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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, Index Copernicus, Embase, Scopus, Proquest, J-Gate Academic Keys, TÜBİTAK/ULAKBİM, Hinari, Oare, Ardi, Goali, Türk Medline Ulusal Atıf İndeksi ve CABI tarafından indekslenmektedir.

Açık Erişim Politikası

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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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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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 reqiuirements 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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3) Editöre Mektuplar:
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5) Eğitim Yazıları:
Bu kategoride otörler osteoporoz, metabolik kemik hastalıkları ve rehabilitasyon konularındaki güncel bilgileri özetlerler.

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

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Türk Osteoporoz Dergisi

TURKISH JOURNAL OF OSTEOPOROSIS

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The Journal publishes papers on all aspects of osteoporosis, metabolic bone diseases and its rehabilitation. In addition to original articles, review articles, original case reports, letters to the editor, scientific letters, educational articles, abstracts from new literature and announcements of future congresses and meetings are also published.
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Türk Osteoporoz Dergisi
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Türk Osteoporoz Dergisi
TURKISH JOURNAL OF OSTEOPOROSIS

Editörden / Editorial

Sevgili Meslektaşlarımız,

Ülkemizi ve Dünyayı etkisi altına alan COVİD-19 hastalığı nedeniyle tüm sağlık personelinin üstün sorumluluk bilinci ve büyük özveriyle çalıştığı bu çok zor günlerin en kısa sürede bitmesini gönülden diliyoruz. Pandemi sürecinde de meslektaşlarımızın akademik faaliyetlere yönelik çabalarının devam ederek, dergimize basım için yayın akışı sürmesinden büyük mutluluk duyuyoruz.

Bu salgın nedeniyle tüm dünyada yapılması planlanan birçok bilimsel kongre iptal edilmiştir veya yüz yüze yapılan kongrelerin yerini online kongreler almıştır. Türkiye Osteoporoz Derneği ev sahipliğinde ve International Osteoporosis Foundation bilimsel desteği ile 08-11 Ekim 2020 tarihlerinde Sheraton Otel Çeşme, İzmir'de yapılması planlanmış olan 7.Ulusal Osteoporoz Kongresi (OSTEO2020) de aynı yerde 07-10 Ekim 2021'e ertelenmiştir. Bu sene kongre gerçekleşemeyince 10-11 Ekim 2020 tarihlerinde bilgi güncellemeye yönelik olarak online "Osteoakademi" eğitim etkinliği başarıyla yapılmıştır. Gene derneğimiz tarafından 1-2 Nisan 2021 tarihlerinde online olarak Osteoporoz Halk Kongresi yapılmıştır.

Osteoporoz,Osteoartrit ve Kas İskelet Sistemi Hastalıkları Dünya Kongresi'nin (WCO-IOF-ESCEO) 26-29 Ağustos 2021 tarihlerinde Londra'da yapılacağı bildirilmiştir.

Siz değerli meslektaşlarımıza bu zor pandemi günlerinde kolaylıklar diler; güzel günlerde görüşmek arzusuyla, sevgi ve saygılarımı sunarım.

Editör
Prof. Dr. Yeşim Kirazlı

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Development of the Protection Against Osteoporotic Fractures Scale

Osteoporotik Kırıktan Korunma Ölçeği'nin Geliştirilmesi

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Abstract

Objective: Osteoporosis is a bone disease that increases the risk of fractures. One out of every two women and one out of every five men are at risk for osteoporosis-related fractures during their lifetime. Bone loss can be prevented by taking precautions in every phase of life. To avoid the serious consequences of osteoporosis, healthy behaviours should be supported using theories of health behaviour as a framework. This study aimed to develop protection against osteoporotic fractures (PROF) scale and to test its validity and reliability.

Materials and Methods: This study was conducted among >55-year-old female outpatients who were admitted to the orthopaedic clinics of Zonguldak Atatürk Public Hospital. Test-retest was applied via face-to-face interviews. The sample size was calculated to be 10 times the number of scale items, resulting in a sample of 400 participants. The theory of planned behaviour provided the theoretical framework for the PROF scale development. Four strategies have been selected for PROF: (1) Bone mineral density measurement, (2) adherence to treatment, (3) physical exercise and (4) regulations to prevent falls at home.

Results: Factor and matrix correlations of the scale ranged from 0.68 to 0.130. Test-retest reliability of the whole scale was 0.95. Cronbach's α value was found to be 0.95. A strong and statistically significant positive correlation was noted between attitudes and subjective norms pertaining to PROF (r=0.520; 0.525; p=0.01, respectively). A moderate and statistically significant positive correlation was noted between intention and behaviour control (r=0.462; p=0.01).

Conclusion: The PROF scale was found to be highly valid and reliable. It can be a part of the public health model aimed at preventing osteoporotic fractures.

Keywords: Osteoporosis, osteoporotic fracture, theory of planned behaviour, scale development, reliability

Öz

Amaç: Osteoporoz kırık oluşma olasılığının arttığı bir kemik hastalığıdır. Her iki kadından biri, her beş erkekten biri hayatlarının bir döneminde osteoporoz ile ilgili kırık riski altındadır. Her dönemde önlemler alarak kemik kaybı önlenebilir. Osteoporozun ciddi sonuçlarından korunmak için sağlık davranış teorileri ile sağlık davranışı desteklenmesi gerekir. Bu çalışmada amaç osteoporotik kırıktan korunma (PROF) ölçeğini geliştirmek, geçerlilik ve güvenirliliği göstermektir.

Gereç ve Yöntem: Çalışma Zonguldak Atatürk Devlet Hastanesi'nin Ortopedi Polikliniği'ne ayaktan başvuran 55 yaş üstündeki kadınlarda yürütülmüştür. Yüz yüze görüşme tekniği kullanılarak test re-test yapılmıştır. Örneklem seçilmeden, örneklem sayısı madde sayısının on katı olarak 400 hesaplanmıştır. Planlı davranış teorisi model olarak alınmıştır. Niyet ve davranış bağımlı değişkenlerdir. Tutum, öznel norm ve davranış kontrolü bağımsız değişkenlerdir. PROF'de dört strateji: 1) Kemik mineral yoğunluğu ölçümü, 2) tedaviye uyum, 3) fiziksel egzersiz ve 4) evde düşmeyi önleyecek düzenlemeler seçilmiştir.

Bulgular: PROF niyeti ile tutum ve öznel norm arasında istatistiksel olarak pozitif yönde, güçlü ve anlamlı bir ilişki vardır (sırasıyla r=0,520; 0,525; p=0,01). Davranış kontrolü ile niyet arasında istatistiksel olarak pozitif yönde, orta güçte ve anlamlı bir ilişki vardır (r=0,462; p=0,01). Güvenirlilik Cronbach α değeri 0,95'dir.

Sonuç: PROF için geliştirilen ölçek yüksek güvenirlilik ve geçerliliğe sahiptir. Osteoporotik kırıklarla mücadelede halk sağlığı modellerinin bir parçası olabilir.

Anahtar kelimeler: Osteoporoz, osteoporotik kırık, planlı davranış teorisi, ölçek geliştirme, güvenirlilik

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Introduction

Osteoporosis (OP) is the most common bone disease. OP is a skeletal system disease with increased risk for fractures and is characterized by reduced bone mineral density (BMD) and deteriorations in the bone tissue microstructure. According to the 2004 report of the World Health Organization, more than 200 million people suffer from OP and approximately 40% of affected people consist of females and people older than 50 years of age. Optimal power-flows (OPF) constitute approximately 1% of disability-adjusted life years pertaining to chronic diseases (1).

There are various risk factors for OP due to its multifactorial nature. Behaviors such as healthy nutrition, adequate physical activity, sensible medicine use, smoking cessation, and avoiding excessive alcohol consumption are important for protection against OP (2). Behaviors which promote bone development including sufficient calcium intake and regular weightlifting may decrease the risk for OP (2,3). Despite the well-documented benefits of exercise, aging women keep pursuing a sedentary lifestyle (4). Health education is a powerful instrument in terms of protection against OP and its consequences. Health behavior and lifestyle changes can be complex (5).

The theory of planned behavior (TPB) proposes a model which can measure how human behavior is shaped. The TPB investigates beliefs and attitudes that underlie health behaviors. According to this model, intention predicts the formation of a deliberate behavior (6).

TPB is determined by three conceptually independent constructs: attitudes towards a behavior, subjective norms, and behavior control. These three behaviors determine attitudes towards a behavior (7,8). Subjective norms are based upon the belief that reference person or groups approve the behavior (9). TPB is a health promotion theory for optimizing OPF. There wasn't any study which to promote positive health behaviors about OPF which was based on the TPB.

The aim of this study was to develop the protection against osteoporotic fractures (PROF) scale based on the TPB model.

Materials and Methods

In this study, based on the TPB model, a measure for protection against osteoporotic fractures in postmenopausal women was developed.

The current study was carried out at the Zonguldak Atatürk Public Hospital Orthopedic Clinics, which is located in the city of Zonguldak. The annual number of outpatients admitted to these clinics is 66,256. Universe of the study consisted of postmenopausal women aged above 55 years who admitted to the Zonguldak Atatürk Public Hospital Orthopedic Clinics. The study sample included postmenopausal women aged above 55 years who were outpatients and who were willing to participate in the study. Each patient was informed about the study and written consent was taken from the patients.

Sample size was determined by multiplying the number of items (40 items) by 10, resulting in a sample size of 400 participants (10,11). The study was conducted with 400 outpatients who admitted to the hospital from May, 21st to September, 10th of the year 2015.

Inclusion criteria: Being a postmenopausal women aged 55 years and above, not undergoing major surgery during the last 2 months, not having an amputation.

Limitations: The sample does not represent all postmenopausal patients since it consisted of volunteering outpatients admitted to an orthopedic clinic. The follow-up period was 6 months and may not be of adequate length in terms of observing the consequences of behavior in the long run.

Definitions and Criteria Related to PROF Scale Variables

The PROF scale was developed according to the TPB. The variables "Attitude", "Subjective Norm", and "Perceived Behavior Control", which affect "Intention", the core of the model, were primary variables. Secondary variables/determinants of the model were beliefs measured through "Behavioral Beliefs", "Normative Beliefs", and "Control Beliefs". Notably, the role of past behavior, in addition to accounting for the influence of habitual behavior in intention and behavior, are evident in earlier studies (6). Therefore, it was decided that the past behavior should be included in the PROF scale.

In the study, 5-point Likert type response categories ranged from "I absolutely disagree" (1) to "I totally agree" (5). Since only the control beliefs difficulties part were negatively worded, the 5-point Likert type responses ranged from "I absolutely disagree" to "I totally agree" (1,5).

The scale was prepared based on the TPB model, which is one of the health promotion models for developing target behaviors (7,9). In the PROF scale, four target activities aimed at protecting women against OPF's included maintaining a calcium-rich diet-sunbathing, use of OP medication when necessary, daily physical activity-programmed exercises, and new house arrangements to prevent falls. Each activity was adapted to the TPB model. For each strategic precaution, the TPB was used to create a pool of 98 items. Forty items were selected from the item pool for draft of PROF scale. Higher scores indicated higher levels of protection, while lower scores indicated insufficient protection. For a standard TPB based study, a draft scale was formed by 5 experts. According to the opinions of the experts, the items that were stated to be problematic were corrected in line with the recommendations and 98 items were subtracted and a draft scale consisting of 40 items was created. Thus, content validity was established. Reliability was tested using the test-retest method, where the scale was readministered after a two week interval.

Ethical approval was obtained from the Bülent Ecevit University Faculty of Medicine Clinical Research Ethics Committee (protocol no: 2015-18-20/05). Administrative permission to conduct the study was obtained from the Zonguldak Public Hospital (document numbered 79914002/900 and record

numbered 7201). Two interviews and a test-retest application were conducted with each volunteering patient via the face-to-face interview method. Data was collected from 400 patients using the sociodemographic data form and the PROF scale. Participants answered the PROF scale by selecting one of the 5-point Likert type response categories (12). Also a questionary which contained a12-item information form questioning sociodemographic and OPF's related characteristics was used.

Statistical Analysis

Statistical analysis of the study was conducted using the SPSS 19.0. Data was tested for normality using the Shapiro-Wilk test. The Mann-Whitney U test was applied to non-normally distributed variables in 2 group comparisons, while the Kruskal-Wallis test was used for 3 group comparisons. Spearman correlation analysis was used to examine the relationship between the variables. Factor analysis was used to determine the subscales of the scale. Cronbach alpha (Cr α) internal consistency coefficient was calculated in evaluating the reliability of the scale. Level of statistical significance was set at $p<0.05$.

Reliability Analyses

Two different methods of reliability, namely internal consistency and time validity, were used of assessing the reliability of the draft of PROF scale which includes 40 items. In order to evaluate reliability, Cr α internal consistency coefficient was first calculated. Cr α is an appropriate internal consistency method when response categories range from 1 to 5 (13). Cr α internal consistency coefficient is calculated by dividing the total item variance to the general variance. This coefficient may range from 0 to 1. A value over 0.70 indicates high levels of reliability (14). The test-retest technique, which evaluates invariance of test scores over time, was used by examining the correlation between pre- and post-test results. For establishing content validity, the content of the scale was logically evaluated by four experts. In order to be able to discover and reveal the dimensions of the scale, a principal components analysis (PCA), which is one of the exploratory factor analysis (EFA) methods, was carried out. To determine the factor structure of the scale, a principal component analysis with varimax rotation, which is a linear rotation technique, was conducted. In factor analysis, factor loadings of 0.60 and above was considered as high, while 0.30-0.59 was considered as moderate loading, regardless of plus and minus signs (14). In the current study, a total of 22 items with rotated factor loadings above 0.30 were included in the factorial construct.

In order to be able to discover and reveal the dimensions of the scale that are required in the scale development process. Confirmatory factor analysis (CFA) procedures were conducted, and all analyses were carried out using the AMOS Version 4.1 software. Data were analyzed in five stages: (1) we conducted EFA with half of the sample using maximum likelihood extraction with oblique rotation using structural equation modeling statistics package AMOS 6.0 (2). We confirmed the fit of the generated factor structure in the second half of the sample by conducting CFA (3).

Extraction and rotation; to determine the factor structure of the scale, principal component analysis was performed with orthogonal (Varimax) rotation, which is a linear rotation technique (11,12). In this study, 22 items with a factor load of 0.30 after rotation were included in the factor structure. Thus, 18 items from the load of 0.29 were removed from the draft scale.

Results

The mean age of the 400 patients was 62.7±7.17. Patients were at the least 55 years old and at the most 86 years old. It was found that 68.5% were married, 31.5% were single, and 10.3% live alone. Among the participants, 79.1% were housewives, 9.3% were retired, 6.8% were in paid employment, and 4.8% reported to be unable to work. Of the women, 43.5% were illiterate, 11.3% were literate, 30.2% were elementary school graduates, 8.5% were high school graduates, and 6.5% were university graduates.

It was found that 80.8% of women were active at home or outside on a daily life (house chores, gardening, shopping).

Among the participants, 35.8% stated that they never fell, 45.5% said they had fallen but did not have bone fractures, 16.3% had a fracture, and 2.5% had multiple fractures. For BMD measurements, bone scan was "never done" in 37.0% of the participants, was done at least once in 63.0%, and was frequently and/or completely done in 9.6%. It was found that 44.8% of the patients never adhered to doctors' medical advice and nutrition recommendations, 32.3% reported to minimally adhere, and 10.8% reported to completely adhere. Among the participants, 63.5% of patients did not regularly engage in physical exercise in the last year, 20.4% rarely exercised, and 6.9% frequently exercised. Of the participants, 63.3% said that they did not make any arrangements in their houses to prevent falling, 19.2% did minimal arrangements, and 5.8% did considerable arrangements.

TPB variables and retest reliability of the PROF scale test were given in Table 1. The PROF scale had a Cr α coefficient of 0.95, while the Cr α coefficients of the variables ranged from 0.70 to 0.89. Test-retest reliability of the entire scale was 0.95 ($p<0.01$) and the test-retest reliability of the variables were 0.72-0.90.

Suitability of data for factor analysis was examined using the KMO value, which was found to be 0.90 (excellent). The Bartlett Sphericity value was $p=0.001$ and below 0.10. These two values indicate that factor analysis can be conducted.

To test construct validity, an exploratory analysis, the PCA, was initially used. Items with factor loadings above 0.30 were determined and the PROF scale was reduced to 22 items. A varimax rotation was conducted, resulting in 6 factors with Eigenvalues above 1. Factor 1 accounted for 36.44% of the total variance, factor 2 accounted for 8.49%, factor 3 accounted for 7.15%, factor 4 accounted for 4.85%, factor 5 accounted for 4.22%, and factor 6 accounted for 3.87%. In the study, total variance was found to be 65.0%. The 28-item factor structure

and total variance of the PROF scale was provided in Table 2.

Table 2 shows the matrix structure of the PROF scale. The items grouped under 6 factors. Sixteen items were removed from the scale.

Factor matrix structure of the sub scales of the PROF scale were given in Table 3 and 4.

Correlations between variables fromed in accordance with the TPB model were shown in Table 4.

A final confirmatory model was proposed that had structure with the six factors being nested within structure of PROF scale. This model also passed the fit criteria, and the results are given at the bottom of Table 5.

CFA model goodness fit indexes of PROF scale with 22 items were very high Table 5.

Relative chi-square index (CMIN/DF) value was found to be 3.41. This value is considered sufficient for the model to be accepted. The adjusted goodness-of-fit index value of 0.834, the goodness-of-fit index (GFI) value of 0.870, the comparative fit index (CFI) value of 0.900. Approximation of the GFI and CFI values to 1 indicates increased compliance. Root mean square of the residuals of 0.078 indicates that the goodness of fit is high. Based on the post-deposition treatment (PDT), the initial 40-item model CFA. According to their calculations, the model was not considered acceptable when looking at the goodness of fit indexes. PROF scale CFA model fit goodness indices The DFA model goodness of fit index of the 22-item. A final confirmatory model was proposed which had the structure of the six factors being nested within the structure of PROF scale. The model also passed the fit criteria, and the results were given at the bottom of Table 5.

In Figure 1 CFA standardized regression coefficients and factor correlation values were seen. There were positive strong correlation with F1 and four factors F2 (r=0.532), F4 (r=0.707), F5 (r=0.803) and F6 (r=0.614). There were were positive strong correlation with F2 and two factors F5 (r=0.571) and F6 (r=0.614). Also F4 and F5 were positive strong correlated (r=0.614).

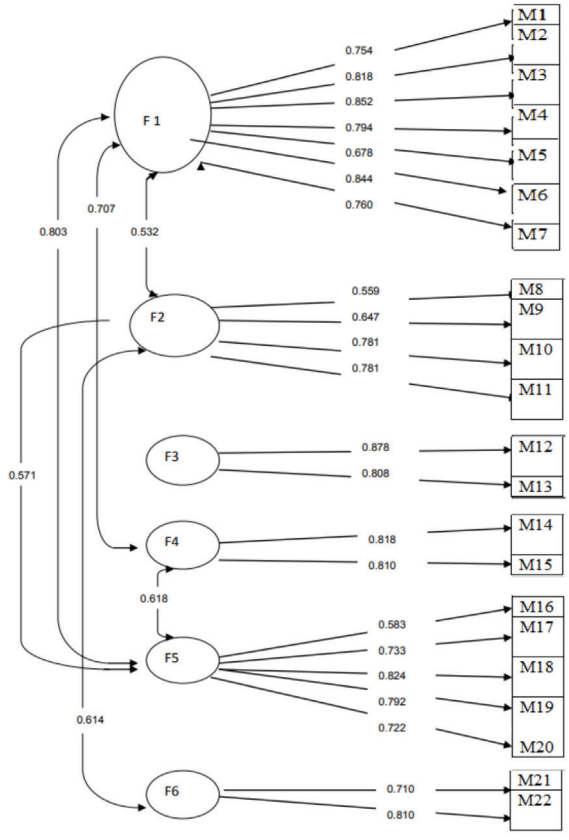

Figure 1. First-level exploratory factor analysis with standardized results

Table 1. Theory of planned behavior variables of protection against osteoporotic fractures scale test and re-test reliability

Factors	Items	Test Cr α	Re-test Cr α
1- Behavioral beliefs (items: 1-7)	7	0.82	0.83
2- Intention (items: 8-11)	4	0.70	0.76
3- Past behavior (items: 12-13)	2	0.73	0.72
4- Subjectif norm (items: 14-15)	2	0.84	0.85
5- Perceived behavioral control (items: 16-20)	5	0.86	0.85
6- Attitute (items: 21-22)	2	0.71	0.72
Total	22	0.95	0.95

Table 2. The factor variance and total variance of the protection against osteoporotic fractures scale

Factor	Eigenvalue	Variance total	Variance	Number of items
1	10.20	36.44	36.44	7
2	2.37	8.49	44.93	4
3	2.00	7.15	52.09	2
4	1.36	4.85	56.95	2
5	1.82	4.22	61.17	5
6	1.08	3.87	65.4	2

Table 3. Factor matrix structure of the sub scales (F1-3) of the protection against osteoporotic fractures scale		
Items	**English version of PROF items**	**r**
Behavioral beliefs (F1)		
1	If I know about the proper physical exercises I can do, it will be easier for me to do physical exercise.	0.778
2	If you exercise physically, you will be protected from bone fractures, and you will live longer without being dependent on anyone.	0.743
3	If I have knowledge about anti-dumping domestic regulations, it will be easier to take measures.	0.657
4	It will be easier for me to follow the recommendation if I know about the medical treatment or supplemental support recommended by the doctor.	0.645
5	If I apply the medical treatment recommendations that my doctor recommends, I should be protected from bones and fractures.	0.636
6	Physical exercise is difficult for me.	0.613
7	It is difficult for me to arrange it in the house to prevent falling.	0.545
Intention (F2)		
8	I intend to measure BMD at certain intervals.	0.694
9	I intend to comply with the medical treatment or supplementary advice suggested by my doctor to protect from bone erosion.	0.678
10	I intend to make an arrangement to prevent my home from falling within a year.	0.678
11	I want to make arrangements in the house to prevent falling.	0.653
Past behavior (F3)		
12	I have done BMD measurements at certain intervals until now.	0.887
13	I applied the medical treatment or supplementary advice suggested by the doctor to protect from bone marrow.	0.904
BMD: Bone mineral density, PROF: Protection against osteoporotic fractures		

Table 4. Factor matrix structure of the some sub scales (F4-6) of the protection against osteoporotic fractures scale		
Items	**English version of PROF items**	**r**
Subjectif norm (F4)		
14	My family and friends are welcomed to exercise physical exercise in order to avoid bone loss.	0.600
15	My family and my friends hopes to make a new arrangement in the house to prevent the fall.	0.599
Perceived behavioral control (F5)		
16	I want to do proper physical exercise.	0.694
17	It is necessary to make a new arrangement in the house to prevent falling.	0.678
18	I have the ability to make arrangements inside the house to prevent falling.	0.678
19	I have a BMD measure.	0.653
20	There is a medical practitioner's advice on medical treatment or supplementary advice.	0.636
Attitute (F6)		
21	It is necessary to carry out BMD measurements at certain intervals.	0.744
22	It is necessary to follow the ecommendations of the doctor for medical treatment or supplementary support.	0.778
BMD: Bone mineral density, PROF: Protection against osteoporotic fractures		

Discussion

The Centers for Disease Control determined people who needed screening. Screening is recommended for Caucasian women aged 65 years or above without any additional risk factors, while it is recommended for younger women who are at risk for OP and fractures (15). Since there are no scales on protection against fractures based on the TPB model, an EFA was undertaken in the current study in order to explore an empirical construct (15,16). According to the results of the factor analysis, which was conducted in order to test the construct validity of the PROF scale, 28 items with factor loadings ranging from 0.39 to 0.77

Table 5. Confirmatory factor analysis model goodness fit indexes of protection against osteoporotic fractures scale with 22 items

CFA model goodness fit indexes of PROF-scale with 22 items							
χ^2	DF	p	CMIN/DF	AGFI	GFI	CFI	RMSEA
734,334	215	0.001	3.416	0.834	0.870	0.900	0.078
CFA model goodness fit indexes of PROF-scale with 40 items							
2894.065	568	0.001	5.095	0.614	0.671	0.763	0.101

CFA: Confirmatory factor analysis, DF: Degree of freedom, CMIN/DF: Relative chi-square index, AGFI: Adjusted goodness-of-fit index, GFI: Goodness-of-fit index, CFI: Comparative fit index, RMSEA: Root mean square of the residuals, PROF: Protection against osteoporotic fractures

were grouped under 6 factors. The 6 factors explained 65% of the total variance. Measurements taken from the same patients were found to be highly reliable. The Cr α coefficient of the entire scale was 0.95 and ranged from 0.70 to 0.89 for the subscales. The factor and matrix correlations of the scale varied from 0.68 to 0.130. Test-retest reliability of the entire scale was 0.95 and varied from 0.72 to 0.90 for the subscales. Accordingly, it was demonstrated that the PROF scale was valid and reliable.

