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Yaka Mah. Yeni Meram Cad. Kasım Halife Sok. No: 11/1 (A Blok) No:
11 (B Blok),Posta Kodu: 42090 Meram / KONYA/TÜRKİYE
Telefon : 0332 221 05 00
E-posta : bilgi@erbakan.edu.tr

Editör asistanı ve sekreter/ Editor assistant and Secreteriat

İlkay Kurt
Tlf: +90 332 223 62 54
E-Mail: ilkayyildiz13@gmail.com

Yayıncı, Grafik ve Kapak tasarım/Publisher, Graphic and Cover design

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Tlf : +90 332 221 0 575, Mobil Tlf: 0 532 262 48 46
E-Mail: bilgi@neuyayin.com

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YAZARLARA BİLGİ/YAZIM KURALLARI

Selçuk Tıp Dergisi (Selcuk Med J), Necmettin Erbakan Üniversitesi'nin bilimsel, bağımsız, hakemli, açık erişimli yayın organıdır. Tıp doktorları, araştırmacılar ve bilim adamlarından oluşan geniş bir kitleye hitap eden disiplinli bir dergidir. Temel amaç Tıp/Sağlık alanında, tanı ve tedavideki güncel gelişmelerin, cerrahi yenilikler ve bilim dünyasına katkıda bulunacak çalışmaların ulusal ve uluslararası literatürde paylaşımının sağlanmasıdır.

Selçuk Tıp Dergisi, tıp bilimine ve akademik çalışmalara katkısı olan, klinik ve deneysel çalışmaları, editöryal yazıları, klinik olgu bildirimlerini, teknik ve eğitici derlemeleri, orijinal görüntü raporlarını ve editöre mektupları yayınlar. Anket/mülakat çalışmaları; Editörün ilk değerlendirmesi sonucunda çok değerli bir katkı sunuyorsa değerlendirmeye alınabilir.

Dergi gönderim kurallarına ve dergi kapsamına uygun görülen, editöryal çalışmalar hariç tüm yazılar alanında uzman hakemlere bilimsel değerlendirme için gönderilir. En az iki hakem kararı aranır. Yayımlanan tüm makaleler çift taraflı kör akran değerlendirmesi sürecine tabidir. Uygunluğunu tartışılan çalışmalarda yardımcı editörler hakemlerin yorumlarını dikkate alarak kendi değerlendirmelerini eklerler. Gönderilen tüm yazılar için nihai karar Baş Editör'e aittir. Bütün makaleler için süreçlerin editör ve yayın kurulu tarafından en geç altı hafta içerisinde sonuçlandırılması hedeflenir. Fakat elde olmayan gecikmelerden dolayı bu süre uzayabilir.

Yayın kurulu kararları ile belirlenen bazı konular hakkındaki yazılar, yayın kurulu üyelerinin tamamının incelemesine sunulur. İncelemeler sonucu oy çokluğuna ulaşan çalışmaların dergideki süreçleri devam edecektir. Yayın kurulu kararları dergi web sitesinde yayınlanmaktadır.

Yayına kabul edilen yazıların her türlü yayın hakkı yazarlara ve Selçuk Tıp Dergisine aittir. Selçuk Tıp Dergisi, ilave olarak websitesinde bulunan telif hakları bildirim belgesinin de yazarlar tarafından onaylanarak imzalanmasını ve ıslak imzalı formun sisteme eklenmesini talep etmektedir. Dergi her yıl Mart, Haziran, Eylül ve Aralık aylarında olmak üzere dört sayı olarak yayımlanmaktadır. Derginin yayın dili İngilizcedir.

Gönderilen yazıların daha önce herhangi bir yerde/dergide yayınlanmamış olması ve yayın için başka bir dergiye gönderilmemiş olması gerekmektedir [Bilimsel kongrelerde sunulan tam metin halinde basılmamış sözlü bildiri ve posterler bildirilmek kaydı ile hariçtir]. Dergide yayımlanan yazıların her türlü sorumluluğu (etik, bilimsel, yasal vb.) yazarlara aittir. Dergide yayımlanan yazılarda ifade edilen ifadeler veya görüşler yazarların görüşleri olup, editörlerin, yayın kurulu ve yayıncının görüşlerini yansıtmaz; editörler, yayın kurulu ve yayıncı, bu tür materyaller için herhangi bir sorumluluk veya yükümlülük kabul etmemektedir. Yazım kurallarına uygun olarak hazırlanmamış olan yazıların incelenmeye alınıp alınmaması Editör ve Editöryal Kurulun insiyatifindedir.

Tüm çalışmalarda etik kurul onayı ve bu onamın belgelendirilmesi gerekmektedir. Tüm çalışmalarda yazarların çalışmaya katkı düzeyi ve onayı bildirilmelidir. Çalışmada veri toplanması, deney aşaması, yazım ve dil düzenlemesi dahil olmak üzere herhangi bir aşamasında finansal çıkar çatışması olmadığı bildirilmelidir. Çalışmada varsa ticari sponsorluk bildirilmelidir. Selçuk Tıp Dergisi'nde intihal programı (iThendicate) kullanılmaktadır. Akademik atıf sınırını aşan benzerlik taşıyan makaleler ve yayın kurallarına uygun olarak hazırlanmamış makaleler değerlendirmeye alınmayacaktır. Dergi intihal tarama raporunu yazardan talep edeceği gibi kendisi de tarama yapabilir.

Derginin yayın politikası ve süreçleri Uluslararası Medikal Dergisi Editörleri Komitesi (International Committee of Medical Journal Editors-ICMJE), Dünya Tıbbi Editörler Derneği (World Association of Medical Editors-WAME), Bilim Editörleri Konseyi (Council of Science Editors-CSE), Avrupa Birliği Derneği Bilim Editörleri (European Association of Science Editors-EASE) ve Yayın Etiği Komitesi (Committee on Publication Ethics-COPE) ve Ulusal Bilgi Standartları Örgütü (National Information Standards Organization-NISO) yönergelerini takip eder. Dergimiz 'Şeffaflık ve Akademik Yayıncılık En İyi Uygulamalar İlkelerine' (Principles of Transparency and Best Practice in Scholarly Publishing) (doaj.org/bestpractice) uygundur. Yayın Kurulu, dergimize gönderilen çalışmalar hakkındaki intihal, atıf manipülasyonu ve veri sahteciliği iddia ve şüpheleri karşısında COPE kurallarına uygun olarak hareket edecektir.

Derginin Yayın Kurulu, itiraz ve şikâyet vakalarını, COPE rehberleri kapsamında işleme almaktadır. Yazarlar, itiraz ve şikayetleri için doğrudan baş editör veya editör/yayın kurulu ile temasa geçebilirler. İhtiyaç duyulduğunda Yayın Kurulu'nun kendi içinde çözemediği konular için tarafsız bir temsilci atanacaktır. İtiraz ve şikayetler için karar verme süreçlerinde nihai kararı Baş Editör verecektir. Yayıncı ve editör gerektiğinde düzeltmeler, açıklamalar, geri çekilmeler ve özürler yayınlamaya her zaman hazırdır.

