, subjects with and without MetS were overweight, with a mean BMI of 31.2±6.09. Therefore, MetS is thought to develop in these people mainly due to unhealthy nutrition habits. It is thought that this is why the difference with the literature in this study. In addition, the difference from the literature may be a result of the limited number of patients.

MetS is a heterogeneous syndrome composed of multiple disorders, each of which has its own unique impact on the metabolism of bone. Greater leptin levels and lower adiponectin, for instance, may affect bone metabolism in people with central obesity, since high levels of leptin and adiponectin have been linked to bone loss in a recent meta-analysis (29). Some studies have showed that adipose tissue causes proinflammatory cytokines, including TNF-alfa, IL-6 and/or IL-1, which are associated with bone loss (30,31). von Muhlen et al. (32) observed the presence of the relationship between lower BMD and MetS. In a cross-sectional research, the mean vertebral BMD of 2475 Korean women was substantially lower in women with MetS, and in the mean vertebral BMD considerably decreased in the presence of other MetS-related factors (33). On the other hand, opposite results have also been reported. Numerous cross-sectional researches have shown a positive relation between BMD and MetS (34). MetS has a multifactorial influence on bone mass, as it is linked to hyperinsulinemia, peripheral aromatization, excess body weight, and mechanical loads (35). Xue et al. (36) found that unadjusted femoral neck and lumbar spine BMD values were greater in MetS participants in comparison to non-MetS participants in a meta-analysis (n=13.122, number of studies=11). The favorable benefits of MetS on bone mass might be attributed to the increased mechanical stress experienced by MetS patients, according to a three-year retrospective longitudinal research of 1,218 postmenopausal women examining annual BMD changes (37). Zhou et al. (35) found a possible gender difference in the

Table 4. Comparison results of QUALEFFO-41 scores between MetS and non-MetS group

QUALEFFO-41	MetS group (n=32)	Non-MetS group (n=83)	p-value
Pain (back pain, sleep disturbance)	29.58±21.23	35.07±19.61	0.191
Physical function and mobility (dressing, bathing, cleaning, cooking, washing, dishes, shopping, standing, bending, kneeling, stairs, walking, body image)	30.83±17.95	30.78±16.03	0.989
Social function (sports, gardening, hobby, friends)	47.03±20.99	52.63±20.12	0.189
General health perception	55.36±14.02	53.15±13.16	0.429
Mental function (fatigue, depression, energy, loneliness, cheerfulness, hope, fear)	42.49±12.05	40.85±13.48	0.549
Total score	53.11±34.14	59.86±52.84	0.505

QUALEFFO-41: The Quality of Life Questionnaire of the European Foundation for Osteoporosis, MetS: Metabolic syndrome
Values are mean ± SD. *p-values with statistical significance (p<0.05)

link between MetS and bone in a meta-analysis and showed that MetS is a risk factor for developing osteoporosis in males, but it might not be a reliable predictor of osteoporosis for women. Consistent with previous studies which found a positive association between MetS and BMD, significant differences in BMD were reported between subjects with and without MetS in this study, so it may be deduced that MetS doesn't have a detrimental effect on bone health in postmenopausal women. Furthermore, preventive mechanisms for bone density may play a larger role in this disease than the deleterious effects on BMD due to inflammation.

Obesity and metabolic disorders have a negative impact on HRQoL (38). HRQoL in postmenopausal women with osteoporotic fractures has been extensively reviewed in previous studies. Briefly, the individuals with multiple vertebral and hip fractures had lower HRQoL than those with a distal forearm or a single vertebral fracture. There are fewer researches that look at HRQoL in individuals with osteoporosis who don't have any fractures. Wilson et al. (39) observed that patients who does not have vertebral fracture had lower values in the QUALEFFO-41 and SF-36 areas than the control group in a systematic study. Several research have looked into the link between MetS and HRQoL, and the most of them have found a link between MetS and a decline in quality of life. However, several studies identified a relationship barely in women, or just when BMI or depression were factors (40). In the present study, the domains of QUALEFFO-41 (mental function, general health perception, social function, physical function, and pain) were similar in postmenopausal women with and without MetS. The difference from the literature may be due to the limited number of patients.

Study Limitations

The study has several limitations. Firstly, PA is a complicated health behavior that is difficult to evaluate. PA levels of the participants were measured using a questionnaire that included self-reported open-ended questions about their most recent 7-day recall of PA. An accelerometer, pedometer, or activity tracker was not used as a more objective assessment tool. As a result, the PA status reported by the participants, was not measurable. Secondly, because the study was conducted in a single center, the number of patients was limited.

Conclusion

Postmenopausal women with and without MetS are overweight and have low-to-moderate PA levels, according to the findings of this study. No significant correlation is observed between MetS and PA level in postmenopausal women. MetS and BMD have a positive relationship in postmenopausal women. More well-designed and comprehensive researches should be undertaken to confirm the link between osteoporosis, MetS, and PA level in postmenopausal women, given the inconsistent results in this field.

Ethics

Ethics Committee Approval: The study was carried out with the Malatya Clinical Research Ethics Committee (decision no: 2019/124, date: 03.07.2019).

Informed Consent: Informing all individuals participating in the research their consent was taken.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: Z.T.B., Concept: A.S., Design: A.S., Data Collection or Processing: Z.T.B., Analysis or Interpretation: Z.T.B., Literature Search: A.S., Writing: Z.T.B.

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Osteoporoz Tanılı Bireylerin Sağlık Okuryazarlığı Düzeyinin Belirlenmesi

Determination of Health Literacy Level in Individuals with Osteoporosis

Fatih Okan, Sevil Okan*

Tokat Gaziosmanpaşa Üniversitesi Sağlık Bilimleri Fakültesi, Halk Sağlığı Hemşireliği Anabilim Dalı, Hemşirelik Bölümü, Tokat, Türkiye
*Tokat Devlet Hastanesi, Fiziksel Tıp ve Rehabilitasyon Bölümü, Tokat, Türkiye

Öz

Amaç: Çalışmada osteoporoz tanılı bireylerin sağlık okuryazarlığı düzeyinin belirlenmesi amaçlandı.
Gereç ve Yöntem: Tanımlayıcı-Kesitsel tipteki çalışma Nisan 2021-Nisan 2022 tarihleri arasında osteoporoz tanılı 156 birey ile gerçekleştirildi. Veriler kişisel özellikler bilgi formu ve Türkiye Sağlık Okuryazarlığı Ölçeği-32 kullanılarak toplandı.
Bulgular: Çalışmaya dahil edilen bireylerin %48,1'inin (n=75) yetersiz, %23,1'inin (n=36) sorunlu-sınırlı, %17,3'ünün (n=27) yeterli, %11,5'inin (n=18) mükemmel sağlık okuryazarlığı düzeyinde olduğu tespit edildi. Sağlık okuryazarlığı toplam puan ortalamasının 65 yaş ve üzeri bireylerde 65 yaş altı bireylere göre; üniversite mezunu olanlarda ilkokul, ortaokul ve lise mezunlarına göre; geniş ailede yaşayanlarda çekirdek ailede yaşayanlara göre; il merkezinde yaşayanlarda ilçe merkezi ve köy/kasabada yaşayanlara göre; geliri giderine eşit ve geliri giderinden fazla olanlarda geliri giderinden az olanlara göre daha yüksek olduğu bulundu ($p<0,05$).
Sonuç: Osteoporoz tanılı bireylerin yaklaşık üçte ikisi sınırlı ya da yetersiz sağlık okuryazarlığı düzeyindedir. Sağlık profesyonelleri osteoporoz tanılı bireylerin sağlık okuryazarlığı düzeyini değerlendirmeli ve bunun sonucunda hastaya uygun bilgilendirme yöntemleri ve eğitim programları planlamalıdır.
Anahtar kelimeler: Osteoporoz, sağlık okuryazarlığı, TSOY-32

Abstract

Objective: The study aimed to determine the health literacy level of individuals diagnosed with osteoporosis.
Materials and Methods: A descriptive cross-sectional study was conducted with 156 individuals diagnosed with osteoporosis between April 2021 and April 2022. Data were collected using the personal information form and the Turkish Health Literacy Scale-32.
Results: It was determined that 48.1% (n=75) of the individuals included in the study had an inadequate, 23.1% (n=36) problematic-limited, 17.3% (n=27) adequate, 11.5% (n=18) excellent level of health literacy. It was found that the total mean score of health literacy was higher in individuals aged 65 and over compared with those under 65 years of age; individuals with university degrees, compared to primary, secondary, and high school graduates; individuals living in an extended family compared to those living in a nuclear family; individuals living in the city center, compared to those living in the district center and village/town; individuals whose income is equal to their expenses and income is more than their expenses than those whose income is less than their expenses ($p<0.05$).
Conclusion: Approximately two-thirds of individuals diagnosed with osteoporosis have limited or insufficient level of health literacy. Health professionals should evaluate the health literacy level of individuals with osteoporosis, and as a result, they should plan appropriate information methods and training programs for the patient.
Keywords: Osteoporosis, health literacy, THLS-32

Giriş

Sağlık okuryazarlığı toplumsal ve bireysel sağlığın önemli bir belirleyicisidir ve hasta merkezli bakımın temel unsuru olarak görülmektedir (1,2). Sağlık okuryazarlığı, uygun sağlık kararları vermek için ilgili sağlık bilgilerini elde etme, işleme ve anlama yeteneği olarak tanımlanır ve sınırlı sağlık okuryazarlığının küresel bir halk sağlığı sorunu olduğu bilinmektedir (3,4). Birçok hasta tıbbi durumlarını, ilaçlarını ve bakım talimatlarını yetersiz sağlık okuryazarlığı nedeniyle anlamakta güçlük çeker (5). Sınırlı sağlık

Yazışma Adresi/Address for Correspondence: Dr. Öğr. Üyesi, Fatih Okan, Tokat Gaziosmanpaşa Üniversitesi Sağlık Bilimleri Fakültesi, Halk Sağlığı Hemşireliği Anabilim Dalı, Hemşirelik Bölümü, Tokat, Türkiye
Tel.: +90 505 877 08 05 **E-posta:** fthokn@yahoo.com **ORCID ID:** orcid.org/0000-0002-7544-9051
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okuryazarlığına sahip hastalar, teşhis ve tedavi protokollerini yetersiz anlamakta ve bu da onları sağlık hizmetlerinin olası kötüye kullanımı ve daha kötü sonuçlar açısından risk altına sokmaktadır (4). Düşük sağlık okuryazarlığı seviyeleri, artan hastane başvuruları ve ölüm oranlarıyla da bağlantılıdır (6). Bunun aksine yüksek sağlık okuryazarlığı ise daha fazla sağlık bilgisi ve kendine güven ile ilişkilidir (7).

Osteoporoz, kemik kütlesinde ve mikromimarisinde sistemik bir bozulma ile karakterize, frajilite kırıklarına neden olan yaygın bir hastalıktır. Menopoz sonrası kadınların yaklaşık %40'ı osteoporozdan etkilenir ve bu sayının nüfusun yaşlanmasından sonra giderek artması beklenmektedir (8). Osteoporoz oldukça yaygındır, ancak genellikle sessiz bir hastalık olduğu için çoğu zaman yetersiz teşhis ve tedavi edilir (9). Hastalar genellikle kırık oluşana kadar hiçbir semptom göstermediklerinden, tedavi almaya değer olduğunu düşünmezler veya risk altında olduklarına inanmazlar (10). Tedaviye uyumsuzluğun önemli bir nedeni de yetersiz sağlık okuryazarlığı düzeyidir (11).

Çalışmada osteoporoz tanılı bireylerin sağlık okuryazarlığı düzeyinin belirlenmesi amaçlandı.

Gereç ve Yöntem

Tanımlayıcı-Kesitsel tipteki çalışma Dünya Sağlık Örgütü (DSÖ) kriterlerine göre Dual X-Işını absorbsiyometri (DXA) ile osteoporoz tanısı konulmuş 18 yaş üzeri 156 birey ile gerçekleştirildi. İletişim kurmayı engelleyecek mental, işitsel ve görsel problemi olanlar, ciddi sistemik hastalığı, osteoporoz dışında metabolik kemik hastalığı, malignitesi, majör psikiyatrik hastalığı, sekonder osteoporoza yol açacak kronik hastalığı olanlar çalışma dışında bırakıldı. Nisan 2021-Nisan 2022 tarihleri arasında Tokat Devlet Hastanesi Fiziksel Tıp ve Rehabilitasyon polikliniğine başvuran osteoporoz tanılı 204 bireyden, okuma-yazma bilmeyen 34, görme ve işitme sorunlarından dolayı iletişim kurulamayan 6, kanser tedavisi gören 5 birey ile çalışmaya katılmak istemeyen 3 birey çalışmaya dahil edilmedi. Çalışmanın yapılabilmesi için Tokat Gaziosmanpaşa Üniversitesi Klinik Araştırmalar Etik Kurulu'ndan (karar no: 21-KAEK-090, 01.04.2021) ve araştırmanın yapıldığı kurumdan gerekli izinler alındı. Çalışmaya dahil edilen bireylerin yazılı ve sözlü onamları alındı.

Veri Toplama Yöntemi

Nisan 2021-Nisan 2022 tarihleri arasında Tokat Devlet Hastanesi Fiziksel Tıp ve Rehabilitasyon polikliniğine başvuran ve osteoporoz tanısı olan veya yeni tanı alan bireylere muayeneleri bitiminde kişisel özellikler bilgi formu ve Türkiye Sağlık Okuryazarlığı Ölçeği-32 (TSOY-32) formu verildi ve gün içinde kendileri tarafından doldurulup getirmeleri istendi. Çalışmada en son yapılan kemik mineral yoğunluğu ölçümleri değerlendirildi.

Veri Toplama Araçları

Kişisel Özellikler Bilgi Formu: Araştırmacılar tarafından oluşturulan kişisel özellikler bilgi formu bireylerin, yaş, cinsiyet, medeni durum, çalışma, eğitim, sosyal güvenceye sahip olma, gelir durumu, hastalık, ilaç kullanma, yaşanılan yer, sigara ve alkol kullanımını sorgulayan toplam 15 sorudan oluşturuldu.