There was a strong and positive correlation between womens' intentions to protect against OPF's and subjective norms. Women who had positive attitudes towards BMD measurement and medicine use (93% and 85%, respectively) had higher intention scores. Women who had positive attitudes towards physical exercise and making arrangements to prevent falling (73% and 70%, respectively) had lower intention scores. High rates of BMD measurement and medicine use (75% and 65%, respectively) in women who perceived the effect of subjective norm values on intention as social pressure from the family indicated that family is a positive element for social pressure.

There was a positive and moderate correlation between intention and perceived behavioral control. Perceived behavior control was evaluated in terms of opportunities and possibilities. Accordingly, 88% of the participants had the opportunity to have a BMD measurement, 84% had the opportunity to apply medical treatment and recommendations, 61% had the opportunity to engage in physical exercise, and 57% had the opportunity to make house arrangements to prevent falls. There was a strong and positive relationship between perceived behavior control and control beliefs. Behavior control was evaluated in terms of opportunities and possibilities. Accordingly, 88% of the participants had the opportunity to have a BMD measurement, 84% had the opportunity to apply medical treatment and recommendations, 61% had the opportunity to engage in physical exercise, and 57% had the opportunity to make house arrangements to prevent falls.

There was a strong and positive relationship between subjective norms and normative beliefs. In normative belief evaluation, it was thought that families would positively respond to BMD measurements and adherence to medicines and medical recommendations (90% and 77%, respectively) and physical exercise and house arrangements (70% and 65%, respectively). The women reported to be willing to have a BMD measurement (92%), to adhere to medicines and medical recommendations (85%), to engage in appropriate physical exercise (60%), and to make house arrangements to prevent falling (50%).

A moderate and positive relationship was found between attitudes and behavioral beliefs. In terms of behavioral beliefs, 90% of the women believed that they can discover whether they have OP or not if they had a BMD measurement, 75% believed that they can protect themselves against OP and OPF's if they adhere to medical treatment and recommendations, 73% believed that they can protect themselves against OP and OPF's and live independently for a long time if they engaged in appropriate physical exercise, and 73% believed that they can decrease the risk for OPF's if they make house arrangements to prevent falls. In order to increase the rate of physical exercise in this population, public health interventions regarding exercise beliefs may prove to be beneficial.

The concepts of PDT were beneficial in terms of understanding commitment to exercise programs or participation in leisure time physical activity (12). In studies which underlined the importance of exercise habits in term of predicting exercise behavior, personal beliefs which were affected by affective interests and social importance predicted intentions. Perceiving regular exercise as a difficult thing and taking or not taking personal responsibility regarding exercise depend upon beliefs (17). It is important to protect the spine by engaging in appropriate daily exercises (18). The belief that falls can be prevented should be supported.

Study Limitations

This study was conducted with female outpatients who were above 55 years of age and who admitted to the orthopedic clinics of Zonguldak Atatürk Public Hospital and cannot be generalized to all female outpatients.

Conclusion

Four out of every five women are active at home or outside, while one is not. Of the women, 65% fell at least once and among those who fell, 69% did not have a fracture as a result and 31% had at least one fracture. One fifth of the sample had an orthopedic surgery during adulthood. Approximately one fourth of the women used an optic or hearing device, while one tenth used assistive walking devices or more than one device. Among the women, 37% never had a BMD measurement, 45% never adhered to medical treatment and recommendations, and 63% never engaged in physical exercise and never made house

arrangements to prevent falling.

The study demonstrated that the majority of women (91%) intended to have a BMD measurement, 87% intended to adhere to medicines and medical recommendations, 60% intended to engage in appropriate physical exercise, and only 50% intended to make house arrangements to prevent falling. 88% believed that it would be easier to have a BMD measurement if they increased their knowledge on the subject, 70.7% believed that it would be easier to adhere to medicines and medical recommendations if they increased their knowledge on the subject, 65% believed that it would be easier to engage in appropriate physical exercise if they increased their knowledge on the subject, and 68% believed that it would be easier to make house arrangements to prevent falling if they increased their knowledge on such arrangements.

The scale had a very high reliability coefficient (Cr α 0.95). Test-retest reliability was also high. The PROF scale was reduced to 28 items by selecting items with factor loadings between 0.39 and 0.77. It was determined that the scale had 6 factors. A strong and positive relationship was found between intentions to protect against OPF's and attitudes and subjective norms, while a moderate and positive association was found between intentions and behavior control. Attitudes and behavioral beliefs were moderately and positively correlated, behavior control and control beliefs were strongly and positively correlated, and subjective norms and normative beliefs were strongly and positively correlated. This self-report scale evaluates how well postmenopausal women protect themselves against OPF's and provides a comprehensible framework by providing strategic steps to develop health behaviors. This scale can be a part of public health models aimed at fighting postmenopausal OP and OPF's.

Ethics

Ethics Committee Approval: Ethical approval was obtained from the Bülent Ecevit University Faculty of Medicine Clinical Research Ethics Committee (protocol no: 2015-18-20/05).

Informed Consent: Each patient was informed about the study and written consent was taken from the patients.

Peer-review: Externally peer-reviewed.

Authorship Contributions

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

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Anthropometric Parameter That Best Predicts the Relationship Between Obesity and Osteoporosis in Kidney Transplant Recipients

Böbrek Nakilli Hastalarda Obezite ve Osteoporoz Arasındaki İlişkiyi En İyi Tahmin Eden Antropometrik Parametre

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Abstract

Objective: This study aimed to investigate the relationship between obesity and osteoporosis in kidney transplant recipients (KTRs) using a body shape index (ABSI), a new anthropometric measurement parameter.

Materials and Methods: In this cross-sectional study, a total of 130 KTRs were included. Laboratory and demographic findings, aetiology of kidney failure, time on dialysis, donor type, time after transplantation, additional diseases, menopausal status for women and medications were recorded from patients' files. Height, weight and waist and hip circumferences were also recorded from the files. ABSI was calculated using a specific formula. Bone mineral density (BMD) was measured using dual X-ray absorptiometry. Patients were divided into the following three groups based on the T-score: Normal, osteopenia and osteoporosis groups, according to the World Health Organization recommendations.

Results: According to the BMD values, 24 patients (18.5%) had normal BMD, 82 patients (63.1%) were osteopenic and 24 patients (18.5%) were osteoporotic. Patients with osteoporosis have significantly higher parathormone hormone and ABSI and lower body mass index (BMI) than patients without osteoporosis ($p<0.05$). A positive correlation of BMI was found in the lumbar ($r=0.294$, $p=0.002$) and femoral T-scores ($r=0.216$, $p=0.024$). A negative correlation was found between ABSI and lumbar T-score ($r=-0.237$, $p=0.014$). Receiver operating characteristic curves showed that ABSI had the optimal power to discriminate patients with/without osteoporosis in both sexes.

Conclusion: ABSI is found to be a more useful tool than anthropometric measurements in predicting osteoporosis in KTRs.

Keywords: ABSI, renal transplant, osteoporosis, obesity

Öz

Amaç: Böbrek nakilli hastalarda obezite ile osteoporoz arasındaki ilişkiyi yeni bir antropometrik ölçüm olan "beden şekil indeksi (ABSI)" kullanarak araştırmayı amaçladık.

Gereç ve Yöntem: Bu kesitsel çalışmaya, takip edilen 130 böbrek nakilli hasta alındı. Laboratuvar ve demografik bulgular, böbrek yetersizliği etiyolojisi, diyaliz süresi, donör tipi, nakil sonrası süre, ek hastalıklar, kadınlarda menopoz durumu, ilaçlar hasta dosyalarından kaydedildi. Boy, kilo, bel ve kalça çevresi de dosyalardan kaydedildi. ABSI, belirli bir formülle hesaplandı. Kemik mineral yoğunluğu (KMY), dual X-ışını absorpsiyometrisi kullanılarak ölçüldü. T-skoruna göre hastalar normal, osteopenik ve osteoporotik olarak üç gruba ayrıldı.

Bulgular: KMY değerlerine göre 24 hasta (%18,5), normal 82 hasta (%63,1) osteopenik ve 24 hastada (%18,5) osteoporotikti. Vücut kitle indeksi ile lomber ($r=0,294$, $p=0,002$) ve femur T-skorları ile arasında pozitif korelasyon bulundu ($r=0,216$ $p=0,024$). Lomber T-skoru ile ABSI arasında negatif korelasyon bulundu ($r=-0,237$, $p=0,014$). ROC eğrileri, ABSI'nın her iki cinsiyette osteoporozu olan ve olmayan hastaları ayırt etmek için en uygun güce sahip olduğunu gösterdi.

Sonuç: ABSI'nın, böbrek nakilli hastalarda osteoporozu tahmin etmede diğer antropometrik ölçümlere kıyasla daha değerli olduğu bulundu.

Anahtar kelimeler: ABSI, böbrek nakli, osteoporoz, obezite

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Introduction

Kidney transplantation is the gold standard method for the treatment of end-stage renal failure. The increase in graft survival is associated with various complications. Among these, osteoporosis and low-energy fractures are important causes of morbidity and mortality (1,2).

Pathogenesis of transplant related osteoporosis is complex and multifactorial. Immunosuppressive agents and immobilization play the main role (3). Weight gain is often observed after kidney transplantation. Although some studies showed that the high body mass index (BMI) is high bone mineral density (BMD), the others claimed that obesity could increase the likelihood of osteoporosis (4,5). Obesity is an inflammatory condition. Obese patients have higher levels of IL-6 and TNF-α proinflammatory cytokines in their blood. This proinflammatory milieu can cause osteoclast activation (6,7).

Computed tomography (CT), magnetic resonance imaging (MRI), and dual energy X-ray absorptiometry (DXA) can accurately assess body fat composition. These methods are expensive and their use in the routine clinical setting are difficult. Different methods are used to evaluate obesity [e.g BMI, waist circumference (WC), hip circumference (HC), waist to hip ratio (WHR), and waist to height ratio (WHtR)]. All these anthropometric measurements have some limitations. BMI cannot differentiate fat mass (FM) from muscle mass and peripheral fat from abdominal fat (8,9). Krakauer and Krakauer (10) developed a new method, "A body shape index (ABSI)", to identify abdominal obesity. Several studies reported that ABSI is independently associated with, metabolic syndrome, diabetes, hypertension (11-13). ABSI is independently associated with a higher mortality rate compared to other anthropometric measures (10,14).

In this study, we investigated the relationship between obesity and osteoporosis in kidney transplant recipients (KTRs) using a new anthropometric measurement "ABSI".

Materials and Methods

All KTRs who were followed up in our clinic were evaluated to be included in the study. The inclusion criteria were as follows: Patients had to have a renal transplant for more than one year, with stable renal function and stable immunosuppressive regimen during the last 6 months. Patients aged younger than 18 years were excluded.

Laboratory and demographic findings regarding age, sex, smoking status, etiology of kidney failure, time on dialysis, donor type, time after transplantation, additional diseases, menopausal status for women, drugs, glucose, urea, creatinine, 25-hydroxyvitamin D, parathormone (PTH), calcium, phosphorus, C-reactive protein (CRP), sedimentation, lipid parameters, were recorded from electronic data bases. Patients' blood pressure, WC and HC, height, weight were also recorded from the files. ABSI was calculated with the following formula:

ABSI: WC (cm)/[$BMI^{2/3}$ x height $(m)^{1/2}$].

BMD was measured using DXA. Measurements of the T-score of the spine at the level of L1-L4 and left femoral neck were estimated. Patients were divided into three groups based on T-score according to the definitions recommended by the World Health Organization (WHO). The results were categorized as T>-1.0 normal, T≤2.5-1.0 as osteopenia and T<2.5 as osteoporosis according to WHO diagnostic criteria. Patients were divided into three groups based on BMD values. Group 1 consisted of patients BMD values were normal, group 2 were osteopenic, group 3 were osteoporotic.

The local ethics committee approved the study protocol (decision no: 2018/0231, date: 15.08.2018). Written informed consent was taken from all subjects before enrolment.

Statistical Analysis

Statistical analyses were performed with SPSS (version 15.0, SPSS Inc, Chicago, IL). The data were expressed as the mean ± standard deviation. The distribution of the variance was analyzed with the Kolmogorov-Smirnov test. The relationship between categorical variables was assessed by the chi-square test. Differences between parametric variables of the two groups were assessed by Student's t-test or Mann-Whitney U test, whichever is appropriate. Partial Spearman correlation coefficients were used to assess the association between anthropometric and biochemical measurements after adjustment for age and sex. To assess the ability of anthropometric measures to discriminate between patients who have or not have osteoporosis, receiver-operating characteristic (ROC) curve analysis was done. A p-value below 0.05 was considered statistically significant. Post-hoc power analysis was calculated using MedCalc for Windows, version 15,0 (mEDcALC Software, Ostend, Belgium).

Results

One hundred and thirty patients were included in the study. Of the 130 patients, 90 (69.2%) were male and 40 (30.8%) were female. The mean age of the patients was 48.9±11.5 years. The number of patients who underwent cadaveric kidney transplantation was 34 (26.2%), and the number of patients undergoing living-related kidney transplantation was 96 (73.8%). When the post-hoc sample size was calculated with 0.05 type 1 error, -0.237 correlation coefficient, 137 were detected.

According to BMD values, 24 patients (18.5%) had normal BMD values, 82 patients (63.1%) were osteopenic and 24 patients (18.5%) were osteoporotic. Patients were divided into two groups based on sex. Eight (20%) of the female patients have normal BMD values, 24 (60%) were osteopenic, 8 (20%) were osteoporotic. In men, 16 (17.5%) of the patients had normal BMD values and 58 (64.4%) were osteopenic, 16 (17.5%) were osteoporotic.

Demographic and laboratory characteristics of the groups are shown in Table 1.

Patients with osteoporosis have significantly higher PTH and ABSI and they have lower BMI than patients without osteoporosis ($p<0.05$).

Table 2 shows the results of partial Spearman correlation coefficients of femoral and lumbar T-scores along with biochemical and anthropometric measurements after adjustment for age and sex. There was a positive correlation of BMI with the lumbar (r=0.294, p=0.002), and femoral T-scores (r=0.216 p=0.024). A negative correlation was found between ABSI and lumbar T-score (r=-0,237, p=0.014) (Table 2).

ROC curves showed that ABSI had the optimal power to discriminate patients with or without osteoporosis in both sexes (Figures 1, 2).

Discussion

In this presented study, we compared the associations between five anthropometric indices (ABSI, BMI, WC, WHR, WHtR) and osteoporosis in KTRs. According to our results, ABSI have better predictive power for predicting osteoporosis than any other anthropometric measures.

Osteoporosis is a skeletal disorder characterized by compromised bone strength. It is characterized by reduced osteoblast proliferation, accelerated osteoclastogenesis, and impaired bone mineralization process that can result in deterioration of trabecular and cortical thickness and density (15). The prevalence of osteoporosis is high in KTRs. The pathophysiology of bone and mineral metabolism in the post-transplant period is complex. Osteoporosis in KTRs is not only caused by uremic osteodystrophy but also caused by risk factors such as age, gender, persistent hyperparathyroidism, vitamin D deficiency, physical inactivity, tobacco, and alcohol use, steroids and immunosuppressive agents (16). The prevalence of high calcium, low phosphorus and/or high PTH before transplantation should be assessed and, if necessary, correction of axial disorders of the calcium-PTH-D vitamin is mandatory (15). Evaluation of post-transplant calcium and PTH levels can identify patients with high fracture risk due to hyperparathyroidism (17). Renal failure is associated with PTH-induced bone-mineral disease following renal transplantation (18). High PTH levels cause a high risk of fracture in obese patients, especially in areas where cortical bone is dense (19). In this study, we found lower mean T-scores with high PTH levels compared to that with lower PTH levels (p=0.006). Previous studies have shown no correlation between serum creatinine, calcium, phosphorus, alkaline phosphatase, vitamin D levels, and BMD outcomes (18,20). Our study results were similar (p>0.05). We think that our standardized follow-up and treatment protocol for KTRs before and after transplantation may have affected this result. Optimal patient adherence to follow-up had also an important impact.

The role of glucocorticoids in the development of osteoporosis in KTRs in the first 6 months after transplantation is already known. The high-dose steroid use in the early period disrupts the activity of osteoblasts and suppresses bone formation. In the

Table 1. Demographic and laboratory characteristics of patients

	Osteoporosis	Osteopenia	Normal	p
Age (years)	44.6±10.6	49.9±11.8	50.4±9.98	0.107
Male/female	16-8	58-24	16-8	0.889
Type of donor/cadaveric living	9-15	17-65	8-16	0.175
Serum calcium (mg/dL)	9.5±0.6	9.7±0.5	9.9±0.6	0.082
Serum phosphorus (mg/dL)	3.25±0.6	3.5±0.65	3.5±0.98	0.351
Vitamin D (ng/mL)	18.9±13.7	18.6±14.0	14.0±6.7	0.428
PTH (pg/mL)	139±88	94.8±61.8	69.7±38.2	0.006*
CRP (mg/dL)	0.93±1.1	0.7±1.01	0.69±1.19	0.243
ESR (mm/h)	23.3±23.4	27.9±24.5	29.2±26	0.737
TG	138.9±73.4	159.8±105	185.7±149.2	0.704
HDL	46.7±12.4	47.7±16.5	47.3±12.3	0.962
LDL	113.7±39.2	121.5±36.3	131.8±27.5	0.286
TC	188.2±48.5	200.4±49	217.9±48.1	0.179
Medicines (fk/cyc/evo)	17-6-1	48-26-8	19-4-1	0.377
Smoke	3	11	5	0.630
BMI (kg/m^2)	23.7±4.2	27.3±4.8	27.3±6.08	0.007*
ABSI ($m^{11/6}\ kg^{-2/3}$)	0.0891±0.00	0.0857±0.0	0.0869±0.00	0.027*
WC (cm)	97.4±9.99	99.9±12.1	100.9±13.9	0.079
WHR	0.90±0.18	0.96±0.9	0.96±0.07	0.287
WHtR	0.58±0.06	0.6±0.07	0.6±0.09	0.164

PTH: Parathormone, BMI: Body mass index, CRP: C-reactive protein, ESR: Erythrocyte sedimentation rate, TG: Triglyceride, HDL: High-density lipoprotein, LDL: Low-density lipoprotein, TC: Total cholesterol, ABSI: A body shape index, WC: Waist circumference, WHR: Waist to hip ratio, WHtR: Waist t height ratio, *p<0.05

later stages of kidney transplantation, reduction in the dose of corticosteroids may ameliorate osteoblast functions, reduction of bone loss and improvement in bone density (21). In our study, no statistically significant correlation was found between the steroid dose and the femur and lumbar T-score (p=0.377).

The prevalence of obesity is an important problem in KTRs (22). The results of studies on the relationship between obesity and osteoporosis are contradictory.

In studies conducted in different patient groups, high BMI has been shown to have a positive effect on BMD (6,23). In a study in which 1,126 patients were evaluated for abdominal FM and fracture risk, women with high abdominal FM had a lower risk of fractures (24). When the relationship between BMI and BMD was evaluated in KTRs, Sezer et al. (20) found a positive correlation between BMI and BMD. On the other hand, recent studies shown that obesity and osteoporosis have common pathophysiological mechanisms. Contrary to the previous results, they suggested that obesity can cause osteoporosis (4,25,26). Kim et al. (27) found that body fat and WC was negatively correlated with BMD. In our study, we also found a positive correlation between BMI and BMD and a negative correlation between ABSI and BMD. We did not find any relation between WC and BMD. WC does not take height into account, therefore it may underestimate visceral fat in short populations. These results indicate that BMI alone is not sufficient in determining fracture risk factors and that obesity assessment methods need to be reviewed again (28). CT, MRI, DXA can be used to accurately measure body fat composition. These methods are expensive and their use in the routine clinical setting are difficult. For these reasons, anthropometric measurements are commonly used in clinical practice.

Studies based on ABSI, a relatively new method, are still emerging and mostly based on cancer and cardiovascular mortality (8,10,11,28). Although there are few studies showing the relationship between ABSI and osteoporosis, negative correlations were found in studies performed in men over 50 and in women with postmenopausal osteoporosis (29,30). In the literature, there were no studies evaluating the relationship between ABSI and osteoporosis in KTRs. In our study, lumbar

Table 2. Partial correlation analysis between parameters and anthropometric indices and lomber- femoral T-scores

	L1-L4		Femur neck	
	R	p	r	p
BMI (kg/m^2)	0.294	0.002*	0.216	0.024*
ABSI (m$^{11/6}$ kg$^{-2/3}$)	-0.237	0.014*	-0.013	0.896
WC (cm)	0.229	0.617*	0.235	0.064*
WHR	0.015	0.880	0.083	0.394
WHtR	0.079	0.106	0.045	0.106

ABSI: A body shape index, WC: Waist circumference, WHR: Waist to hip ratio, WHtR: Waist t height ratio, *p<0.05

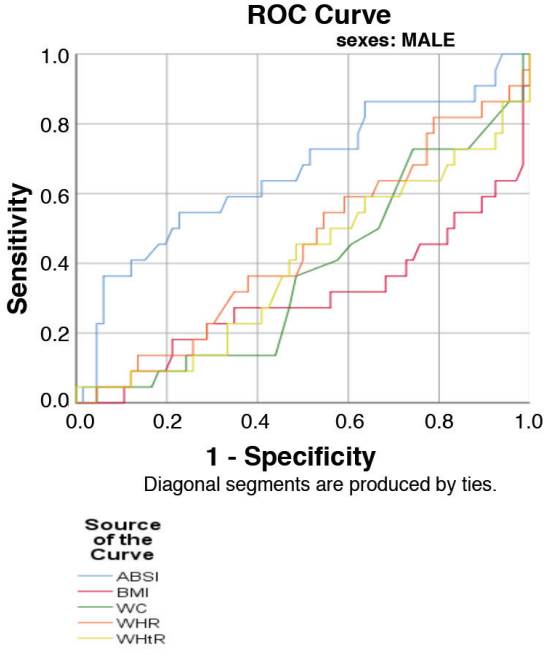

Figure 1. Receiver-operating characteristic curves for anthropometric measure to predict osteoporosis in men

ROC: Receiver-operating characteristic, ABSI: A body shape index, WC: Waist circumference, WHR: Waist to hip ratio, WHtR: Waist t height ratio, BMI: Body mass index

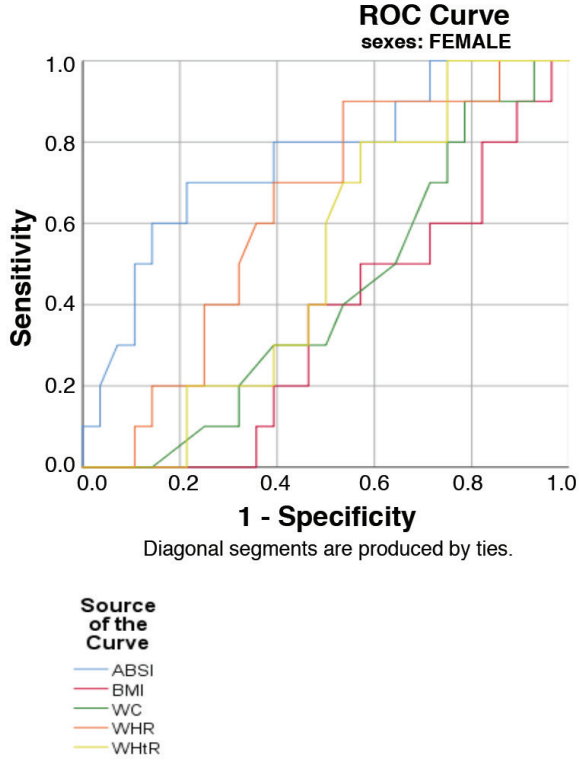

Figure 2. Receiver-operating characteristic curves for anthropometric measure to predict osteoporosis in women

ROC: Receiver-operating characteristic, ABSI: A body shape index, WC: Waist circumference, WHR: Waist to hip ratio, WHtR: Waist t height ratio, BMI: Body mass index

vertebra T-scores were found to be low in the high ABSI group and high ABSI may increase the risk of vertebral fractures in the renal KTRs.