Selçuk Tıp Dergisi ile ilgili tüm yazışmalar, makale gönderme, makalenin takibi, danışman raporları, düzeltmelerin yapılıp yüklenmesi, kabul yazısı gönderimi ve diğer tüm makale ile ilgili formların yüklenmesi https://www. selcukmedj.org sayfasından yapılacaktır. Bu site üzerinden yüklenecek makaleler için kurallar aşağıda belirtilmiştir.

Selçuk Tıp Dergisi, ücretsiz, açık erişim politikası benimsemektedir. Bu bağlamda dergide yayınlanan tüm yazılar https://www. selcukmedj.org adresinden erişime açık olup yazarlardan hiçbir ek ücret talep edilmeyecektir.

Yazarlık

Selçuk Tıp Dergisi'ne gönderilen çalışmalarda yazar olarak listelenen herkesin ICMJE (www.icmje.org) tarafından önerilen yazarlık koşullarını karşılaması gerekmektedir. ICMJE, yazarların aşağıdaki 4 koşulu karşılamasını önermektedir:

- Çalışmanın konseptine/tasarımına; ya da çalışma için verilerin toplanmasına, analiz edilmesine ve yorumlanmasına önemli katkı sağlamış olmak;
- Yazı taslağını hazırlamış ya da önemli fikirsel içeriğin eleştirel incelemelerini yapmış olmak;
- Yazının yayından önceki son halini gözden geçirmiş ve onaylamış olmak;
- Çalışmanın herhangi bir bölümünün geçerliliği ve doğruluğuna ilişkin soruların uygun şekilde soruşturulduğunun ve çözümlendiğinin garantisini vermek amacıyla çalışmanın her yönünden sorumlu olmayı kabul etmek.

Yazar olarak belirtilen her kişi yazarlığın dört koşulunu karşılamalıdır ve bu dört koşulu karşılayan her kişi yazar olarak tanımlanmalıdır. Yazar olarak atanan tüm kişiler yazarlık için hak kazanmalı ve hak kazanan herkes listelenmelidir. Dört kriterin hepsini karşılamayan kişilere makalenin başlık sayfasında teşekkür edilmelidir. Finansman alımı, veri toplanması ya da araştırma grubunun genel gözetimi, kendi başlarına, yazarlığı haklı çıkarmaz. Bir ya da daha fazla yazar, çalışma başlangıcından yayınlanmış makaleye kadar, bütün olarak çalışmanın bütünlüğünün sorumluluğunu üstlenmelidir. Çok merkezli çalışmalarda yazarlık bir gruba atfedilir. Yazar olarak adlandırılan grubun tüm üyeleri, yukarıdaki yazarlık kriterlerini tam olarak karşılamalıdır. Bu kriterleri karşılamayan grup üyeleri, onayları ile birlikte listelenmelidir. Mali ve maddi destek de kabul edilmelidir.

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Yazar Değişikliği Talepleri
Yazar listesindeki yazar isimlerinin eklenmesi, silinmesi veya yeniden düzenlenmesi ancak makale kabul edilmeden önce ve ancak dergi Editörü tarafından onaylandığı takdirde yapılabilir.
Böyle bir değişikliği talebi olursa Editör, sorumlu yazardan (a) yazar listesindeki değişikliğin nedeni ve (b) tüm yazarlardan eklemeyi kabul ettiklerine dair yazılı onay (e-posta), talep eder. Editör, yalnızca istisnai durumlarda, makale kabul edildikten sonra yazarların eklenmesini, silinmesini veya yeniden düzenlenmesini dikkate alacaktır.

Makale Yazımı
Orijinal araştırma makalesi kaleme alanlar, konuyu özgün bir şekilde ve nesnel bir tartışma ile ele almalıdır. Makale, başkalarının çalışmayı tekrarlamasına izin vermek için yeterli ayrıntı ve referansları içermelidir. Hileli veya bilerek yanlış beyanlar etik dışı davranış teşkil eder ve kabul edilemez.

Özgünlük
Yazar makalenin orijinal olduğu, daha önce başka bir yerde yayınlanmadığı ve başka bir yerde, başka bir dilde yayınlanmak üzere değerlendirmede olmadığı konusunda teminat sağlamalıdır. Makale yazımının yapay zekâ sistemleri kullanılarak yapıldığı çalışmalar kabul edilmemektedir. Yapay zekâ sistemleri, sadece yazıların dil düzenlemeleri için kullanılabilir.

Orijinal Kaynak Kullanımı ve Atıf Yapma
Yazarlar, tamamen özgün eserler yazdıklarından ve başkalarının eserlerini veya sözlerini kullanmışlarsa, bunun uygun şekilde alıntılandığından emin olmalıdır. Üçüncü taraflarla konuşma, yazışma veya tartışmalarda olduğu gibi özel olarak elde edilen bilgiler, kaynağın açık ve yazılı izni olmadan kullanılmamalıdır.

Veri Erişimi ve Muhafazası
Yazarlardan, editör incelemesi için makalelerini destekleyen araştırma verilerini sağlamaları ve/veya derginin açık veri gereksinimlerine uymaları istenebilir. Yazarlar, mümkünse, bu tür verilere kamu erişimi sağlamaya ve bu tür verileri yayınlandıktan sonra makul bir süre boyunca saklamaya hazır olmalıdır. Dergimiz, araştırma verilerinin TUBITAK'ın Aperta Portalı'na yüklenmesini tavsiye etmektedir.

Çoklu ve Eşzamanlı Yayın
Bir yazar aynı araştırmayı içeren makalesini birden fazla dergisinde yayımlamamalıdır. Aynı makalenin aynı anda birden fazla dergiye gönderilmesi etik dışı davranıştır. Bir yazar, özet şeklinde yayınlanmış olması dışında, daha önce yayınlanmış bir makaleyi başka bir dergide değerlendirilmek üzere sunmamalıdır.

Anket ve Mülakata Dayanan Çalışmaların Yayını ve Etik Kurul Onamları
Etik kurul izni gerektiren, tüm bilim dallarında yapılan araştırmalar için (etik kurul onayı alınmış olmalı, bu onay makalede belirtilmeli ve belgelendirilmelidir. Etik kurul izni gerektiren araştırmalarda, izinle ilgili bilgilere (kurul adı, tarih ve sayı no) yöntem bölümünde, ayrıca makalenin ilk/son sayfalarından birinde; olgu sunumlarında, bilgilendirilmiş gönüllü olur/onam formunun imzalatıldığına dair bilgiye makalede yer verilmelidir. Anket çalışmaları ve mülakata dayanan çalışmaların etik kurul onam belgeleri alınmış olmalı ve makale yüklenirken dergi sistemine eklenmelidir.

Çıkar Çatışması
Kişinin yaptığı işte çelişkiye düşmesine yol açacak, objektifliğini önemli oranda bozabilecek veya herhangi bir kişi ya da kuruluş lehine adil olmayan avantaj sağlayabilecek herhangi finansal ya da diğer tür çıkarlardır. Araştırmanın yürütülmesi ve makalenin hazırlanması sürecinde alınan tüm mali destek kaynakları ve sponsorların çalışmadaki rolü açıklanmalıdır. Finansman kaynağı yoksa bu da belirtilmelidir. Açıklanması gereken olası çıkar çatışması örnekleri arasında danışmanlıklar, maaş alımı, hibeler yer alır. Potansiyel çıkar çatışmaları mümkün olan en erken aşamada açıklanmalıdır.