TSOY-32: TSOY-32, on beş yaş üzeri ve en az ilkokul mezunu olan kişilerde sağlık okuryazarlığını değerlendirmek amacıyla geliştirilmiş öz bildirim ölçeğidir. Ölçek, Avrupa Sağlık Okuryazarlığı Araştırma Konsorsiyumu (12) tarafından geliştirilen kavramsal çerçeveye dayanmaktadır. Ancak, TSOY-32, orijinal ölçekten farklı olarak, üç değil, iki temel boyut alınarak, 2X4'lük bir matrise dayanarak yapılandırılmıştır. Buna göre, matris iki boyut (tedavi ve hizmet; hastalıklardan korunma/sağlığın geliştirilmesi) ile dört süreç (sağlıkla ilgili bilgiye ulaşma, sağlıkla ilgili bilgiyi anlama, sağlıkla ilgili bilgiyi değerlendirme, sağlıkla ilgili bilgiyi kullanma/uygulama) olmak üzere toplam sekiz bileşenden oluşmaktadır. Ölçeğin Türkçe'de güvenirliği; iç tutarlık (Cronbach alfa) ile değerlendirilmiştir. Ölçeğin genel iç tutarlık katsayısı; 0,927 olarak saptanmıştır. Birinci boyut olan "Tedavi ve Hizmet Alt Boyutu"nun iç tutarlık katsayısı 0,880'dir. İkinci boyut olan "Hastalıklardan Korunma ve Sağlığın Geliştirilmesi Boyutu"nun iç tutarlık katsayısı 0,863'tür. Bu çalışmada genel iç tutarlık katsayısı 0,972; birinci boyut olan "Tedavi ve Hizmet Alt Boyutu"nun iç tutarlık katsayısı 0,957; ikinci boyut olan "Hastalıklardan Korunma ve Sağlığın Geliştirilmesi Boyutu"nun iç tutarlık katsayısı 0,949 bulundu.

Ölçeğin Türkçe geçerlilik ve güvenirliği Okyay ve ark. (13) tarafından yapılmıştır. Ölçekte 0 puan en düşük sağlık okuryazarlığını, 50 puan en yüksek sağlık okuryazarlığını göstermektedir. Sağlık okuryazarlığı düzeyi, elde edilen puana göre dört kategoride değerlendirilmiştir; 0-25 puan yetersiz sağlık okuryazarlığı, >25-33 puan sorunlu - sınırlı sağlık okuryazarlığı, >33-42 puan yeterli sağlık okuryazarlığı, >42-50 puan mükemmel sağlık okuryazarlığı.

Kemik Mineral Yoğunluğu Ölçümü (KMY): Lomber vertebra, femur boyun ve femur total bölgelerinin KMY T-skoru değerlendirmeleri DXA tekniği ile; Hologic Discovery 4500 QDR kullanılarak yapıldı. Osteoporoz tanısı DSÖ sınıflandırmasına göre yapıldı. T-skoru -1 ve üstünde olanlar normal, -1 ile -2,5 olanlar osteopeni, T-skoru -2,5 ve altında olanlar osteoporoz olarak kabul edildi (14). Femur boynu ve femur total T-skoru hesaplamasında referans değer olarak "National Health and Nutrition Examination Survey" III verileri, lomber vertebra T-skoru hesaplamasında ise üretici firma veri tabanı (Hologic database) kullanıldı.

İstatistiksel Analiz

Araştırmada elde edilen verilerin istatistiksel analizleri SPSS (Versiyon 22.0, SPSS Inc., Chicago, IL, USA) paket programı kullanılarak gerçekleştirildi. Tanımlayıcı istatistikler ortalama ± standart sapma, kategorik verilerin frekans dağılımları sayı ve yüzde (%) olarak raporlandı. Normallik dağılımı Kolmogorov–Smirnov testi ile incelendi. Sürekli değişkenler için bağımsız iki örneklem ortalama karşılaştırmalarında Mann-Whitney U testi kullanıldı. Sürekli değişkenlerin gruplar arası çoklu karşılaştırılmasında Bonferroni Düzeltmeli Kruskal-Wallis H testi kullanıldı. Parametreler arasındaki ilişkiyi saptamak için Spearman korelasyon analizi kullanıldı. İstatistiki anlamlılık düzeyi için $p<0,05$ olarak kabul edildi.

Bulgular

Çalışmada yaş ortalaması 63,62±8,78'dir (min:46- maks:88). Çalışmada 65 yaş ve üzeri bireylerin sağlık okuryazarlığı toplam puan ortalaması 65 yaş altı bireylere göre anlamlı olarak daha yüksek bulundu (sırasıyla 31,79±11,18, 21,11±11,41, p<0,001). Üniversite düzeyi eğitim seviyesinde olanları sağlık okuryazarlığı toplam puan ortalaması ilkokul, ortaokul ve lise düzeyi eğitim seviyesinde olanlara göre daha yüksek bulundu (p<0,001). Memur statüsünde çalışanların sağlık okuryazarlığı toplam puan ortalaması, ev hanımı, emekli ve çiftçi olanlara göre daha yüksekti (p<0,001). Geniş ailede yaşayanların sağlık okuryazarlığı toplam puan ortalaması, çekirdek ailede yaşayanlara göre anlamlı olarak daha yüksek saptandı (sırasıyla 30,16±11,63, 25,11±12,51 p=0,046). İl merkezinde yaşayanların sağlık okuryazarlığı toplam puan ortalaması ilçe merkezi ve köy/kasabada yaşayanların puan ortalamasına göre daha yüksek saptandı (p=0,004). Geliri giderinden az olanların sağlık okuryazarlığı toplam puan ortalaması 19,53±11,24, geliri giderine eşit 28,67±12,67 ve geliri giderinden fazla olanlara göre 26,46±10,50 daha düşük bulundu (p<0,001). Bireylerin sağlık okuryazarlığı toplam puan ortalaması cinsiyet, medeni durum ve sigara içme durumuna göre benzer bulundu (p>0,05) (Tablo 1).

Çalışmada sağlık okuryazarlığı ölçeği toplam puanı 26,18±12,47, sağlık okuryazarlığı ölçeği tedavi ve hizmet alt boyutu puan ortalaması 24,98±13,02, hastalıklardan korunma/sağlığın geliştirilmesi alt boyutu puan ortalaması 27,37±13,04 olarak bulundu (Tablo 2).

Kemik mineral yoğunluğu ölçümlerinden femur boynu T-skoru ortalması -1,47±1,00, femur total T-skoru ortalaması -1,29±1,11, lomber vertebra total T-skoru ortalması -2,79±0,69 olarak bulundu. Sağlık okuryazarlığı ölçeği toplam puanı ile femur boynu T-skoru ortalaması (r=-0,097), femur total T-skoru ortalaması (r=0,016), lomber vertebra total T-skoru ortalması (r=-0,125) arasında anlamlı korelasyon tespit edilmedi (p>0,05) (Tabloda gösterilmemiştir).

Çalışmaya dahil edilen bireylerin %48,1'inin (n=75) yetersiz sağlık okuryazarlığı, %23,1'inin (n=36) sorunlu-sınırlı sağlık okuryazarlığı, %17,3'ünün (n=27) yeterli sağlık okuryazarlığı, %11,5'inin (n=18) mükemmel sağlık okuryazarlığı düzeyine sahip olduğu tespit edildi (Şekil 1).

Tartışma

Çalışmada osteoporoz tanılı bireylerin %71,2'sinin yetersiz ya da sınırlı sağlık okuryazarlığı düzeyine sahip olduğu tespit edildi. İran'da 60 yaş üzeri 347 osteoporoz tanılı hasta ile gerçekleştirilen çalışmada sağlık okuryazarlığı, tedavi uyumu, kemik mineral yoğunluğu ve yaşam kalitesi arasındaki ilişki değerlendirilmiş ve hastaların çoğunun (%70) sağlık okuryazarlığı düzeyinin orta düzeyde olduğu; hastaların yanlızca %11,50'sinin sağlık okuryazarlığı düzeyinin yeterli olduğu tespit edilmiştir (15). Sağlık okuryazarlığı ile 3 yaygın kas-iskelet sistemi hastalığı (artrit ve alt tipleri, gut ve osteoporoz) arasındaki ilişkiyi değerlendiren bir başka çalışmada osteoproz tanılı bireylerin %70,4'ünün (n=159) sağlık okuryazarlığı düzeyinin yetersiz ve risk altında olduğu bulunmuştur (16). İsrail'de osteoporoz tanılı 303 kadının değerlendirildiği kesitsel çalışmada da bireylerin yaklaşık %75'inin sağlık okuryazarlığı düzeyi düşük ya da orta düzeyde saptanmıştır (17). Türkiye'de yapılan bir çalışmada ise toplumun %64,6'sının "yetersiz" (%24,5) veya "sorunlu" (%40,1) sağlık okuryazarlığı kategorilerinde olduğu görülmüştür (18). Sağlık Bakanlığı Sağlığın Geliştirilmesi Genel Müdürlüğü tarafından yürütülen Türkiye sağlık okuryazarlığı düzeyi ve ilişkili faktörlerin araştırıldığı çalışmada araştırmaya katılanların TSOY-32 ile saptanan sağlık okuryazarlığı düzeyinin %68,9'unun yetersiz ve sorunlu-sınırlı olduğu tespit edilmiştir (19). Osteoporozlu bireylerde tespit ettiğimiz sağlık okuryazarlığı düzeyi Türkiye'deki genel popülasyonla benzer oranlardadır. Fakat tedaviye uyum ve takip gerektiren, morbidite ile ilişkili osteoporozda yeterli sağlık okuryazarlığı düzeyine sahip bireylerin oranının artırılmasın gerektiğini düşünmekteyiz. Bulgularımızın aksine yaş ortalaması 53,7 olan Avusturalyalı bireylerde sağlık okuryazarlığının değerlendirildiği çalışmada ise katılımcıların %68,5'inin sağlık okuryazarlığı düzeyinin yüksek olduğu bildirilmiştir (20). Bu durum çalışmaya katılan Avusturalyalı bireylerin eğitim düzeylerinin ve gelir durumlarının yüksek olması ile ilişkili olabilir. Osteoporoz, hem erkekleri hem de kadınları etkileyen, morbidite ve mortalite ile ilişkili kronik bir hastalıktır (21). Kronik hastalığı olan kişilerde düşük sağlık okuryazarlığının etkisi önemlidir (22). Düşük sağlık okuryazarlığı seviyesinin daha az fiziksel aktivite yapma ve sigara içme gibi davranışların benimsenmesi ile de ilişkili olduğu tespit edilmiştir (23). Distal radius fraktürü tanılı hastaların sağlık okuryazarlığının sonraki osteoporoz tedavisine uyumu üzerindeki etkisinin değerlendirildiği bir çalışmada düşük enerjili travmanın neden olduğu distal radius fraktürü olan toplam 116 hastanın (kadın, 50 yaş üzeri) %19'unun (n=22) sınırlı sağlık okuryazarlığına; %33'ünün (n=38) ise potansiyel olarak sınırlı sağlık okuryazarlığına sahip olduğu görülmüştür (11). Bu nedenle çalışmamızda bireylerin önemli bir kısmında düşük tespit edilen sağlık okuryazarlığı düzeyinin osteoporoz tanılı hastalarda koruyucu olabilecek sağlıklı yaşam davranışlarının uygulanmasını engelleyebileceği, tedaviye uyumu etkileyebileceği göz önünde bulundurularak sağlık okuryazarlığı düzeyini artırabilecek önlemler alınmalıdır. Düşük sağlık okuryazarlık düzeyine sahip bireylere hastalıklarının tanısı, tedavisi ve takibi ile ilgili detaylı bilgilendirmeler yapılmalı, danışmanlık ve eğitimler planlanmalıdır.

Çalışmada 65 yaş ve üzeri bireylerin sağlık okuryazarlığı toplam puan ortalaması 65 yaş altı bireylere göre daha yüksek bulundu. Bulgularımızın aksine Türkiye'de 50 yaş üzeri, kronik hastalığı olan 322 bireyin değerlendirildiği kesitsel çalışmada 50-65 yaş arası bireylerin sağlık okuryazarlığı toplam puan ortalamalarının 65 yaş üzeri bireylerin sağlık okuryazarlığı puan ortalamalarından daha yüksek olduğu tespit edilmiştir (24). Litaratürde artan yaşın düşük sağlık okuryazarlığı ile ilişkili olduğunu bildiren çalışmalar mevcuttur (20,25). Fakat bu çalışmalara 18 yaş üzeri bireyler dahil edilmiştir ve genç grubun sağlık okuryazarlığı düzeyinin yüksek bulunması bununla ilişkili olabilir. Buchbinder ve ark. (26)

Tablo 1. Bireylerin demografik özelliklerine göre sağlık okuryazarlığı ölçeği toplam puanlarının karşılaştırılması

Demografik özellikler		N	Sağlık okuryazarlığı puanı Ort ± SS	Test
Yaş/yıl	<65	82	21,11±11,41	U=1556.500
	≥65	74	31,79±11,18	**p=0,001**
Cinsiyet	Kadın	12	27,99±13,09	U=797.500
	Erkek	144	26,03±12,45	p=0,658
Medeni durum	Evli	136	26,38±12,76	U=1240.500
	Dul/Boşanmış	20	14,81±10,41	p=0,526
Eğitim durumu	İlkokul	80	17,70±8,45[a]	KW=85.048 **p=0,001***
	Ortaokul	36	32,74±8,84[b]	
	Lise	28	35,17±9,35[bc]	
	Üniversite	12	42,01±8,58[c]	
Meslek	Ev Hanımı	92	22,55±10,47[a]	KW=80.048 **p=0,001***
	Emekli	33	32,10±10,78[b]	
	Memur	18	41,92±8,33[c]	
	Çiftçi	13	15,02±8,07[a]	
Aile tipi	Çekirdek	123	25,11±12,51	U=1589.000
	Geniş	33	30,16±11,63	p=0,046
Yaşanılan yer	İl merkezi	83	30,58±10,67[a]	KW=11.228 **p=0,004***
	İlçe merkezi	62	23,43±12,48[b]	
	Kasaba/Köy	11	22,11±15,37[b]	
Gelir durumu	Gelir giderden az	36	19,53±11,24[a]	KW=13.914 **p=0,001***
	Gelir gidere eşit	93	28,67±12,67[b]	
	Gelir giderden fazla	27	26,46±10,50[b]	
Sigara içme durumu	Evet	12	24,17±17,54	U=757.500 p=0,479
	Hayır	144	26,34±12,02	

SS: Standart sapma, KW: Kruskal-Wallis H, U: Mann-Whitney U, Ort: Ortalama
Mann-Whitney U testi kullanıldı. *Bonferroni düzeltmeli Kruskal-Wallis H testi kullanıldı.
[a,b,c]: Aynı harfe sahip ortalamalar istatistiksel olarak benzerdir.