CRP levels are higher in obese subjects. The elevation of CRP also results in an increase in serum bone turnover markers, a decrease in BMD and a higher risk of bone fracture (6). In our study, no significant relationship was found between CRP elevation, ABSI and BMD values (p=0.243). Immunosuppressive treatment may have a negative effect on these results.

When we examined the relationship between BMD and living-related and cadaveric kidney transplantation, no statistically significant relationship was found between BMD and the type of donor (p=0.175) (31).

Study Limitations

The main limitations of our study were the relatively small patient sample and the use of cross-sectional study design. Our patients were heterogeneous in terms of factors such as age, duration of renal failure and dialysis, time after transplantation, number of rejection episodes, menopausal status in women and immunosuppressive medications used.

Conclusion

Osteoporosis is more prevalent among patients with KTRs and associated with increased mortality and morbidity in this group. Therapy options were limited as bisphosphonates are not recommended in KTRs because of their adverse side effects. Obesity is one of the most important risk factors for developing osteoporosis. There is a clinical benefit in showing relationship of obesity and osteoporosis in KTRs. It is especially important to establish an accurate and precise diagnosis of obesity. According to our results, ABSI was a more useful tool to predict osteoporosis in KTRs, compared to anthropometric measurements. There is a need for more extensive studies to justify good predictors of osteoporosis in this special set of patients.

Ethics

Ethics Committee Approval: The İstanbul Medeniyet University, Göztepe Training and Research Hospital Clinical Research Ethics Committee approved the study protocol (decision no: 2018/0231, date: 15.08.2018).

Informed Consent: Written informed consent was taken from all subjects before enrolment.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Concept: S.M., G.Ş., Design: S.M., G.Ş., Data Collection or Processing: S.M., G.Ş., Analysis or Interpretation: S.M., G.Ş., Writing: S.M.

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Sociodemographic and Clinical Characteristics of Patients with Behçet's Disease Followed Up in the Physical Therapy and Rehabilitation Department of a Tertiary Hospital

Üçüncü Basamak Bir Hastanenin Fizik Tedavi ve Rehabilitasyon Kliniği Tarafından Takip Edilen Behçet Hastalarının Sosyodemografik ve Klinik Özellikleri

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Abstract

Objective: Behçet's disease (BD) is a multisystemic inflammatory disease that causes significant morbidity worldwide. In this study, we aimed to evaluate the clinical and demographic characteristics of the patients with BD.
Materials and Methods: Patients admitted to our physical medicine and rehabilitation clinic between January 2015 and December 2018 were evaluated retrospectively. One hundred sixty patients who met the diagnostic criteria of the International Study Group for BD were included in the study. In addition to the patients' demographic characteristics, their clinical features, including age at onset, symptoms on initial admission, disease duration, systemic/organ involvement and medical treatments used, were recorded.
Results: The mean age of the 160 patients included in the study was 40.48±10.0 [minimum (min): 19, maximum (max): 72]. The mean age at disease onset was 30.54±8.46 (min: 14, max: 62). The most common involvement type in BD was mucocutaneous manifestations, and oral aphthae were the most common mucocutaneous symptom, with an occurrence rate of 100%. Regarding clinical manifestations, 36.3% (n=58) of patients showed ocular involvement, 16.9% (n=27) had vascular involvement and 15% (n=24) had musculoskeletal involvement. The rarest involvement was that of the genitourinary system, with a rate of 0.6% (n=1). Colchicine was the most commonly used therapeutic agent, whereas steroids, azathioprine, cyclosporine and various biologicals could also be used, depending on clinical status.
Conclusion: The results of our study suggest that, although the most common manifestation of BD is mucocutaneous involvement, the involvements of various systems, such as the ocular, musculoskeletal and neurological systems, are not rare and are associated with severe morbidity and mortality. Treatment modalities vary according to the systems and organs involved. Therefore, it is very important to systematically evaluate patients with BD and to arrange appropriate and effective treatment.
Keywords: Behçet's disease, ocular involvement, uveitis, oral aphthae, musculoskeletal involvement, epidemiology

Öz

Amaç: Behçet hastalığı (BH) dünyada önemli morbiditelere neden olan, multisistemik enflamatuvar bir hastalıktır. Bu çalışmada BH tanılı hastalarımızın klinik ve demografik özelliklerini incelemeyi amaçladık.
Gereç ve Yöntem: Ocak 2015-Aralık 2018 tarihleri arasında fiziksel tıp ve rehabilitasyon kliniğine başvuran hastaların kayıtları retrospektif olarak incelendi. Uluslararası Behçet Hastalığı Çalışma Grubu'nun tanı kriterlerini karşılayan 160 hasta çalışmaya dahil edildi. Hastaların demografik özelliklerine ek olarak hastalığın başlangıç yaşı, ilk başvuru yakınması, hastalık süresi, sistemik bulgular ve kullanılan medikal tedaviler de dahil olmak üzere klinik özellikler kayıt altına alındı.
Bulgular: Çalışmaya alınan 160 hastanın yaş ortalaması 40,48±10,0 [minimum (min): 19, maksimum (maks): 72] idi. Hastalığın ortalama başlangıç yaşı 30,54±8,46 (min: 14, maks: 62) olarak hesaplandı. Hastalığın en sık tuttuğu sistemlerin başında deri yer alırken; en sık deri bulgusu %100 ile oral aftlardı. Sırasıyla diğer en sık tutulum bölgeleri %36,3 (n=58) ile göz, %16,9 (n=27) ile vasküler yapılar ve %15 (n=24) ile eklemlerdi. En nadir tutulum %0,6 (n=1) ile genitoüriner sistemdi. Tedavide en sık kullanılan ajan kolşisin olup hastanın klinik durumuna göre steroidler, azatiopürin, siklosporin ve çeşitli biyolojik ilaçlar tedavide kullanılan farklı gruplardan ajanlardır.
Sonuç: Çalışmamızın sonuçları BH'nin en sık görülen tutulum şekli mukokütanöz tutulum olsa da; oküler, kas-iskelet sistemi ve nörolojik sistem tutulumu gibi ciddi morbidite ve mortalite ile ilişkili farklı tutulumların da nadir olmadığını göstermektedir. Tedavi, tutulan sistem ve organlara göre değişir. Bu nedenle, BH hastalarını sistematik olarak değerlendirmek ve uygun ve yeterli tedaviyi düzenlemek çok önemlidir.
Anahtar kelimeler: Behçet hastalığı, göz tutulumu, üveit, oral aft, kas iskelet sistemi tutulumu, epidemiyoloji

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Introduction

Behçet's disease (BD) is a multisystemic inflammatory disease characterized by recurrent oral aphthae (OAs), genital ulcers (GU), skin lesions, uveitis, joint involvement and vascular lesions. It was first described by a Turkish dermatologist, Hulusi Behçet, in 1937, with recurrent OAs, GU and hypopionic iridocyclitis triple symptom (1). The underlying pathology in BD is known to be vasculitis. However, the etiopathogenesis of the BD is still unclear. Central nervous system, genitourinary system (GUS), gastrointestinal system (GIS) and respiratory system involvements can also be seen in BD. Myocardial infarction, pericarditis and glomerulonephritis due to BD are rare. Therefore, BD is not only a serious cause of morbidity but also a serious cause of mortality. BD diagnosis is based on the diagnostic criteria of the International Study group for Behçet's Disease (ISGBD). According to ISGBD criteria; in addition to recurrent OAs that cannot be explained with any other clinical situation; at least two of the four findings (GU, ocular lesions, skin lesions and pathergy test positivity) are diagnosed as BD (2). Although BD is reported from different parts of the world, it is more common in the Mediterranean, the Middle East and the Far East regions. In epidemiological studies, Turkey is the most prevalent country for BD with 370-420/100,000 (3,4). Although BD starts more often at the age of 20-40 years, it can be seen in all ages, including childhood and old ages (5,6). Involvement types may vary in different societies and geographical regions. For example, gastrointestinal involvement was more frequent in Japanese and Americans (7); on the other hand pathergy positivity rather high in Turkey and Japan, it is low in western countries such as America and England (8). Neurological, ophthalmologic and pulmonary involvements of BD may cause severe complications that may result in complete loss of vision or even death. Therefore, the aim of this study is to determine the prototypic features of BD in our country retrospectively by evaluating the demographic and clinical characteristics of the patients with BD admitted to our clinic and to draw attention to possible morbidity and mortality risks of BD.

Materials and Methods

One hundred sixty patients diagnosed with BD according to ISGBD criteria (9) admitted to our outpatient clinic between January 2015 and December 2018 were included to this study. In accordance with the Declaration of Helsinki, ethics committee approval was obtained from the Clinical Studies Ethics Committee of Tokat Gaziosmanpaşa University Faculty of Medicine with protocol number 19.02.2019/19-KAEK-034.

The data of the patients were analyzed retrospectively from the electronic media files in the hospital automation system. Informed consent could not be obtained from the patients due to the retrospective design of the study. In addition to the demographic characteristics of the patients, clinical features including age at onset, initial admission symptom, disease duration, systemic findings and medical treatments used were recorded. Systemic involvement findings were evaluated as follows:

Mucocutaneous involvement: OAs, GU, papulopustular lesions, erythema nodosum, pathergy response.

Ocular involvement: Anterior uveitis, posterior uveitis, panuveitis, total loss of vision.

Musculoskeletal system involvement: Foot, knee, hip, elbow, shoulder, sacroiliac joint.

Vascular involvement: Systemic arterial, pulmonary vascular, venous occlusion, varices.

Neurological involvement: Seizure, paresthesia, hemiplegia/ hemiparesis, diplopia.

GIS involvement: Fistula/ulcer, portal venous thrombosis.

GUS involvement: Epididymitis, orchitis.

Cardiac involvement: Myocarditis, pericarditis, endocarditis.

Pulmonary involvement: Pleuritis, pulmonary parenchymal involvement, pulmonary vascular involvement.

Medical treatments: Colchicine, steroids, azothiopurine, cyclosporine, anti-tumor necrosis factor-alfa (anti TNF-α) agents were recorded.

Systemic examinations of the patients were performed by specialists of the related clinics (dermatology, ophthalmology, cardiovascular surgery, neurology, gastroenterology, cardiology). Iridocyclitis was evaluated as anterior uveitis; vitritis, retinitis and vasculitis were evaluated as posterior uveitis. Findings not related to BD were not recorded. The patients who were examined for musculoskeletal involvement were found to have arthritis with direct radiography, scintigraphy or magnetic resonance imaging (MRI). Doppler ultrasonography (USG), computed tomography (CT) or conventional angiography findings of the patients examined for vascular system involvement were accepted as involvement. Only the findings of CT, MRI, venography/ angiography and electroencephalography examinations of the patients who were examined for neurological involvement were considered to be related with BD. Echocardiography was used for the evaluation of cardiac involvement and direct X-ray and CT results were taken into consideration while pulmonary involvement was evaluated. Subjective complaints such as headache and dizziness were not evaluated. Only one patient with a complaint of GUS was evaluated in the relevant clinic diagnosed as epididymitis. USG, endoscopy and colonoscopy findings were taken into consideration while evaluating GIS involvement. The Pathergy skin test was performed under sterile conditions by a 20 gauge needle and evaluated by a dermatologist 48 hours later. The test was not administered to systemic drug users and the presence of papules or pustules was considered positive.

Statistical Analysis

Descriptive analyzes were used to give information about the general characteristics of the study groups. Data of continuous variables are in the form of mean ± standard deviation; data on categorical variables are given as n (%). When comparing the means of the quantitative variables between the groups,

the significance of the difference between two means test was used. Cross-tables and chi-square tests were used to evaluate whether there is a relationship between qualitative variables. P values less than 0.05 is considered to be statistically significant. In analyzes, computerized statistical software program "IBM SPSS Statistics 19" was used (IBM SPSS Statistics 19, SPSS inc., an IBM Co., Somers, NY).

Results

One hundred and sixty patients participated in our study and 59.4% (n=95) of the cases were female; 40.6% (n=65) were male. The mean age of the females was 40.54±10.57 [minimum (min): 19, maximum (max): 72], while the mean age of the males was 40.38±9.18 (min: 23, max: 60) (p=0.925). The distribution of ages at onset and at the time of admission; and the duration of the disease are shown in Table 1.

The most common involvement type was mucocutaneous manifestations in BD and OA was the most common mucocutaneous symptom with 100% of the patients. This is a normal result of the diagnostic criteria used in our study. Regarding clinical manifestations, 36.3% (n=58) of the patients showed ocular involvement, 16.9% (n=27) vascular involvement and 15% (n=24) musculoskeletal involvement.

The most rarely seen involvement is GUS with 0.6% (n=1). OA was present in 76.9% (n=123) of the patients. The second most common involvement type at admission was ocular involvement with 19.4% (n=31). The onset admission symptoms and age characteristics by gender are shown in Table 2. The characteristics of the patients by clinical involvements and used medical treatments are as follows:

Mucocutaneous involvement: Recurrent OAs was observed in all of the patients according to ISGBD criteria. Eighty-seven patients (54.4%) had recurrent GUs. Papulopustular lesions were seen in 67 patients (41.9%) and erythema nodosum was seen in 32 patients (20%). Pathergy test was positive in 24 (15%) patients.

Ocular involvement: Ocular involvement was detected in 58 patients (36.3%). Nineteen (11.8%) patients had isolated anterior uveitis and 39 (24.3%) had panuveitis. However, 9 (5.6%) patients had total loss of vision due to panuveitis.

Musculoskeletal system involvement: Joint involvement was detected in 24 patients (15%). The most commonly involved joints were ankle joint (15 patients, 9.37%), sacroiliac joint (12 patients, 7.5%), wrist joint (5 patients, 3.1%), knee joint (4 patients, 2.5%), elbow joint (3 patients, 1.9%) and hip joint (1 patient, 0.6%). In 16 (10%) patients with joint involvement, more than one joint was involved.

Vascular involvement: Twenty-seven patients (22.5%) had vascular involvement. Five patients (3.1%) had systemic arterial vasculitis. Two patients (1.3%) had pulmonary artery aneurysm, 12 patients had venous occlusion and 14 patients had varicose veins. The distribution of the cases with venous occlusion was in the form of deep vein thrombosis in 7 patients, superficial venous thrombosis in 2 patients and portal vein thrombosis in 3 patients. In addition, 6 patients with varicose veins also had a history of venous thrombosis. Vascular involvement was significantly higher in males (p=0.031).

Neurological involvement: There were 10 (6.3%) patients who were followed up as neuro-Behçet disease (NBD). Paresthesia was present in 7 patients (4.4%), hemiparesis in 2 patients (1.3%) and diplopia in 1 patient (0.6%). Headache was not evaluated as neurological involvement unless it was accompanied by other neurological examination findings and pathological imaging tests, but all patients followed up as NBD had headache.

GIS involvement: Three patients (1.9%) had Budd-Chiarri

Table 1. The distribution of ages at onset and at the time of admission; and the duration of the disease

	Mean ± standard deviation	Median [Min-Max]
Age at admission	40.48±10	39 [19-72]
Age at onset	30.54±8.46	29 [14-62]
Duration of the disease	9.78±5.65	8 [1-31]

Min: Minimum, Max: Maximum

Table 2. The onset admission symptoms and age characteristics by gender

	Gender		p
	Female	Male	
Onset admission symptoms			
Oral aphthae	79 (83.2)	44 (67.7)	0.145
Genital ulcers	1 (1.1)	0 (0)	
Ocular involvement	12 (12.6)	19 (29.2)	
Musculoskeletal involvement	1 (1.1)	1 (1.5)	
Neurological involvement	1 (1.1)	1 (1.5)	
Gastrointestinal system involvement	1 (1.1)	0 (0)	
Age at admission	40.54±10.57	40.38±9.18	0.925
Age at onset	31.27±8.82	29.46±7.84	0.184

For qualitative variables chi-square test and for quantitative variables the significance of the difference between two means test were used

syndrome due to portal venous thrombosis. Two patients (1.3%) had ileocecal ulcers.

GUS involvement: One patient (0.6%) was referred to the urology outpatient clinic because of scrotal pain. He was diagnosed as epididymitis by detailed examination and scrotal USG.

Cardiopulmonary involvement: Three patients (1.9%) had pericardial effusion and 2 (1.3%) patients had pleural effusion (see vascular involvement). All 3 patients with cardiac involvement were male.

Except vascular and cardiac involvement, there was no statistically significant difference in organ and system involvement by gender ($p>0.05$).

Medical treatments: Colchicine was the most commonly used treatment with 98.1%. Seventeen patients (10.6%) were taking steroids with colchicine treatment. There were 37 patients (23.1%) receiving azothiopurine (28 patients for ocular involvement, 4 patients for vascular involvement, 3 patients for neurological involvement, 1 patients for musculoskeletal system involvement, 1 patients for GIS involvement), 7 patients (4.4%) using cyclosporine A (all for ocular involvement), and 8 patients (5%) using anti-TNF agents. Of these 8 patients; 5 were using infliximab (3 for ocular involvement, 2 for neurological involvement), 2 were using adalimumab (for ocular involvement) and 1 were using etanercept (for musculoskeletal system involvement).

Discussion

This study presents the demographic and clinical characteristics of 160 patients diagnosed with BD over a 3-year period. Mucocutaneous manifestations are the most common symptoms in BD. As in our study, the only symptom seen in all patients was painful OAs with recurrent character. There are studies reporting that ethnicity and environmental factors change the prevalence and clinical manifestations of BD. BD may begin especially in the third decade and rarely in childhood (10).

The mean age at onset of the disease was 27.6±7.2 in males and 29.0±9.3 in females in the study of Soylu et al. (11). The mean age at onset of the disease was found to be 28.03±7.57 in Brazil, 35.52±9.25 in Greece and 33.2±10.2 in Korea (12-14). The mean age at onset of the patients included in our study was found to be 30.54±8.46 and was consistent with the literature. In the literature, there are some studies reporting that the disease starts at an earlier age in individuals with BD in their family (15). However, there was no regular information about family histories in the retrospective scanned files of the patients in our study group. Therefore, the relationship between family history and early onset of the BD could not be evaluated.

Mucocutaneous findings in BD are the most common onset admission symptom in many studies (10,16,17) and even the diagnostic criteria of ISGBD have identified OAs, one of the mucocutaneous findings, as a prerequisite for diagnosis (9). In our study, OAs were observed in all of our patients because patients were included in the study according to the diagnostic criteria of ISGBD.

In a study by Soylu et al. (11), GUs were detected in 82.8% of the patients, whereas 54.4% of the patients had GUs in our study. Pathergy test positivity has been reported by various researchers at different rates (16,17). In the study of Tursen et al. (16), Patergy positivity was 56.1%. In our study, Pathergy test was positive in 24 (15%) patients. Whether this is caused by test standardization or other factors, such as drug use, is unclear and requires further investigation.

Ocular involvement is one of the most important causes of morbidity in BD. In addition, ocular involvement is the second most common onset admission symptom after mucocutaneous manifestations (18). In general evaluation, the frequency of ocular involvement is around 50-68% in BD (18,19). When ocular controls are not performed regularly, some cases carry a risk of poor prognosis that may go up to total vision loss. In 31 (19.4%) of our cases, the onset admission symptom was ocular involvement, whereas the second most common involvement after mucocutaneous manifestations was ocular involvement in general, and 58 (36.3%) of the patients had ocular involvement. Nine (5.6%) of the patients had total loss of vision. Therefore, ocular involvement should be considered carefully and it is important to evaluate asymptomatic Behçet's patients for ocular involvement.

Vascular involvement is one of the poor prognostic factors in BD. The risk for other vascular complications increases after the first vascular manifestation. The prevalence varies between 5-40% in the literature. This difference may be due to different reasons such as the clinic in which the study was conducted or the ethnic origin of the patients participating in the study (20-24). In our study, vascular involvement was observed in twenty-seven patients (22.5%). It is also known that the prevalence of vascular involvement, which is the cause of serious morbidity and even mortality, is increased in the follow-up periods (20). For this reason, careful monitoring of vascular complications in patients with BD is necessary; provided that one who has experienced a vascular event once, more closely.

Although musculoskeletal problems in the form of arthritis or arthralgia are not included in the ISGBD criteria, it is a major finding in approximately half of the patients with BD (25). Articular involvement has been reported from 16% to 93% from different countries (26-28). Although BD tends to involve the large joints of the lower extremity, it may also involve the large joints of the upper extremity, the small joints of the hand and foot, and the sacroiliac joint (29,30). In our study, articular involvement was detected in 24 patients (15%) and our results are consistent with the literature. Although Behçet's arthritis is usually self-limiting, intermitant and non-erosive; it may rarely cause erosion in the joint (31). Articular involvement has been shown to have a negative effect on the quality of life (QoL) of the patient (32). In order to improve the QoL and to prevent the complications that may occur due to arthritis/arthralgia, it would

be appropriate to use different techniques such as scintigraphy and MRI in case of clinical suspicion.

NBD is a rare manifestation of BD associated with severe morbidity and mortality. One of the most serious organ involvement is NBD and the frequency was reported as 3-10% in large BD cohorts (33,34). In our study, there were 10 patients (6.3%) followed with NBD. Our results were consistent with the literature. Patients with NBD may present with different clinical findings such as venous thrombosis, intracranial vasculitic involvement and brain stem involvement. Bolek et al. (32) found that ocular involvement is also common in patients with NBD. In our study, 40% (n=4) of the patients with NBD also had ocular involvement. Therefore, to evaulate patients with ocular involvement in terms of presence of NBD and patients with NBD in terms of ocular involvement is important both for the regulation of appropriate treatment and for the prevention of possible comorbidities.

Epididymitis is common in BD. It is even considered one of the minor criteria of BD (35). In a study, epididymitis was detected in 17% of the patients with routine scrotal USG performed independently of complaints in BD (36). It is known that pain due to GUs and epididymitis can be confused with each other. In our study, urogenital examination was performed in only one patient due to pain and epididymitis was detected. In order to prevent urogenital comorbidity, routine urogenital examinations of the patients especially with GU may be useful.

GIS involvement is important because it is associated with serious morbidity and mortality in BD patients, and its prevalence has been reported in the literature at rates ranging from 2.8% to 60% (31,37-41). In our study, three patients (1.9%) had Budd-Chiari syndrome as a result of portal venous thrombosis and two patients (1.3%) had ileocecal ulcers. Our results are consistent with the literature showing gastrointestinal involvement rate in Turkey (16). Routine gastroenterological examination and endoscopic evaluations will contribute to the detection of subclinical involvement and accuracy of the data.

Cardiac involvement is a rare manifestation of BD but there are variable involvement types. Endocarditis, myocarditis, pericarditis, coronary arteritis and coronary artery aneurysms are some of the cardiac manifestations of BD (42). Also, pulmonary manifestations of BD are rare and can be summarized as follows: Pleuritis, pulmonary vasculitis, pulmonary fibrosis, pulmonary embolism and pulmonary infections (43). In our study, 3 patients (1.9%) had pericardial and 2 patients had pleural effusion (1.3%). Pulmonary artery aneurysm was also detected in two patients (1.3%).

The main goal of the treatment in BD is to achieve remission and improve the QoL of the patient. The clinical presentation and involved systems determine the basis of the treatment in BD. Comorbid conditions, involved organs, disease severity, age and sex of the patients are the main parameters to make a decision for treatment. Colchicine, steroidal and nonsteroidal anti-inflammatory agents, azathioprine, cyclosporine A, cyclophosphamide, biological agents and monoclonal therapies are among the main agents used in treatment (44). In our study, colchicine was the most commonly used agent in our patients with 98.1% while the number of the patients using anti TNF-α agents was 8 (5%). The frequency of organ involvement in BD may vary depending on the diagnostic criteria used in the study and the clinic in which the study was conducted (45). Therefore, the involvement rates of the systems show significant differences in different studies. In addition, it is clear that in prospective studies, different system involvements may be included to the patients' clinic during the follow-up periods.