Hata Bildirimi
Bir yazar yayınlanmış çalışmasında önemli bir hata veya yanlışlık fark ettiğinde, derhal dergiye bildirimde bulunmalıdır. Editör tarafından gerekli görüldüğü takdirde makaleyi geri çekmek veya düzeltmek için iş birliği yapmak da yazarın yükümlülüğüdür. Editör veya yayıncı, yayınlanan bir çalışmanın hata içerdiğini üçüncü bir şahıstan öğrenirse, yazarın konu hakkında editöre bilgi vermek de dahil olmak üzere editörle iş birliği yapması yazarın yükümlülüğüdür.

Görüntü Bütünlüğü
Bir görüntüde belirli bir özelliği geliştirmek, karartmak, taşımak, kaldırmak veya eklemek kabul edilemez. Yazarlar, dergi tarafından uygulanan grafik görseller için belirlenen politikaya uymalıdır.

Düzeltme ve Yayından Geri Çekme Talepleri
Selçuk Tıp Dergisi tarafından yayımlanan makaleler nihai versiyondur. Bu nedenle yayımlandıktan sonra düzeltme talepleri, Yayın Kurulu tarafından **COPE** yönergelerine göre değerlendirilir. Yayından geri çekme talepleri, makale kabulünden önce yapılmalıdır ve Editör Kurulu onayına tabidir. Makale kabulü sonrasında henüz yayınlanmadan önce bir geri çekme talebi olursa, gerekçesi ile birlikte baş editöre mail yolu ile ulaştırılmalıdır. Gerekçeler editör kurulu toplantısında değerlendirilerek nihai karar verilecek ve yazara mail yolu ile bildirilecektir. **Yayın aşamasına alınmış bir makalenin geri çekme talep başvuruları dikkate alınmayacaktır.** Yayımlanmadan önce çalışmasını geri çekme talebinde bulunmak isteyen yazar (lar), Geri çekme formunu doldurarak her bir yazarın ıslak imzası ile imzalanmış ve taratılmış halini editor@selcukmedj.org.tr adresi üzerinden e-posta aracılığıyla Baş Editör ve Editör kuruluna iletmekle yükümlüdür. Geri çekme formuna web sitemizin indirmeler sayfasından ulaşabilirsiniz(https://www.selcukmedj.org/tr-tr/indirmeler/). Editör Kurulu geri çekme bildirimini inceleyerek en geç 15 gün içerisinde dönüş sağlar.
Yazar isimleri, bağlantıları, makale başlıkları, özetler, anahtar kelimeler, herhangi bir bilgi yanlışı ve dijital nesne anımlayıcılardaki [digital object identifier (DOI)] yazım hataları, bir "erratum" ile düzeltilebilir.

Makale Değerlendirme Süreci
Dergiye gönderilen makalelerin hızlı bir şekilde değerlendirilmesi ve yayınlanması hedeflenmiştir. Tüm makaleler çift kör hakem değerlendirme sürecine tabidir. Makaleler, içerik, özgünlük, alandaki önem, istatistiksel analizin uygunluğu ve sonuçların çıkarılması için alanında uzman hakemler tarafından gözden geçirilecektir. En az iki hakem kararı aranacaktır. Hakemler arasında tutarsızlıklar olması durumunda, makale üçüncü ya da dördüncü bir hakeme gönderilebilecektir. Hakem kararları yardımcı editörler tarafından değerlendirilerek değerlendirme sonuçları baş editöre gönderilecektir. Gönderilen makalelerin kabulüne ilişkin nihai karar, baş editöre aittir.

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Hakemler tarafından bildirilen ve yazarlar için faydalı oldukları değerlendirilen yorum ve değerlendirmeler yazarlara gönderilir. Hakemler tarafından yapılan talimat, itiraz ve talepler kesinlikle yerine getirilmelidir. Hakem(ler)e cevap dosyası ayrıca bir Word belgesi halinde oluşturulmalıdır. Yazının gözden geçirilmiş şekliyle yazarlar, bu dosyada, hakemlerin taleplerine uygun olarak atılan her adımı açık ve net bir şekilde belirtmelidir. Yazar açıklama notları, hakemlerin değerlendirme sırasına göre numaralandırılmış olarak listelenmelidir. Ayrıca makale içerisinde de gerekli değişiklikleri yapmalı ve bunları makale içerisinde belirterek (boyayarak), revize edilmiş makale ve hakem önerilerine verilmiş yanıtları içeren formlar https://www. selcukmedj.org adresinden titizlikle yüklenmelidir.

Yazıların Gönderilmesi

Yazarlar Yayın Hakları Bildirim Formunu sisteme yüklemelidir. Tüm yazışmalar sorumlu yazara gönderilecektir. İlgili sorumlu yazarın, tüm diğer yazışmalar için bir e-posta adresi bildirilmelidir. Yazarlar makalelerininin alındığından kendisine verilen numara ile haberdar edilirler. Bildirilen makale numarası yapılan tüm yazışmalarda kullanılmalıdır. Yazarlara beyan edilir ki; editör ofisinin ilk değerlendirmesi sonucu okuyucunun menfaatine dönük olarak makalelerin içeriği dolayısıyla makalesi geri iade edilebilir. Bu hızlı reddetme süreci, yazarın başka bir yerde makalesini yayınlanmasına olanak sağlar.
Selçuk Tıp Dergisi'ne makale gönderilmesi, tüm yazarların, derginin yayın politikalarını ve yayın etiğini okuduğu ve kabul ettiği anlamına gelir. Makale gönderimi ve ilgili diğer tüm işlemler https://www. selcukmedj.org adresinden online olarak yapılacaktır.

Yazıların Hazırlanması

Yazarların, materyallerini göndermeden önce aşağıdaki kuralları okumaları ve makalelerini bu kurallara uygun halde sisteme yüklemeleri gerekmektedir:

Genel yazı biçimi: Tüm makaleler, her tarafta 2,5 cm genişliğinde kenar boşlukları bulunan standart A4 boyutunda bir word dosyası kullanılarak yazılmalı, kaynaklar, resim şekil ya da tablolar metinde geçiş sırasına göre numaralandırılmalıdır. Metin, sol hizalı ve heceli satır sonları olmayan 12 puntolu bir fontta çift boşluk kullanılarak ve Times New Roman karakterinde yazılmalıdır. Kelimeler arasında ve cümle noktası sonrasında tek boşluk bırakmaya özen gösterilmelidir. Paragraf için sol girintiyi sekme tuşu ile bir kez tıklayarak ayarlanmalıdır. Ölçüm birimleri için Uluslararası Birimler Sistemi (SI) kullanılmalıdır. Makalenin tüm sayfaları sayfa sonunda numaralandırılmalıdır. Tüm yazılar yazım kurallarına uymalı, noktalama işaretlerine uygun olmalıdır.

Tüm makalelerde; Kapak sayfası, Ön yazı (cover letter), makale dosyası, Etik kurul onay Belgesi (kurumdan alınan), intihal analiz raporu, Şekiller ve Resimler, Telif Hakları Devir Formu, ve gerekli ise hasta onam formu ayrı dosyalar olarak yüklenmelidir.
Kaynaklar makale dosyasında, makale biter bitmez değil ayrı bir sayfada başlamalıdır. Tablolar, tablo açıklamaları, resim/şekiller ve resim/şekil açıklamaları ayrıca makale ana dosyasına kaynakların ardından ayrı bir sayfada eklenmelidir. Tablo/Resim/şekil açıklamaları; Tablo/Resim/şekillerin hemen altlarında olmalıdır.