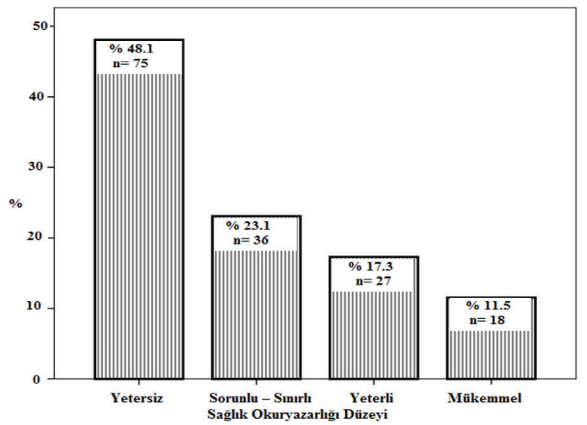
tarafından yapılan çalışmada ise Tıpta Yetişkin Okuryazarlığının Hızlı Tahmini (*Rapid Estimate of Adult Literacy in Medicine-REALM*) kullanılmış ve yaş ile sağlık okuryazarlığı arasında ilişki tespit edilememiştir. Çalışmamızda 65 yaş altı bireylerin sağlık okuryazarlığı toplam puanının 65 yaş üzeri bireylere göre daha düşük olmasının sebebi 65 yaş üzerindeki bireylerin hastane başvurularının kronik hastalıkları sebebi ile daha fazla olabileceği, hastalıklarının takibi ve tedavisi ile ilgili daha tecrübeli olabilecekleri ve yaşlandıkça sağlıkla ilgili terimlere daha aşina hale gelmeleri ile açıklanabilir. Öte yandan bu çalışmada 65 yaş altındaki bireylerin yetersiz ya da sınırlı sağlık okuryazarlığı düzeyi %85,3, 65 yaş üzerindeki bireylerin ise %55,4 bulunması nedeniyle her iki grubunda yetersiz sağlık okuryazarlığı açısından değerlendirilmesi gerektiği düşünülmektedir.

Çalışmada cinsiyete göre sağlık okuryazarlığı toplam puanları arasında anlamlı farklılık saptanmadı. Bulgularımızla benzer şekilde cinsiyet ile sağlık okuryazarlığı arasında ilişki tespit edilmeyen çalışmalar olduğu gibi (20,27); kadınlarda erkeklere göre sağlık okuryazarlığı düzeyinin yüksek olduğunu (28) ya da düşük olduğunu bildiren çalışmalar da mevcuttur (29). Cinsiyet ile sağlık okuryazarlığı düzeyi arasındaki ilişkiye dair sonuçlar literatürde farklılıklar göstermektedir. Genel olarak cinsiyete göre sağlık okuryazarlığı düzeylerine bakıldığında bireylerin çoğunluğununun yetersiz ve sınırlı (erkeklerde %66,7, kadınlarda %71,5) sağlık okuryazarlığına sahip olması nedeni ile her iki cinsiyetteki bireyler sağlı okuryazarlığı açısından değerlendirilmeli ve eğitim planları her iki grubu da kapsayacak şekilde planlanmalıdır.

Çalışmamızda geniş ailede yaşayanların sağlık okuryazarlığı toplam puan ortalaması, çekirdek ailede yaşayanlara göre daha yüksek saptandı. Birçok aile üyesinin bir arada yaşadığı geniş ailelerde, bu aile üyeleri arasında daha fazla iş birliği ve dayanışma vardır; sonuç olarak, aile üyeleri kronik hastalığı olan bireylerin bakımında yardımcı olabilir (30). Çalışmamızın aksine çekirdek ailede yaşayan bireylerin sağlık okuryazarlığının geniş ailede yaşayanlara göre daha yüksek olduğunu bildiren çalışma olduğu gibi (31) aile tipi ile sağlık okuryazarlığı arasında ilişki tespit etmeyen çalışmalar da bulunmaktadır (30). Çalışmamızda

Tablo 2. Sağlık okuryazarlığı ölçeği toplam ve alt boyut bileşen puanları

Sağlık okuryazarlığı ölçeği alt boyut bileşenleri	**Ort ± SS**
Tedavi ve hizmet	24,98±13,02
Sağlıkla ilgili bilgiye ulaşma alt boyut	26,92±14,31
Sağlıkla ilgili bilgiyi anlama alt boyut	24,83±13,27
Sağlıkla ilgili bilgiyi değerlendirme alt boyut	24,43±13,01
Sağlıkla ilgili bilgiyi kullanma/Uygulama alt boyut	24,14±13,22
Hastalıklardan korunma/Sağlığın geliştirilmesi	27,37±13,04
Sağlıkla ilgili bilgiye ulaşma alt boyut	27,16±13,80
Sağlıkla ilgili bilgiyi anlama alt boyut	28,09±13,80
Sağlıkla ilgili bilgiyi değerlendirme alt boyut	27,21±14,81
Sağlıkla ilgili bilgiyi kullanma/Uygulama alt boyut	27,83±13,92
Sağlık okuryazarlığı ölçeği toplam puanı	26,18±12,47
SS: Standart sapma, Ort: Ortalama	



Şekil 1. Bireylerin sağlık okuryazarlığı düzeyine göre dağılımları

il merkezinde yaşayanların sağlık okuryazarlığı ilçe merkezi ve köy/kasabada yaşayanlara göre daha yüksek saptandı. Kanser hastalarının değerlendirildiği bir çalışmada da kırsal kesimdeki hastaların kentsel bölgedekilere göre daha düşük sağlık okuryazarlığına sahip olma olasılığının %33 daha yüksek olduğu tespit edilmiştir (32). Benzer şekilde Ulusal Sağlık Okuryazarlığı Araştırması verilerinin değerlendirildiği çalışmada kırsal nüfusun tüm okuryazarlık türleri için daha düşük okuryazarlık seviyelerine sahip olduğu bildirilmiştir (33). Öte yandan yaşanılan yer ile sağlık okuryazarlığı arasında herhangi bir ilişki tespit etmeyen çalışmalar da mevcuttur (34,35). Literatürde her ne kadar aile tipi, yaşanılan yer ve sağlık okuryazarlığı arasındaki ilişkiye dair farklı sonuçlar bulunsa da osteoporoz tanılı bireylerden özellikle çekirdek ailede, ilçe merkezi ve köyde yaşayanlar; düşük sağlık okuryazarlığı varlığı açısından değerlendirilmeli ve hastalığın takibi, ilaçların yönetimi konusunda detaylı bilgilendirme yapılmalıdır.

Çalışmada geliri giderinden az olanların sağlık okuryazarlığı düzeyi daha düşük tespit edildi. Benzer şekilde osteoporoz tanılı bireylerin değerlendirildiği bir çalışmada geliri daha yüksek olanların daha yüksek sağlık okuryazarlığına sahip olduğu saptanmıştır (17). Ülkemizde yapılan tanımlayıcı kesitsel bir çalışmada da gelir durumu giderden fazla olan bireylerin toplam sağlık okuryazarlığı puanlarının gelir durumu giderden az ve gidere eşit olan bireylerden daha yüksek olduğu bildirilmiştir (24). Çalışmamızda üniversite mezunu olanların sağlık okuryazarlığı toplam puan ortalaması ilkokul, ortaokul ve lise mezunlarına göre daha yüksek bulundu. Yapılan çalışmalarda daha düşük eğitimli kişilerin, yüksek eğitimli kişilere kıyasla daha düşük sağlık okuryazarlığına sahip oldukları tespit edilmiştir (20,27).

Sağlık okuryazarlık düzeyi yüksek olan kadınların osteoporoz taramalarını yaptırma olasılıklarının da daha yüksek olduğu bilinmektedir (36). Düşük okuryazarlık aynı zamanda optimal sağlık hizmeti almanın önünde önemli bir engel olabilir ve kronik hastalığı olan hastalarda zayıf okuryazarlık becerilerinin hastalık süreci hakkında bilgi eksikliği ve zayıf öz-yönetim becerileri ile ilişkili olduğu bulunmuştur (26). Osteoporoz ve sonuçları, eğitim, korunma, zamanında teşhis, öz bakım ve bu sorunun yönetimi ile önlenebilir. Bu nedenle insanların sağlık okuryazarlığı ve farkındalığını geliştirmek önemli stratejilerden biridir (37). Okuryazarlık değerlendirmesinin yararlarını akılda tutmak, hemşireleri, hastanın okuryazarlık düzeyine uygun bakım sağlamanın yollarını bulmaya motive edebilir. Hastaların okuryazarlık seviyelerine göre uyarlanmış bakımın sağlanması, hastaların bakım sürecine katılmalarını sağlayabilir. Okuryazarlık değerlendirmesi; hemşirenin daha iyi bir tıbbi öykü çıkarmasına, bir tedavi planını anlaşılır terimlerle açıklamasına ve hastanın tedavi önerilerini olağan günlük rutinlerine entegre etmesine yardımcı olan, etkili ileri düzey hemşire-hasta iletişiminin önemli bir bileşenidir (38).

Çalışmanın Kısıtlılıkları

Bu çalışma ülkemizde osteoporoz tanılı bireyerde sağlık okuryazarlığı düzeyini değerlendiren ilk çalışmadır fakat bazı limitasyonları mevcuttur. Osteoporoz alanında sağlık okuryazarlığını ölçmek için spesifik bir ölçek olmadığı için genel sağlık okuryazarlığı ölçeği kullanılmıştır. Diğer yandan, bu çalışmanın sonuçlarının genellenebilmesi için çalışmanın diğer illerdeki osteoporoz tanılı bireylerle de gerçekleştirilmesi önerilebilir.

Sonuç

Sonuç olarak osteoporoz tanılı bireylerin yaklaşık üçte ikisi sınırlı ya da yetersiz sağlık okuryazarlığı düzeyindedir. Bu durum hastaların osteoporoz tanısı, takibi, tedavisi ile ilgili bilgileri anlamalarını sınırlayabilir ve potansiyel olarak olumsuz sağlık sonuçlarına yol açabilir. Bu nedenle sağlık profesyonelleri osteoporoz tanılı bireylerin sağlık okuryazarlığı düzeyini değerlendirmelidir. Böylece hastaya uygun bilgilendirme stratejileri geliştirebilir (görsel materyaller vs.), bakım planı uygulayabilir ve sağlık okuryazarlığı düzeyini artırmak için eğitim programları planlayabilir.

Etik

Etik Kurul Onayı: Tokat Gaziosmanpaşa Üniversitesi Klinik Araştırmalar Etik Kurulu tarafından onaylandı (karar no: 21-KAEK-090, tarih: 01.04.2021).

Hasta Onayı: Araştırmaya katılan tüm bireylere bilgi verilerek onamları alındı.

Hakem Değerlendirmesi: Editörler kurulu dışında olan kişiler tarafından değerlendirilmiştir.

Yazarlık Katkıları

Konsept: F.O., S.O., Dizayn: F.O., Veri Toplama veya İşleme: F.O., S.O., Analiz veya Yorumlama: F.O., S.O., Literatür Arama: F.O., S.O., Yazan: F.O., S.O.

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Osteoporoz Tanısı Olan ve Olmayan Postmenopozal Kadınların Fiziksel Aktivite Düzeyleri ve Yaşam Kalitelerinin Karşılaştırılması

Comparison of Physical Activity Levels and Quality of Life of Postmenoposal Women with and Without Osteoporosis

Erkan Erol, Fatih Okan*, Sevil Okan**

Tokat Gaziosmanpaşa Üniversitesi Sağlık Bilimleri Fakültesi, Fizik Tedavi ve Rehabilitasyon Anabilim Dalı, Fizyoterapi ve Rehabilitasyon Bölümü, Tokat, Türkiye
*Tokat Gaziosmanpaşa Üniversitesi Sağlık Bilimleri Fakültesi, Halk Sağlığı Hemşireliği Anabilim Dalı, Hemşirelik Bölümü, Tokat, Türkiye
**Tokat Devlet Hastanesi, Fiziksel Tıp ve Rehabilitasyon Kliniği, Tokat, Türkiye

Öz

Amaç: Osteoporoz, kemik dokusunun mikro-mimarisinin bozulması ve düşük kemik mineral yoğunluğu ile karakterize önemli bir halk sağlığı sorunudur. Çalışmamızda osteoporoz tanısı olan ve olmayan postmenopozal kadınların fiziksel aktivite düzeyleri ve yaşam kalitelerinin karşılaştırılması amaçlandı.

Gereç ve Yöntem: Kesitsel tipteki çalışma, 104 postmenopozal kadın ile gerçekleştirildi (52 osteoporoz-52 osteoporoz olmayan). Değerlendirmede kişisel özellikler veri formu, [Uluslararası Fiziksel Aktivite Anketi (UFAA) Kısa Form] ve Avrupa Osteoporoz Derneği Yaşam Kalitesi Anketi-41 (QUALEFFO-41) kullanıldı.

Bulgular: Osteoporoz tanılı bireylerin QUALEFFO-41 mobilite, QUALEFFO-41 zihinsel fonksiyonlar ve QUALEFFO-41 toplam puanı osteoporoz tanısı olmayan bireylere göre anlamlı şekilde yüksek bulundu (sırasıyla; p=0,046, p=0,001, p=0,024). Osteoporoz tanısı olan ve olmayan bireylerin fiziksel aktivite düzeyleri UFAA sınıflamasına göre benzer bulundu (p>0,05). Osteoporozu olan bireylerin UFAA toplam skorları ile QUALEFFO-41 toplam skorları arasında negatif yönlü zayıf ilişki bulundu (p=0,007).

Sonuç: Osteoporoz tanılı postmenopozal kadınların yaşam kalitesi düşük düzeydedir ve fiziksel aktivite düzeyindeki artış daha iyi yaşam kalitesi ile ilişkilidir. Osteoporoz tanılı postmenopozal kadınlarda fiziksel aktivite düzeyini artırmak yaşam kalitesini iyileştirmek açısından pozitif etkili olabilir.

Anahtar kelimeler: Osteoporoz, yaşam kalitesi, fiziksel aktivite, postmenopozal, kemik mineral yoğunluğu

Abstract

Objective: Osteoporosis is an important public health problem characterized by the deterioration of the microarchitecture of bone tissue and low bone mineral density. In our study, we compared the physical activity levels and quality of life of postmenopausal women with and without osteoporosis.

Materials and Methods: A cross-sectional study was conducted with 104 postmenopausal women (52 osteoporosis-52 non-osteoporosis). Personal characteristics data form, International Physical Activity Questionnaire (IPAQ), Short Form and Quality of Life Questionnaire of The European Foundation for Osteoporosis (QUALEFFO-41) were used for evaluation.