Study Limitations

The main limitations of our study were that the retrospective design of the study did not allow us to evaluate the family history of the patients and the initial symptoms until the diagnosis. New multicentred and multidisciplinary researches will provide a better definition of the clinic of BD and will also contribute to the standardization of the parameters used in BD follow-ups.

Conclusion

The results of our study suggest that, although the most common manifestation of BD is mucocutaneous involvement, different involvements which are associated with severe morbidity and mortality, such as ocular, musculoskeletal and neurological systems are not rare. Treatment varies according to the involved systems and organs. Therefore, it is very important to systematically evaluate patients with BD and to arrange appropriate and adequate treatment.

New studies evaluating the immunopathogenesis, clinical characteristics and epidemiology of BD will contribute to many different subjects such as developing new laboratory tests, new diagnostic criteria, measuring disease activity and determining the best treatment methods.

Ethics

Ethics Committee Approval: In accordance with the Declaration of Helsinki, ethics committee approval was obtained from the Clinical Studies Ethics Committee of Tokat Gaziosmanpaşa University Faculty of Medicine with protocol number 19.02.2019/19-KAEK-034.

Informed Consent: Informed consent could not be obtained from the patients due to the retrospective design of the study.

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Authorship Contributions

Surgical and Medical Practices: N.Y., Concept: N.Y., O.D., Design: N.Y., O.D., Data Collection or Processing: N.Y., O.D., Analysis or Interpretation: N.Y., O.D., Literature Search: N.Y., O.D., Writing: N.Y., O.D.

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HIV Pozitif Erkek Hastalarda Osteoporoz Sıklığı ve Serum CD4+ T Hücre Seviyesi ile İlişkisinin İncelenmesi

Osteoporosis Prevalence in Patients Infected with Human Immunodeficiency Virus and Its Correlation Between CD4+ T Cell Levels

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Öz

Amaç: İnsan bağışıklık yetmezlik virüsü (HIV) pozitif hastalarda osteopeni ve osteoporoz sık karşılaşılan bir komorbiditedir. Biz bu çalışmamızda HIV pozitif erkek hastalarda düşük kemik mineral yoğunluğu prevelansını saptamayı ve CD4+ T hücre düzeyini kullanarak, kemik mineral yoğunluğu ile hastalık aktivitesi arasındaki ilişkiyi araştırmayı amaçladık.

Gereç ve Yöntem: Polikliniğimize 2016-2019 yılları arasında başvurmuş olan 18-50 yaş arası 50 HIV pozitif erkek hasta çalışmaya dahil edildi. Hastaların dual enerji X-ışını absorpsiyometri ölçümlerindeki kemik mineral yoğunlukları ve CD4+ T hücre sayıları retrospektif olarak tarandı.

Bulgular: Hastaların 19'unda (%38) osteoporoz ve 16'sında (%32) osteopeni olmak üzere toplam 35'inde (%70) kemik mineral yoğunluğunda azalma tespit edilmiştir. Hastaların CD4+ T hücre sayısı ile kemik mineral yoğunluk değerleri arasındaki korelasyon incelenmiş, anlamlı korelasyon saptanmamıştır (p>0,05).

Sonuç: HIV pozitif erkek hastalarda, kemik mineral yoğunluğundaki azalma prevelansı oldukça sık bir problem olmakla beraber, etiyolojisini sadece hastalığın kendisine veya viral yüke bağlamak mümkün görünmemektedir. Antiretroviral tedavilere naif daha fazla sayıda hasta ile yapılacak çalışmalara ihtiyaç duyulmaktadır.

Anahtar kelimeler: Osteoporoz, HIV, antiretroviral ajanlar

Abstract

Objective: Osteopenia and osteoporosis are frequent comorbidities observed in patients infected with human immunodeficiency virus (HIV). This study aimed to investigate the prevalence of reduced bone mineral density among male patients with HIV and correlation between disease activity and bone mineral density by using Cluster of Differentiation 4 (CD4)+ T cell levels.

Materials and Methods: A total of 50 men with HIV, aged between 18 and 50 years admitted to our clinic from 2016 to 2019 were included in this study. Bone mineral density results measured by dual energy X-ray absorptiometry and CD4+ T cell levels were retrospectively screened.

Results: Decreased bone mineral density was observed in 35 (70%) patients, whereas 19 (38%) had osteoporosis and 16 (32%) had osteopenia. No significant correlation was found between the CD4+ T cell levels and bone mineral density values of patients (p>0.05).

Conclusion: The prevalence of decreased bone mineral density in male patients with HIV is a common problem, and its aetiology is not attributable by the disease itself or viral load. Further studies with more patients naive to antiretroviral treatments are necessary.

Keywords: Osteoporosis, HIV, antiretroviral agents

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Giriş

Son dekadlarda insan bağışıklık yetmezlik virüsü (Human immunodeficiency virus-HIV) ile enfekte bireylerin beklenen yaşam süreleri, antiretroviral tedavilerin (ART) gelişimi ile birlikte anlamlı düzeyde uzamıştır. Beklenen yaşam sürelerinde uzama bazı komplikasyonların artışını da beraberinde getirmiştir. Düşük kemik mineral yoğunluğu bu hastalarda sık karşılaşılan komplikasyonlardan biridir (1,2). Genel popülasyonla karşılaştırıldığında HIV pozitif bireylerde osteoporoz ve osteopeni riskinin sırasıyla 3,7 ve 6,4 kat artmış olduğu bildirilmiştir (3).

HIV ile enfekte bireylerdeki osteopeni veya osteoporozun etiyolojisinde yaşam sürelerindeki uzama ile beraber sistemik enflamasyon, viral yük ve antiretrovirallerin kemik mineral yoğunluğu üzerindeki negatif etkileri sorumlu tutulan ana faktörlerdir. Ayrıca HIV pozitif bireylerde daha sık rastlanan sedanter yaşam, düşük vücut kitle indeksi, malnütrisyon, keyif verici madde bağımlılığı ve yetersiz kalsiyum ve vitamin D alımı gibi risk faktörleri de daha sık görülebilmektedir (4-6). Son yıllarda yapılan çalışmalarda sıklıkla antiretroviral ajanların kemik mineral yoğunluğu üzerindeki etkileri araştırılmış; tenofovir ve efavirenz en riskli ajanlar olarak bildirilmişlerdir (7-9). Öte yandan kronik immün aktivasyon ve enflamatuvar sitokinlerin artışı HIV pozitif bireylerde kemik mineral yoğunluğundaki azalmada rol oynayabilmektedir (10). Tümör nekroz faktör ve interlökin-6 gibi pro-enflamatuvar sitokinlerin artışı osteoklastik aktiviteyi stimüle edebilmektedir (11). ART'ye rağmen persistan sitokin disfonksiyonunun kronikleşmiş HIV enfeksiyonunda devam eden demineralizasyonu açıklayabileceği düşünülmektedir (12).

Biz çalışmamızda hastalık aktivasyon belirteçlerinden $CD4^+$ T hücre düzeyini kullanarak, kemik mineral yoğunluğu ile hastalık aktivitesi arasındaki ilişkiyi araştırmayı amaçladık. Mevcut literatür daha çok yaş ve cinsiyet açısından heterojen grupları içerdiğinden 50 yaş altı erkek hastaları çalışmaya dahil ettik.

Gereç ve Yöntem

Ocak 2016 ve Şubat 2019 tarihleri arasında polikliniğimize başvuran 18-50 yaş arası 50 HIV pozitif erkek hasta çalışmaya dahil edildi. Çalışmaya dahil edilen tüm hastaların onamları alındı. Sekonder osteoporoz nedenlerine (hipotiroidizm, hipertiroidizm, hiperparatiroidizm, hipogonadizmi diabetes mellitus...) sahip olan hastalar çalışmaya dahil edilmedi. Hastaların ilk başvurularındaki çift enerjili X-ışını absorbsiyometri (dual energy X-ray absoptiometry-DEXA) ölçümlerindeki kemik mineral yoğunlukları ve $CD4^+$ T hücre sayıları retrospektif olarak tarandı. Hastalar $CD4^+$ T hücre sayısı 500/mm^3 ve daha fazla olan hastalar (n=28) ile daha az olan (n=22) hastalar olmak üzere iki gruba ayrıldı (13). Antiretroviral naif hastalar ile tedavinin ilk 6 ayında olan hastalar çalışmaya dahil edildi.

Her gruptaki osteopeni ve osteoporoz prevelansları belirlenerek gruplar arasında karşılaştırıldı. Uluslararası Klinik Dansitometri Derneği'nin (International Society of Clinical Densitometry-ISCD) 50 yaş altı erkeklerde kullanılmasını önerdiği üzere Z skoru -1 ile -2 arasında olan hastalar osteopenik, Z skoru -2 ve daha altında olan hastalar osteoporotik olarak tanımlandı (14).

İstatistiksel Analiz

Çalışmada tanımlayıcı veriler kategorik verilerde n, % değerleri, sürekli verilerde ise ortalama ± standart sapma ve minimum-maksimum değerleri ile gösterilmiştir. Kategorik verilerin karşılaştırılmasında ki-kare testi ve Fisher Exact testi kullanılmıştır. Ölçümsel veriler normal dağılım varsayımı için Kolmogorov-Smirnov testleri ile sınanmıştır. Ölçümsel verinin korelasyonun incelenmesinde Spearman korelasyon analizi kullanılmıştır. Tüm analizlerde istatistiksel anlamlılık için $p<0,05$ kabul edilmiştir. Analizler IBM © SPSS programı 20 sürümü ile gerçekleştirilmiştir.

Bulgular

Hastaların yaş ortalaması 39,7±10,9 yıl, vücut kitle indeksi ortalama 23,8±2,8 kg/m^2 olarak tespit edilmiştir. Hastaların 19'unda (38%) osteoporoz ve 16'sında (32%) osteopeni olmak üzere toplam 35'inde (70%) kemik mineral yoğunluğunda azalma tespit edilmiştir.

Hastaların $CD4^+$ T hücre sayısı ile kemik mineral yoğunluk değerleri arasındaki korelasyon incelenmiş, anlamlı korelasyon saptanmamıştır ($p>0,05$) (Tablo 1).

Hastaların $CD4^+$ T hücre sayıları 500'ün altı ve üstü olarak gruplanmıştır. Subgrup analizlerde de $CD4^+$ T hücre sayısı ile kemik mineral yoğunluk değerleri arasında anlamlı korelasyon saptanmamıştır ($p>0,05$).

Hastaların $CD4^+$ T hücre düzeyleri ile Z skorları karşılaştırılmış, anlamlı farklılık saptanmamıştır ($p>0,05$) (Tablo 2).

Tartışma

HIV pozitif erkek hastalarda osteopeni ve osteoporoz sıklığını incelediğimiz bu çalışmada, toplam 35 hastada (%70) kemik mineral yoğunluğunda azalma tespit edilmiştir. Bu durum kadın cinsiyetin ve 50 yaş üstü erkek hastaların dahil edildiği diğer çalışmalarla benzerlik göstermektedir (7). Güncel rehberlerde HIV pozitif hastaların DEXA ile takip edilmesi ve tedavi önerileri daha çok 50 yaş üstü erkek ve postmenopozal kadınları kapsamakta iken çalışmamızda 50 yaş altı erkek hastalarda da, yüksek oranda kemik mineral yoğunluğunda azalma olduğunu saptadık (15,16).

Tablo 1. Hastaların $CD4^+$ T hücre sayısı ile kemik mineral yoğunluk değerleri arasındaki korelasyonun incelenmesi

	$CD4^+$ T hücre sayısı	
	Rho	**p**
L1-L4 KMY	-0,184	0,202
F boyun KMY	-0,044	0,763
F total KMY	-0,197	0,170

*Spearman korelasyon analizi, L: Lomber, KMY: Kemik mineral yoğunluğu, F: Femur

Çalışmamızda hastaların CD4+ T hücre düzeyleri ile kemik mineral yoğunlukları arasında bir korelasyon saptanmamıştır (p>0,05). CD4+ T hücre sayıları 500'ün altında olan hastaların %68'inde kemik mineral yoğunluğunda azalma görülürken, CD4+ T hücre sayıları 500'ün üstü olan hastaların %71'inde kemik mineral yoğunluğunda azalma görülmüştür. Bu sonuç ART'nin erken dönemindeki hastalarda CD4+ T hücre sayılarındaki hızlı düzelmeye bağlı olabilir. Bu konuda ART'ye naif daha fazla sayıda hasta ile yapılacak çalışmalara ihtiyaç duyulmaktadır.

Hem ART alan hem de naif hastaların dahil edildiği güncel bir çalışmada CD4+ T hücre sayısı ile L1-L4 lomber vertebra kemik mineral yoğunluğu arasında pozitif bir korelasyon saptanmıştır (17). Bizim çalışmamızda da lomber bölgedeki kemik mineral yoğunluğundaki azalma (%70) total femur (%44) ve femur boyun (%46) bölgelerine göre daha fazla görülmüştür. Yong ve ark.'larının (18) yaptığı bir çalışmada, CD4+ T hücre seviyesi düşük olan hastalarda frajilite kırıklarının sıklığının arttığı tespit edilmiştir. HIV pozitif kadın hastaların da dahil edildiği bu çalışmada ART süresi ile frajilite kırıklarının sıklığı arasında bir ilişki bulunmamıştır.

Kronik immün aktivasyon ve proenflamatuvar sitokinlerin artışı HIV pozitif bireylerde, kemik mineral yoğunluğundaki azalmada rol oynayabilmektedir (10). *In vitro* çalışmalarda HIV gp120 proteininin osteoblast fonksiyonları üzerine inhibitör etkisi olduğu ve kemiğe spesifik "runt bağımlı transkripsiyon faktörü-2"nin ekspresyonunu azalttığı gösterilmiştir (19). Shaiykova ve ark.'nın (20) yaptığı güncel bir çalışmada ise bizim çalışmamıza benzer şeklide, hastalık aktivitesi baskılanmış olgularda yüksek oranda düşük kemik mineral yoğunluğu saptanmıştır. Bu durum HIV pozitif bireylerdeki düşük kemik mineral yoğunluğunu tek bir nedene bağlamanın mümkün olmadığı görüşünü desteklemektedir.

Son yıllarda yapılan çalışmalarda ART'de kullanılan proteaz inhibitörlerinin kemik mineral yoğunluğu üzerindeki etkileri araştırılmış; tenofovir ve efavirenz en riskli ajanlar olarak bildirilmişlerdir (7-9). Aukrust ve ark.'nın (11) yaptığı bir çalışmada ART alan hastalarda osteokalsin düzeyinin arttığı ve proenflamatuvar sitokin düzeylerinin azaldığı gösterilmiştir. Tedavinin viral yük, CD4+ T hücre seviyeleri ve TNF bileşenleri üzerindeki etkisi ile ilişkili şekilde serum osteolkalsin seviyelerinde artış olduğu görülmüştür. Ayrıca hem kemik yıkımının hem de yapımının eş zamanlı arttığını destekleyecek şekilde osteokalsin ve C-telopeptid düzeylerinde korele bir artış gözlenmiştir. Viral yükü baskılamada etkinlikleri kanıtlanmış olan bu ajanların hem direkt hem de renal fosfat kaybını artırarak ayrıca D vitamini metabolizmasını bozarak indirekt etkilerle kemik mineral yoğunluğunda azalmaya yol açtığı bilinmektedir (21-24). Özellikle ART süresinin ilk 3 yılında bu riskin daha fazla olduğu bildirilmiştir (20).

Çalışma Kısıtlılıkları

Çalışmamızın retrospektif özellikte olması ve hasta sayısının 50 ile sınırlı olması, çalışmamızın kısıtlılıklarındandır. ART'nin etkisini gözlemlemek açısından uzun takip süreli, daha geniş hasta gruplarında yapılmış çalışmalara ihtiyaç vardır.

Sonuç

Elli yaş altı HIV pozitif erkek hastalarda, kemik mineral yoğunluğundaki azalma, prevelansı oldukça sık bir problem olmakla beraber; etiyolojisini sadece hastalığın kendisine, viral yüke ya da ART'ye bağlamak mümkün görünmemektedir. Morbidite ve hatta mortalite riski olan osteoporotik kırıkları önlemek için HIV pozitif hastaların kemik mineral yoğunluklarının yakın takibi ve tedavisi önem arz etmektedir.

Tablo 2. Çalışmaya katılan hastaların CD4+ T hücre düzeyleri ile Z skorlarının karşılaştırılması

		CD4+ T hücre düzeyleri				p
		CD4 hücre sayısı 500'ün altında		CD4 hücre sayısı 500'ün üstünde		
		n	(%)	n	(%)	
F boyun Z skor	Normal	12	(54,5)	15	(53,6)	>0,999[a]
	Osteopeni	8	(36,4)	10	(35,7)	
	Osteoporoz	2	(9,1)	3	(10,7)	
L total Z skor	Normal	7	(31,8)	8	(28,6)	0,970[b]
	Osteopeni	9	(40,9)	12	(42,9)	
	Osteoporoz	6	(27,3)	8	(28,6)	
F total Z skor	Normal	14	(63,6)	14	(50,0)	0,732[a]
	Osteopeni	7	(31,8)	12	(42,9)	
	Osteoporoz	1	(4,5)	2	(7,1)	
Herhangi bir bölgede Z skor	Normal	7	(31,8)	8	(28,6)	0,965[b]
	Osteopeni	7	(31,8)	9	(32,1)	
	Osteoporoz	8	(36,4)	11	(39,3)	

[a]Fisher Exact testi, [b]Ki-kare testi, F: Femur, L: Lomber

Etik

Etik Kurul Onayı: Çalışma, Etik Kurul Onay Belgesi gerektirmemektedir.

Hasta Onayı: Çalışmaya dahil edilen tüm hastaların onamları alındı.

Hakem Değerlendirmesi: Editörler kurulu tarafından değerlendirilmiştir.

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Brown Tumor and Hyperparathyroidism in Orthopaedic Surgery

Ortopedide Brown Tümörü ve Hiperparatiroidizme Yaklaşım

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Abstract

Objective: This study aimed a better diagnosis for patients with primary hyperparathyroidism (PHPT), who could be referred to misdiagnosis and treatment and be able to demonstrate a well analysis of patient before orthopaedic surgery.

Materials and Methods: A total of 12 patients admitted to our orthopaedics outpatient clinic between 2003 and 2017, examined and treated due to the bone lesion or fracture and diagnosed with PHPT, were included in this study. Patients were referred to the general surgery clinic for adenectomy. Direct radiograph was used to follow cysts recession after adenectomy.

Results: Patients have the mean age of 36.6±13.4 years, wherein seven were female and five were male. Individual bone involvement was observed in three patients, whereas nine patients had multiple bone involvement. Eight patients had pathological fractures. Biopsy was conducted on all patients, revealing an increased osteoclastic activity and multinuclear giant cells, and a report was issued for these findings.

Conclusion: Brown tumor is very rare reactive lesions developed in bone tissues during hyperparathyroidism. In order to make a definitive diagnosis for the cystic and lytic lesions, suspecting the patient's clinical status and keeping any possible diagnosis in mind is necessary.

Keywords: Brown tumor, giant cell tumour, primary hyperparathyroidism, metastatic bone lesion

Öz

Amaç: Primer hiperparatiroidizmi (PHPT) olup yanlış tanı ve tedaviye yönlendirilebilecek hastalar için, ortopedik cerrahi öncesinde daha iyi analiz edilmesine yol gösterecek bir çalışma planladık.

Gereç ve Yöntem: 2003-2017 yılları arasında ortopedi polikliniğimize başvuran, kemik lezyonu veya kırığı nedeniyle muayene edilip tedavi edilen ve PHPT tanısı alan 12 hasta çalışmaya alındı. Hastalar adenektomi için genel cerrahi kliniğine sevk edildi. Adenektomi sonrası kistlerin durgunluğunu takip etmek için direkt radyografi kullanıldı.

Bulgular: Hastaların ortalama yaşı 36,6±13,4 yıl idi. Çalışmaya dahil edilen hastaların 7'si kadın, 5'i erkekti. Üç hastada bireysel kemik tutulumu gözlenirken, 9 hastada çoklu kemik tutulumu gözlendi. Sekiz hastada patolojik kırık vardı. Artmış osteoklastik aktivite ve çok çekirdekli dev hücreler gösteren tüm hastalara biyopsi yapıldı ve bu bulgular için bir rapor yayınlandı.

Sonuç: Brown tümör, hiperparatiroidizm sırasında kemik dokularında gelişen çok nadir reaktif lezyonlardır. Kistik ve litik lezyonlar için kesin bir tanı koymak için, hastanın klinik durumundan şüphelenmek ve olası herhangi bir tanıyı akılda tutmak gerekir.

Anahtar kelimeler: Brown tümör, dev hücreli tümör, primer hiperparatiroidizm, metastatik kemik lezyonu

Introduction

Primary hyperparathyroidism (PHPT) is the most common cause of hypercalcemia in patients with asymptomatic hypercalcemia, who applies to the hospital outpatient clinics. Its prevalence rate is 1/1,000 person. Although it can be observed in all age groups, it is mostly observed in individuals at the age of 60s. Female to male ratio of PHPT is 3/2. The main finding of PHPT is the presence of elevated calcium and parathyroid hormone (PTH) levels (1).

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Hyperparathyroidism (HPT) may be accompanied with endocrinological weakness and getting exhausted quickly. Symptoms related to the renal and skeletal system are also observed. Early detection of the disease provides a minimal demineralization in the skeletal system (2,3). In general, nothing is detected as a radiological finding, but less frequently osteoporosis is observed. Other skeletal system findings include subperiosteal resorption of the distal phalanx, thinning of the distal ends of the clavicle, salt and pepper appearance of the skull, bone cysts in long bones, and Brown tumors (BTs).

BTs are very rare reactive lesions developed in the bone tissues during HPT. They represent 1% of all tumor-like bone lesions and 5% of all primary benign bone tumors (4). BTs, which are one of the subgroups of giant cell tumors (GCT), are caused by excessive proliferation of osteoclasts as a result of a hormonal stimulus. Osteoclast-rich tumors are brown. The source of the color is hemosiderin pigment, which occurs as a result of hemorrhage due to rich vein network it contains (3). Although there are no characteristic findings, all giant cell lesions may be BTs (5,6). It is important to remember that BT is not a pathognomonic finding for HPT. The most important factor in establishing the correct diagnosis is to suspect possible pathologies.

This study included the patients who were admitted to the orthopaedic clinic with HPT. We aimed to report better orthopaedics approach for these patients to avoid the mis-diagnosis and wrong surgical treatment.

Materials and Methods

This study was approved by the Fatih Sultan Mehmet Training and Research Hospital Institutional Review Board/Ethics Committee and conducted according to the ethical principles stated in the Declaration of Helsinki (decision no: 17073117-050.06, date: 03.02.2020). After approval of the institutional review board, informed consent was obtained from the all participants.

This retrospective study included 12 patients who were admitted to our orthopaedics outpatient clinic between 2003 and 2017 with bone lesions. Patients were examined and treated due to the bone lesion or fracture, and diagnosed with PHPT, were included in the study. Laboratory tests were performed for the patients. Endocrinology consultation was requested for patients who had HPT. Patients were confirmed to have no secondary or tertiary HPT after parathyroid scintigraphy, thyroid ultrasound, renal function tests, chest radiographs and all abdominal computed tomographies (CTs) were taken. As a result of these tests parathyroid adenoma was detected in all patients. The patients were referred to the general surgery clinic for adenectomy. Direct radiograph was used to follow the recession of the cysts after adenectomy.

Statistical Analysis

There was no statistical analysis applied in the study. This study was designed as a case series.

Results

The mean age of the patients was 36.6±13.4 years and 7 of the patients included in the study were female, while 5 were male. In 8 patients, pathological fractures were detected in different bone regions. One patient was operated for the cyst. Individual bone involvement was observed in 3 patients while 9 patients had multiple bone involvement. Demographic data, place of involvement, fracture locations, laboratory findings and treatment modalities are presented in Table 1.

Biopsy was conducted in all patients which revealed increased osteoclastic activity and multinuclear giant cells. Each patient with cyst did not receive any additional operation other than stabilization since the calcium, phosphorus and PTH values that were found to be compatible with HPT. Only the patient numbered 9, who had biopsy, had curettage and grafting in the second session due to the fact that the lesion in the talus was isolated and involved a large part of the talus to prevent early load and fracture.