Makale bölümleri hakkında

1-Kapak Sayfası: Makalenin İngilizce tam başlığı ve 50'den fazla karakter içermeyen kısa bir başlık, tüm yazarların açık şekilde adları ve soyadları, ORCID numaraları, kurumları, sorumlu yazar ismi iş veya cep telefonu, e-posta ve yazışma adresi belirtilmelidir.Makale daha önce tebliğ olarak sunulmuş ise tebliğ yeri ve tarihi belirtilmelidir. Yazarlar ve kurumları hakkındaki bilgiler başlık sayfası haricinde ana metinde (materyal metot bölümü dahil), tablolarda, şekillerde ve video dokümanlarında yer almamalıdır. Herhangi bir hibe ya da diğer destek kaynaklarının detayları, makalenin hazırlanmasına katkıda bulunan ancak yazarlık kriterlerini karşılamayan bireylere teşekkür bölümü de kapak sayfasına eklenmelidir.

2-Ana makale dosyası; Ana makale dosyası, yazar isimleri ve kurumları gibi bilgiler içermemelidir. Ana makale dosyası:
1. Başlık, 2. Özet ve Anahtar Kelimeler, 3. Makale ana metni, 4. Kaynaklar, 5. Tablolar ve açıklamaları, 6. Resim ve Şekil açıklamaları ile birlikte resim ve şekiller, 7. Alt yazılar şeklinde dizilmelidir.
Başlık: Makale Word dosyasında en baş kısımda makalenin yazım dilinde tek uzun başlığı yer almalıdır.
Özet: Editöre Mektup haricinde tüm yazılar özet içermelidir. Orijinal araştırma makalelerinin özetleri Amaç, Gereçler ve Yöntem, Bulgular ve Sonuç alt başlıklarını içermelidir. Özetler; kaynak, şekil veya tablo numarası içermemelidir. Sözcük sayısı ve özellikler için Tablo 1'deki veriler dikkate alınmalıdır.
Anahtar sözcükler: Özelerin sonunda en az üç ile en fazla beş anahtar sözcük bildirilmelidir. Anahtar sözcükler kısaltmalar olmaksızın tam olarak listelenmeli birbirinden virgül ya da noktalı virgül kullanılarak ayrılmalıdır. Anahtar kelimeler, "Tıbbi Konu Başlıklarına **(MESH)"** uygun olmalıdır (Bakınız: www.nlm.nih.gov/mesh/MBrowser.html).
Kısaltmalar: Özetlerde ve başlıklarda kısaltmalar kullanılmamalıdır. Makalede kullanılacak kısaltmalar, mümkünse ulusal veya uluslararası kabul görmüş olmalı, ilk kullanıldığında metin içinde tanımlanmalı ve parantez içinde yazılmalıdır. Daha sonra metin boyunca o kısaltma kullanılmalıdır. Yaygın olarak kabul edilen kısaltmalar ve kullanım için lütfen "Bilimsel Stil ve Biçim"e bakınız. (https://www.scientificstyleandformat.org/Home.html). Ana metinde Bir ticari markalı ilaç, ürün, donanım veya yazılım programı ana metinde yer aldığında, ürün bilgisi, ürünün adını, ürünün imalatçısını ve şirket ile şirket merkezinin bulunduğu ülkeyi aşağıdaki biçimde parantez içinde verilmelidir: "Discovery St PET / CT tarayıcı (General Electric, Milwaukee, WI, ABD).
Makale ana metni:
Giriş: Konuyu ve çalışmanın amacını açıklayacak spesifik bilgilere yer verilir.
Gereç ve Yöntemler: Çalışmanın gerçekleştirildiği yer, zaman ve çalışmanın planlanması ile kullanılan elemanlar ve yöntemler bildirilmelidir. Verilerin derlenmesi, hasta ve bireylerin özellikleri, deneysel çalışmanın özellikleri ve istatistiksel metotlar detaylı olarak açıklanmalıdır. Çalışmaya alınanlar ve çalışmayı yürütmek için kullanılan tüm yöntemler ayrıntılı olarak açıklanmalıdır. Kullanılan yeni veya modifiye yöntemler ayrıntılı olarak açıklanmalı kaynak belirtilmelidir. İlaçların ve kimyasal ajanların dozları, konsantrasyonları, verilme yolları ve süresi belirtilmelidir. Elde edilen verileri özetlemek ve önerilen hipotezi test etmek için kullanılan tüm istatistiksel yöntemlerin kısa bir raporu, istatistiksel olarak anlamlı farklılık için belirlenen p değeri ölçütleri de dahil olmak üzere bir alt başlık altında sunulmalıdır. Yapılan istatistiksel değerlendirme ayrıntılı olarak açıklanmalıdır. Olabildiğince standart istatistiksel yöntemler kullanılmalıdır. Nadiren kullanılmış veya yeni istatistiksel yöntemler kullanılmışsa konuya ilişkin ilgili referanslar belirtilmelidir. Gerekirse, olağandışı, karmaşık veya yeni istatistiksel yöntemlerle ilgili daha ayrıntılı açıklamalar, çevrimiçi ek veri olarak okuyucular için ayrı dosyalarda verilmelidir.
Bulgular: Elde edilen veriler istatistiksel sonuçları ile beraber ayrıntılı olarak verilmelidir. Bulgular şekiller ve tablolar ile desteklenmelidir. Rakam ve tablolarda verilen bilgilerin gerekli olmadıkça metinde tekrarlanmamasına özen gösterilmelidir.
Tartışma: Çalışmanın sonuçları literatür verileri ile karşılaştırılarak değerlendirilmeli, yerel ve/veya uluslararası kaynaklarla desteklenmelidir. Yazıyla alakasız veya gereksiz genel bilgiler eklenmemeli, yazının amacına uygun yeterli uzunlukta olmalıdır.
Kaynaklar: Kaynaklar ayrı bir sayfaya yazılmalıdır. Kaynaklar APA 7 sistemine uygun olarak belirtilmelidir. Buna göre, kaynak numaraları cümle sonuna nokta konmadan () içinde verilmeli, nokta daha sonra konulmalıdır. Kaynak yazar isimleri cümle içinde kullanılıyorsa ismin geçtiği ilk yerden sonra () içinde kaynak verilmelidir. Birden fazla kaynak numarası veriliyorsa arasına ",", ikiden daha fazla ardışık kaynak numarası veriliyor ise rakamları arasına "-" konmalıdır [ör. (1,2), (1-4) gibi. Yazar sayısı 3 ve daha azsa tüm yazarların ismi olmalı, 3'dan daha fazla ise ilk3 yazar yazılıp diğerleri için et al. kullanılmalıdır. Kaynaklar metindeki kullanılış sırasına göre numaralandırılıp listelenmelidir. Atıf doğruluğu, yazarın sorumluluğundadır. Kaynaklar orijinal yazım, aksan, noktalama vb. ile tam olarak uyumlu olmalıdır. Metin içindeki tüm kaynaklar belirtilmelidir. Kaynak listesinde mükerrer yazım yapılmamalıdır. Farklı yayın türleri için kaynak stilleri aşağıdaki örneklerde sunulmuştur:

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Araştırma Makalesi:

- Mirza E, Oltulu R, Oltulu P, et al. Dry eye disease and ocular surface characteristics in patients with keratoconus. Saudi J Ophthalmol. 2022;36(1):117-21. doi: 10.4103/sjopt.sjopt_37_21.
- Vikse BE, Aasarød K, Bostad L, et al. Clinical prognostic factors in biopsy-proven benign nephrosclerosis. Nephrol Dial Transplant. 2003;18(3):517-23. doi: 10.1093/ndt/18.3.517.