Results: QUALEFFO-41 mobility, QUALEFFO-41 mental functions, and QUALEFFO-41 total scores of individuals with osteoporosis were found to be significantly higher than individuals without a diagnosis of osteoporosis (p=0.046, p=0.001, p=0.024, respectively). Physical activity levels of individuals with and without a diagnosis of osteoporosis were found to be similar according to the IPAQ classification (p>0.05). There was a weak negative correlation between the IPAQ total scores and the QUALEFFO-41 total scores of individuals with osteoporosis (p=0.007).

Conclusion: The quality of life of postmenopausal women with osteoporosis is low, and the increase in physical activity level is associated with a better quality of life. Increasing the level of physical activity in postmenopausal women with osteoporosis may have a positive effect on improving the quality of life.

Keywords: Osteoporosis, quality of life, physical activity, postmenopausal, bone mineral density

Yazışma Adresi/Address for Correspondence: Dr. Öğr. Üyesi, Erkan Erol, Tokat Gaziosmanpaşa Üniversitesi Sağlık Bilimleri Fakültesi, Fizik Tedavi ve Rehabilitasyon Anabilim Dalı, Fizyoterapi ve Rehabilitasyon Bölümü, Tokat, Türkiye
Tel.: +90 554 792 01 18 **E-posta:** erkanerol@gmail.com **ORCID ID:** orcid.org/0000-0002-0087-1821
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Giriş

Osteoporoz, kemik dokusunun mikro-mimarisinin bozulması ve düşük kemik mineral yoğunluğu ile karakterize önemli bir halk sağlığı sorunudur. Kemikte meydana gelen değişiklikler sonucu kemiğin mukavemeti azalır, kırılganlığı artar (1). Osteoporozun en yaygın klinik sonuçları; insidansı yaşla birlikte artan kalça, vertebra ve el bileği kırıklarıdır. Osteoporotik kırıklar morbidite, mortalite, yaşam kalitesinde azalma, iş gücü kaybı ve ekonomik maliyetlerden sorumludur (2,3). Kırığa sebep olan önemli nedenlerden biri olarak düşük kemik kütlesi gösterilmektedir ve dolayısıyla osteoporozun önlenmesi bu açıdan önemlidir (1,2). Kullanmama ve hareketsizliğin, iskelet sisteminin yükünü azaltarak kemik kütlesinin azalmasına neden olduğu düşünülmektedir. Bunun tersi olarak, fiziksel aktivite artışı neticesinde kemik büyümesinin sağlandığı ve kemik kütlesinin korunduğu bilinmektedir. Fiziksel aktivite, boş zamandaki fiziksel aktiviteyi (egzersiz, spor), günlük yaşam aktivitelerini, ev ve iş yerinde yapılan işleri içeren bir şemsiye terimdir (4). Fiziksel aktivitenin sağlıklı yaşlanma için faydaları bilinmektedir (5) ve osteoporozun önlenmesi ve tedavisi için çeşitli fiziksel aktiviteler önerilmektedir (6).

Sağlıkla ilgili yaşam kalitesi; fiziksel, zihinsel ve sosyal refahı ifade eder ve yaşam kalitesinin bir alt kümesidir (7). Klinik çalışmalarda, "sağlıkla ilgili yaşam kalitesi" kısaca "yaşam kalitesi" olarak adlandırılır (8). Osteoporozun sağlık durumu üzerinde olumsuz etkileri vardır ve bu etkiler yaşam kalitesine yansır (9). Osteoporozlu postmenopozal kadınlarda yaşam kalitesini değerlendirmek, bu popülasyonda osteoporozu önleme ve tedavi uygulamaları için önemli bilgiler sağlar (9).

Literatüre baktığımızda osteoporozda fiziksel aktivitenin ve egzersizin etkilerini inceleyen çalışmalar mevcuttur. Ayrıca osteoporozlu bireylerle yapılan çeşitli çalışmalarda yaşam kalitesi de değerlendirilmiştir. Ancak osteoporozlu bireylerin fiziksel aktivite düzeyi ile yaşam kaliteleri arasındaki ilişkiyi incelen çalışmaya rastlanmamıştır. Çalışmamızda osteoporozu olan ve olmayan postmenopozal kadınlarda yaşam kalitesi ve fiziksel aktivite düzeylerini karşılaştırmayı ve osteoporozu olan kadınlarda yaşam kalitesi ile fiziksel aktivite düzeyi arasındaki ilişkiyi incelemeyi amaçladık.

Gereç ve Yöntem

Kesitsel tipteki çalışma 50 yaş üzeri 104 postmenopozal kadın katılımcı ile gerçekleştirildi (52 osteoporoz tanısı olan-52 osteoporoz tanısı olmayan). Çalışmanın örneklem büyüklüğü G*power 3.1.9.4 programında yapılan güç analizi neticesinde %80 güç, 0,50 etki büyüklüğü, 0,05 yanılma payı ile her grupta 51 kişi olacak şekilde toplam 102 kişi olarak hesaplandı. Çalışmaya 01.05.2022-31.06. 2022 tarihleri arasında Tokat Devlet Hastanesi Fiziksel Tıp ve Rehabilitasyon Polikliniği'ne başvuran, postmenopozal dönemdeki 50 yaş üstü 113 birey değerlendirildi. Belirgin kognitif bozukluğu ve iletişim kurma problemi olan 3, kanser tanısı olan 1, fiziksel aktivitesini kısıtlayacak derecede kronik hastalığı olan 3, çalışmaya katılmak istemeyen 2 birey çalışmaya dahil edilmedi. Çalışmada yazılı ve sözlü onamı alınan bireylerden veriler bireylerin poliklinik muayenesi sonrasında yüz yüze görüşme yöntemiyle elde edildi. Bireylerin kemik mineral yoğunluğu ölçümleri çalışmada değerlendirildi. Tokat Gaziosmanpaşa Üniversitesi Klinik Araştırmalar Etik Kurulu'na başvurularak çalışma için etik kurul izni alınmıştır (karar no: 22-KAEK-092, tarih: 31.03.2022).

Veri Toplama Araçları

Kişisel Özellikler Veri Formu

Katılımcıların yaş, meslek, eğitim düzeyi, doğum sayısı, menopoz yaşı ve osteoporoz süresi kaydedildi. Boy ve kilo ölçümleri yapılarak beden kitle indeksi (BKİ) hesaplandı.

Fiziksel Aktivite Düzeyi Değerlendirmesi

Fiziksel aktivite düzeyi, [Uluslararası Fiziksel Aktivite Anketi (UFAA) Kısa Form] ile değerlendirildi. UFAA 7 sorudan oluşmaktadır ve son bir hafta içindeki fiziksel aktivite düzeyini değerlendirmektedir. Son bir haftada ne kadar süre şiddetli fiziksel aktivite, orta şiddetli fiziksel aktivite, yürüyüş yapıldığını ve oturularak geçirilen süreyi sorgular. 2020 yılında yayınlanan bir meta analizde fiziksel aktiviteyi değerlendirmek için UFAA kullanımının en geçerli ve güvenilir kendi kendine raporlama yöntemlerinden biri olduğu bildirilmiştir (10).

Yaşam Kalitesi Değerlendirmesi

Yaşam kalitesinin değerlendirmesinde Avrupa Osteoporoz Derneği Yaşam Kalitesi Anketi-41 (*Quality of Life Questionnaire of the European Foundation for Osteoporosis-41 - QUALEFFO-41*) kullanıldı. QUALEFFO-41, Avrupa Osteoporoz Derneği tarafından geliştirilmiş, osteoporozda yaşam kalitesini değerlendiren, 41 maddeden oluşan ve hasta tarafından doldurulan ankettir. QUALEFFO-41, ağrı (5 madde), fiziksel fonksiyon (17 madde), boş zaman ve sosyal aktiviteler (7 madde), genel sağlık değerlendirmesi (3 madde) ve zihinsel fonksiyonlar (9 madde) alt gruplarındaki toplam 41 maddeden oluşmaktadır. Türkçe için geçerlilik ve güvenirliği Koçyigit ve ark. (11) tarafından yapılmıştır.

Kemik Mineral Yoğunluğu Ölçümü (KMY): Lomber vertebra, femur boyun ve femur total bölgelerinin KMY T-skoru değerlendirmeleri çift enerjili X-ışını absorbsiyometri (DEXA); Hologic Discovery 4.500 QDR kullanılarak yapıldı. Osteoporoz tanısı Dünya Sağlık Örgütü sınıflandırmasına göre yapıldı. T-skoru -1 ve üstünde olanlar normal, -1 ile -2,5 olanlar osteopeni, T-skoru -2,5 ve altında olanlar osteoporoz olarak kabul edildi. Femur boynu ve femur total T-skoru hesaplamasında referans değer olarak "National Health and Nutrition Examination Survey" verileri, lomber vertebra T-skoru hesaplamasında ise üretici firma veri tabanı Hologic database kullanıldı.

İstatistiksel Analiz

Çalışmada toplanan verilerin istatistiksel analizleri için SPSS (Versiyon 22.0, SPSS Inc., Chicago, IL, USA) programı kullanıldı. Tanımlayıcı istatistikler ortalama ± standart sapma, kategorik verilerin frekans dağılımları sayı ve yüzde (%) olarak gösterildi.

Normallik dağılımı Kolmogorov-Smirnov testi ile incelendi. Sürekli değişkenler için bağımsız iki örneklem ortalama karşılaştırmalarında parametrik test varsayımları sağlandığında iki Ortalama Arasındaki Farkın Önemlilik Testi, sağlanmadığı durumlarda ise Mann-Whitney U testi ile yapıldı. Gruplar arasında kategorik değişkenlerin oran karşılaştırmaları için ki-kare testi ile yapıldı. Parametreler arasındaki ilişkiyi saptamak için Spearman korelasyon analizi kullanıldı. İstatistiki anlamlılık düzeyi için p<0,05 olarak kabul edildi.

Bulgular

Bireylerin tanımlayıcı özellikleri Tablo 1'de sunulmuştur. Osteoporoz tanılı bireylerin yaş ortalaması (64,29±8,85) osteoporoz tanısı olmayan bireylere (60,27±8,36) göre daha yüksek, BKİ ortalaması (29,02±5,12) ise osteoporoz tanılı bireylere göre (33,49±4,89) daha düşük bulundu (sırasıyla p=0,014, p=0,001). Osteoporoz tanılı bireylerin menopoza girme yaşının osteoporoz tanısı olmayan bireylere göre anlamlı şekilde daha düşük olduğu tespit edildi (sırasıyla 45,02±5,81, 47,88±4,79 p=0,007). Osteoporoz tanısı olan ve olmayan bireylerin eğitim durumu, medeni durumu, gelir durumu, sigara kullanma durumu ve doğum sayısı benzer bulundu (p>0,05).

Bireylerin UFAA ve QUALEFFO-41 parametrelerinin karşılaştırılması Tablo 2'de gösterilmiştir. Osteoporoz tanılı bireylerin QUALEFFO-41 mobilite, QUALEFFO-41 zihinsel fonksiyonlar ve QUALEFFO-41 toplam puanları osteoporoz tanısı olmayan bireylere göre anlamlı şekilde yüksek bulundu (sırasıyla p=0,046, p=0,001, p=0,024). Osteoporoz tanısı olan ve olmayan bireylerin UFAA toplam skor, QUALEFFO-41 ağrı, QUALEFFO-41 günlük yaşam aktiviteleri, QUALEFFO-41 ev işleri, QUALEFFO-41 boş zaman ve sosyal aktiviteler, QUALEFFO-41 genel sağlık puan ortalamaları arasında istatistiksel olarak anlamlı fark saptanmadı (p>0,05). Osteoporoz tanısı olan ve olmayan bireyler UFAA sınıflamasına göre benzer bulundu (p>0,05).

Osteoporoz tanılı bireylerde UFAA, QUALEFFO-41 ve diğer parametrelerin ilişkisi Tablo 3'te sunulmuştur. Osteoporozu olan bireylerin UFAA toplam skor ile QUALEFFO-41 toplam skor arasında negatif yönlü zayıf ilişki bulundu (p=0,007).

Tartışma

Osteoporoz, fiziksel, sosyal ve ekonomik etkileri olan kronik bir durumdur, bu nedenle osteoporozun yaşam kalitesine etkisi birçok çalışmada araştırma konusu olmuştur. Bu çalışmada osteoporozu olan ve olmayan bireylerin yaşam kaliteleri karşılaştırıldığında, osteoporozu olan bireylerin yaşam kalitesinin daha düşük olduğu görüldü (QUALEFFO-41 toplam skoru). Ayrıca QUALEFFO-41'in alt parametreleri olan mobilite ve zihinsel fonksiyonların da osteoporozu olan bireylerde daha çok etkilendiği tespit edildi. İspanya'da 60 osteoporozlu kadınla yapılan bir çalışmada osteoporozlu, kadınlarda yaşam kalitesinin genel popülasyona kıyasla daha düşük olduğu bildirilmiştir (12). Korkmaz ve ark. (13) 46 osteoporozlu ve 46 sağlıklı bireyle yaptıkları çalışmada, osteoporoz grubunda QUALEFFO-41'in mobilite, boş zaman ve sosyal aktiviteler, genel sağlık ve zihinsel fonksiyonlar alt

Tablo 1. Bireylerin tanımlayıcı özelliklerinin karşılaştırılması

Özellikler		Osteoporoz olan n (%)	Osteoporoz olmayan n (%)	Test
Eğitim durumu	Okuryazar değil	12 (23,1)	16 (30,8)	x^2=0,814 p=0,666
	İlköğretim mezunu	35 (67,3)	31 (59,6)	
	Lise mezunu	5 (9,6)	5 (9,6)	
Medeni durumu	Evli	38 (73,1)	46 (88,5)	x^2=5,33 p=0,069
	Bekar	3 (5,8)	3 (5,5)	
	Dul/Boşanmış	11 (21,2)	3 (5,5)	
Gelir durumu	Gelir giderden az	22 (42,3)	23 (44,2)	x^2=4.743 p=0,093
	Gelir gidere eşit	26 (50,0)	18 (34,6)	
	Gelir giderden fazla	4 (7,7)	11 (21,2)	
Sigara kullanma durumu		4 (7,7)	6 (11,5)	x^2= 0,443 p=0,371
Yaş (Ort ± SS)		64,29±8,85	60,27±8,36	t= -2.882* **p=0,014**
BKİ (Ort ± SS) kg/m^2		29,02±5,12	33,49±4,89	t=4.572* **p=0,001**
Menopoz yaşı (Ort ± SS) yıl		45,02±5,81	47,88±4,79	t=2.742* **p=0,007**
Doğum sayısı		3,94±2,31	3,42±1,70	U=1220.00** p=0,383