Two patients were operated another orthopaedic clinic for eccentric bone tumor. Tumor resection prosthesis was performed for a patient with the diagnosis of osteosarcoma, while other patient underwent curettage and grephonage due to a GCT of bone (Figure 1).

Cysts and fractures of our patients were tried to be treated by using non-surgical methods. The most simple and comfortable method was tried to be chosen for the fractures requiring surgery (Figure 2). The main purpose of the surgery was to protect the patient's own bone tissue and not to treat cysts (such as giant cell bone tumor or malignant tumors).

During follow-up, bone fusion was observed, cysts were seen to be regressed, and the patient was observed to gain her healthy bone tissue rapidly following the adenectomy (Figure 3).

Discussion

BTs are very rare reactive lesions developed in the bone tissues during HPT. In order to make a definitive diagnosis for the cystic and lytic lesions, it is necessary to suspect the patient's clinical status and to keep any possible diagnosis in mind to prevent the wrong and over treatments in orthopaedics.

These tumoral structures associated with PHPT are reversible pathologies that can be healed through the excision of the parathyroid adenomas or removal of the glands (3,4). Following removal of the adenoma, osteoclastic activity stops suddenly and bone healing is observed instead of bone destruction (5,7). However, it is possible to leave them in areas where there are multi-localized BTs (8).

In the diagnosis of PHPT pathology, serum calcium, phosphorus, alkaline phosphatase and PTH are more significant than the histopathological examination. In HPT, GCTs are smaller and have a nodular appearance and they particularly have rounded hemorrhage foci; their stromal cells are more spindle-shaped and tender. The presence of bone metaplasia in stroma is also important. In these regions, osteoclastic and osteoblastic

Table 1. Demographic changes of the patients

Patient no.	Gender	Age	Complaint	Involvement	Fracture	Laboratory	Treatment
1	F	12	Pain and functional limitation and Fracture findings	Humerus, radius, femur, tibia, ribs, iliac, mandible	Femoral neck and diaphysis, humerus	Ca: 9.9 mg/dL, P: 2.6 mg/dL, PTH: 142 pg/mL	Adenomectomy for fractures conservative
2	M	20	Pain and fracture formed 2 months ago	Humerus, femur	Humerus	Ca: 14. 1 mg/dL, P: 2.28 mg/dL, PTH: 738 pg/mL	Adenomectomy for fractures conservative
3	F	25	Pain and difficulty in walking	Femur, tibia, fibula, rib, scapula, radius, metacarpus, phalanx, s. pubis	No	Ca: 10.8 mg/dL, P: 1.8 mg/dL, PTH: 1,385 pg/mL	Adenomectomy conservative for cysts
4	F	31	Pain and movement limitation	Femur neck	Femur neck	Ca: 10.5 mg/dL, P: 2.1 mg/dL, PTH: 419 pg/mL	Adenomectomy + osteosynthesis with cannula screw for fracture
5	F	19	Widespread body pain and shoulder prosthesis application and tumor diagnosis at the age of 16	Vertebra, sacrum, iliac, ribs	No	Ca: 15.7 mg/dL, P: 2.3 mg/dL, PTH: 1,548 pg/mL	Adenomectomy conservative for cysts
6	M	46	Fracture findings	Both femur, cranium, humerus, tibia	Femur diaphysis	Ca: 11.2 mg/dL, P: 3.8 mg/dL, PTH: 724 pg/mL	Adenomectomy + osteosynthesis with femoral nail
7	F	34	Pain and movement limitation	Femur, humerus	Humerus	Ca: 9 mg/dL, P: 2 mg/dL, PTH: 956 pg/mL	Adenomectomy conservative for cysts and fractures
8	M	49	Fracture findings	Femur	Femur supracondylar	Ca: 13 mg/dL, P: 1.7 mg/dL, PTH: 1,008 pg/mL	Adenomectomy + osteosynthesis with plate
9	M	66	Ankle pain	Talus	No	Ca: 13.2 mg/dL, P: 1.4 mg/dL, PTH: 912 pg/mL	Adenomectomy + curettage and grafting
10	F	38	Widespread body pain and fracture findings + curettage and grafting for eccentric talus	Femur, talus, iliac, foot phalanx	Femur diaphysis	Ca: 12.9 mg/dL, P: 2.2 mg/dL, PTH: 1,025 pg/mL	Adenomectomy + osteosynthesis with femoral nail
11	M	48	Hip pain	Acetabulum	Acetabulum	Ca: 10.7 mg/dL, P: 2.7 mg/dL, PTH: 1,014 pg/mL	Adenectomy + osteosynthesis with screw + grafting
12	F	52	Ankle and knee pain	Tibia, femur, fibula, iliac	No	Ca: 11.4 mg/dL, P: 1.5 mg/dL, PTH: 825 pg/mL	Adenectomy + conservative

Ca: Calcium, PTH: Parathyroid hormone, P: Phosphorus, M: Male, F: Female

activities improved with peritrabecular fibrosis may be observed. In our case series, biopsy was performed during the fracture surgery which revealed mature bone lamellae with multinuclear giant cells accompanied by mild mononuclear inflammatory cell infiltration. Bone tissues showing fibrosis and mildly inflamed reactive changes, focal bone resorption, and increased osteoclastic activity were also observed in the biopsy results. Due to this pathology, it is not possible to differentiate GCT and

BT. In the diagnosis of BTs, histopathologic examination helps to differentiate malignancy to a certain extent, however, it is not enough alone to make the final diagnosis.

GCTs are locally aggressive lesions containing connective tissues and stromal cells. They are usually present in bone metastases and are mostly located in the femur, tibia, radius, and humerus (3,5). Apart from long bones, they can be seen in the bones of the hand by 5%. The tumor can have monofocal or multifocal localization. Serum calcium level is the only beneficial laboratory finding to be used. This lesion is radiologically seen as lucent and expansile and looks like the enchondroma of the bone or aneurysmal bone cyst (5). In a study by Cicconetti et al. (9), it has been reported that the differential diagnosis of BT is very difficult which may be attributed to the fact that similar radiological images (cyst-like radiolucent) are seen in other pathologies. Morano et al. (7) reported in their study that the diagnosis of the patients was osteocalcytoma until their patients were diagnosed with PHPT in recovery period. They removed the parathyroid adenoma and found that their pathological diagnosis was BT. In our study, PHPT was tried to be excluded by performing biochemical laboratory tests to each patient whose initial diagnosis was bone cyst or lytic lesion when they admitted to the outpatient clinic. It should be kept in mind that BTs may mimic all kinds of lesions and may be atypical. If the PTH effect is not eliminated, relapse will occur in the same or another site, regardless of how BTs are treated.

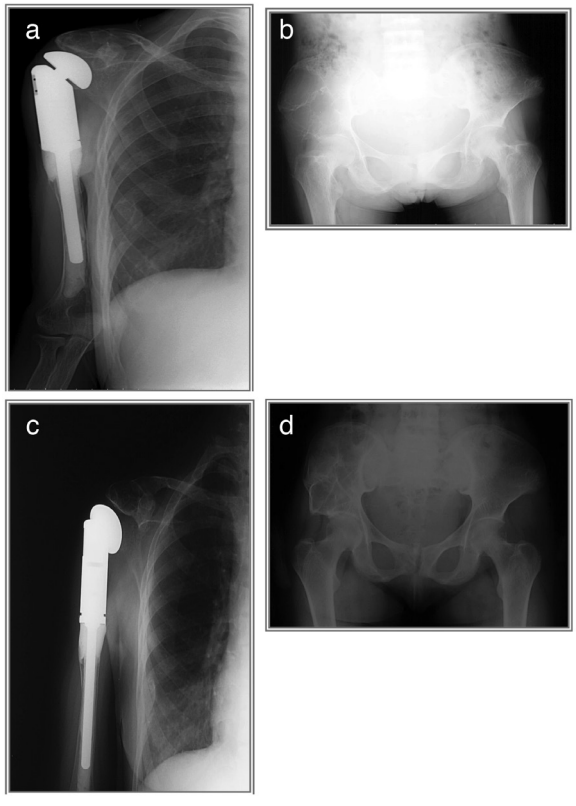

Figure 1. A 19-year-old female patient who underwent eccentric tumor resection due to right humeral lesion (patient numbered five) -; the significant change of the cyst in the iliac crest is particularly seen very well on the direct radiograph
a: Distal lesions of the acromion and clavicle of the patient, b: Large cystic lesion in the right half of the iliac crest, c and d: Control radiographs of the patient three years after the parathyroidectomy

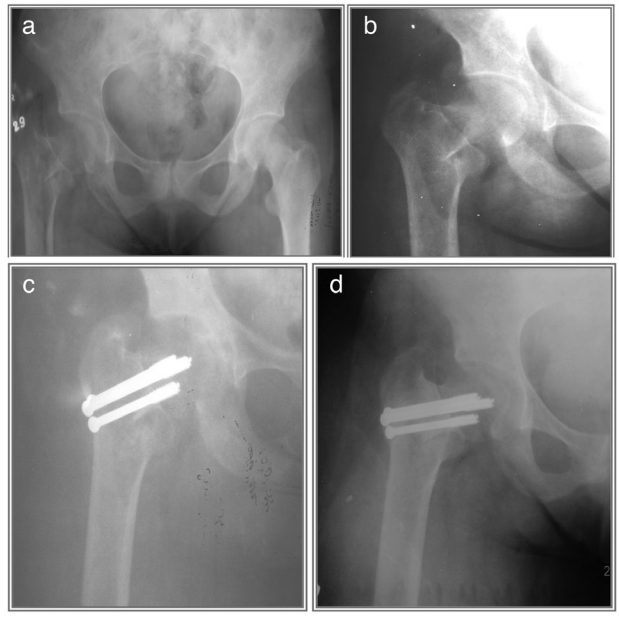

Figure 2. A 31-year-old female patient who underwent osteosynthesis due to a femoral neck fracture (patient numbered four)
a and b: Proximal femur fracture radiographs, c: Post-operative radiograph first day, d: bone fusion six months after the surgery

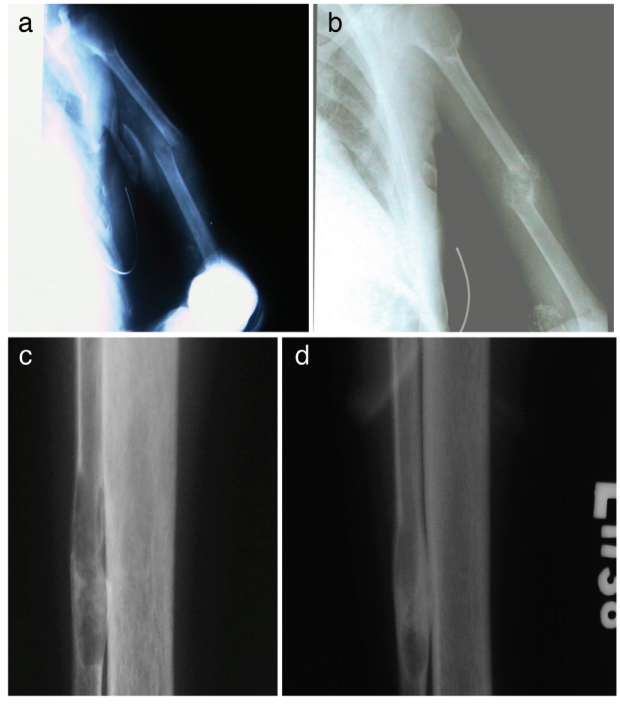

Figure 3. Patient numbered seven
a and b: First fracture and four-month follow-up radiograph of the patient who admitted to our clinic because of the pathologic fracture of the left humerus, c and d: Anteroposterior radiography of the patient (patient numbered three) at the time of the first diagnosis of the cyst in the right fibula and one-year follow-up radiograph

Pezzilo et al. (10) treated a femoral cyst case with the diagnosis of aneurysmal bone cyst and an isolated humerus cyst case with the diagnosis of GCT. Jouan et al. (11) applied a brutal operation for a BT case by performing fifth ray amputation. Some studies diagnosed osteolytic lesion of the distal ulna and radius as GCT and they performed resection to ulna and curettage and cement to the radius (12,13). Rossi et al. (14) reported that asymptomatic PHPT should be followed after adenoma excision. After excision, the curettage and denosumab are good treatment since there was no regression in the cyst. Ouzaa et al. (15) reported that performig curettage, cementoplasty, and iliac bone graft for GCT was successful. Similarly, in a patient included in our study, curettage and cementoplasty were performed for the eccentric lytic lesion on the talus, which was diagnosed as GCT (patient numbered 10). Another patient in our series underwent tumor resection prosthesis with the diagnosis of primary bone malignancy, which was actually lytic lesion in the humerus, however, similar lesions were observed in other parts of the body in the post-operative follow-up and treatment. In the first examinations of the patient, the diagnosis of PHPT was made and the cysts were followed up (patient numbered 5, Figure 1).

BT is mostly seen in the craniofacial localization (15-19). Since we included patients who applied to the orthopedics outpatient clinic, the number of patients with lesions in the craniofacial region was two. The most involved area was the femur which was seen in 9 patients out of 12.

Particularly in patients presenting with multiple bone involvement, BTs mimic bone metastases is the first diagnosis come to mind since it is common (19-22). Therefore, patients are diagnosed with PHPT during primary tumor investigation and continue their treatment as simpler and more satisfying. Since we analyzed the calcium, PTH and phosphorus values of the patients presenting with cystic bone lesions during the examination phase, we made very few mistakes in such a large number of complicated patients. De Crea et al. (23) reported that they performed right leg amputation in one patient and en bloc resection in one patient. Kirdak et al. (24), PHPT patients in two different countries were compared and it was reported that patients with PHPT in the developing country had higher serum PTH levels, more bone lesions, and larger adenomas. We believe that the wrong diagnosis and over-treatment are started to be more frequent in the differential diagnosis since PHPT-related BTs are seen less in developed countries.

Particular attention should be paid in differential diagnosis because GCT of bone, enchondroma, and aneurysmal bone tumor are very similar to BTs (6). It is important to note that histological examination alone is not sufficient to make a diagnosis. Therefore, it would be the most accurate and reliable approach to eliminate the diagnosis of PHPT by performing a simple blood test before performing the biopsy.

Once the adenoma is removed, the lesions are rapidly regressing and the bone is able to gain its former strength (3,7,8,16-18). The results of the patients followed in our strongly support this treatment (Figure 3). Particularly BTs developed in the lower extremity load-bearing bones can cause pain and pathological fracture. Therefore, the lesion should be treated surgically. Simple methods should be preferred in surgery and existing bone stock of the patient should be preserved. In a study by Yang et al. (25), which is one of the largest BT series in the literature, three of eight patients had pathological fractures. All of the fractures were in the lower extremities that were treated surgically. Our approach was similar to the literature; we treated our patients as it was a tumor in the diagnosis, while as a fracture in the treatment. Therefore, no overtreatment was observed in our patients (Figure 2, 3). It should be noted that lesions in other regions will disappear following removal of the adenoma. The most important matter is to keep these pathologies in mind during the diagnosis process and to suspect the diagnosis. The reason we report very few wrong procedures with the largest CT case in the literature may be the fact that the necessity of taking blood tests for PHPT in every patient with bone cyst or tumor before the biopsy stage is learned clearly during the education process.

Study Limitations

One of the limitations of our study was its retrospective pattern. The other limitation was the patient number. But we believe that our case number was good to report for a very rare disease. Another limitation was the absence of the control group to compare. But this is theoretically impossible to designate a control group for a comparison for this disease.

Conclusion

Evaluating the laboratory tests well during the treatment of the BTs in the orthopaedic discipline before proceeding to invasive procedures protect both the patient and physicians from over and wrong treatments.

Ethics

Ethics Committee Approval: This study was approved by the Fatih Sultan Mehmet Training and Research Hospital Institutional Review Board/Ethics Committee and conducted according to the ethical principles stated in the Declaration of Helsinki (decision no: 17073117-050.06, date: 03.02.2020).

Informed Consent: After approval of the institutional review board, informed consent was obtained from the all participants.

Peer-review: Internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: Y.Ö., H.M.Ö., Concept: Y.Ö., B.E.K., Design: B.E.K., Data Collection or Processing: A.V., E.A.Y., Analysis or Interpretation: B.E.K., Literature Search: O.G., Y.Ö., Writing: Y.Ö., B.E.K.

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Long-stem Prosthesis for Intertrochanteric and Femoral Neck Fractures in the Elderly: Retrospective Comparison of Short-term Clinical Outcomes

Yaşlılarda İntertrokanterik ve Femur Boyun Kırıklarında Uzun Stemli Protezler: Kısa Dönem Klinik Sonuçlarının Retrospektif Karşılaştırılması

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Abstract

Objective: Hip fracture treatment in elderly patients remains challenging. This study aimed to evaluate short-term clinical results of long-stem cementless arthroplasty in elderly patients with femoral neck and intertrochanteric fractures.

Materials and Methods: We collected data of patients we treated with long-stem cementless arthroplasty between January 2011 and December 2019 due to hip fractures. This study included 48 patients (≥65 years of age) with femoral neck and intertrochanteric fractures. The patients underwent either bipolar or total hip arthroplasty. A 2-year follow-up was conducted in all the patients. Outcomes were evaluated with the Harris hip score (HHS), Koval categories, complications and hip and mid-thigh pain. We compared clinical results of patients with femoral neck fractures and those with intertrochanteric fractures.

Results: The mean follow-up period was 57 (34-92) months. Sixteen patients had femoral neck fractures and 32 had intertrochanteric fractures. No difference in demographic characteristics and comorbidities was noted between groups. The mean preoperative Barthel index of activities of daily living score was 79. At the last follow-up, the mean HHS of the control group was 77 and the mean Koval categories score was 3. Revision surgeries were conducted in two patients due to dislocation. Infection was observed in one patient and was treated by debridement and anti-biotherapy. Implant loosening and periprosthetic fractures were not noted.

Conclusion: With fair outcomes, long-stem cementless arthroplasty is a potential treatment for hip fractures in elderly patients. A longer follow-up to evaluate the efficacy of these prostheses is warranted.

Keywords: Femoral neck fractures, intertrochanteric fractures, arthroplasty, cementless, long-stem

Öz

Amaç: Yaşlılarda kalça kırıklarının tedavisi hala güçlükler içermektedir. Çalışmamızda; femur boyun ya da intertrokanterik kırığı olan yaşlı hastalarda uzun stemli çimentosuz artroplastinin kısa dönem klinik sonuçlarını değerlendirmeyi amaçladık.

Gereç ve Yöntem: Ocak 2011'den Aralık 2019'a kadar kalça kırığı nedeniyle uzun stemli çimentosuz artroplasti ile tedavi ettiğimiz hastaların verilerini topladık. Femur boyun ya da intertrokanterik kırığı olan 48 hasta (≥65 yaş) çalışmaya dahil edildi. Hastalara bipolar veya total kalça artroplastisi uygulandı. Tüm hastalar en az 2 yıl takip edildi. Sonuçlar Harris kalça skoru (HHS), Koval kategorileri, komplikasyon, kalça ağrısı ve uyluk önü ağrısı açısından değerlendirildi. Femur boyun kırığı olan hastalarla ve intertrokanterik kırığı olan hastaların klinik sonuçlarını karşılaştırdık.

Bulgular: Ortalama takip süresi 57 (34-92) aydı. On altı hastada femur boyun kırığı, 32 hastada intertrokanterik kırık vardı. Demografik özellikler ve komorbiditeler açısından gruplar arasında fark yoktu. Preoperatif, Barthel günlük yaşam aktivite indeksi puanı ortalama 79 olarak hesaplandı. Son kontrollerde ortalama HHS 77 ve Koval kategorileri 3'tü. Çıkık sebebiyle 2 hastaya revizyon uygulandı. Sadece 1 hastada enfeksiyon vardı ve debridman ve antibiyoterapi ile tedavi edilebildi. İmplant yetersizliği veya periprostetik kırık hiçbir hastada görülmedi.

Sonuç: İyi klinik sonuçlarla, uzun stemli çimentosuz artroplasti yaşlı hastalarda kalça kırıklarının tedavisi için bir seçenek olabilir. Bu protezlerin etkinliğini değerlendirmek için daha uzun takip süreleriyle yapılmış çalışmalar daha uygun olacaktır.

Anahtar kelimeler: Femur boyun kırığı, intertroknaterik kırık, artroplasti, çimentosuz, uzun stem

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Introduction

Hip fractures are significant causes of mortality and morbidity in elderly (1). Hip fractures incidence is increasing and 6.26 million hip fractures per year is estimated for 2050 (2,3). Elderly patients with hip fractures show up with comorbidities including hypertension, cardiac disease, and diabetes. Consequently, early mobilization is needed in order to lower complications (4). Treatment modalities differ with type of hip fracture. Arthroplasty is chosen mostly for treatment of displaced femoral neck fractures (5). But treatment of unstable intertrochanteric fractures still remains controversial (6). Although most of the studies advise proximal femoral nail anti-rotation for these cases, recent papers show satisfactory outcomes with bipolar hemiarthroplasty (BHA) (7,8). Some authors prefer internal fixation due to advantage of lower post-operative complications. However; cut out of lag screw, loss of reduction and conversion to arthroplasty are still debating issues of internal fixation with intramedullary nails (9,10).

Type of arthroplasty is chosen regarding mobilization, cognitive functions, and tolerability of anesthesia. Patients who can walk out-doors with or without one walking stick, without cognitive disfunctions and those can tolerate longer anesthesia can be treated with total hip arthroplasty (THA) (11). Most of elderly with hip fractures are treated controversially with BHA. There are cemented and cementless options for arthroplasty. Cemented arthroplasty has advantages as; good fixation, lower aseptic loosening rated and less reported thigh pain (11). But due to increased risk of interoperative cardiac and respiratory complications; sufficient stability with cementless arthroplasty was tried to be achieved (12). Different types of cementless prosthesis were used by orthopedic surgeons. Although there are lots of studies at the literature over cementless arthroplasty elderly patients with hip fracture few reports are found investigating long-stem cementless arthroplasty in treatment of elderly patients with hip fractures. Long-stem cementless prosthesis were used mostly for revision surgeries. Outstanding long-term outcomes were achieved espeically in cases with femoral defects. Long-stem cementless prosthesis was thought by some orthopedic surgeons as an option for primary surgeries in osteoporotic patients regarding additional stability. In treatments of unstable intertrochanteric fractures; cementless long-stem designs fit stabily beginning from just distal site of the defected region and bone ingrowth to stem provides additional stability. In our study we aimed to show short term clinical outcomes of elderly patients with hip fractures; who were treated with cementless long-stem prosthesis.

Materials and Methods

We collected the data of the patients ≥65 years of age with hip fractures from January 2011 to December 2019. The study was designed retrospectively. All procedures were conducted in accordance with the ethical standards of the Helsinki Declaration of 1975, as revised in 2000. Due to retrospective design of the study, additional informed consent was not obtained from the patients. Patients who were treated with long-stem prosthesis (Echelon, Smith & Nephew, USA) due to hip fracture and had a minimum 2-year follow up was included in the study. All the fractures were osteoporotic fractures. Prosthesis used was same in all patients as; 190 mm, manufactured from cobalt chromium and porous coated (Figure 1, 2). The treatment was either bipolar or THA. Patients with pathological fractures, concomitant pelvic fractures, with fractures older than seven days, patients who were prefracture bedridden or patients who were lost during follow-up were excluded from the study. A

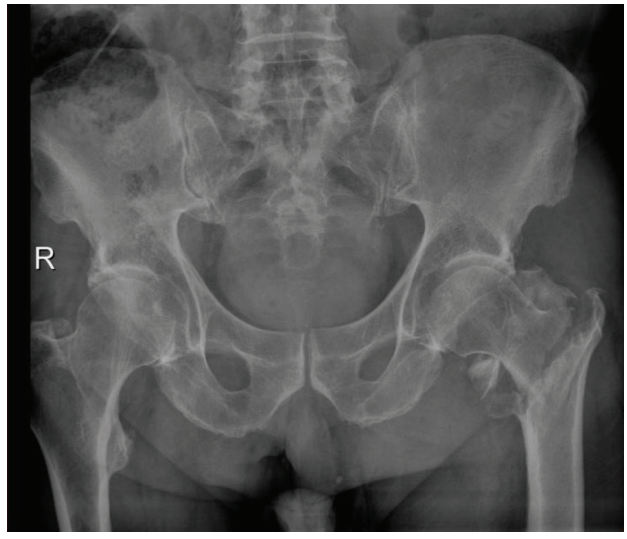

Figure 1. Preoperative X-ray showing intertrochanteric fracture

Figure 2. Post-operative X-ray showing treatment with long-stem cementless bipolar hemiarthroplasty

total of 48 patients (38 female, 10 male) with a mean age of 81 (65-96) were evaluated. For assessments; age, gender, interval between fracture and operation, type of fracture, body mass index (BMI), American Society of Anesthesiologists (ASA) score, comorbidities, prefracture walking ability regarding score of Koval categories, prefracture Barthel index of activities of daily living (ADL) score, type of anesthesia, surgical time, number of blood transfusions, hospitalization day, type of prosthesis follow-up duration of the patients were recorded. Follow-up controls were performed at post-operative 6 weeks, 3, 6, 12 months and every year thereafter. On the follow-up controls for assessment of clinical outcomes, Koval categories, and Harris hip score (HHS) was used. The mobilisation ability of the patients were evaluated with score of Koval categories in every control (Figure 3) (Table 1) (13). The progression or regression of ambulatory capacity was compared with the prefracture and previous follow-up controls. Post-operative activities of the patients were evaluated regarding HHS (14). HHS was recorded for patients in every follow-up control and clinical improvement and returning to physical ability status of prefracture term was evaluated with HHS. Mid-thigh pain was also questioned in controls as a possible complaint of patients treated with cementless arthroplasty (15). For the pain located around hip visual analogue scale (VAS) was assessed in controls (16). Additionally early post-operative and late complications were recorded. Mean of score of Koval categories, HHS and VAS of the last control of the patients were assessed for comparison between both groups.