Tek Yazarlı Kitaplar:

- Danovitch GM. Handbook of Kidney Transplantation. Boston: Little, Brown and Company (Inc.), 1996: 323-8.

Kitap Bölümü:

- Soysal Z, Albek E, Eke M. Fetüs hakları. Soysal Z, Çakalır C, ed. Adli Tıp, Cilt III,İstanbul Üniversitesi Cerrahpaşa Tıp Fakültesi Yayınları, İstanbul, 1999:1635-50.
- Davison AM, Cameron JS, Grünfeld JP, et al. Mesengiocapillary glomerulonephritis In: Williams G, ed. Oxford Textbook of Clinical Nephrology.New York:Oxford University Press, 1998: 591- 613.

Baskıdan önce çevrim içi olarak yayımlanan dergi makalesi:

- Doğan GM, Sığırcı A, Akyay A, et al. A Rare Malignancy in an Adolescent: Desmoplastic Small Round Cell Tumor. Turkiye Klinikleri J Case Rep. 10.5336/caserep.2020-77722. Published online: 31 December 2020.
- Cai L, Yeh BM, Westphalen AC, et al. Adult living donor liver imaging.DiagnIntervRadiol. 2016 Feb 24.doi: 10.5152/dir.2016.15323. [Epub ahead of print].

Toplantı Raporları:

- Bengisson S. Sothemin BG. Enforcement of data protection, privacy and security in medical informatics. In: Lun KC, Degoulet P, Piemme TE, Rienhoff O, editors. MEDINFO 92. Proceedings of the 7th World Congress on Medical Informatics; 1992 Sept 6-10; Geneva, Switzerland. Amsterdam: North-Holland; 1992. pp.1561-5.

Bilimsel veya Teknik Rapor:

- Cusick M, Chew EY, Hoogwerf B, et al. Early Treatment Diabetic Retinopathy Study Research Group. Risk factors for renal replacement therapy in the Early Treatment Diabetic Retinopathy Study (ETDRS), Early Treatment Diabetic Retinopathy Study Kidney Int: 2004. Report No: 26.

Tez:

- Kaplan SI. Post-hospital home health care: elderly access and utilization (dissertation). St Louis (MO): Washington Univ; 1995.

Web sayfası ve Sosyal Medya araçları: Yazar. Başlık. Erişim linki: URL. Erişim tarihi ve yılı

3-Tablolar ve açıklamaları: Tablolar, ana makale metnine dahil edilmelidir, kaynak listesinden sonra sunulmalı ve ayrı bir sayfada olmalıdır. Ana metinde yer alan sıraya göre numaralandırılmalıdır. Her bir tablonun üzerine açıklayıcı bir başlık konulmalıdır. Tabloda kullanılan kısaltmalar, tablonun altında dipnotlarla tanımlanmalıdır (ana metin içerisinde tanımlanmış olsa bile). Tablolar kolay okunması için açık bir şekilde düzenlenmelidir. Tablolarda sunulan veriler, ana metinde sunulan verilerin tekrarı olmamalı, ancak ana metni desteklemelidir.

4-**Şekil ve Resimler:** Şekil, grafik ve resimler makale gönderim sistemi aracılığıyla ayrı dosyalar (TIFF veya JPEG formatında) halinde yüklenmeli ilaveten ana makale dosyasında ayrı bir sayfada tablolardan sonra ana metin içinde de gösterilmelidir. Sisteme ayrı olarak yüklenmeyen sadece makale içerisinde geçen resimler kabul edilmeyecektir. Şekil ve resimler mutlaka isimlendirilmeli ve numaralandırılmalı, metin içinde sıralamaya dikkat edilerek belirtilmelidir. Ana metine eklenecek resim, şekil ve grafik altına açıklamaları da eklenmelidir. Resimler minimum 300 dots per inch (dpi) çözünürlüğünde ve net olmalıdır. Şekil ve resim altlarında kısaltmalar kullanılmış ise, kısaltmaların açılımı alfabetik sıraya göre alt yazının altında belirtilmelidir. Mikroskobik resimlerde büyütme oranı ve tekniği açıklanmalıdır. Yayın kurulu, yazının özünü değiştirmeden gerekli gördüğü değişiklikleri yapabilir. Şekil alt birimleri olduğunda, alt birimler tek bir görüntü oluşturmak için birleştirilebilir. Şekiller, alt birimleri göstermek için işaretlenmeli ve her birinin açıklamaları (a, b, c, vb.) yazılmalıdır. Şekilleri desteklemek için kalın ve ince oklar, ok uçları, yıldızlar, yıldız işaretleri ve benzer işaretler kullanılabilir. Makale içeriği gibi şekiller de kör olmalıdır. Bir birey ya da kurumu tanımlayabilecek resimlerdeki olası bilgiler anonimleştirilmelidir. Hasta fotoğrafı paylaşımlarında kimliğin birebir tanınmamasına özen göstermeli, hastalığı belirlemeye yetecek yeterlilikte görüntü paylaşılmalıdır. Hastanın kimliğini açık eden resim paylaşımları için, hastanın resminin paylaşımına izin verdiği onam formu şarttır.

Tablo 1. Makale türlerine göre sınırlamalar

Makale türü	Sözcük sınırı	Özet sınırı	Kaynak sınırı	Tablo sınırı	Şekil sınırı
Araştırma makalesi	4000	300	50	6	6
Derleme	6000	300	85	6	10
Olgu sunumu	1500	200	15	3	5
Editöre mektup	1000	Özet yok	8	Tablo içermez	Şekil içermez
Editöryal	1000	Özet yok	20	3	3
Orijinal görüntü raporu	200	Özet yok	5	1	3

Makale Türleri

Selçuk Tıp Dergisi'nde aşağıda kısaca açıklanan makale türleri yayınlamaktadır:

Araştırma Makaleleri: Orijinal araştırmalara dayanan yeni sonuçlar sağlayan en önemli makale türüdür. Orijinal makalelerin ana metni Giriş, Yöntemler, Bulgular, Tartışma, Sonuç ve Kaynaklar alt başlıklarıyla yapılandırılmalıdır. Sözcük sayısı ve özellikler için lütfen Tablo 1'e bakınız. İstatistiksel analiz genellikle sonuçları desteklemek için gereklidir. İstatistiksel analizler uluslararası istatistik raporlama standartlarına uygun olarak yapılmalıdır (Altman DG, Gore SM, Gardner MJ, Pocock SJ. Statistical guidelines for contributors to medical journals. Br Med J 1983:7;1489–93). İstatistiksel analizler hakkında bilgi Materyaller ve Yöntemler bölümünde ayrı bir alt başlık ile sağlanmalı ve süreç boyunca kullanılan istatistiksel yazılım belirtilmelidir. Birimler Uluslararası Birimler Sistemine (SI) uygun olarak hazırlanmalıdır.
Makalenin kısıtlılıkları, sakıncalar ve eksik yönler, sonuç paragrafından önce Tartışma bölümünde belirtilmelidir.