*t-test, **Mann-Whitney U test, Ort: Ortalama, SS: Standart sapma, BKİ: Beden kitle indeksi

Tablo 2. Bireylerin UFAA ve QUALEFFO41 parametrelerinin karşılaştırılması

	Osteoporoz olan (Ort ± SS)	Osteoporoz olmayan (Ort ± SS)	Test
QUALEFFO-41 ağrı	34,90±29,58	36,53±26,83	U=1295.50 p=0,711
QUALEFFO-41 günlük yaşam aktiviteleri	26,56±20,37	19,59±17,24	U=1083.00 p=0,078
QUALEFFO-41 ev işleri	38,65±27,77	28,75±22,94	U=1085.00 p=0,081
QUALEFFO-41 mobilite	37,62±21,98	28,75±22,94	U=1045.50 **p=0,046**
QUALEFFO-41 boş zaman ve sosyal aktiviteler	70,75±21,34	62,83±20,78	U=1099.50 p=0,100
QUALEFFO-41 genel sağlık	60,09±19,19	54,48±18,26	U=1109.50 p=0,111
QUALEFFO-41 zihinsel fonksiyonlar	54,27±17,41	43,05±13,05	U=750.50 **p=0,001**
QUALEFFO-41 toplam skor	47,14±17,81	39,44±12,81	U=1006.00 **p=0,024**
UFAA toplam skor	1108.42±1916.27	1166.73±1988.61	U=1262.00 p=0,557
UFAA sınıflama n (%)			
İnaktif	29 (55,8)	30 (57,7)	x^2=0,446 p=0,800
Minimal aktif	17 (32,7)	18 (34,6)	
Çok aktif	6 (11,5)	4 (7,7)	

Ort: Ortalama, SS: Standart sapma, QUALEFFO-41: Avrupa osteoporoz derneği yaşam kalitesi anketi, UFAA: Uluslararası fiziksel aktivite anketi

Tablo 3. Osteoporoz tanılı bireylerde UFAA, QUALEFFO-41 ve diğer parametrelerin ilişkisi

			1	2	3	4	5
1	UFAA toplam skor	r p	1	- 0.372** **0.007**	0.030 0.835	0.015 0.914	0.081 0.567
2	QUALEFFO-41 toplam skor	r p	- 0.372** **0.007**	1	0.263 0.059	0.019 0.895	0.069 0.627
3	Osteoporoz tanı süresi (ay)	r p	0.030 0.835	0.263 0.059	1	- 0.012 0.935	0.038 0.788
4	BKİ	r p	0.015 0.914	0.019 0.895	-0.012 0.935	1	- 0.077 0.588
5	Menopoz yaşı (yıl)	r p	0.081 0.567	0.069 0.627	0.038 0.788	-0.077 0.588	1

QUALEFFO-41: Avrupa osteoporoz derneği yaşam kalitesi anketi, UFAA: Uluslararası fiziksel aktivite anketi, BKİ: Beden kitle indeksi

parametreleri ile QUALEFFO-41 toplam skorunun daha yüksek (azalmış yaşam kalitesini gösterir) olduğunu bildirmişlerdir. Çalışmamızda da benzer şekilde QUALEFFO-41 mobilite ve zihinsel fonksiyonlar alt parametreleri açısından osteoporoz grubunun daha çok etkilendiği, QUALEFFO-41 boş zaman ve sosyal aktiviteler ile genel sağlık parametrelerinde ise istatistiksel olarak anlamlı fark olmadığı ancak osteoporozu olan bireylerin daha yüksek skorlar aldığı görüldü. Bu veriler ışığında osteoporozlu bireylerde genel olarak yaşam kalitesinin etkilendiğini ancak mobilite ve zihinsel fonksiyonların diğer parametrelere göre daha fazla etkilendiğini, oluşturulacak tedavi programlarında bunun göz önüne alınması gerektiğini düşünüyoruz.

Düzenli fiziksel aktivitenin, özellikle postmenopozal kadınlarda kemik mineral yoğunluğunu artırdığı ve osteoporozu önlemede etkili olduğu görülmüştür (14). Fiziksel aktivite, osteoporozun hem önlenmesinde hem de tedavisinde önerilmektedir. Naharcı ve ark. (15) düzenli egzersiz yapan yaşlı erkeklerde hareketsiz bireylere kıyasla daha az oranda osteoporoz görüldüğünü bildirmişlerdir. Ancak bizim çalışmamızda osteoporozu olan ve olmayan kadınlar arasında fiziksel aktivite düzeyi açısından fark görülmedi. Fark görülmemesinin sebebi çalışmaya dahil edilen her iki gruptaki bireylerin yarısından fazlasının inaktif katergoride olması ve fiziksel olarak aktif birey sayısının az olması olabilir.

Fiziksel olarak aktif olan kadınların olmayanlara göre yaşam kalitelerinin daha iyi olduğu görülmektedir (16). Pamuk ve ark. (17) postmenopozal 280 kadınla yaptıkları çalışmada fiziksel aktivite düzeyindeki artışın yaşam kalitesini artırdığını bildirmişlerdir. Teoman ve ark. postmenopozal kadınlarla yaptıkları çalışmada aerobik egzersizin yaşam kalitesini artırdığını göstermişlerdir (18). Çalışmamızda literatürle benzer şekilde osteoporozlu bireylerde fiziksel aktivite düzeyi arttıkça yaşam kalitesinin de arttığı görüldü. Postmenopozal dönemdeki osteoporozlu kadınlarda yaşam kalitesini artırmak için fiziksel aktivite düzeyinin artırılması faydalı olabilir.

Kilolu bireylerde osteoporoz görülme riskinin zayıf bireylere göre daha az olduğu düşünülmektedir (15). Yapılan bir çalışmada, yaşlılarda diyetle kilo verme sonucu kemik yıkım hızının arttığı ve kalçada kemik mineral yoğunluğunun azaldığı bildirilmiştir (19). Naharcı ve ark. (15) yaptıkları çalışmada osteoporozu olan bireylerin BKİ'sini, olmayanlara göre daha düşük bulmuşlardır. Vücuttaki yağ dokusu artışının kemik kitlesinin korunmasını sağlayabileceğini bildirmişlerdir. Yağ dokusundan salgılanan adiponektin ve leptin gibi hormonların kemik mineral yoğunluğunu korudukları gösterilmiştir (20). Çalışmamızda da benzer şekilde osteoporozu olan kadınların BKİ'si, olmayanlara kıyasla daha düşük bulundu. Ayrıca BKİ ile yaşam kalitesi arasında bir ilişki olmadığı görüldü. Literatüre baktığımızda çalışmamızın sonucuyla benzer şekilde Pamuk ve ark. (17) ile Adıgüzel ve ark.'da (21) osteoporozu olan postmenopozal kadınlarda yaptıkları çalışmalarda BKİ ile yaşam kalitesi arasında ilişki olmadığını bildirmişlerdir.

Menopoza girme ile birlikte östrojen miktarındaki azalma sonucu kemik kaybı hızlanmaktadır. Bu nedenle menopoza girme yaşı düştükçe osteoporoz riski artmaktadır. Çalışmamızda osteoporoz olan grupta menopoza girme yaşı istatistiksel olarak anlamlı düzeyde daha düşük bulundu. Ancak osteoporozu olan bireylerde menopoza girme yaşı ile yaşam kalitesi veya fiziksel aktivite arasında ilişki olmadığı görüldü.

Çalışmamızın bazı kısıtlılıkları bulunmaktadır. Birincisi, çalışma sadece kadınlarda yapıldığı için elde edilen sonuçlar tüm osteoporozlu bireyler için genellenemez. Çalışmamızın kadınlarda yapılmasının nedeni, kadınlarda osteoporoz insidansının erkeklere kıyasla daha fazla olmasıdır. İkinci kısıtlılık, çalışmadaki ölçüm araçlarının sübjektif sonuçlar sunmasıdır. Yaşam kalitesi değerlendirmesi doğası gereği sübjektif verilere dayanır ancak fiziksel aktivite değerlendirmesinde pedometre, akıllı bileklik/saat, cep telefonu gibi kişinin hareket miktarını objektif olarak ölçen cihazlar kullanılabilir ve bu cihazlar kişinin sübjektif olarak raporladığına kıyasla daha doğru bilgiler verir. Bundan sonra yapılacak çalışmalarda bunların göz önüne alınması önerilir.

Sonuç

Sonuç olarak osteoporozu olan bireylerde yaşam kalitesi osteoporozu olmayanlara kıyasla daha kötüdür. Osteoporoz, yaşam kalitesini ciddi şekilde etkileyen yaygın bir rahatsızlıktır. Elde ettiğimiz sonuçlara göre yaşam kalitesinin özellikle mobilite ve zihinsel fonksiyonlar alt basamaklarının etkilendiği görüldü. Osteoporozun yönetiminde bunların göz önünde bulundurulması yönetimin başarısını artıracaktır. Ayrıca osteoporozlu bireylerde yaşam kalitesindeki artışın fiziksel aktivite düzeyinde artışla ilişkili olduğu bulundu. Bu nedenle osteoporozlu bireylerde fiziksel aktivite düzeyini artırmanın ve egzersiz yapmanın yaşam kalitesini artırmak açısından pozitif etkileri olabileceği düşünülebilir.

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Investigation of the Relationship Between Bone Mineral Density, Kinesiophobia, Fear of Falling, Anxiety and Depression Levels in Patients with Osteoporosis

Osteoporoz Tanılı Hastalarda Kemik Mineral Yoğunluğu, Kinezyofobi, Düşme Korkusu, Anksiyete ve Depresyon Düzeyleri Arasındaki İlişkinin İncelenmesi

Cansın Medin Ceylan, Merve Damla Korkmaz*

İstanbul Physical Medicine and Rehabilitation Training and Research Hospital, Clinic of Physical Medicine and Rehabilitation, İstanbul, Turkey
*University of Health Sciences Turkey, Kanuni Sultan Süleyman Training and Research Hospital, Clinic of Physical Medicine and Rehabilitation, İstanbul, Turkey

Abstract

Objective: To evaluate the relationship between kinesiophobia, fear of falling, anxiety, and depression levels in women with osteoporosis (OP).

Materials and Methods: Female participants with OP were included in our cross-sectional observational study and their fear of falling and movement, anxiety and depression levels were questioned. Demographic data (age, body mass index, fracture history), and dual X-ray absorptiometry data were recorded. Tampa Scale of Kinesiophobia (TSK), Fall Efficacy Scale (FES), Hospital Anxiety, and Depression Scale were used.

Results: Based on their history of fracture, 77 individuals were divided into two groups: OP with fracture (n=33) and OP without fracture (n=44). The findings of the bone mineral density correlated negative with the TSK, FES, and depression levels ($p<0.05$). FES, TSK, anxiety, and depression scores were positively correlated (r=0.232; r=0.241; r=0.296). Only the existence of the fracture and anxiety levels showed a statistical relationship in the inter-group analysis (p=0.003). No statistically significant differences were detected between the fracture history and TSK, FES, and depression scores ($p>0.05$).

Conclusion: Fall efficacy was associated with kinesiophobia, anxiety, and depression. Therefore, care should be taken when warning OP patients to prevent negative consequences that may occur due to fracture. In addition to the negative consequences of fractures, balance and strengthening exercises and how to reduce falls should be emphasized.

Keywords: Osteoporosis, kinesiophobia, fall efficacy, fracture

Öz

Amaç: Osteoporoz'lu (OP) kadınlarda; kinezyofobi, düşme korkusu, anksiyete ve depresyon düzeyleri arasındaki ilişkiyi değerlendirmektir.

Gereç ve Yöntem: Kesitsel gözlemsel çalışmamıza OP olan kadın katılımcılar dahil edilerek düşme ve hareket korkuları, anksiyete ve depresyon düzeyleri sorgulanmıştır. Demografik verileri (yaş, vücut kitle indeksi, kırık öyküsü) ve dual X-ışını absorpsiyometri verileri kaydedilmiştir. Tampa Kinezyofobi Ölçeği (TKÖ), Düşme Etkinlik Ölçeği (DEÖ), Hastane Anksiyete ve Depresyon Ölçeği kullanılmıştır.

Bulgular: Kırık öyküsüne göre 77 kişi iki gruba ayrıldı: Kırıklı OP (n=33) ve kırıksız OP (n=44). Kemik mineral yoğunluğu ile TKÖ, DEÖ ve depresyon düzeyleri arasında negatif korelasyon mevcuttu ($p<0,05$). Düşme Etkinlik Ölçeği, TKÖ, anksiyete ve depresyon puanları arasında pozitif korelasyon bulunmuştur (r=0,232; r=0,241; r=0,296). Gruplar arası analizde sadece kırık varlığı ve anksiyete düzeyleri istatistiksel bir ilişki göstermiştir (p=0,003). Kırık varlığı ile TKÖ, DEÖ ve depresyon puanları arasında istatistiksel olarak anlamlı fark saptanmamıştır ($p>0,05$).

Sonuç: Düşme etkinliğinin kinezyofobi, anksiyete ve depresyon ile ilişkili olduğu bulunmuştur. Bu nedenle kırık nedeniyle oluşabilecek olumsuz sonuçları önlemek için OP hastaları uyarılırken dikkatli olunmalıdır. Ek olarak kırığın olumsuz sonuçlarının yanında denge ve kuvvetlendirme egzersizleri ile düşmelerin nasıl azaltılacağı üzerinde durulmalıdır.

Anahtar kelimeler: Osteoporoz, kinezyofobi, düşme etkinliği, fraktür

Address for Correspondence/Yazışma Adresi: Cansın Medin Ceylan MD, İstanbul Physical Medicine and Rehabilitation Training and Research Hospital, Clinic of Physical Medicine and Rehabilitation, İstanbul, Turkey
Phone: +90 531 575 95 39 **E-mail:** cansinmedin@hotmail.com **ORCID ID:** orcid.org/0000-0003-1552-8986
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Introduction

Osteoporosis (OP), a systemic skeletal condition that worsens bone fragility and raises the risk of fracture, is characterized by the deterioration of the microarchitecture of bone tissue and low bone mass (1). Older persons living in the community frequently struggle with OP. The World Health Organization describes OP as having a bone density that is 2.5 standard deviations below what is typical for a young adult (2). According to estimates, 200 million individuals worldwide have OP, and one in three women and one in five men are susceptible to developing an OP fracture (3,4).

The risk of fractures from falls increases quickly in people with OP due to their increased bone fragility (5,6). Due to the increased risk of fracture from falling during physical exercise in patients with OP, this may enhance their fear of falling (FOF) and, in this scenario, kinesiophobia (7).