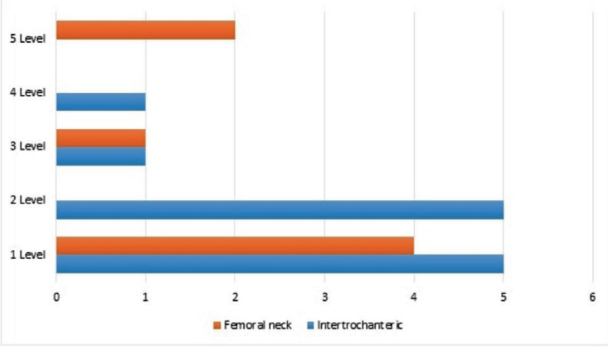

Figure 3. Regression of score Koval categories at the last control compared with preoperative levels

Table 1. Categories of walking ability by Koval

Categories of walking ability by Koval	Scores
Independent community ambulatory	1
Community ambulatory with cane	2
Community ambulatory with walker	3
Independent household ambulatory	4
Household ambulatory with cane	5
Household ambulatory with walker	6
Non-functional ambulator	7

Surgical Technique

Operations were performed by the same surgical team general or spinal anesthesia.

For BHA lateral approach was used in lateral decubitus position. Following capsulotomy, femoral head and fractured fragments were removed. Femoral canal was reamed and prepared for rasping. After rasping with help of stem trial, the stability, leg length and the size of them stem were controlled. Femoral stem was inserted to femoral canal. Then displaced trochanteric fragments were fixed with cerclage wires. Reduction was done after deciding bipolar neck length and size with trial reduction. The operation was completed closing wounds. For THA after removing femoral head, before femoral canal preparation acetabular component was implanted. In order to prepare acetabulum retractors were positioned. After verifying landmarks acetabulum was reamed. Acetabular component was implanted. Then femoral stem was implanted as describe above. Insert was set after trial reduction was performed. And the operation was completed with closing wounds. For antibiotic prophylaxis 1 gr cefazolin was begun intravenously; within 30 minutes before the incision and continued with three doses next 24 hours. Low molecular weight heparin was used daily for 30 days for thromboembolism prophylaxis. Drains were removed 24 hours after surgery. Blood was performed with hemoglobin <85 g/L and regarding patients' complaints and symptoms. All the patients were encouraged with full weight bearing mobilization on the post-operative first day.

Measurements were done; hospitalization duration and time from fracture to operation as days, blood transfusion in terms of units and surgical time as skin-to-skin in minutes. Clinical outcomes were defined as HHS at the last control, changes in score of Koval categories comparing preoperative status with the last control in terms of average. Complications were recorded as early post-operative and late complications. Mid-thigh pain was also questioned and pain in the operated hip was calculated with VAS.

Statistical Analysis

Statistical analysis was performed using statistical package SPSS version 17 SPSS. Quantitative data were expressed with mean ± standard and for categorical variables data were presented as percentage. Shapiro-Wilk test showed that quantitative data were not normally distributing and consequently non-parametric tests were used. Existence of statistically significant difference between quantitive data of two independent groups was analyzed by Mann-Whitney U test and existence of statistically significant difference between categorical data was analyzed by chi-square test. When values in cells were 5 or above 5 Pearson test was used, when below 5 Fisher's Exact test was used. P value was accepted as p=0.05 in 95% confidence interval. P<0.05 was accepted as statistically significant.

Results

Fourty eight patients were followed up minimum 2 years with mean 57 (24-92) months. Sixteen patients had femoral neck fractures and 32 had intertrochanteric fractures, in 21 patients' fracture was in left hip and in 27 in right hip. All the fractures were presented as osteoporotic fractures. Mean BMI of the patients was 26 (18-39). Hypertension (26) was the most common comorbidity, followed by diabetes (13) and cardiac disorders (12). Six patients had diagnosis of dementia. Preoperative ADL score was an average of 79 and mean score of Koval categories was 2. Time from fracture to surgery was mean 2 days. Mean ASA score of the patients was 2 (Table 2). Thirty nine patients underwent BHA and 9 patients underwent THA. Seven patients were operated under general anesthesia and 41 patients under spinal anesthesia. Surgical times was average of 77 minutes. Mean hospitalization duration was 6 days and average of blood transfusion given was two units per patient. At the last follow-up control mean HHS was 77 and mean score of Koval categories, was seen to be regressed to 3. VAS was calculated as an average of 1 and mid-thigh pain was present in 6 (12.5%) patients. At the early post-operative stage one patient with BHA suffered from urinary tract infection and one patient with THA needed debridement a month after operation due to wound infection. One patient with THA had dislocation three weeks after the operation. Closed reduction was performed. Cause having redislocation three weeks later, the patient was taken to revision surgery. As a late complication one of our patients had dislocation on 9th month for two times, revision surgery was done also to this patient after 2nd dislocation, following closed reduction in the first dislocation. At the last follow-up control, three patients were nonfunctional ambulatory. The patients were divided in two groups. Patients with femoral neck fractures were defined as group 1 and patients with intertrochanteric fractures were defined as group 2. There was no statistically significant difference between two groups of regarding demographic and preoperative functional status. There was also no significant difference on hospitalization days, blood transfusions and post-operative complications. HHS and score Koval categories were also found similar in both groups (Table 3).

Table 2. Demographic characteristics and preoperative status of the patients

	Femoral neck	Intertrochanteric	p
Number of patients	16	32	-
Mean age of operation (year)	81 (67-88)	81 (65-96)	0.776*
Gender (female:male)	15:1	23:9	0.132**
ASA classification			
I	0	3	0.492*
II	8	15	
III	8	13	
Preoperative ADL (mean)	81	78	0.371*
Preoperative score of Koval categories (mean)	2	3	0.709*
Body mass index	26	26	0.904*

ASA: American Society of Anesthesiologists, ADL: Activities of daily living
*Mann-Whitney U test, **Fisher's Exact test

Table 3. Intraoperative and post-operative variables of the groups

	Femoral neck	Intertrochanteric	p
Prosthesis (number)			
Bipolar hemiarthroplasty	15	24	0.238*
Total arthroplasty	1	8	
Mean unit of transfusion (number)	2	2	0.138**
Time from fracture to surgery (day)	1	2	0.732**
Mean duration of hospitalization (day)	6	6	0.347**
Complications (number)			
Early	0	2	0.546*
Late	2	2	0.592*
Score of Koval categories in last control (mean)	3	3	0.911**
Harris hip score in last control (mean)	76	78	0.709**

*Fisher's Exact test, **Mann-Whitney U test

Discussion

In treatment of hip fractures in elderly, in order to avoid mortality and morbidities; main purpose is thought as achieving prefracture mobilization status and functions as early as possible. For this reason, arthroplasty is advised by some authors regarding mobilization with early weight bearing and few implant failures (17,18). Arthroplasty can be performed either cementless or cemented. Cemented stems have been chosen by some surgeons suggesting as being initially more stable when compared with cementless stems (19,20). But intraoperative cardiopulmonary complications are still debating issues of cemented prosthesis. Though cementless prosthesis seem as good options to avoid these problems, increasing stability of these stems have become concerning. Recent studies show good outcomes with cementless stems without any complication related with stability (4,21). Cementless prosthesis are available with short, standard, and long-stems. Although there are lots of studies at the literature over cementless stems, few studies are reported on long-stem cementless prosthesis in treatment of hip fractures in elderly (4,22,23).

In our study, we observed that, in treatment of hip fractures in elderly, long-stem cementless prosthesis provided satisfactory clinical outcomes with low complication rates. The patients could restore their prefracture functions with early mobilization. We have not come upon to any perioperative cardiopulmonary complications. Only two of our patients needed revision surgery, both due to dislocation related with traumas. We observed implant related infection in one patient, which recovered after debridement and antibiotherapy without need of implant removal. Although there are studies suggesting that rate of periprosthetic fracture is increased with cementless arthroplasty, we have not seen any periprosthetic fracture (24,25). We saw that pain was not present in most of our patients. In our mean 59 months follow-up none of our patients suffered from implant failure.

Although there are studies showing good outcomes with cemented stems in treatment of hip fractures, bone cement implantation syndrome is still a debating issue. The syndrome is presented just after cementing; with sudden hypotension, arrhythmia, hypoxia, pulmonary hypertension, cardiogenic shock and even with cardiac arrest (26). The mechanism is still not clear but, thermic, anaphylactic, and inflammatory processes have been accused (27). Cemented arthroplasty related intraoperative mortality rates were shown as 0.11-4.3% in studies over hip fractures, differing by type of fracture and type of arthroplasty (27,28). The rates were 0.20% for intracapsular and 1.6% for intertrochanteric fractures. We choose cementless stems in order to avoid perioperative cardiopulmonary complications. We did not experience any such complications in our cases. And we think that our outcomes were compatible with studies reporting treatment of in hip fractures in elderly with cemented hemiarthroplasty (29,30).

Choy et al. (21) presented 40 patients treated with cementless bipolar arthroplasty with diagnosis of intertrochanteric fracture. Mean age of the patients was 78.8. Mean follow-up period of the patients was 40.5 months. Most of the patients could be able to return to their daily activities. HHS at the last controls was calculated with an average of 80.6. They did not experience any intraoperative death or periprosthetic fracture. Only in 3 patients superficial infection developed and all could be treated without implant removal. They achieved good functional outcomes in their patients with cementless bipolar arthroplasty and none of the patients had implant loosening in follows.

In the study of Lee et al. (22), clinical outcomes of 96 patients treated with cementless BHA were reported. Significant number of patients had regression in mobilization status regarding score of Koval categories similar with our study. Only 3 patients had activity related mid-thigh pain and in small number of patients they observed cortical porosis but none of the patients needed revision surgery due to implant failure.

Chang et al. (1) published outcomes of patients consisting femoral neck and intertrochanteric fractures treated with cementless BHA. The patients were in similar age and preoperative clinical status with our study. They reported few surgical complications in both group with satisfactory clinical results. HHS was found mean 66.9 in intertrochanteric group and 68.1 in femoral neck group. As short term results they did not have any implant related complication.

Kim et al. (23) reported their midterm functional outcomes and survival rates of elderly patients with intertrochanteric fractures, whom they treated with long-stem BHA. They followed their patients for mean of 61.8. They did not experience any stem implant failure. Two of their patients had dislocation and 6 of the patients had periprosthetic fracture caused by falling. They also saw that score of Koval categories regress during elongated as the follow-up duration but clinical scores were fair at the last controls of the patients with mean 77 points of HHS. Except periprosthetic fractures findings of our study was comparable with this study similar demographic characteristics of patients. In our study there were also patients with femoral neck fractures and these patients' clinical outcomes were also outstanding like those of intertrochanteric fractures.

Study Limitations

Our study has several limitations. First, our study was designed retrospectively. Second, study consists of limited number of patients that were not so homogeneous. Another issue was lacking of control groups. Comparison with group of patients who had cemented arthroplasty would be more informative. Since we were not preferring cemented arthroplasty due to perioperative complications only, there were only few patients in this group and the number was not enough for comparison. The follow-up period was also not so long. This has always become a challenging issue for hip fractures in elderly patients because of high mortality rates and difficulties to go on with regular follow-up controls. Despite these limitations, we believe that our study

shows that long-stem cementless arthroplasty is advisable for elderly patients with hip fractures.

Conclusion

We observed clinical outcomes of our patients for a mean of 57 months. HHS of the patients were fair and most of the patients were able to ambulate with or without any support. None of our patients suffered from loosening. With outstanding functional results, we believe that long-stems prosthesis can be chosen as a treatment option hip fractures in elderly. At the literature long-stem prosthesis was used for treatment of intertrochanteric fractures. We used these type of prosthesis also for femoral neck fractures. Long-stem prosthesis has an advantage of additional stability with diaphyseal press fit locking. We think that long-stem cementless prosthesis can be preferred in elderly patients with femoral neck fractures among those with poor bone quality.

Ethics

Ethics Committee Approval: Research was performed without any conflict of ethical issues.

Informed Consent: All procedures were conducted in accordance with the ethical standards of the Helsinki Declaration of 1975, as revised in 2000. Due to retrospective design of the study, additional informed consent was not obtained from the patients.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

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

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Role of FRAX in the Evaluation of Osteoporosis in Patients with Chronic Obstructive Pulmonary Disease

Kronik Obstrüktif Akciğer Hastalığı Hastalarında Osteoporozu Değerlendirmede FRAX'ın Rolü

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Abstract

Objective: The incidence of osteoporosis increased in patients with chronic obstructive pulmonary disease (COPD), and fractures due to osteoporosis are a significant cause of morbidity. Thus, risk assessment and taking necessary precautions are essential in these patients. This study aimed to assess the fracture risk of patients with COPD scanned with dual-energy X-ray absorptiometry (DXA) using the fracture risk assessment tool (FRAX) and to identify their treatment status.

Materials and Methods: Patients who presented to the Physical Therapy Outpatient Clinic of Aydın Atatürk State Hospital and diagnosed with COPD between January 2014 and January 2019 were included in the study. Results of DXA and pulmonary function test performed within the last year were recorded. According to the DXA results, patients were divided into osteoporotic, osteopaenic and normal groups. Patients were also classified into group A, B, C and D according to the Global Initiative for Chronic Obstructive Lung Disease classification. FRAX values were calculated using an online calculator.

Results: Ninety-five patients with COPD were enrolled in the study. According to their DXA values, 39 (41.1%), 41 (43.2%) and 15 (15.8%) patients were allocated in the osteoporotic, osteopaenic and normal groups, respectively. The 10-year major osteoporotic and hip fracture risks, calculated using FRAX, was the highest in the osteoporotic group, followed by the osteopaenic group ($p<0.001$ and $p<0.001$, respectively). Thirty-six patients (92.3%) in the osteoporotic group received medical treatment for osteoporosis, whereas only 13 (31.7%) patients in the osteopaenic group received medical treatment. FRAX assessment revealed that both major osteoporotic and hip fracture risks were higher in groups C and D ($p=0.002$ and $p=0.002$, respectively).

Conclusion: All patients with COPD, particularly those in groups C and D, should be assessed with both DXA and FRAX, regarding osteoporosis and fracture risks, and preventive measures/treatment should be planned when required.

Keywords: Osteoporosis, COPD, FRAX

Öz

Amaç: Kronik obstrüktif akciğer hastalığı (KOAH) hastalarında osteoporoz sıklığı artmıştır ve osteoporoz sonucunda ortaya çıkan kırıklar önemli bir morbidite nedenidir. Bu nedenle bu hastalarda kırık riskinin değerlendirilmesi ve gereken olgularda önlem alınması gereklidir. Bu çalışmada çift enerjili X-ışını absorbsiyometri (DXA) ile taranan KOAH hastalarının kırık risk değerlendirme aracı (FRAX) ile kırık riskini değerlendirmeyi ve bu hastaların tedavi durumlarını belirlemeyi amaçladık.

Gereç ve Yöntem: Ocak 2014- Ocak 2019 tarihleri arasında Aydın Atatürk Devlet Hastanesi Fizik Tedavi Polikliniği'ne başvuran ve KOAH tanısı olan hastalar çalışmaya alındı. Sistemdeki DXA sonuçları ve son bir yıl içerisinde yapılmış olan solunum fonksiyon test sonuçları kaydedildi. Hastalar DXA sonuçlarına göre osteoporotik, osteopenik ve normal olarak 3 gruba ayrıldı. Hastalar ayrıca Kronik Obstrüktif Akciğer Hastalığına Karşı Küresel Girişim sınıflamasına göre A, B, C ve D olarak 4 sınıfa ayrıldı. Hastaların web üzerinden FRAX değerleri hesaplandı.

Bulgular: Çalışmaya 95 KOAH hastası alındı. DXA değerlerine göre sınıflandırıldığında 39'u (%41,1) osteoporotik, 41'i (%43,2) osteopenik ve 15'i (%15,8) normal gruptaydı. FRAX ile hesaplanılan 10 yıllık majör osteoporotik ve kalça kırık riski en yüksek osteoporotik grupta daha sonra ise osteopenik grupta bulundu (p değerleri sırasıyla <0,001 ve <0,001). Osteoporozu olan hastaların 36'sı (%92,3) osteoporoz için medikal tedavi almışken, osteopenik grupta 13 (%31,7) hasta medikal tedavi almıştı. Osteopenik grupta tedavi almayan 28 hastanın 5'i (17,8) kalça fraktürü açısından yüksek riskli bulundu. FRAX ile yapılan değerlendirmede C ve D grubunda olan hastalarda hem majör osteoporoz riski hem de kalça fraktürü riski daha yüksekti (p değerleri sırasıyla 0,002 ve 0,002).

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Öz

Sonuç: Başta C ve D grubu olmak üzere tüm KOAH hastaları osteoporoz ve kırık riski açısından hem DXA hem de FRAX ile birlikte değerlendirilerek gereken olgularda koruyucu ve medikal tedavi planlanmalıdır.
Anahtar kelimeler: Osteoporoz, KOAH, FRAX

Introduction

Chronic obstructive pulmonary disease (COPD) has pulmonary and extrapulmonary effects, has numerous comorbidities, and is characterized by chronic and progressive airway destruction (1,2). Associated comorbidities lead to impairment of the quality of life and increasing duration of hospitalization in COPD patients. One of these comorbidities is osteoporosis, a disorder with a course of reduction in both the mass and microarchitecture of bone, eventually leading to fractures (3,4). Conducted studies have reported an increased incidence of osteoporosis, and that this might be related to the causes such as the drugs used, inactivity, cachexia, malnutrition, and inflammation (5). Assessment with dual-energy X-ray absorptiometry (DXA) is considered the golden standard in diagnosing and treating osteoporosis (6,7). Fractures occurring as a consequence of osteoporosis in COPD patients reduce the quality of life of the patient. The hip fracture disables the patient's mobilization, leading to more reduction of the already low exercise capacity, and kyphosis due to vertebral fractures causes a further reduction of the respiratory reserve (8). When individuals with osteoporotic fractures were considered, it was found that fractures occurred not only in the presence of osteoporosis but also in those with osteopenia (9). Thus, the World Health Organization (WHO) constituted a fracture risk assessment tool (FRAX), a web-based algorithm table, to calculate the fracture risk (10). A 10-year hip and major osteoporotic fracture risks are calculated with FRAX (11,12). During the calculation process, a country-based datasheet is used. Data such as age, gender, height, body weight, previous fracture history, fracture history of the parents, smoking status, steroid use, presence of rheumatoid arthritis or secondary osteoporosis, alcohol use, and the femoral neck score measured by DXA are recorded, and the 10-year hip fracture and major osteoporotic fracture risks are calculated. The obtained fracture risk results guide selection patients to be careful about and apply preventive measures early. In a patient with not too low DXA measurement, a high fracture risk may be calculated with FRAX. In this case, such patients should be warned regarding preventive measures, an exercise program should be given to prevent falls, and they should be assessed for treatment.

In our study, we aimed to evaluate the fracture risk with FRAX in COPD patients screened with DXA and identify these patients' treatment status.

Materials and Methods

The study was initiated following the approval of the Aydın Adnan Menderes University Ethics Committee for Non-Interventional Clinical Research (protocol no: 2019/26, date: 07.02.2019). In our study, the data of the patients who presented to the Physical Therapy Outpatient Clinic of Aydın Atatürk State Hospital and diagnosed with COPD between January 2014 and January 2019 were investigated in the digital environment. Information was given to the phone-reached patients who had a pulmonary function test (PFT) result within the last year and whose DXA data for osteoporosis was accessed in the system. Patients who agreed to participate in the study and signed the informed consent form were included. Patients with conditions that can affect DXA measurements, such as extensive degenerative disorders, laminectomy, or prosthesis, were excluded from the study.

Study Protocol

The patients' demographic characteristics, such as age, gender, and body mass index (BMI), were recorded. BMI was calculated using the formula [BMI=body weight/height^2 (kg/m^2)]. The patients were divided into three groups according to their DXA results found in the system as osteoporotic, osteopenic, and normal based on the WHO classification (13). Based on this categorization, patients with an L1-L4 vertebra total T-score or femoral neck T-score or femur total T-score was equal or under -2.5 were considered osteoporotic, those between -1 and -2.5 osteopenic, and those over -1 normal. All three groups were questioned regarding whether they had received medical treatment for osteoporosis. Previous fracture history, fracture history of the parents, smoking status and alcohol use, steroid use, rheumatoid arthritis, or causes of secondary osteoporosis were questioned and recorded. The patient's information and the femoral neck T-score were entered in the internet database, and the FRAX algorithm on the web site provided by WHO for Turkey was applied for each patient (14). The 10-year hip fracture and major osteoporotic fracture risks of the patients were calculated. Using the fracture risk threshold values suggested by the National Osteoporosis Foundation, the patients were divided into high-fracture-risk and low-fracture-risk groups. Patients with a 10-year hip fracture risk of over 3% were considered high-risk, and those equal to or under 3% were low-risk. Patients with a major osteoporotic fracture risk above 20% were considered high-risk, and those equal to or below 20% as low risk (15).

PFTs of the patients performed within the last year were evaluated. Forced vital capacity (FVC) %, forced expiratory volume 1st second (FEV1) %, and FEV1/FVC were recorded. Modified Medical Research Council (mMRC) dyspnea scale and COPD assessment test (CAT) were performed in all cases for clinical assessment. mMRC dyspnea scale reveals the activity limitation due to shortness of breath and is graded between 0

and 4 (16). CAT is a test measuring the health status of COPD patients, and there are eight items related to symptoms, exercise limitation, sleep status, and confidence level of the patient. The patient's answer for each test item is scored between 0 and 5, and the total score ranges between 0 and 40 (17).

COPD patients in the study were classified into four groups based on the Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2017 criteria. According to this, patients with a high symptom frequency were placed in groups B or D, and those with high exacerbation risk in groups C or D (1). Patients were divided into two separate groups as those in groups A and B with less frequent exacerbation and those in groups C and D with more frequent exacerbation.

Statistical Analysis

The data obtained were analyzed using the SPSS software package (SPSS 23, IBM Corp., released in 2015, IBM SPSS Statistics for Windows, Version 23., Armonk, NY, USA). The Kolmogorov-Smirnov test analyzed the conformity of variables to normal distribution. Regarding the continuous variables, those with a normal distribution were expressed as mean ± standard deviation and those not in conformity with normal distribution as median (25%-75%). Categorical variables were expressed as numbers and percentages. The Student t-test was used to compare two groups regarding continuous variables with a normal distribution and the Mann-Whitney U test for those not showing a normal distribution. For comparison of three or more groups regarding continuous variables with a normal distribution, One-Way Analysis of Variance and Tukey HSD test, one of the multi-comparison tests, were used, and for variables not showing normal distribution, the Kruskal-Wallis test, and the Bonferroni-Dunn test, which is another multi-comparison test, were used. The Pearson chi-square and Fisher Exact tests were used for the evaluation of categorical variables. $P<0.05$ was considered statistically significant.