Derleme Makaleleri: Yeterli sayıda bilimsel makaleyi tarayıp, konuyu bugünkü bilgi ve teknoloji düzeyinde özetleyen, değerlendirme yapan ve bulguları karşılaştırarak yorumlayan yazılar olmalıdır. Temel ve uygulamalı bilim alanlarında tüm gelişmeleri ile birlikte son bilimsel çalışmalardaki teknik ve uygulamalar değerlendirilir. Belirli bir alan hakkında kapsamlı bilgi sahibi olan ve bilimsel geçmişi yüksek atıf potansiyeli olan yazarlar tarafından hazırlanan derlemeler dergimiz tarafından kabul edilecektir. Bu yazarlardan makale kabul şekli davet yöntemiyle de olabilir. Ana metin Giriş, Klinik ve Araştırma Sonuçları ve Sonuç bölümlerini içermelidir. Sözcük sayısı ve özellikler için lütfen Tablo 1'e bakınız.

Olgu Sunumları: Tanı ve tedavide zorluk teşkil eden, yeni tedaviler sunan veya literatürde yer almayan bilgileri ortaya koyan nadir olgu veya durumlar hakkında eğitici olgu sunumları dergimizde yayınlanmak için kabul edilir. Olgu sunumu, Giriş, Olgu Sunumu ve Tartışma ve Sonuç alt başlıklarını içermelidir.

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İlginç ve sıra dışı resimler değerlendirme sürecinde bir avantajdır. Hasta tanımlayıcı resimlerde hasta kimliği açık ediliyorsa resmin paylaşımına izin veren hasta onamı mutlaka olmalıdır. Sözcük sayısı ve özellikler için lütfen Tablo 1'e bakınız.

Editöre Mektuplar: Bu yazı türü, daha önce yayınlanmış bir makalenin önemli kısımlarını, gözden kaçan yönlerini veya eksik kısımlarını tartışır. Derginin dikkatini çekebilecek konular başta olmak üzere, okuyucuların dikkatini çekebilecek konular hakkında makaleler, özellikle eğitici konularda Editöre Mektup şeklinde sunulabilir. Okuyucular, yayınlanmış yazılar hakkındaki yorumlarını Editöre Mektup olarak da sunabilirler. Özet, Anahtar Sözcükler ve Tablolar, Şekiller, Görüntüler ve diğer medya eklenmemelidir. Metin alt başlıkları içermemelidir. Sözcük sayısı ve özellikler için lütfen Tablo 1'e bakınız.

Editöryal: Tıbbın herhangi bir alanında bir görüşün açıklandığı ya da başkalarının görüşlerinin yayınlandığı, kısa makalelerdir. Normal bir dergi makalesine göre daha yaratıcı yazabilme olanağı sağlar. Dergide yakın zamanda yayınlanmış bir makale tartışılabilir, Tarihi materyal, Halk sağlığına dair konular, Sağlık politikaları, Tıp Eğitimi ve Tıpta teknolojik gelişmeler hakkındaki yazılar bu bölümde değerlendirilebilir. Tam bir derleme olamayacak bir konuda kısa derleme bu başlık altında değerlendirilebilir. Dergi editörü; okuyuculara kişisel mesaj iletmek, aynı sayıdaki bir makale ile ilgili yorum yapmak, okuyucunun dikkatini yeni gelişmelere çekmek isterse bu bölüme yazabilir. Bilimsel makalelerin tipik yazım bölümlerini içermez. Temel mesaj bir cümlede özetlenebilmelidir. Bu cümleyi editoryali yazmaya başlamadan belirlemek yazımı kolaylaştırır. Bu mesaj konusunda okuyucuyu ikna etmek için mantıklı bir tartışma yürütmelidir. Şekiller, Görüntüler ve diğer medya eklenebilir. Sözcük sayısı ve özellikler için lütfen Tablo 1'e bakınız.

Orijinal Görüntü Raporu: Tıbbın her alanına ait ilgi çekici, tanımlayıcı veya eğitici görüntüler (ilustrasyon ya da Fotoğraf) birkaç satırlık açıklayıcı metin ve referanslarla birlikte bu bölümde değerlendirmeye sunulabilir. Makale uzunluğu 200 kelimeyi geçmemelidir. Özet, tartışma veya sonuca gerek yoktur ancak kısa bir başlık eklenmelidir. Sözcük sayısı ve özellikler için lütfen Tablo 1'e bakınız.

Hakem Raporu Sonrasında Değerlendirme

Yazarlar hakem raporunda belirtilen düzeltme istenen konuları maddelendirerek bir cevap olarak kendilerine ayrılan cevap bölümüne yazmalıdırlar ve hakem (ler)e cevap başlıklı ek bir dosya şeklinde https://www. selcukmedj.org adresinden yüklenmelidir. Ayrıca makale içerisinde de gerekli değişiklikleri yapmalı ve bunları makale içerisinde belirterek (boyayarak) online olarak tekrar gönderilmelidir.

Son Kontrol

1. Yayın hakkı devir ve yazarlarla ilgili bildirilmesi gereken konular formu gereğince doldurulup imzalanmış,
2. Ana makale metni ve özetlerde gerekli kelime sayıları aşılmamış
3. Yeterli sayıda anahtar kelime eklenmiş,
4. Başlık uzun ve kısa başlık şeklinde yazılmış,
5. Kaynaklar kurallara uygun olarak yazılmış,
6. Tablo, resim ve şekillerde bütün kısaltmalar açıklanmış olmalıdır.

Online Yükleme Basamakları, https://www. selcukmedj.org sayfasında;

1. Makale türü *
2. Uzun Başlık *
3. Kısa başlık *
4. Özet*
5. Anahtar kelimeler *
6. Yüklenmesi gerekli bölümler (Kapak sayfası, Ön yazı (cover letter), makale dosyası, Etik kurul onay Belgesi (kurumdan alınan), intihal analiz raporu, Şekiller ve Resimler, Telif Hakları Bildirim Formu ve gerekli ise hasta onam formu şeklinde tamamlanmalıdır.

Dergi Sahibi
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Yayıncı
Necmettin Erbakan Üniversitesi yayınları (Neü Press)
Yaka Mah. Yeni Meram Cad. Kasım Halife Sok. No: 11/1 (A Blok)
Meram / KONYA/TÜRKİYE
Tlf : +90 332 221 0 575
Mobil Tlf: 0 532 262 48 46
E-Mail: bilgi@neuyayin.com

Baş Editör
Doc. Dr. Sinan Demircioğlu
Necmettin Erbakan Üniversitesi, İç Hastalıkları Anabilim Dalı,
Hematoloji Bilim Dalı, Konya/Türkiye
Tel: 0 332 223 72 87
E-posta: editor@selcukmedj.org,
sinandemircioglumd@gmail.com

Sekreter ve yazı işleri müdürü
İlkay Kurt
E-posta: info@selcukmedj.org , ilkayyildiz13@gmail.com

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INFORMATION FOR AUTHORS/WRITING RULES

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- Mirza E, Oltulu R, Oltulu P, et al. Dry eye disease and ocular surface characteristics in patients with keratoconus. Saudi J Ophthalmol. 2022;36(1):117-21. doi: 10.4103/sjopt.sjopt_37_21.
- Vikse BE, Aasarød K, Bostad L, et al. Clinical prognostic factors in biopsy-proven benign nephrosclerosis. Nephrol Dial Transplant. 2003;18(3):517-23. doi: 10.1093/ndt/18.3.517.