Kinesiophobia is a fear of movement brought on by the perception of injury susceptibility and is connected to decreased levels of physical exercise (8). According to recent studies, numerous chronic musculoskeletal conditions cause fear of mobility because patients believe they will hurt worse when they move (9,10). Researchers have discovered that OP patients exhibited greater degrees of kinesiophobia than healthy patients who were age and sex-matched controls. Women who have OP are more likely to sustain fractures from falls (11). They proposed that an individual with OP might experience kinesiophobia, which is possibly connected to a fear of fracture (7).

FOF is a significant issue for many people in society, and it gets worse as people get older. It is more prevalent in women, particularly those who have OP (12). An key risk factor for acquiring a FOF is having previously fallen (12,13). Activity avoidance is frequently caused by a FOF. Therefore, leading a sedentary lifestyle raises the risk. An important risk factor for immobilization bone loss is a sedentary lifestyle (14). Sale et al. (15) discovered that patients with OP are aware of the danger of fracture, and this is coupled with healthy lifestyle adjustments like exercising and practicing mindfulness. It has also been underlined that psychological issues associated with falling, particularly in women with OP, can cause significant challenges in eveyday life. Elderly women in the community who participated in a qualitative study on the impact of FOF on daily life said that they accepted and adjusted to their FOF and that they as a result decreased their independence and participation in the outside world (16).

Falling is an important issue for OP patients. In addition, FOF and kinesiophobia, which are likely to develop in OP patients, will lead to a decrease in patients' participation in the outside world. This may cause an increase in the depression and anxiety scores of the patients. On the other hand, in the literature, there are few studies these are evaluating the relationship between kinesiophobia and fear of movement in OP.

The purpose of present study is to assess the link between kinesiophobia, fall fear, anxiety, and depressive symptoms in OP affected women.

Materials and Methods

A total of 100 patients were involved in present cross-sectional observational study conducted between November 31, 2021 and May 31, 2022. Before starting the study, the protocol was approved by University of Health Sciences Turkey Kanuni Sultan Süleyman Traning Research Hospital Ethics Committee decision no: 2021.11.308, date: 26.11.2021). All selected participants signed an informed consent form. The Declaration of Helsinki's guiding principles were followed in conducting the study. Demographic data [age, weight, height, body mass index, fracture history of the patients were questioned; the fear of movement was evaluated with the Tampa Scale of Kinesiophobia (TSK), the FOF was evaluated with the Fall Efficacy Scale (FES), the presence of anxiety and depression was evaluated with the Hospital Anxiety and Depression Scale (HADS)].

Inclusion criteria were being 45-75 years, having diagnosed with OP [lumbar spine (L1-L4) or femoral neck/total hip T-score values below -2.5], and presence of community ambulation.

Exclusion criteria were the lack of cognitive ability to understand the test instructions, being illiterate, aphasia, a psychiatric disease with a known neurological or orthopedic disease that may affect mobility, and having endocrinological diseases.

TSK, which is used for the subjective assessment of fear of movement/kinesiophobia, includes 17 items related to fear of movement and re-injury. A four-point Likert-type scale with the options "strongly disagree" and "strongly agree" is used to score each item. The overall score is between 17 and 68. High scores are associated with higher levels of kinesiophobia (17). Yılmaz et al. (18) evaluated the reliability and validity of the Turkish version of the TSK.

The FES is a self-report questionnaire that assesses the degree of anxiety related to falls. The questionnaire has 16 items, each of which is scored on a four-point scale (1 being the least interested, and 4 being the most concerned), giving a total score that ranges from 16 (no worries) to 64 (extremely worried). Ulus et al. (19) evaluated the validity and reliability of the FES-I in Turkish.

A popular self-assessment tool designed to measure psychological distress in non-psychiatric patients is the HADS. It has two subscales: a seven-item anxiety scale (HADS-A) and a seven-item depression scale (HADS-D) (20). The patient answered to each item on a 4-point (0-3) scale, hence the range of possible scores for each of the two subscales is 0 to 21. Better mood is indicated by low scores on the depression and anxiety subscales. Aydemir et al. (21) evaluated the validity and reliability of the Turkish version of HADS.

Statistical Analysis

SPSS version 23.0 was used to conduct the statistical analysis (MacOs, IBM Corp., Armonk, NY, USA). Using the German-made G*Power software version 3.1.9, the sample size for the study was estimated to meet the objectives of $\alpha<0.05$ and $\beta=80\%$. For the purpose of determining the normal distribution, the Shapiro-Wilk W test was employed. Mean (standard deviation) was used for descriptive statistics. Pearson and/or Spearman correlation

coefficient were used for correlation analysis. The Mann-Whitney U test and independent t-test test were preferred for intergroup analysis depending on whether or not the data was distributed parametrically. Correlation coefficients were also utilized.

Results

One hundred participants with OP who visited to Physical Medicine and Rehabilitation clinic were evaluated to include in the study. Fifteen participants were not willing to participate the study, 5 of them had endocrinological diseases, and 3 participants were immobile. Seventy seven participants were included in the study. Participants were randomized according to presence of fracture: Group 1 (OP with fracture; n=33) and group 2 (OP without fracture; n=44). Table 1 shows the participant's demographic details.

A positive correlation was detected between TSK scores and age, FES, and depression scores according to the study's variables' correlation analyses (p=0.041, r=0.233; p=0.043, r=0.232; and p=0.046, r=0.229, respectively). TSK scores and bone mineral density (BMD) values for the femoral neck, whole hip, and lumbar spine were found to be negatively correlated (p<0.001, r= -0.418; p=0.022, r=-0.260; and p=0.024, r= -0.257, respectively). A positive correlation was found between FES scores and age, TSK, anxiety and depression scores (p=0.01, r=0.292; p=0.043, r=0.232; p=0.034, r=0.241, and p=0.009, r=0.296, respectively), where as a negative correlation was found between FES scores, and T-scores and BMD values of the femoral neck and total hip (p=0.008, r=-0.299; r=-0.275; p=0.004, and p=0.016, r=-0.326; p=0.012, r=-0.285, respectively). A positive correlation was detected between anxiety scores and FES and depression scores (p=0.034, r=0.241; and p<0.001, r=0.657). Also, it was found a negative correlation between depression scores and bone density test results (Table 2).

According to inter-group analysis, there was only statistical difference between presence of the fracture and anxiety scores (p=0.003). There were no statistically differences between presence of the fracture and bone density test results, TSK, FES, and depression scores (Table 3).

Discussion

In this study, it was determined that the presence of fracture history was unrelated to the demographic data, dual X-ray absorbsiometri (DXA) values, FES, HAD and kinesiophobia scores of the patients. Only patients without fracture had higher anxiety scores than the group with fractures. There was a correlation between age and FES and TKS, and between the increase in OP levels and TKS, FES and depression scores according to the correlation analysis. The association between FES scores and age, TKS, anxiety, and depression scores was shown to be positive. Additionally, a positive correlation was detected between the FES and depression scores and the anxiety score. A diagnosis of OP was associated with an increased risk of falling. According to prior studies, people with OP are more likely to fall because of their advanced age, weakened balance, and diminished strength (22,23). Those who are older, female, and of the black race are less likely to engage in exercise or other forms of physical activity, according to research by Barkley (24). Age, FES, and TKS were found to positively correlate in our investigation, corroborating these findings. On the contrary, Resnick et al. (11) found no relationship between demographic data, FOF, and exercise participation.

Considering the serious consequences that can be experienced after falling, it is not surprising that approximately 40-60% of people who fall have reported FOF (13,25,26). Women and the elderly are more likely than men to fear falling (27,28). Although there aren't many research examining people with OP's FOF, those that have been done have revealed a connection between the two conditions (17,28,29). These findings are supported by our investigation, which found a negative connection between FES scores, T and BMD values for the femoral neck and total hip. Maggio et al. (28) argue that those who know that they have OP are likely to be afraid of fracture in any fall, which exacerbates their fear. However, in our study, contrary to this data, the presence of a history of fracture was not associated with an increase in FOF or with kinesiophobia. Unfortunately, the FOF frequently prevents people from exercising or engaging in other types of physical activity, which contributes to a loss of independence that goes beyond what is necessary to prevent bodily harm from falls or normal aging changes (11,29,30). According to Mahler and Sarvimäki (16) elderly women in the community accepted and adjusted to their FOF, and as a result, they decreased their independence and engagement in society.

Additionally, it has been noted that OP patients are very likely than the general population to experience psychological issues such anxiety and depression (31). Additionally, a lower BMD is

Table 1. Demographical characteristics of the participants

	Group 1 (n=33)	Group 2 (n=44)	p
Age (year)	65.6 (7.9)	65.8 (7.8)	0.642
BMI (kg/m^2)	29.0 (5.1)	28.5 (4.5)	0,.342
Ca (mg/dL)	9.6 (3.7)	9.6 (0.3)	0.349
PTH (pg/mL)	36.3 (16.8)	45.2 (18.3)	0.646
25-OH vitamin D_3 (ng/mmol)	23.7 (11.2)	24.0 (11.2)	0.092

BMI: Body mass index, Ca: Calcium, PTH: Parathormon
P values for homogenity. There were no statistically significant differences between age, BMI, level of calsium, parathormon and 25-OH vitamin D_3

Table 2. Correlations between the variables of the study

	TSK	FES	HADS-anxiety	HADS-depression
Age				
r	0.233	0.292	-0.117	0.076
p	0.041*	0.010*	0.310	0.509
T-score (femoral neck)				
r	-0.170	-0.299	-0.053	-0.277
p	0.140	0.008*	0.648	0.015*
Z-score (femoral neck)				
r	-0.045	-0.218	-0.091	-0.259
p	0.697	0.056	0.433	0.023*
BMD (femoral neck)				
r	-0.418	-0.326	-0.123	-0.301
p	<0.001*	0.004*	0.288	0.008*
T-score (total hip)				
r	-0.096	-0.275	-0.110	-0.303
p	0.480	0.016*	0.341	0.007*
Z-score (total hip)				
r	0.027	-0.110	-0.182	-0.327
p	0.816	0.339	0.114	0.004*
BMD (total hip)				
r	-0.260	-0.285	-0.172	-0.398
p	0.022*	0.012*	0.134	<0.001*
T-score (L1-L4)				
r	0.129	0.164	0.098	0.142
p	0.263	0.154	0.395	0.218
Z-score (L1-L4)				
r	0.093	0.097	0.091	0.107
p	0.422	0.402	0.430	0.355
BMD (L1-L4)				
r	-0.257	0.146	-0.035	0.034
p	0.024*	0.205	0.762	0.770
TSK				
r	1	0.232	0.153	0.229
p	-	0.043*	0.185	0.046*
FES				
r	0.232	1	0.241	0.296
p	0.043*	-	0.034*	0.009*
HADS-anxiety				
r	0.153	0.241	1	0.657
p	0.185	0.034*	-	<0.001*
HADS-depression				
r	0.229	0.296	0.657	1
p	0.046*	0.009*	<0.001*	-

TSK: Tampa scale of kinesiophobia, FES: Fall efficacy scale, HADS: Hospital anxiety and depression scale, BMD: Bone mineral density
There was a positive correlation between TSK scores and age, FES, and depression scores. TSK scores and BMD values for the femoral neck, whole hip, and lumbar spine were found to be negatively correlated. Positive correlation was found between FES scores and age, TSK, anxiety and depression scores whereas a negative correlation was found between FES scores, and T scores and BMD values of the femoral neck and total hip. There was a positive correlation between anxiety scores and FES and depression scores. Also, it was found a negative correlation between depression scores and bone density test results

associated with higher levels of depression or anxiety (32,33). In present study, patients with OP without a fracture history had higher levels of anxiety than those with a fracture history. And while depression levels do correlate with BMD, anxiety levels do not. The presence of fracture was not found to be associated with the depression levels of the patients. Considering the serious consequences that can be experienced after falling, the fear of experiencing a fracture may have led to an increase in the anxiety levels of the patients. Moreover, a positive correlation was detected between FES and depression score, anxiety score, and tampa score in our study. Kinesiophobia caused by the FOF have caused the fear of movement in the patients, and their

Table 3. Comparison of the both groups according to presence of the fracture

	Group 1 (n=33)	Group 2 (n=44)	p	95% Confidence interval of the difference	
				Lower	Upper
Femur neck T-score	-2.2 (0.9)	-2.1 (0.9)	0.476	-0.53	0.30
Femur neck Z-score	-0.8 (0.8)	0.6 (1.0)	0.473	-0.58	0.27
Femur neck BMD	0.701 (0.114)	0.710 (0.119)	0.737	-0.063	0.044
Femur total T-score	-1.7 (0.9)	-1.8 (0.8)	0.481	-0.24	0.52
Femur total Z-score	-0.6 (0.8)	-0.7 (0.9)	0.568	-0.29	0.52
Femur total BMD	0.775 (0.104)	0.765 (0.101)	0.679	-0.037	0.056
L1-L4 T-score	-2.3 (1.2)	-2.3 (0.6)	0.247	-0.42	0.51
L1-L4 Z-score	-0.7 (1.6)	-0.9 (0.9)	0.315	-0.27	0.89
L1-L4 BMD	0.884 (0.159)	0.863 (0.104)	0.829	-0.38	0.08
TSK	36.8 (6.0)	38.4 (5.0)	0.198	-4.15	0.87
FES	26.7 (6.9)	29.0 (8.9)	0.221	-5.99	1.51
HADS					
Anxiety	5.6 (1.9)	7.7 (3.9)	0.003*	-3.46	-0.73
Depression	5.4 (2.9)	6.9 (4.4)	0.085	-3.11	0.20

TKS: Tampa scale of kinesiophobia, FES: Fall efficacy scale, HADS: Hospital anxiety and depression scale
There was only statistical difference between presence of the fracture and anxiety scores. No statistically differences were found between presence of the fracture and bone density test results, TSK, FES, and depression scores, BMD: Bone mineral density

participation in the outside world decreased, which may have led to an increase in the depression and anxiety levels of the patients.

The literature have few studies that evaluate kinesiophobia in OP patients (3,7,34). According to Gunendi et al. (7) They found that OP patients had higher kinesiophobia levels than healthy individuals of similar age and gender. In addition, Mısırcı et al. (3) found similar levels of kinesiophobia in patients with postmenopausal OP and osteopenia, and the level of kinesiophobia in both patient groups was found to be higher than in healthy controls. Patients with OP and osteopenia may have similar degrees of kinesiophobia since it is difficult to differentiate between the two conditions as a result of a lack of knowledge.