Results

Data of a total of 226 COPD were reached regarding the specified dates. One hundred thirty-one patients with no DXA or PFT result within the last year of their follow-up were excluded from the study. A total of COPD 95 patients with an average age of 66.26±8.51 years, consisting of 80 (84.2%) males and 15 (15.8%) females, were included in the study. While 27 (28.4%) patients were active smokers, 61 (64.2%) were ex-smokers, and 7 (7.4%) had never smoked. The average smoking amount of the patients was 42.75±28.33 pack years. The medical histories of all non-smokers involved biomass exposure. According to the GOLD classification system, 21 (22.1%) patients were in group A, 31 (32.6%) in group B, 8 (8.4%) in group C, and 35 (36.8%) in group D. The mean femoral neck T-score of the patients measured with DXA was -1.66±1.25, the mean femur total T-score was -1.29±1.2, and the mean L1-L4 total T-score was -1.73±1.38. According to the calculated FRAX values, the mean 10-year major osteoporotic fracture risk was 13.66±8.97%, and the mean 10-year hip fracture risk was 6±7.08%. The demographic, functional, and laboratory data of the patients were presented in Table 1.

When the patients were grouped according to the DXA criteria determined by WHO, 39 (41.1%) patients were osteoporotic, 41 (43.2%) were osteopenic, and 15 (15.8%) were normal. All three groups were similar regarding the age, female/male ratio, amount of smoking, and COPD duration ($p=0.199$, $p=0.253$, $p=0.066$, and $p=0.660$, respectively). The FEV1/FVC value was significantly higher in the normal group than the osteopenic group ($p=0.032$). BMI was highest in the normal group and lowest in the osteoporotic group ($p<0.001$). The mMRC dyspnea scale and CAT scores, which reveal the clinical status, were similar in all three groups ($p=0.300$ and $p=0.296$, respectively).

The 10-year major osteoporotic fracture and hip fracture risks,

Table 1. The demographic, functional, and laboratory data of the patients with chronic obstructive pulmonary disease

Characteristics	Patients with COPD 95
Age (years)	66.46±8.07
Gender, n (%)	
Female	15 (15.8)
Male	80 (84.2)
BMI (kg/m^2)	25.31±4.59
Smoking history, n (%)	
Non-smoker	7 (7.4)
Ex-smoker	61 (64.2)
Active smoker	27 (28.4)
Smoking (packs/year)	40 (20-60)
Duration of COPD	8 (5-12)
FVC % pred	73.28±15.93
FEV1 % pred	52.47±15.94
FEV1/FVC	57.25 (50.73-63.39)
mMRC score	2 (1-3)
CAT score	16 (9-22.5)
COPD group, n (%)	
A	21 (22.1)
B	31 (32.6)
C	8 (8.4)
D	35 (36.8)
Femoral neck T-score	-1.66±1.25
Femur total T-score	-1.29±1.2
L1-L4 total T-score	-1.73±1.38
Major osteoporosis	11 (7.57-16)
Hip fracture	3.65 (1.47-7.72)

BMI: Body mass index, COPD: Chronic obstructive pulmonary disease, FVC: Forced vital capacity, % pred: Percent predicted, FEV1: Forced expiratory volume in one second, mMRC: Modified Medical British Research Council dyspnea questionnaire, CAT: COPD assessment test

calculated according to FRAX, were significantly different in all three groups (p<0.001 and p<0.001, respectively). Regarding major osteoporotic fractures, the fracture risk was high in 7 (%) patients in the osteoporotic group and 2 (%) patients in the osteopenic group. Regarding hip fractures, the fracture risk was high in 27 (69.2%) patients in the osteoporotic group and 14 (34.1%) patients in the osteopenic group. In all patients with normal DXA results, both fracture risks were low. According to the T-score, 36 (92.3%) patients with osteoporosis and 13 (31.7%) patients with osteopenia had received medical treatment for osteoporosis. Five (17.8%) of 28 patients in the osteopenic group who had not received any treatment were found to be at high risk regarding hip fracture (Table 2).

Regarding the COPD groups, 52 patients were in groups A and B, which had fewer exacerbations and hospitalizations, and 43 patients were in groups C and D. The patients in groups C and D were older and had a longer duration of COPD diagnosis (p=0.003 and p<0.001, respectively). Both groups were similar regarding the female/male ratio, BMI, and the amount of smoking (p=0.905, p=0.903, and p=0.163, respectively). The FVC %, FEV1 %, FEV1/FVC values, and the mMRC dyspnea scale and CAT scores were higher in the patients in groups C and D (p<0.001, p<0.001, p=0.001, p<0.001, and p<0.001, respectively). Evaluation with FRAX revealed that both the major osteoporosis and hip fracture risks were significantly higher in the patients in groups C and D when compared to those in groups A and B (p=0.002 and p=0.002, respectively). On the other hand, both groups were similar regarding the administered medical treatment according to DXA measurements (p=0.115) (Table 3).

Table 2. Demographic, functional, and laboratory data of the patients grouped according to their DXA results

Characteristics	Normal group (n=15)	Osteopenic group (n=41)	Osteoporotic group (n=39)	p
Age (years)	66.6±7.22	64.85±7.58	68.1±7.58	0.199
Gender, n (%)				
Female	2 (13.3)	4 (9.8)	9 (23.1)	0.253
Male	13 (86.7)	37 (90.2)	30 (76.1)	
BMI (kg/m^2)	29.42±4.01	25.66±4.24	23.37±4.07	<0.001*
Smoking, n (%)				
Non-smoker	1 (6.7)	2 (4.9)	4 (10.3)	0.896
Ex-smoker	10 (66.7)	26 (63.4)	25 (64.1)	
Active smoker	4 (26.6)	13 (31.7)	10 (25.6)	
Smoking (packs/year)	50 (40-75)	40 (30-55)	30 (20-50)	0.066
COPD duration	8 (6-10)	7 (5-10)	10 (5-15)	0.660
FVC (% pred)	76.38±12.93	76.07±14.67	69.24±17.6	0.116
FEV1 (% pred)	58.88±12.02	54.02±15.92	48.41±16.49	0.067
FEV1/FVC	62.77 (58.04-64.84)	56.46 (48.06-62.97)	57.2 (51.38-62.3)	0.082$^{\gamma}$
mMRC score	2 (1-3)	2 (1-3)	2 (2-3)	0.300
CAT score	12 (6-20)	14 (8.5-21.5)	19 (12-23)	0.296
Major osteoporosis risk	2.7 (2.2-3.2)	4.7 (3.5-7.8)	11 (6.3-18)	<0.001*
Major osteoporosis risk, n (%)				
Low	15 (100)	39 (95.1)	32 (82.1)	0.033$^{\tau}$
High	0 (0)	2 (4.9)	7 (17.9)	
Hip fracture risk	0.4 (0.2-0.7)	1.8 (0.85-3.8)	5 (2.4-11)	<0.001*
Hip fracture risk, n (%)				
Low	15 (100)	27 (65.9)	12 (30.8)	<0.001*
High	0 (0)	14 (34.1)	27 (69.2)	
Treatment status, n (%)				
Non-treated	15 (100)	28 (68.3)	3 (7.7)	<0.001*
Treated	0 (0)	13 (31.7)	36 (92.3)	

BMI: Body mass index, COPD: Chronic obstructive pulmonary disease, FVC: Forced vital capacity, % pred: Percent predicted, FEV1: Forced expiratory volume in one second, mMRC: Modified Medical British Research Council dyspnea questionnaire, CAT: COPD assessment test, *Significant differences were present among the three groups. $^{\gamma}$Significant difference was present between groups 1 and 2. $^{\tau}$Significant difference was present between groups 1 and 3

Discussion

Hip and vertebral fractures occurring due to osteoporosis cause both impairments of patients' quality of life and significantly burden the country's economy. Thus, identifying the patient groups at risk, and in addition to preventive measures, administering medical treatment to such patients when required might reduce the occurrence of fractures.

Besides osteoporosis, the incidence of balance disorder and falls are also increased in COPD patients (18,19). For this reason, the COPD patient group is a group that should immensely be paid attention to during screening for osteoporosis. Because fractures due to osteoporosis prevent mobilization and reduce the pulmonary reserve even further, the quality of life is impaired in COPD patients (3). Among these patients, with an evaluation made by DXA only, some at risk of fracture might escape the attention. When patients with a fracture history were analyzed, osteoporotic fractures were more frequent in the osteoporotic group and the osteopenic group (20). In our study also, a high 10-year hip fracture risk was determined in 14 (34.2%) patients in the osteopenic group, but five (35.7%) of these patients had not received any treatment.

When fracture risk evaluation was performed according to the subgroups of COPD, significantly higher FRAX values were determined in groups C and D than groups A and B.

Table 3. Demographic, functional, and laboratory data of the patients grouped according to their COPD groups

	COPD groups A+B (n=52)	COPD groups C+D (n=43)	p
Age (years)	64.25±8.06	69.13±7.32	0.003
Gender, n (%)			
Female	8 (15.4)	7 (16.3)	0.905
Male	44 (84.6)	36.8 (83.7)	
BMI (kg/m^2)	25.36±3.91	25.26±5.34	0.913
Smoking status, n (%)			
Non-smoker	5 (9.6)	2 (4.7)	0.631
Ex-smoker	33 (63.5)	28 (65.1)	
Active smoker	14 (26.9)	13 (30.2)	
Smoking (pack year)	37.5 (20-50)	40 (25-60)	0.163
COPD duration (years)	6 (5-8)	10 (7-15)	<0.001
FVC (% pred)	80.52±14.81	64.7±12.72	<0.001
FEV1 (% pred)	58.92±14.5	44.81±14.19	<0.001
FEV1/FVC	59.86 (55.03-64.84)	54.43 (47.2-60.3)	0.001
mMRC score	1.5 (1-2)	3 (2-3)	<0.001
CAT score	10 (8-17.5)	20 (16-24)	<0.001
Femoral neck T-score	-1.37±1.09	-2.02±1.34	0.011
Femur total T-score	-1.01±1.08	-1.63±1.26	0.012
L1-L4 total T-score	-1.51±1.29	-2.01±1.45	0.073
Major osteoporosis	4.7 (3.4-8.25)	8.8 (4.9-17)	0.002
Major osteoporosis risk, n (%)			
Low	50 (96.2)	36 (83.7)	0.043
High	2 (3.8)	7 (16.3)	
Hip fracture	1.65 (0.55-3.8)	3.9 (1.7-10)	0.002
Hip fracture risk, n (%)			
Low	38 (73.1)	16 (37.2)	<0.001
High	14 (26.9)	27 (62.8)	
Treatment status, n (%)			
Non-treated	29 (55.8)	17 (39.5)	0.115
Treated	23 (44.2)	26 (60.5)	

BMI: Body mass index, COPD: Chronic obstructive pulmonary disease, FVC: Forced vital capacity, % pred: Percent predicted, FEV1: Forced expiratory volume in one second, mMRC: Modified Medical British Research Council dyspnea questionnaire, CAT: COPD assessment test

Besides, all of the osteopenic patients with a high hip fracture risk according to FRAX but who had not received any treatment were in group D. We think that because COPD patients in the C and D groups are patients who encounter more frequent exacerbations, hospitalizations, and receive steroid treatment more frequently (1), fracture risk is higher in these groups. We also think that COPD patients who are identified as osteopenic when evaluated with DXA only, particularly those in groups C and D, should be evaluated more carefully and that early-onset treatment can prevent fractures that might occur in the future.

As a result of our study, we think that FRAX has various weaknesses in evaluating COPD patients. First of all, during the FRAX calculation, current smoking status is marked as "no" if the patient is not an active smoker. However, most of the COPD patients who quit smoking have a long duration of smoking in their lives. It is well known that smoking increases fracture risk. With the increasing amount and duration of smoking, the risk of fracture also increases (21,22).

On the other hand, there are not enough studies on how the risk of fracture changes following smoking cessation. A study reported that at least ten years must have passed after smoking cessation for smoking to be ineffective regarding fracture risk (23). In our study, 64.2% of the patients were ex-smokers, and most of them had quit smoking recently. The mean cigarette use of the patients was as high as 42.75±28.33 packs/year. We think that questioning previous smoking status and its amount besides the current smoking status during FRAX calculation will reflect fracture risk more accurately.

Secondly, during FRAX calculation, current steroid use is questioned, and if the patient is not using systemic steroids at that period, that section is marked as "no". As a result, the osteoporosis risk is calculated as low. Most COPD patients, particularly those in groups C and D, use inhaled steroids known to increase osteoporosis risk (3). On the other hand, patients in these groups use systemic steroids from time to time due to their frequent exacerbations or hospitalizations. We think that evaluating after adding inhaled steroids to the datasheet will be more accurate in FRAX calculation.

According to the recommendations of WHO, while treatment is indicated in normal patients who have a lumbar vertebra total T-score, femoral neck score, or femur total T-score equal to or over -2.5, in COPD patients, it is indicated in the osteopenic group with a score equal to or over -1 (24). However, in our study, 28 (68.3%) patients in the osteopenic group had not received any treatment, suggesting that treatment might have been neglected while evaluating the osteopenic group among COPD patients. According to DXA, when we evaluated the fracture risk of untreated patients in the osteopenic group, we determined that the hip fracture risk was high in 17.8% of the group. We think that this ratio will increase when the deficiencies of FRAX are corrected. Despite shortcomings of FRAX evaluation, if both DXA and FRAX are used together, the physician's awareness would increase, leading to requestion the necessity of treatment in particularly the osteopenic group.

The number of studies related to FRAX in determining the fracture risk has increased in recent years (9,25-28). However, enough data regarding which disorders FRAX should be used in or which treatment should be preferred and its combined use with DXA during follow-up has not accumulated yet (29). As such studies increase in number, the necessity of use, priority, or deficiencies of FRAX will be manifest more clearly.

Study Limitations

There are some limitations in our study. Firstly, the number of female patients in our study was small because of the higher rate of patients with COPD in men. Secondly, the number of patients was small in the COPD subgroups.

Conclusion

In the calculation of FRAX, the parts on the current smoking status and steroid use should be rearranged. All COPD patients, particularly those in groups C and D, should be assessed with both DXA and FRAX regarding the risks of osteoporosis and fracture, and then preventive and medical treatment should be planned when required.

Ethics

Ethics Committee Approval: The study was initiated following the approval of the Aydın Adnan Menderes University Ethics Committee for Non-Interventional Clinical Research (protocol no: 2019/26, date: 07.02.2019).

Informed Consent: Patients who agreed to participate in the study and signed the informed consent form were included.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: O.Y., Ş.D.Y., Concept: O.Y., Ş.D.Y., Design: O.Y., Ş.D.Y., Data Collection or Processing: O.Y., Ş.D.Y., Analysis or Interpretation: O.Y., Ş.D.Y., Literature Search: O.Y., Ş.D.Y., Writing: O.Y., Ş.D.Y.

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Case Report / Olgu Sunumu

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Differential Diagnosis of Thyroid Dermopathy and Acropachy with Arthritis

Tiroid Dermopati ve Akropaçisinin Artritlerle Ayırıcı Tanısı

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Abstract

Thyroid acropachy is a rare manifestation of autoimmune thyroid disease with characteristic imaging findings. Clinically, it is almost always associated with thyroid ophthalmopathy and dermopathy. It presents as nail clubbing and swelling of the digits and toes. Especially, symmetrical swelling of the hands and feet as well as clubbing of the nails may require differential diagnosis with many hepatic, pulmonary, renal and even rheumatologic diseases. Radiologically, soft-tissue swelling and periosteal new bone formations are particularly significant. We present a 22-year-old female with Graves' disease who presented with bilateral swelling of the hands and feet and was diagnosed with thyroid acropachy following clinical and radiological evaluations.

Keywords: Graves' disease, thyroid, acropachy, dermopathy, ophthalmopathy

Öz

Tiroid akropaçisi, karakteristik görüntüleme bulgularının gözlendiği nadir otoimmün tiroid hastalığının nadir bir tezahürüdür. Klinik olarak, neredeyse her zaman tiroid oftalmopati ve dermopatisi ile ilişkilidir. Tırnaklarda çomaklaşma ve el ve ayak parmaklarında şişlikler şeklinde görülür. Özellikle ellerin ve ayakların simetrik şişmesi ve tırnakların çomaklaşması birçok hepatik, pulmoner, renal ve hatta romatolojik hastalıkla ayırıcı tanı gerektirebilir. Radyolojik olarak yumuşak doku şişmesi ve periosteal yeni kemik oluşumları özellikle önemlidir. Burada, el ve ayaklarda bilateral şişlik ile başvuran ve klinik ve radyolojik değerlendirmelerle tiroid akropaçisi tanısı alan 22 yaşında Graves tanılı bir kadın hasta sunuldu.

Anahtar kelimeler: Graves hastalığı, tiroid, akropaçi, dermopati, oftalmopati

Introduction

Thyroid acropachy is an extrathyroidal clinical manifestation of autoimmunity that affects less than 1% of the patients with Graves' disease (GD) and can be seen in euthyroid or hypothyroid patients within weeks and years after treatment for thyrotoxicosis (1). It is more common in females and the peak age range is 50s (2,3). The clinical feature of thyroid acropachy is that it is usually symmetrical and bilateral (4). In thyroid acropachy, nail clubbing caused by glycosaminoglycan accumulation, proliferation in the diaphysis and hypertrophy of the surrounding soft tissues are observed (1). It is almost always associated with thyroid ophthalmopathy and dermopathy (5). We present a 22-year-old female patient with a history of total thyroidectomy due to GD in an euthyroid status after operation with the complaint of diffuse swelling and pain of the hands and feet; diagnosed as thyroid ophthalmopathy, dermopathy and acropachy after clinical and radiological evaluations.

Case Report

A 22-year-old female patient was referred to our outpatient clinic with a prediagnosis of arthritis due to swelling of both hands and feet, especially bulking of bilateral dorsum of the feet. The patient also complained of range of motion limitation and pain. The patient had these complaints for the last two years but showed a progressive deterioration especially in the last one year. There was no change in temperature or skin color of the joints. There was no trauma history. However, the patient's anamnesis revealed that she had been received anti-thyroid drug treatment for a while with the diagnosis of GD before total thyroidectomy; however, total thyroidectomy was performed because there was no clinical and laboratory improvement; and she had been receiving levothyroxine sodium 100 mcg/day after the operation. The physical examination demonstrated bilateral eyelid retraction compatible with thyroid ophthalmopathy and significant myxedematous changes to the

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bilateral hands, fingers, ankles, especially in the dorsum of the both feet (Figure 1, 2). The patient had no physical examination findings suggesting arthritis, but described pain in bilateral hands and feet. There were signs of nail clubbing of the hands (Figure 2). Hepatic and renal functions and blood electrolytes were found to be normal in the laboratory evaluation. Serological tests for rheumatologic diseases were negative. Erythrocyte sedimentation rate and C-reactive protein values were within normal limits. Serum thyroid stimulating hormone (TSH) level was 0.874 mIU/L (N: 0.3-4.5 mIU/L) and serum free T4 level was 1.29 ng/dL (N: 0.8-1.8 ng/dL). Direct X-ray imaging of the feet demonstrated bilateral soft tissue swelling (Figure 3). In addition, periosteal new bone formations were present in the 1st and 5th metatarsals of the right foot (Figure 4). Magnetic resonance imaging was performed for both feet. Muscle planes and tendons that entered the plane of bilateral examination had normal signal characteristics. There was significant edema

Figure 1. Swelling in the dorsum of the foot consistent with myxedema involving the ankle (left foot)

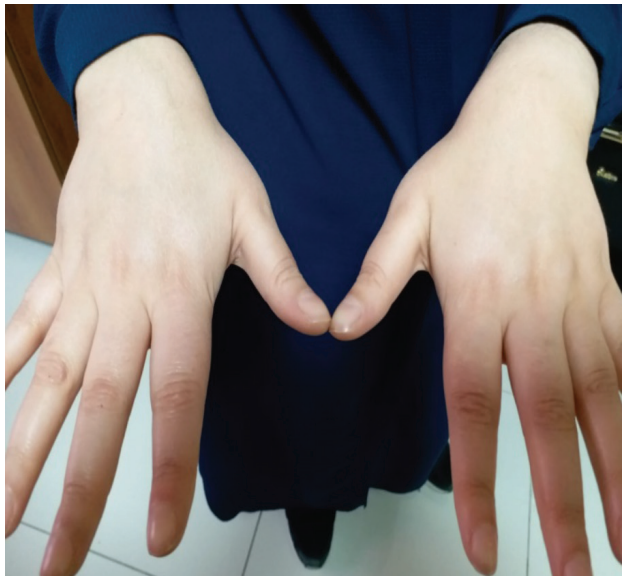

Figure 2. Swelling and nail clubbing in both hands extending up to the level of the proximal interphalengeal joint

Figure 3. Increased thickness and edema of the dorsum of the foot on T1-weighted magnetic resonance imaging of the right foot (white arrow)

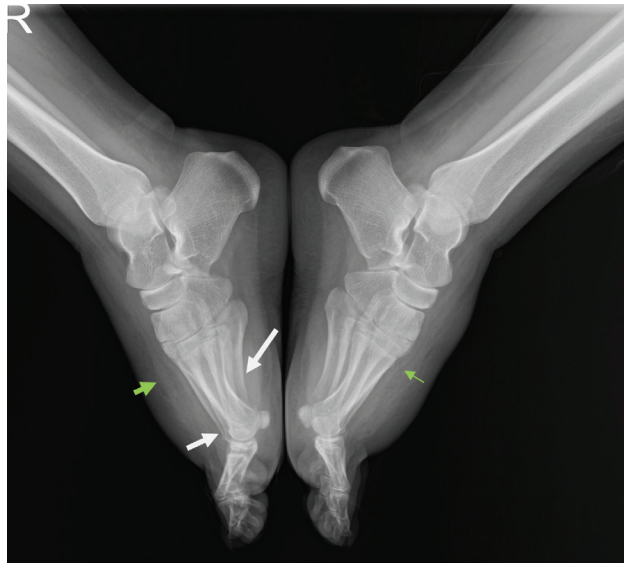

Figure 4. White arrows indicate periosteal new bone formation in the 1st and 5th metatarsal bones. Green arrows indicate soft tissue edema in the dorsum of both feet

and thickening of the bilateral foot dorsals. These findings were consistent with thyroid dermopathy and associated thyroid acropachy. The patient was followed by the ophthalmology clinic for thyroid ophthalmopathy. The patient was consulted with the dermatology clinic for thyroid dermopathy and acropachy. The patient was informed about regular follow-up visits to endocrinology clinic in terms of thyroid dysfunction, and non-steroidal anti-inflammatory agents (NSAIDs) could be used for pain complaints, also pentoxifylline 600 mg 2*1 treatment was initiated. The patient with a smoking history of 3 packs/year was recommended to quit smoking. In addition, our patient was informed about the case presentation and informed consent was obtained.

Discussion

Thyroid acropachy is the least seen extrathyroidal manifestation of autoimmune thyroid diseases (1). Graves' acropachy was first reported in a female patient with GD who was treated with thyroidectomy in 1933 (6). The coexistence of the triad of ophthalmopathy, dermopathy and acropachy in GD is very rare and occurs only in 0.8 to 1% of the patients with Graves ophthalmopathy (3,5). Graves acropachy is strongly associated with severe Graves ophthalmopathy and dermopathy and almost all cases occur simultaneously with ophthalmopathy and dermopathy (5). In fact, the chronological sequence of the extrathyroidal manifestations of autoimmune thyroid disease is that first thyroid dysfunction, next ophthalmopathy, then dermopathy, and finally acropachy are revealed (5). Most patients have nail clubbing and periosteal reactions in the phalanges. Lower extremity pain, skin and nail changes may indicate acropachy (5). Although the exact etiology is not known, autoantibodies against TSH and insulin like growth factor-1 receptors are thought to be involved in the pathophysiology of thyrotoxicosis and ophthalmopathy in GD (7,8). It is thought that TSH receptor autoantibodies bind to TSH receptors of the fibroblasts in the periosteum and trigger inflammatory response by increased cell proliferation and accumulation of glycosaminoglycans (5,9). Some studies have shown that smoking is a predisposing factor for acropachy in patients with GD (10-12). In our case, the ophthalmopathy, dermopathy and acropachy trio were present together and our patient had a history of smoking. In this respect, it is thought that smoking may play a role in the progression of the complaints of our patient despite being euthyroid as laboratory.