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Single Author Books:
- Danovitch GM. Handbook of Kidney Transplantation. Boston: Little, Brown and Company (Inc.), 1996: 323-8.

Book Chapter:
- Soysal Z, Albek E, Eke M. Fetüs hakları. Soysal Z, Çakalır C, ed. Adli Tıp, Cilt III,İstanbul Üniversitesi Cerrahpaşa Tıp Fakültesi Yayınları, İstanbul, 1999:1635-50.
- Davison AM, Cameron JS, Grünfeld JP, et al. Oxford Textbook of Clinical Nephrology. In: Williams G, ed. Mesengiocapillary glomerulonephritis. New York: Oxford University Press, 1998: 591- 613.
- **Journal article published online ahead of print:**
- Doğan GM, Sığırcı A, Akyay A, et al. A Rare Malignancy in an Adolescent: Desmoplastic Small Round Cell Tumor. Turkiye Klinikleri J Case Rep. 10.5336/caserep.2020-77722. Published online: 31 December 2020.
- Cai L, Yeh BM, Westphalen AC, et al. Adult living donor liver imaging.DiagnIntervRadiol. 2016 Feb 24.doi: 10.5152/dir.2016.15323. [Epub ahead of print].

Meeting Reports:
- Bengisson S. Sothemin BG. Enforcement of data protection, privacy and security in medical informatics. In: Lun KC, Degoulet P, Piemme TE, Rienhoff O, editors. MEDINFO 92. Proceedings of the 7th World Congress on Medical Informatics; 1992 Sept 6-10; Geneva, Switzerland. Amsterdam: North-Holland; 1992. pp.1561-5.

Scientific or Technical Report:
- Cusick M, Chew EY, Hoogwerf B, A et al. Early Treatment Diabetic Retinopathy Study Research Group. Risk factors for renal replacement therapy in the Early Treatment Diabetic Retinopathy Study (ETDRS), Early Treatment Diabetic Retinopathy Study Kidney Int: 2004. Report No: 26.

Thesis:
- Kaplan SI. Post-hospital home health care: elderly access and utilization (dissertation). St Louis (MO): Washington Univ; 1995.

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When sharing patient photos, ensure that the identity is not recognized one-to-one, and images sufficient to identify the disease should be shared. For sharing images that reveal the patient's identity, a consent form in which the patient authorizes the sharing of the image is necessary.

Table 1. Limitations according to article types

	limitation of article	abstract	references	Tables	Figures
Research Article	4000	300	50	6	6
Review	6000	300	85	6	10
Case Presentations	1500	200	15	3	5
Letters to the Editor	1000	(-)	8	(-)	(-)
Editorial	1000	(-)	20	3	3
Original Image Report	200	(-)	5	1	3

Article Types

Selcuk Medical Journal publishes the types of articles briefly described below:

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Review Articles: Review articles should be articles that review a sufficient number of scientific articles, summarize the subject at the current level of knowledge and technology, evaluate and interpret the findings by comparing them. Techniques and applications in the latest scientific studies with all the developments in basic and applied sciences are evaluated. Reviews prepared by authors who have extensive knowledge of a particular field and have a scientific background with high citation potential will be accepted by our journal. Acceptance of manuscripts from these authors can also be by invitation. The main text should include Introduction, Clinical and Research Results and Conclusion. Please see Table 1 for word count and specifications.

Case Reports: Educational case reports on rare cases or conditions that pose difficulties in diagnosis and treatment, offer new treatments or reveal information not included in the literature are accepted for publication in our journal. The case report should include the subheadings Introduction, Case Presentation and Discussion and Coclusion. Interesting and unusual pictures are an advantage in the evaluation process.

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If patient identity is disclosed in patient-identifying pictures, patient consent must be provided to share the picture. Please see Table 1 for word count and specifications.

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Selcuk Med J 2025;41(4): 171-175

OPEN ARAŞTIRMA MAKALESİ / RESEARCH ARTICLE

Evaluation of Depression and Anxiety in Patients with Chronic Central Serous Chorioretinopathy

Kronik Santral Seröz Koryoretinopatili Hastalarda Depresyon ve Anksiyetenin Değerlendirilmesi

Berrin Okka[1], Ali Osman Gundogan[2], Bekir Sen[2]

[1]Necmettin Erbakan University, Faculty of Medicine, Department of Medical History and Ethics, Konya, Türkiye
[2]Necmettin Erbakan University, Faculty of Medicine, Department of Ophthalmology, Konya, Türkiye

ÖZET

Amaç: Kronik Santral Seröz Koryoretinopati (SSKR) hastalarında Beck Depresyon Ölçeği, Beck Anksiyete Ölçeği ve Anksiyete Duyarlılık İndeksi-3 ölçeği kullanılarak hastaların psikolojik durumlarını sağlıklı olgularla karşılaştırmak.

Gereç ve Yöntemler: Çalışmamız kesitsel klinik çalışma olarak planlanıp, Kasım 2023- Haziran 2024 tarihleri arasında Kronik SSKR tanısı ile Necmettin Erbakan Üniversitesi Tıp Fakültesi Hastanesi Retina biriminde takip ve tedavi altında olan 18-60 yaş arası 25 kronik SSKR hastası çalışma grubunu oluşturdu. Yaş ve cinsiyet uyumlu rutin göz kontrolü için polikliniğe başvuran 25 olgu da kontrol grubuna dahil edildi. Hasta ve kontrol grubuna en iyi düzeltilmiş görme keskinliği ve intraoküler basınç ölçümü, detaylı bir ön segment ve fundus muayenesini içeren tam oftalmolojik muayene yapıldıktan sonra Anksiyete Duyarlılığı İndeksi-3 (ADİ-3), Beck Depresyon Ölçeği (BDÖ) ve Beck Anksiyete Ölçeği (BAÖ) testleri uygulandı.

Bulgular: İki grup arasında ortalama yaş ve cinsiyet açısından istatistiksel olarak anlamlı fark saptanmadı (sırayla p=0.336, p=0.774). SSKR grubunda kontrol grubuyla karşılaştırıldığında BDÖ ve BAÖ skoru istatistiksel olarak anlamlı derecede yüksek bulundu (sırasıyla, p<0.001, p=0.013). Ayrıca SSKR grubunda ADİ-3 skoru da istatistiksel olarak anlamlı derecede yüksekti. (p=0.015)

Sonuç: Kronik SSKR hastalarında sağlıklı bireylere kıyasla depresyon ve anksiyete skorlarının daha yüksek olduğu tespit ettik. Çalışmamızın sonuçları, psikolojik faktörlerin SSKR ile ilişkili olduğunu göstermektedir. Sağlık profesyonellerinin, uzun tedavi sürecinde ortaya çıkabilecek sorunları göz önüne alarak hasta merkezli ve etik değerlere uygun bir şekilde, yapıcı bir yaklaşımla her hasta için bireyselleştirilmiş olarak ve fiziksel sorunların yanı sıra psikososyal sorunların da yönetimini içeren uygulamalara yönelmelidir. Oftalmologlar, SSKR hastalarını tedavi ederken psikososyal destek veya müdahaleler için hastaları yönlendirmesi gerektiğini akılda tutmalıdırlar.