However, in our study, contrary to this data, kinesiophobia increases as the level of OP increases. A negative correlation was found between TKS and BMD values of femoral neck, total hip and lumbar spine. In addition, the history of fracture was not considered to be associated with kinesiophobia. The level of kinesiophobia was found to be correlated with anxiety and depression in both OP and osteopenia patients. In addition, high kinesiophobia scores are associated with anxiety and depression (3). There is only one study in the literature comparing kinesiophobia and FOF, and a weak-moderate positive correlation was found between the two (3). Similarly, a positive correlation was found between fall efficacy and tampa in our study. Additionally, it was discovered that patients with high kinesiophobia had greater FOF than those with low kinesiophobia. It might be said that FOF may worsen kinesiophobia or that kinesiophobia may cause FOF (3).

It is critical to comprehend the idea of FOF in older persons with OP in order to be able to construct fall prevention programs and to best address the FOF. Regardless of the extent of the disease, even just knowing you have OP can cause you to reduce your physical activity, which can lead to deconditioning and an increase in risk. Informing older persons with OP of the increased risk of falling should therefore be done with caution (35). In order to lower the risk of falling and to prevent falls, patients should be informed. How patients can improve their balance and strength and prevent falls through the use of the proper exercise techniques should be covered in this information.

Study Limitations

The limitations of the study are the small number of patients included in the study. Correlations observed are weak due to the small number of patients. For this reason, new studies with larger number of patients are needed.

Conclusion

As OP deepens, the patients' fall efficacy, kinesiophobia and depression levels increase. However, this situation was not associated with the presence of fracture. In addition, there is a relationship between FOF, kinesiophobia and depression. For this

reason, caution should be exercised when warning OP patients in order to prevent the negative consequences that may occur due to fractures. In addition to the negative consequences of the fracture, balance and strengthening exercises and how to reduce falls should be emphasized.

Ethics

Ethics Committee Approval: Approval for the study was granted by the University of Health Sciences Turkey, Kanuni Sultan Süleyman Training and Research Hospital Ethics Committe. (decision no: KAEK/2021.11.308, date: 26.11.2021).
Informed Consent: Consent form was obtained from all patients participating in the study.
Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: M.D.K., Concept: C.M.C., M.D.K., Design: C.M.C., M.D.K., Data Collection or Processing: C.M.C., M.D.K., Analysis or Interpretation: M.D.K., Literature Search: C.M.C., Writing: C.M.C.
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Case Report / Olgu Sunumu

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Pelvic Insufficiency Fractures in Patients with Rheumatoid Arthritis: A single Case Report

Romatoid Artritli Hastalarda Pelvik Yetmezlik Kırıkları

Emel Ekşioğlu, Yasemin Tombak, Zeynep Şener, Ajda Bal

University of Health Sciences Turkey, Dışkapı Yıldırım Beyazıt Training and Research Hospital, Clinic of Physical Medicine and Rehabilitation, Ankara, Turkey

Abstract

One of the risk factors for pelvic insufficiency fractures is rheumatoid arthritis (RA). Unfortunately, the diagnosis of these fractures is difficult in these patients and their treatment is delayed. When a patient with RA comes a complaint of pain in the groin or lower back without a trauma, it should be considered that this may be an insufficiency fracture, and careful clinical assessment and appropriate imaging methods should be used. Insufficiency fractures are a rare complication of RA. In our case a 70-year old woman with RA presented with acute onset severe left groin pain. Computed tomographic scan of the left hip showed that there is probably an old fracture on the left anterior to the acetabular roof and superior-inferior pubic ramus. Fractures in the patient were treated conservatively. Early diagnosis followed by proper treatment may help improve the quality of life and prevent disability of these patients.
Keywords: Insufficiency fracture, rheumatoid arthritis, quality of life, disability

Öz

Pelvik yetmezlik kırıkları için risk faktörlerinden biri romatoid artrittir (RA). Ne yazık ki bu hastalarda bu kırıkların tanısı güç olmakta ve tedavisi gecikmektedir. Bir RA hastası non-travmatik kasık veya bel ağrısı şikayeti ile geldiğinde bunun bir yetmezlik kırığı olabileceği düşünülmeli ve dikkatli klinik değerlendirme ve uygun görüntüleme yöntemleri kullanılmalıdır. Yetmezlik kırıkları RA'nın nadir görülen bir komplikasyonudur. Olgumuzda 70 yaşında RA'lı kadın akut başlangıçlı şiddetli sol kasık ağrısı ile başvurdu. Sol kalçanın bilgisayarlı tomografisi, asetabular çatının ve superıor-inferior pubis ramusunun önünde muhtemelen eski bir kırık olduğunu gösterdi. Hastadaki kırıklar konservatif olarak tedavi edildi. Erken teşhis ve ardından uygun tedavi, bu hastaların yaşam kalitesinin iyileştirilmesine ve sakatlıkların önlenmesine yardımcı olabilir.
Anahtar kelimeler: Yetmezlik kırığı, romatoid artrit, yaşam kalitesi, engellilik

Introduction

Insufficiency fractures are a subtype of stress fracture that occurs as a result of normal or physiological stress applied to the bone with reduced resistance. Major risk factors for insufficiency fractures are primary osteoporosis and secondary osteomalacia often in combination with old age and female gender. Other predisposing factors are rheumatoid arthritis (RA) renal failure, diabetes mellitus, hyperparathyroidism, long-term steroid use, previous radiotherapy, Cushing disease, liver cirrhosis, multiple myeloma and Wegener's diasease (1-3).

Resulting from their reduced walking capacity, disease-related inflammation, and glucocorticoid use, patients with RA have a higher risk of osteoporosis and fracture than the general population (4). Recently, chronic inflammation has been recognized as a potential risk factor for osteoporotic fractures (5). In a the Health Aging and Body Composition Study, it was shown that elevated inflammatory markers, such as Interleukin-2, interleukin-6, C-reactive protein (CRP) and tumor necrosis factor-α, were associated with osteoporotic fracture (6). insufficiency fractures in RA patients can occur anywhere in the body, and one of the most common sites is the pelvis.

This case report highlights a 70-year-old patient with RA who presented to the hospital with left groin discomfort and was diagnosed with a pubic ramus and iliac ala fracture. Parasymphyseal fractures with iliac ala fractures are uncommon, just as they were in our case (7).

Address for Correspondence/Yazışma Adresi: Yasemin Tombak MD, University of Health Sciences Turkey, Dışkapı Yıldırım Beyazıt Training and Research Hospital, Clinic of Physical Medicine and Rehabilitation, Ankara, Turkey
Phone: +90 312 596 2996 **E-mail:** yasemintombak@hotmail.com **ORCID ID:** orcid.org/0000-0003-0065-5376
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According to earlier reports, most of RA patients experiencing pelvic insufficiency fractures react favorably to conservative treatment. Subject fractures are mostly stable and the pain can be managed with bed rest (7).

Case Report

A female patient at her seventy with known RA (Rheumatoid factor: 187 IU/mL, anti-cyclic citrullinated peptide: 7 IU/mL), primary hypertension and diabetes mellitus complained of left groin pain with sudden onset and gradually becoming more severe. Three months after initial presentation she was admitted to our hospital. She had not been through anything traumatic recently, while she was unable to weight bear. A radiography of the pelvis showed a suspicious fracture line at the level of the left iliac side and pubic ramus (Figure 1). Then patient underwent computerized tomography (CT) imaging of the left hip joint. CT showed displaced and partially fragmented fracture lines, which are thought to be probably belong to the old fracture, in the anterior of the acetabular roof and superior-inferior pubic ramus on the left, and nodular hypodense soft tissue densities with indistinct borders in the intramedullary area (Figure 2a, b).

The patient's erythrocyte sedimentation rate was 39 mm/h and CRP was 11 mg/L.

The renal functions were as the following: alanine transaminase: 18.9 U/L, aspartate transaminase: 27.3 U/L, creatinine: 0.82 mg/dL, ure: 43.5 mg/dL, 25-OH vitamin D: 48 ng/mL, calcium: 9.38 mg/dL, phosphorus: 2.92 U/L, parathormone: 88.9 pg/dL. Patient's bone mineral density T-score was -2.1 in the left femur total, -3.0 in the L1-L4 vertebrae. She has been using prednisolone 5 mg/day for 15 years, leflunomide 20 mg/day and hydroxychloroquine 400 mg/day for 8 years for the treatment of RA.

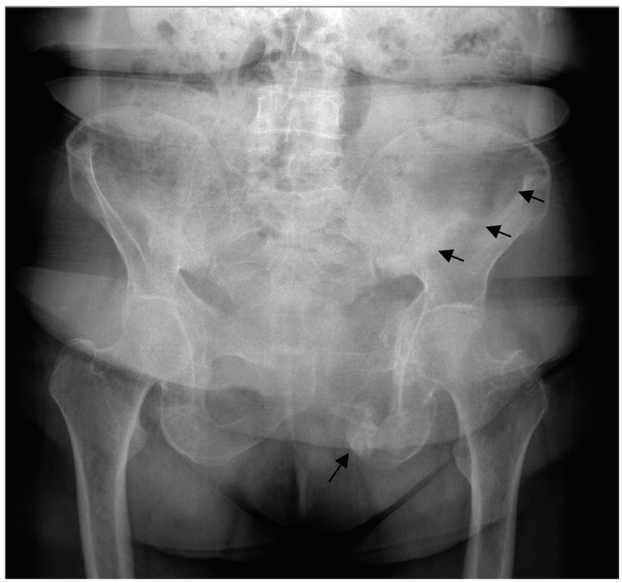

Figure 1. Fracture line at the level of the left iliac side and pubic ramus

On physical examination, the patient did not have swollen and tender joints and had no morning stiffness. [Disease Activity Score 28 (DAS 28): 3.26], Health Assessment Questionnaire (HAQ): 0.1 Short Form 36 (SF-36): 52, her pain with [visual analog scale (VAS), 0-10 mm): 7]. The patient was ambulatory with a single cane and had a Trendelenburg gait pattern. Left hip range of motion was normal. There is weakness in the lower extremity muscles, espicially in the abductor muscles.

Zoledronic acid 5 mg/100 mL was administered intravenously to the patient for the osteoporosis. The patient's physical therapy and rehabilitation program was started. Gait-balance exercises, strengthening exercises for the muscles of the lower extremities (especially hip abductors), cold pack and transcutaneous electrical nerve stimulation (TENS) application on the left posterior pelvis were performed daily. Tramadol 50 mg/day was started for her pain. After 2 weeks later the patient's left hip pain complaint regressed. It was observed that the patient was independently ambulated with minimal Trendelenburg gait at discharge with DAS 28: 2.21, HAQ: 0.05, SF-36: 54%, pain with VAS: 1 at discharge.

Discussion

Pelvic insufficiency fractures, according to the definition, occur when bone fails under normal physiologic load. Hence,

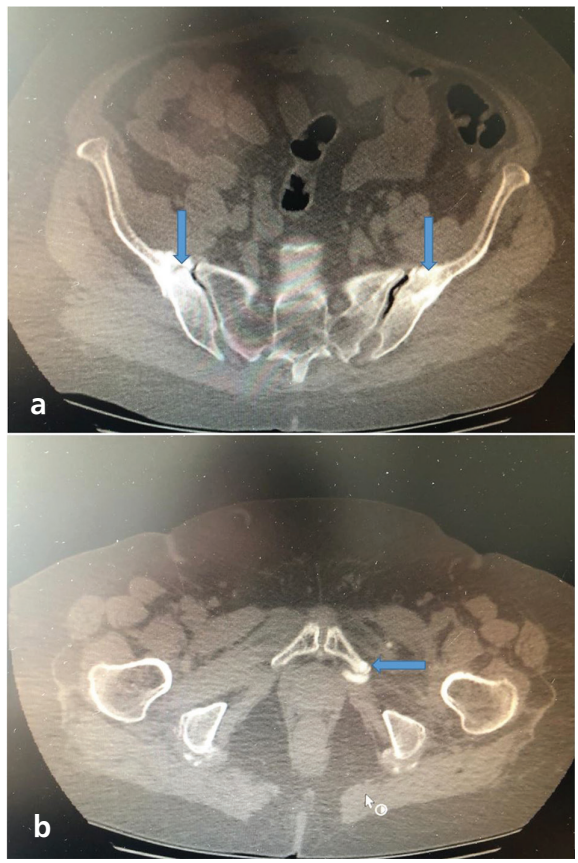

Figure 2a, b. Computerized tomography imaging of the right and left iliac bone fracture and left inferior ramus fracture

any disease that reduces bone density might be a risk factor (8,9). The incidence of insufficiency fractures is believed to be between 1 and 5 percent, depending on the referral population (1,10). Several conditions may consist bone density and strength, predisposing patients to insufficiency fractures and postmenopausal osteoporosis being the most cause among them. Other risk factors are chronic systemic diseases such as RA, long term glucocorticoid use and the use of radiotherapy (1,4). Pelvis insufficiency fractures are becoming more common, and they can cause significant disability in the elderly (8). Previously, pelvic insufficiency fractures and parasymphyseal fractures are separately described in RA patients. Less common are parasymphyseal fractures with iliac ala fractures (7). These combination fractures are hypothesized to be caused by the pelvic ring structure and the vertical shear stress delivered to this location (11). In our case; the patient has also multiple risk factors such as RA, long term glucocorticoid treatment and postmenapousal osteoporosis. Particularly, in our patient, the pelvic ring was grossly unstable due to a combination of parasymphyseal and iliac ala fractures, resulting in an inability to walk. Radiography and CT scan of the pelvis showed displaced and partially fragmented fracture lines in the anterior of the acetabular roof and superior-inferior pubic ramus and at the level of the left iliac side, supporting the diagnosis of pelvic insufficiency fracture.

The majority of pelvic insufficiency fractures are treated conservatively with bed rest and analgesia, followed by gradual mobilisation (9). Our patient's treatments involved physical therapy for example gait-balance exercises, strengthening exercises for the muscles of the lower extremities (especially hip abductors), cold pack and TENS. And for her pain relief we used tramadol 50 mg/day. At the end of 2 weeks, the patient's pain regressed to a great extent and she started walking unaided.

In conclusion, pelvic insufficiency fracture does not appear very often in patients with RA and diagnosis is often delayed. Expanded mindfulness of this condition and determination of suitable radiological examination methods will result in a faster and more precise conclusion and early detection of these fractures followed by appropriate treatment may aid in improving the quality of life and preventing disability.