Acropachy is usually asymptomatic, but the main clinical symptoms may include nail clubbing, pain in small joints, soft tissue swelling, reactive changes in the periosteum, and changes in the skin and nails of the fingers (5). This disorder mostly involves the metacarpophalangeal and proximal interphalangeal joints of the upper extremity; in the lower extremity, it especially involves the ankles and the metatarsophalangeal joints (13). There is no temperature increase in soft tissue edema and is often associated with bone changes (13). Acropachy is extremely rare before the onset of thyrotoxicosis, 95% of the patients with acropachy develop the disease during GD treatment (14). In patients with clubbing of the fingers, the diagnosis is based on only the clinical findings (5). Histological examination shows that there is nodular fibrosis in the distal periosteum (13). Similarly, our patient's complaints were revealed when she was being treated for GD and our patient described pain especially on her hands.

There is no specific treatment for acropachy, high potency corticosteroids have been used and some patients have been successfully treated with rituximab (14,15). Patients with joint pain can be treated with NSAIDs such as ketoprofen (14). It is known that pentoxifylline intradermal, intravenous and oral use regresses dermatological symptoms in the treatment of pretibial myxedema (16,17). Treatment of thyrotoxicosis may lead to an improvement in the clinical manifestations of acropachy, but the role of thyroid function control in acropachy is uncertain (5,14). Despite the fact that our case is euthyroid, the progression of her complaints is consistent with the literature suggesting that the role of thyroid function control in acropachy is uncertain. Although the primary treatment of our patient is planned to maintain the euthyroid status and to use oral pentoxifylline in addition to NSAIDs for joint pain, at controls further treatment options will be evaluated according to the clinical status of our patient.

Acropachy is a rare presentation of thyroid autoimmunity. Corticosteroids, NSAIDs, pentoxifylline and in some cases rituximab may be good treatment alternatives. To provide and maintain euthyroidism is one of the main objectives; however the clinical benefit of euthyroidism in acropachy is unclear. Thyroid acropachy is a relatively benign condition that is usually asymptomatic. Clinical recognition of this condition is very important, because clubbing and swelling of the extremities may cause unnecessary research for many pulmonary, cardiac, hepatic or rheumatologic diseases.

Ethics

Informed Consent: Written informed consent was obtained from the patient prior to the drafting of the manuscript.
Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: N.Y., P.G.O., Concept: N.Y., P.G.O., Design: N.Y., P.G.O., Data Collection or Processing: N.Y., P.G.O., Analysis or Interpretation: N.Y., P.G.O., Literature Search: N.Y.,P.G.O., Writing: N.Y., P.G.O.

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Case Report / Olgu Sunumu

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An Overview of the Musculoskeletal Comorbidity of Acromegaly: A Case with Non-traumatic Spontaneous Rectus Femoris Rupture

Akromegalinin Kas-iskelet Sistemi Komorbiditesine Genel Bir Bakış: Travmatik Olmayan Spontan Rektus Femoris Rüptürü Olgusu

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Abstract

Acromegaly is a chronic endocrinopathy with pathologically increased levels of growth hormone (GH) and insulin-like growth factor-1 due to a pituitary adenoma that produces GH. One of the partially irreversible complications of acromegaly is arthropathy associated with severe morbidity in these patients. Joint complaints, such as pain, stiffness, or functional limitations, often occur with typical radiological abnormalities at an early age. We present a case of a 24-year-old acromegalic male patient with non-traumatic spontaneous right rectus femoris muscle rupture and an accompanying intramuscular haematoma.

Keywords: Acromegaly, growth hormone, muscle rupture

Öz

Akromegali, büyüme hormonu (BH) üreten hipofiz adenomuna bağlı olarak patolojik olarak artmış BH ve insülin benzeri büyüme faktörü-1 seviyelerinin söz konusu olduğu kronik bir endokrinopatidir. Akromegalinin kısmen geri dönüşümsüz komplikasyonlarından biri, bu hastalarda ciddi bir morbidite ile ilişkilendirilen artropatidir. Eklem ilişkili şikayetler ağrı, sertlik veya fonksiyonel kısıtlılık gibi, genellikle erken yaşlarda tipik radyolojik anormalliklerle kendisini gösterir. Burada non-travmatik spontan sağ rektus femoris kas rüptürü ve eşlik eden kas içi hematomu olan 24 yaşında akromegalik bir erkek olguyu sunmaktayız.

Anahtar kelimeler: Akromegali, büyüme hormonu, kas rüptürü

Introduction

Acromegaly is a chronic endocrinopathy characterized by excessive secretion of growth hormone (GH) and consequently increased levels of insulin-like growth factor-1 (IGF-1) (1). The disease usually develops in the second and third decades of life and it is known that females are affected more frequently than males (2). Patients generally present with complaints of fatigue, joint pain, headache and excessive sweating (3,4). However, clinical findings such as somatic disorders, vocal changes and extremity enlargement are considered pathognomonic and support the diagnosis (5,6). Musculoskeletal findings of this syndrome are common and almost all patients develop symptoms or signs of arthropathy. Acromegalic arthropathy occurs in approximately 50% of the patients, and it is a result of soft tissue and cartilage hypertrophy affecting both the peripheral and axial skeleton due to increased bone turnover associated with excessive GH secretion. In the early stages of the disease, cartilage hypertrophy predominates, and then degenerative changes and osteoarthritic findings occur. Arthropathy can only be reversed when GH and IGF-1 levels return to normal at very early stages of the disease. If the disease is not treated for a long time, osteoarticular sequelae cannot be modified by subsequent acromegaly treatment (6,7). Musculoskeletal findings of acromegaly may be a stimulant for early diagnosis. Thickening of peripheral nerves, such as carpal tunnel or cubital tunnel syndrome, increased disc height and vertebral scalloping (an exaggeration of the normal concavity of the posterior surface of one or more vertebral bodies due to soft-tissue hypertrophy in the spinal canal and increased bone resorption), spondylolisthesis, Baastrup's disease, diffuse idiopathic skeletal hyperostosis, facet hypertrophy and fatty infiltration of the paraspinal muscles are some of the typical musculoskeletal findings of acromegaly (3,8). Due to the insidious course of acromegaly, there are diagnostic delays.

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The most important therapeutic approach in acromegaly is the early diagnosis at that insidious stage of the disease. In this early stage of the disease, patients refer to many different specialists including musculoskeletal system specialists. The main objective in the treatment of acromegaly is to eliminate morbidity and to make mortality similar to healthy people for the same age group and sex. Therefore, especially musculoskeletal system specialists should recognize the early musculoskeletal manifestations of acromegaly, which is the most common cause of the first referral to health care professionals of acromegalic patients, and direct the suspected patients for endocrinological evaluation. Herein, we present a case of a 24-year-old acromegalic male patient with non-traumatic spontaneous right rectus femoris muscle rupture and accompanying intramuscular hematoma.

Case Report

A 24-year-old male patient was admitted to our outpatient clinic with pain and swelling on the anterior aspect of his right thigh. The patient's pain was present for less than 24 hours. The patient reported that his pain suddenly began while he was walking downstairs. There was no other history of trauma. On physical examination, knee and hip joint range of motions were complete but painful. There was an increase in stiffness and temperature in the anterior aspect of the right thigh. There was also a 2 cm diameter increase in the right thigh compared to the left side. The patient's visual analogue scale (VAS) score for his pain was 10. When the patient's history was questioned, it was learned that he had applied to various clinics with fatigue and joint pain in the last 3 years. Lumbar magnetic resonance imaging (MRI) taken 2 years ago with the complaint of sciatic pain revealed hypertrophy of lumbar facets, increased disc heights of L4-L5 and L5-S1, and left paramedian disc protrusion at L5-S1 level (Figure 1, 2). One year ago, the patient applied to the endocrinology clinic with complaints of fatigue, enlargement in hands and feet, and excessive sweating. In the pituitary MRI, a 19*16.9 mm diameter macroadenoma was detected in the left half of the pituitary gland extending from the central section of the pituitary gland. The patient underwent transsphenoidal pituitary surgery with the diagnosis of acromegaly. The patient was using long-acting somatostatin analogue (lanreotide subcutaneous 60 mg 1*1- per month) and prolactin inhibitor (0.5 mg cabergoline 1*1- 2 times per week) post-operatively. There was no pathological finding in the laboratory examinations. The platelet count was 228,000; activated partial thromboplastin time, prothrombin time and international normalized ratio were within normal ranges. Ultrasonographic imaging revealed a 2 cm transverse hematoma in the widest segment of the right rectus femoris muscle and a partial rupture of the musculotendinous junction at the proximal rectus femoris. In addition to topical and oral nonsteroidal anti-inflammatory treatments, immobilization and cold pack applications (3 times per day) were recommended to the patient. On the third day of the treatment, the patient's pain was better and VAS score decreased to 3 from 10.

Our patient was informed about the case presentation, verbal and written informed consents were obtained.

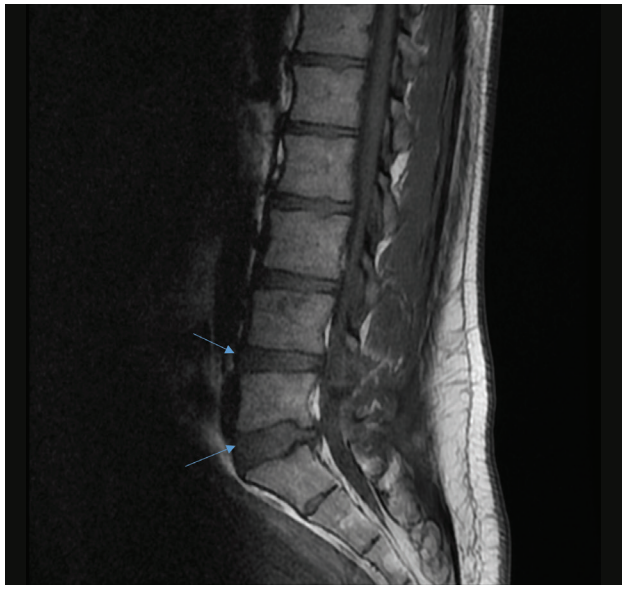

Figure 1. Increased disc heights of L4-L5 and L5-S1 (blue arrows), and left paramedian disc protrusion at L5-S1 level

Discussion

Active acromegaly is associated with severe comorbidity and decreased quality of life (QoL). Joint problems observed in acromegaly are the main cause of the decrease in QoL. Joint complaints appear as the earliest symptom of the disease in a significant proportion of the patients (9,10). The incidence of acromegaly is 2.78 per million-person-years, with little gender predominance (female vs. male, 49.5% vs. 50.5%, respectively)

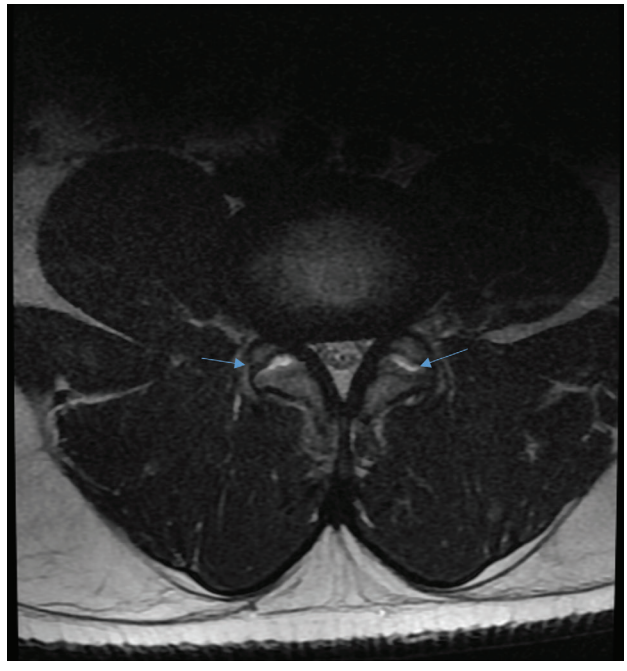

Figure 2. Hypertrophy of lumbar facets (blue arrows)

(11). The low incidence of the disease may be associated with the diagnostic delay due to the insidious course of the disease (6).

In acromegaly, there is a joint-related comorbidity reaching 77%. Therefore, knowing the typical musculoskeletal findings of acromegaly will provide both early diagnosis and treatment of this rare and insidious disease; as well as early initiation of acromegaly treatment will prevent not only joint-related comorbidity, but also cardiovascular, metabolic, respiratory and psychosocial comorbidities (8,9). Arthropathy in acromegaly has been known since Pierre Marie's classic definition of the disease in 1886 (5). Joint-related complaints such as pain, stiffness or functional limitations are often seen with typical radiological abnormalities at very early ages (12). Both weight-bearing and non-weight-bearing joints are affected. Notably, even after long-term remission of acromegaly, the prevalence of clinical and radiographic osteoarthritis is 12 times higher than in the general population (13). There are two basic mechanisms in the pathogenesis of acromegalic arthropathy; the first is endocrine changes, the second is mechanical changes. In the early course of the disease, high levels of GH and IGF-1 cause hypertrophy of articular cartilage and periarticular ligaments (7). During this period, there is a pseudo expansion in the joint space. In lumbar vertebral imaging, an increase in the intervertebral disc distance and vertebral scalloping can be observed (8). Changing joint structure with recurrent intra-articular trauma and further deterioration of the joint with an exaggerated repair reaction leading to subchondral cysts and osteophyte formations occurs and arthropathy due to biomechanical changes becomes irreversible (8,13). Acromegalic arthropathy includes the lumbar spine and also peripheral joints such as shoulder, knee, wrist, hip and fingers (8,9,14). Considering the age of our patient, the findings in lumbar MRI taken before the acromegaly diagnosis were characteristic changes for acromegaly and could be a stimulant for early diagnosis.

In the literature, there were no reports of spontaneous tendon rupture associated with acromegaly. However, it is known that some endocrinopathies such as diabetes mellitus and hyperparathyroidism, various rheumatic diseases such as lupus or gout, drug using such as quinolone or glucocorticoids, chronic renal failure and renal transplantation can cause spontaneous tendon rupture without significant mechanical bearing (15).

The non-traumatic spontaneous tendon rupture in our patient may be associated with acromegaly-related endocrine disorders and changes in joints, muscles and ligaments (10). In addition, it is known that somatostatin analogs reduce the nociceptive responses by affecting the central and peripheral nervous system (16). This may have weakened the muscle tendon due to chronic uncontrolled loading.

Acromegaly is a rare and insidious disease. However, joint complaints are frequently observed in acromegaly and show some characteristic features. For this reason, the knowledge of the musculoskeletal system findings of acromegaly by radiologists and physiatrists who are especially interested in the musculoskeletal system; will enable early diagnosis and treatment of this insidious disease, in which cardiac, respiratory, metabolic and psychosocial comorbidity is frequently observed.

Ethics

Informed Consent: Written informed consent was obtained from the patient prior to the drafting of the manuscript.
Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: N.Y., P.G.O., Concept: N.Y., P.G.O., Design: N.Y., P.G.O., Data Collection or Processing: N.Y., P.G.O., Analysis or Interpretation: N.Y., P.G.O., Literature Search: N.Y., P.G.O., Writing: N.Y., P.G.O.

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Case Report / Olgu Sunumu

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A Rare Case of Posterior Knee Pain: Synovial Osteochondramatosis

Nadir Bir Diz Arkası Ağrı Sebebi Olgusu: Sinovyal Osteokondromatozis

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Abstract

Synovial osteochondromatosis (SOC) is an uncommon benign condition characterized by the proliferation of the synovium with cartilaginous metaplasia. It can develop in any joint where synovium exists but is most prevalent in the knee. It generally occurs in the knee's anterior compartment, but it can also be seen in the posterior fossa. In this article, we report a 58-year-old woman with knee pain and swelling secondary to SOC. The detection of calcific nodules in both plain radiography and magnetic resonance imaging of the knee determined the diagnosis. SOC needs attention due to its high morbidity rates and possibility of malignant transformation.
Keywords: Osteochondromatosis, knee pain, synovium

Öz

Sinovyal osteokondromatozis (SOC) sinovyumun kıkırdaksı metaplazisi ile proliferasyonu ile karakterize benign nadir bir durumdur. SOC sinovyumun olduğu herhangi bir eklemde görülmesine rağmen en sık dizde görülür. Genellikle dizin ön kompartımanında görülse de posterior fossada da görülebilmektedir. Bu olguda, SOC nedeniyle dizde ağrı ve şişlik şikayetleri bulunan 58 yaşında kadın bir hasta sunulmuştur. Direkt radyografi ve manyetik rezonans görüntülemede kalsifik nodüllerin görülmesi tanıyı desteklemiştir. SOC yüksek morbidite oranı ve malign transformasyon ihtimali nedeniyle ayrıca dikkat edilmesi gereken bir durumdur.
Anahtar kelimeler: Osteokondromatozis, diz ağrısı, sinovyum

Introduction

Synovial chondromatosis is a rare idiopathic disease affecting the synovial joints, tendon sheaths and bursa (1). It has been estimated an incidence of one case for 100,000 people (2). It is characterized by multiple cartilage foci and metaplasia formation in the intima layer of the synovial membrane of the joint. Multiple and cartilaginous nodules are formed in the synovium because of that the nodules formed in the synovial membrane of the joint break off and become free (3). The term synovial osteochondromatosis is used in cases where the cartilage lesion is ossified. Although the etiology is unknown, it is thought that it may develop as a result of synovial irritation due to trauma or infection.

There are two forms of synovial osteochondromatosis. Primary synovial osteochondromatosis is almost always monoarticular and involves large joints, especially the knee. The diagnosis is determined generally between 3rd-5th decades of life and is more common in males. The more common secondary form is seen in older age and after pathologies such as trauma, osteoarthritis, osteochondritis dissecans or neuropathic arthropathy (4).

Although non-steroidal anti-inflammatory drugs reduce symptoms, surgery is often preferred for the treatment of synovial osteochondromatosis. Due to the relapse of the disease and malignant degeneration, complete resection of the involved synovium is necessary as well as removal of free intraarticular bodies (5).

In this case report, a patient diagnosed as synovial osteochondromatosis is presented.

Case Report

A 58-year-old female patient was referred to our outpatient clinic with complaints of pain and swelling in the posterior aspect of her left knee for six months. Her symptoms relieved when using non-steroidal anti-inflammatory drugs (asemetazine, diclofenac), however the symptoms repeated

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when she ceased the medications. There was no prior trauma or any known knee disease. Physical examination revealed a swelling in the posterior of the left knee. There was no range of motion limitation and redness in the knee joint. The patient reported a pain intensity of 8 on the 10-cm visual analogue scale. No abnormal finding was seen in blood tests. X-ray showed narrowing of the joint space, osteophytes and irregular calcified nodular opacities in the popliteal fossa (Figure 1). Hypointense nodular lesions were detected in the popliteal fossa in T2 sequences by magnetic resonance imaging (MRI) (Figure 2). The images were consistent with synovial osteochondroma of the knee joint. The patient was referred to the orthopedics clinic for surgery. Written consent was taken from patient.

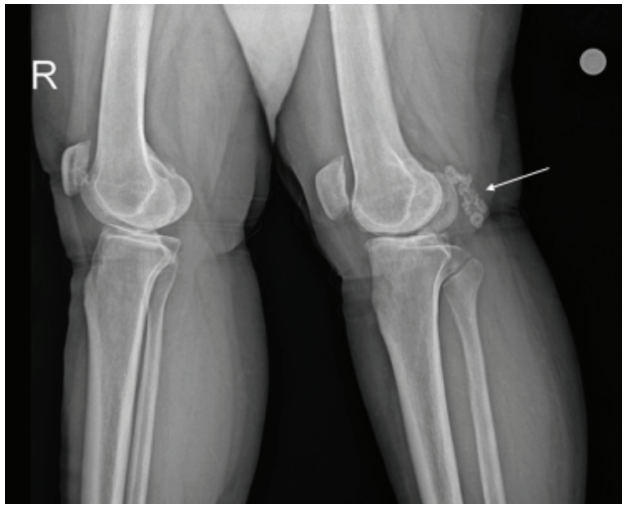

Figure 1. Lateral direck radiography of the left knee showed irregular calcified nodular opacities in the popliteal fossa

Figure 2. Knee magnetic resonance imaging with sagittal T2 sequences demonstrate hypointense nodular lesions in the popliteal fossa

Discussion

Although synovial osteochondromatosis can develop in any joint where synovium exists, it is most prevalent in the knee (5). It is reported to be detected in the elbow, ankle, hip and shoulder joints after the knee joint. It has rarely been shown to involve small joints (6). The disease generally occurs in the anterior compartment of the knee such as the suprapatellar pouch, infrapatellar fat pad and medial-lateral gutter (7,8). In the present case, it was seen that the disease appeared in the posterior fossa in the posterior compartment of the knee.

The disease process is insidious and the diagnosis can be made years later (9). Clinically, patients with synovial osteochondromatosis have progressively increased joint pain and swelling. Joint pain is associated with damage to the joint surface, which may lead to joint locking and instability over time (10,11). The patient in this case had joint pain and swelling that persisted for six months, increased over time, and responded positively to non-steroidal anti-inflammatory drugs, but there was no limitation of joint mobility and locking feel because of the posterior localization of the calcific nodules. The patient's advanced age, degenerative changes in the joints and no history of trauma or infection suggest the diagnosis of secondary synovial osteochondromatosis.

The pathogenesis of the disease involves a metaplastic error of synovial cells. Chondroid bodies usually appear at the ends of the synovial villi. The cells surrounding the bodies turn into chondroblasts. These cartilage clusters grow in the form of spherical bodies connected to the vilus with their pedicles: Later, these cartilage clusters can separate from the pedicles and fall into the joint and form loose bodies. These loose bodies feed on synovial fluid and continue to grow. With the emergence of osteoblasts, cellular metaplasia occurs and bone nidus may occur (7).

Diagnosis of synovial osteochondramatosis can be difficult especially in the early chondromatosis stage and calcified formations within the joint may be radiologically confused with degenerative osteoarthritis, osteochondritis dissecans, pigmented villonodular synovitis, neuropathic arthropathy and gout. Direct radiography is important for the diagnosis of calcific nodules, but in 5-30% of cases it cannot be diagnosed because the nodules are not calcified yet (12). MRI is the most useful test in the early diagnosis of the disease. MRI supports the diagnosis of non-calcified nodules as well as detecting changes in joint and bone structures adjacent to the lesion (12). It also distinguishes the disease from other diseases associated with synovial proliferation, such as synovial hemangioma, synovial sarcoma and pigmented villonodular synovitis. In this case, since the nodules were calcific, both plain radiography and MRI supported the diagnosis of synovial osteochondramtosis.

Surgery is the most commonly used method in the treatment of synovial osteochondromatosis. Recurrence and malignant degeneration may be seen, although not frequent. Therefore, no chondromatosis focus should be left in the joint during surgical

treatment. In this regard, cases that underwent synovectomy due to synovial osteochondromatosis and residual cartilage lesions that grow into chondrosarcoma have been reported (13). Therefore, the patient should be followed up at certain times after the operation for recurrence. Non-steroidal anti-inflammatory drugs and physical therapy agents have been used to reduce symptoms if patients do not accept the operation (14). The patient in this case stated that using non-steroidal anti-inflammatory drugs for a long time reduced his symptoms.

Synovial osteochondromatosis may cause complications such as osteoarthritis, nerve entrapment, tendon tear, malignant transformation and patellar subluxation when not treated (15-17). In the study of Biazzo and Confalonieri (18), it was found that 67.1% of synovial osteosarcomas originated from synovial osteochondromatosis and the mean tumor formation time was 11.2 years.

Synovial osteochondromatosis is a rare pathology involving the knee joint. The disorder should be kept in mind in the differential diagnosis of knee pain.

Ethics

Informed Consent: Written consent was taken from patient.
Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: B.A., Ö.K., Concept: B.A., S.K., Design: B.A., Ö.K., S.K., Data Collection or Processing: Ö.K., E.Y. Analysis or Interpretation: B.A., E.Y., Literature Search: B.A., Ö.K., S.K., Writing: B.A., E.Y.

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

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