Ethics

Informed Consent: Was obtained from the patient regarding the case report.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: E.E., Y.T., Concept: E.E., A.B., Design: E.E., A.B., Data Collection or Processing: Y.T., Z.Ş., Analysis or Interpretation: E.E., Y.T., Z.Ş., A.B., Literature Search: E.E., Y.T., Z.Ş., Writing: E.E., A.B.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

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Post-stroke Complication of Shoulder Dislocation and Fracture of the Humeral Head Due to Osteoporosis: A Case Report

İnme Sonrası Osteoporoza Bağlı Komplikasyon Olarak Gelişen Omuz Çıkığı ve Humerus Başı Kırığı: Bir Olgu Sunumu

Özgür Zeliha Karaahmet, Gülnur Çelik, Yasemin Tombak Yıldızkan, Ece Ünlü Akyüz

University of Health Sciences Turkey, Dışkapı Yıldırım Beyazıt Training and Research Hospital, Clinic of Physical Medicine and Rehabilitation, Ankara, Turkey

Abstract

Fracture of the humeral head and posterior or anterior dislocations of the shoulder joint due to osteoporosis are rare. Bilateral shoulder fracture dislocation has recently begun to appear in the literature. Moreover, the occurrence of this lesion following an ischemic stroke appears to be another new element in its ethiopathogenesis. Here, it was presented as a case report of bilateral shoulder fracture and dislocation in a patient who previously developed left hemiplegia due to stroke. To our knowledge, this is the first case of o shoulder fracture-dislocation developed after minor trauma due to osteoporosis in a former stroke patient.
Keywords: Shoulder dislocation, shoulder fracture, hemiplegia, osteoporosis

Öz

Osteoporoz nedeniyle humerus başı kırığı ve omuz ekleminin posterior veya anterior çıkıkları nadirdir. Bilateral omuz kırıklı çıkığı yeniden literatürde yer almaya başlamıştır. Ayrıca, bu lezyonun bir iskemik inmeyi takiben ortaya çıkması, etiyopatogenezinde başka bir yeni unsur gibi görünmektedir. Burada daha önce inme nedeniyle sol hemipleji gelişen bir hastada bilateral omuz kırığı ve çıkığı olgusu sunuldu. Bildiğimiz kadarıyla bu olgu, inme geçirmiş bir hastada osteoporoza bağlı minör travma sonrası gelişen ilk omuz kırıklı çıkığı olgusudur.
Anahtar kelimeler: Omuz çıkığı, omuz kırığı, hemipleji, osteoporoz

Introduction

Stroke is the second most common cause of mortality worldwide (1). Stroke generally affects the elderly population. The elderly population is also at risk for osteoporosis and fractures. Post-stroke patients experience many complications in the early and late stages, one of which is osteoporosis. Post-stroke metabolic disorders and physical inactivity cause acceleration of bone mass loss (2-4). It has been reported in studies that the risk of hip fractures after stroke is two to four times higher than healthy controls matched by age (5). Many studies have shown that significant bone mineral loss is higher especially on the paretic side in patients with stroke (6).

The rare cases of dislocation of bilateral shoulder fractures occur during epileptic seizures or in the course of trauma that occurs during convulsions (7). According to reports from today, divergence form of these bilateral shoulder fracture dislocation is a new aspect. Moreover, the occurrence of this lesion following an ischemic stroke appears to be another new element in its ethiopathogenesis (8).

Herein, it was presented as a case report of bilateral shoulder fracture and dislocation in a patient who previously developed left hemiplegia due to stroke. The patient consent was obtained.

Case Report

A 69-year-old male patient had left hemiplegia due to a stroke in September 2009. The patient could be ambulatory in the house with the support of a single person and with a cane. The patient was withdrawn from his left shoulder while being helped during the transfer in June 2019, and a fracture and dislocation occurred in the left shoulder. Later, in September 2019, a fracture and dislocation occurred in the right shoulder as a result of excessive pulling on the right shoulder during the transfer of

Address for Correspondence/Yazışma Adresi: Özgür Zeliha Karaahmet Assoc. Prof., University of Health Sciences Turkey, Dışkapı Yıldırım Beyazıt Training and Research Hospital, Clinic of Physical Medicine and Rehabilitation, Ankara, Turkey
Phone: +90 505 815 15 85 **E-mail:** drozguroz@gmail.com **ORCID ID:** orcid.org/0000-0002-1338-8935
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the patient. The dislocated shoulder was reduced and remained in a cast for 20 days (The direct radiography of the patient's right shoulder before and after reduction is shown in Figure 1). The patient, who had fractures and dislocations in both shoulders within 4 months, was admitted to the physical medicine and rehabilitation clinic for rehabilitation at wheelchair level. In the physical examination, the patient had a short-term sitting balance. His ambulation was at wheelchair level. FIM motor was 17, FIM cognitive was 35, total was 52. Brunnstrom upper limb on the left was 2, hand was 2, lower limb was 3. Range of motion: Right shoulder passive abduction was 90, internal rotation was 90, external rotation was 70; left shoulder passive abduction was 60, flexion was 90, internal rotation was 90, external rotation was 70. His left supraspinatus and infraspinatus muscles were markedly atrophied. In laboratory tests; his bone mineral density (BMD) of the femur neck was -3.4, L1-L4 BMD was -3.4. Hemogram, biochemical tests, parathormone, calcium, phosphorus, and alkaline phosphatase values, and 24-hour urinary calcium values were within normal limits in the blood tests of the patient. Apart from stroke, the patient did not have a history of any other disease that could cause osteoporosis or any medication use. Calcium-vitamin D treatment (1.000 mg/day calcium, 800 IU/day vitamin D) and zoledronate treatment (5 mg/year) were initiated for the patient.

The patient was initiated upper extremity electrical stimulation, ROM exercises, pendulum and stretching exercises as physical therapy, in addition to balance and coordination exercises, ambulation training, trunk balance, and bicycle ergometer. Afterward, walking training was started with auxiliary devices, first in a parallel bar, then with a rollator. The patient was discharged after 6 weeks with the help of a walker and ancillary orthosis, with ambulation.

Discussion

A review of literature revealed more than 15 cases of bilateral fracture-dislocations of shoulder. Fractures and dislocations of the shoulder which have been seen in patients with stroke are associated with epileptic seizures (8). In the literature, we did not find a case of shoulder fracture-dislocation developed after minor trauma due to osteoporosis in a former stroke patient.

Physical inactivity is a problem that increases the risk of both stroke and osteoporosis. Immediately after stroke, patients were found to have lower BMD compared with law-matched controls (4). Studies have shown that ambulation is very important in the first two months after stroke. The therapeutic effects of exercise have been reported in the elderly, especially those with chronic diseases and those at risk of stroke, osteoporosis and falling. Low FIM scores correlated with bone loss (9). Serious osteoporosis was detected in the case we presented. It was learned that the patient had a stroke 10 years ago and was able to walk with a cane and person support. As can be understood from here, it is seen that the patient has a serious sedentary life and received assistance during ambulation and transfers. As a matter of fact, while he was getting help, he had fractures and dislocations in his left shoulder and then right shoulder.

In conclusion, low BMD may be associated with limited ambulation and low FIM. Early mobilization should be targeted in stroke rehabilitation.

Ethics

Informed Consent: Informed consent was obtained from the patient regarding the case report.

Peer-review: Internally peer-reviewed.

Authorship Contributions

Concept: Ö.Z.K., Y.T.Y., E.Ü.A., Design: Ö.Z.K., E.Ü.A., Data Collection or Processing: Ö.Z.K., G.Ç., Analysis or Interpretation: Ö.Z.K., Y.T.Y., E.Ü.A., Literature Search: Ö.Z.K., Y.T.Y., Writing: Ö.Z.K., G.Ç.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

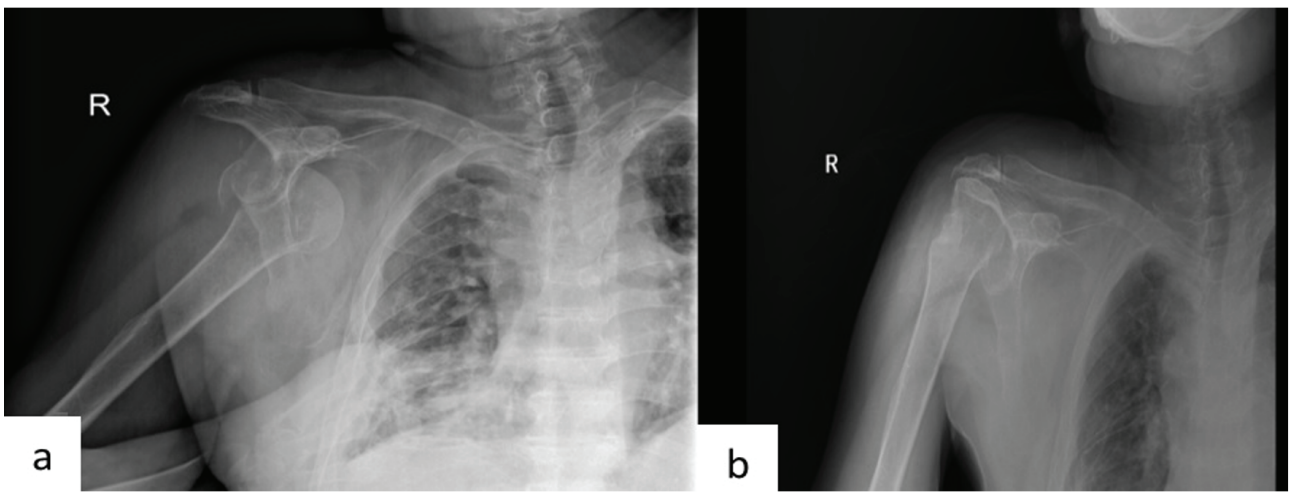

Figure 1. a. Right shoulder radiography posterior dislocation and femoral head fracture, **Figure 1. b.** Right shoulder radiography after reduction

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Letter to the Editor / Editöre Mektup

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We Can Avoid Vasovagal Syncope with the Simple Positioning Rule

Basit Pozisyonlama Kuralı ile Vazovagal Senkoptan Korunabiliriz

Ebru Kübra Taşpolat, Mustafa Turgut Yıldızgören*, Fatih Bağcıer

University of Health Sciences, Başakşehir Çam and Sakura City Hospital, Clinic of Physical Medicine and Rehabilitation, İstanbul, Turkey
*Fizikon Medical Center, Department of Physical Medicine and Rehabilitation, Konya, Turkey

Dear Editor;

Myofascial trigger points constitute a common and complex entity that manifests with different symptoms depending on their localization. Conventional techniques and invasive treatment approaches are used (1). Invasive treatment modalities include dry needling, local anesthetic administration, and botox injections. During treatment, side effects may appear directly depending on the needle penetration sites or indirectly in autonomic nervous system activation. Complications like neurovascular injuries, pneumothorax damage, and abdominal wall damage are side effects of the needle penetration site (2). On the contrary, vasovagal syncope is an indirect side effect caused by autonomic nervous system activation (3).

Vasovagal syncope is the transient loss of consciousness resulting from instantaneous cerebral hypoperfusion characterized by rapid onset, short duration, and complete spontaneous recovery. Various conditions, including pain, stress, needle phobia, and prolonged standing, can trigger it. Vasovagal syncope can be observed after prodromal symptoms like nausea, pallor, sweating, dizziness, tinnitus, gray out, and faintness (3). Therefore, the physician should be aware of this and monitor the patient for such symptoms. Notably, vasovagal syncope can be encountered both during and after treatment. Therefore, monitoring the patient for up to 10 minutes following treatment would be beneficial.

An important issue that should be addressed while applying myofascial trigger point therapy is ensuring the physician's and patient's correct positioning during needling. This way, the physician can ensure procedural ergonomics and access the treatment site easily. Another critical issue, which can be overlooked, includes the practices adopted at outpatient clinics wherein myofascial trigger point therapy is administered. At the same time, the patient is in a seated position (Figure 1a). Considering this, the authors recommend administering the treatment while the patient lies, regardless of the involved muscle (Figure 1b) (4). Although unnecessary, this approach minimizes the possibility of vasovagal syncope. Although case presentations in the literature suggest the association of thicker needles with vasovagal syncope, there is no clear information about such an association (3).

The algorithm suggested here is to ensure verbal or physical communication with the patient during treatment. If prodromal symptoms appear, the first step is to provide the patient with a safe environment, not overreact, and elevate the patient's legs (4). Nothing is probably required other than terminating treatment and observing the patient (5). It is recommended to refer the patient to the emergency department if the symptoms persist or the patient does not feel well. In relatively rare cases, when the patient loses consciousness, the patient's head should be turned to one side to facilitate breathing. It is recommended to check the vital signs, perform electrocardiography, and immediately conduct necessary medical interventions (4).

In conclusion, vasovagal syncope is not a rare occurrence. Studies in this field would be very important for predicting the

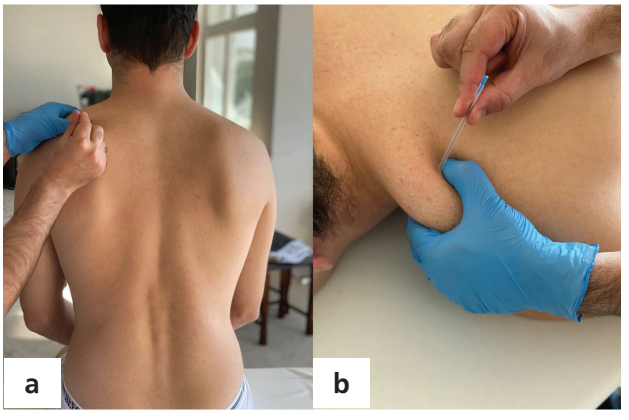

Figure 1. Two different patient position a) dry needling treatment for upper trapezius muscle in a sitting position, b) dry needling treatment for upper trapezius muscle in a supine position

Address for Correspondence/Yazışma Adresi: Ebru Kübra Taşpolat Asst, University of Health Sciences, Başakşehir Çam and Sakura City Hospital, Clinic of Physical Medicine and Rehabilitation, İstanbul, Turkey
Phone: +90 534 721 96 05 **E-mail:** ebrutaspolat@gmail.com **ORCID ID:** orcid.org/0000-0003-0686-0653
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possible risks and reducing the rate of autonomic reflexes. When encountered, an algorithmic intervention approach should be planned.

Keywords: Myofascial trigger point, vasovagal syncope, positioning, dry needling
Anahtar kelimeler: Miyofasyal tetik noktası, vazovagal senkop, pozisyonlama, kuru iğneleme
Peer-review: Externally and internally peer-reviewed.
Conflict of Interest: No conflict of interest was declared by the authors.
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