Anahtar Kelimeler: Santral seröz koriyoretinopati, beck depresyon ölçeği, beck anksiyete ölçeği, anksiyete duyarlılığı indeksi-3

ABSTRACT

Objective: To compare the psychological status of patients with chronic central serous chorioretinopathy (CSCR) with healthy controls using the Beck Depression Inventory (BDI), Beck Anxiety Inventory (BAI), and Anxiety Sensitivity Index-3 (ASI-3).

Materials and Methods: This cross-sectional clinical study included 25 patients aged 18-60 with chronic CSCR who were followed and treated at the Retina Unit of Necmettin Erbakan University Faculty of Medicine Hospital between November 2023 and June 2024. A control group of 25 age- and sex-matched individuals undergoing routine eye check-ups was also recruited. All participants underwent a complete ophthalmological examination, including best corrected visual acuity, intraocular pressure measurement, and detailed anterior segment and fundus examination. The ASI-3, BDI, and BAI were administered.

Results: There were no statistically significant differences between the CSCR and control groups in terms of mean age and sex (p=0.336 and p=0.774, respectively). The CSCR group had significantly higher BDI and BAI scores compared to the control group (p<0.001 and p=0.013, respectively). The ASI-3 score was also significantly higher in the CSCR group (p=0.015).

Conclusion: Patients with chronic CSCR exhibited higher levels of depression and anxiety compared to healthy individuals, suggesting an association between psychological factors and CSCR. Healthcare professionals should adopt a patient-centered, ethical, and constructive approach, incorporating the management of psychosocial issues alongside physical concerns in individualized care plans for CSCR patients. Ophthalmologists should consider referring these patients for psychosocial support or interventions.

Keywords: Central serous chorioretinopathy, beck depression inventory, beck anxiety inventory, anxiety sensitivity index-3

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Sorumlu Yazar/Corresponding Author: Ali Osman Gundogan, Necmettin Erbakan University, Faculty of Medicine, Department of Ophthalmology, Konya, Türkiye
e-mail: aogundogan@hotmail.com

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INTRODUCTION

Central serous chorioretinopathy (CSCR) is characterized by serous fluid accumulation between the retinal pigment epithelium and the outer segments of photoreceptors, leading to neurosensory retinal detachment. The etiology is often idiopathic. Common symptoms include blurred vision, metamorphopsia, impaired color vision, and micropsia, often with a gradual onset and progression. Bilateral involvement occurs in 10% of patients. The disease predominantly affects males between 20 and 50 years of age, with an incidence approximately six times higher in men than women. Recurrence typically occurs within the first year in 31% of CSCR patients (1).

CSCR can present in acute or chronic forms. The acute form is more common and usually self-resolves within 2-3 months. The chronic form, characterized by diffuse retinal pigment epithelial abnormalities with retinal pigment epithelium atrophy, pigment clumping, and shallow serous retinal detachment, occurs in approximately 5% of cases (2). Recent studies define fluid accumulation lasting longer than 3 months as chronic CSCR (3).

The etiology and pathophysiology of CSCR are not fully understood. Systemic hypertension, obstructive sleep apnea, endogenous or exogenous corticosteroids, pregnancy, alcohol, and tobacco use have been associated with the disease (4-7). One study reported a close association between CSCR and Type A personality traits (8). Recent studies suggest a strong link between psychological factors and CSCR etiology, highlighting the importance of stress and anxiety management in disease management (9). Psychological stress and Type A personality, risk factors for CSCR, are also risk factors for depression (10). One study demonstrated a significantly increased risk of developing depression in CSCR patients (11). This study aimed to compare the psychological status of chronic CSCR patients with healthy controls using the BDI, BAI, and ASI-3.

MATERIALS AND METHODS

This study was designed as a cross-sectional clinical study and included 25 chronic CSCR patients aged 18-60 who were being followed and treated at the Retina Unit of Necmettin Erbakan University Faculty of Medicine Hospital between November 2023 and June 2024. The control group consisted of 25 age- and sex-matched individuals who attended the outpatient clinic for routine eye check-ups. Individuals with systemic diseases such as diabetes, hypertension, cerebrovascular or cardiovascular diseases, those with a psychiatric illness or a history of using medication that could affect mental status, those with any eye disease other than CSCR, a history of intraocular surgery or trauma, alcohol or tobacco use, or a history of COVID-19 were excluded from the study.

All patients and controls underwent a complete ophthalmological examination, including best-corrected visual acuity and intraocular pressure measurement, and a detailed anterior segment and fundus examination. Following the ophthalmological examination, the Anxiety Sensitivity Index-3 (ASI-3), Beck Depression Inventory (BDI), and Beck Anxiety Inventory (BAI) tests were administered.

The study was conducted with the approval of the Necmettin Erbakan University Ethics Committee and in accordance with the principles of the Declaration of Helsinki (Ethics Committee Decision No: 2024/5051). Written informed consent was obtained from all participants.

Beck Depression Inventory (BDI)

The BDI is a widely used 21-item instrument for measuring depressive symptoms. Created by Aaron T. Beck and first published in 1961 (12), it assesses emotional, behavioral, and somatic symptoms. Symptom severity can be categorized as minimal depression (0-9), mild depression (10-16), moderate depression (17-29), and severe depression (30-63). The reliability and validity of the Turkish version were established by Hisli (1988) (13). In this study, individuals with BDI scores ≤ 9 were considered to have no depressive symptoms, while those with scores > 9 were considered to have depressive symptoms.

Beck Anxiety Inventory (BAI)

The BAI, developed by Beck et al. (14), is a 21-item scale assessing the degree of discomfort experienced during the past week for each item. Scores are interpreted as minimal/normal anxiety (0-7), mild anxiety (8-15), moderate anxiety (16-25), and severe anxiety (26-63). The validity and reliability of the Turkish version were established by Ulusoy et al. (15). In this study, individuals with BAI scores > 7 were considered to have anxiety symptoms.

Anxiety Sensitivity Index-3 (ASI-3)

The ASI-3 comprises 18 items across three subscales: physical, social, and cognitive, each containing six items. It uses a 5-point Likert scale, ranging from 0 (very little) to 4 (very much). Participants rate their agreement with each statement based on their past experiences or how they anticipate feeling in that situation if they haven't experienced it (16). The reliability and validity of the Turkish version were established by Mantar et al. (17).

Statistical Analysis

Statistical analysis was performed using IBM SPSS Statistics version 29.0 (IBM Corp, Armonk, NY, USA). Normality was assessed using the Shapiro-Wilk test for continuous variables. Continuous variables with normal and non-normal distributions were expressed as mean ± standard deviation (SD) and median [interquartile range, IQR], respectively. Categorical variables were presented as number (n) and percentage (%). Independent samples t-tests and Mann-Whitney U tests were used to compare continuous variables with normal and non-normal distributions, respectively. Pearson's chi-square test was used to compare categorical variables. A p-value < 0.05 was considered statistically significant.

RESULTS

The study included 25 chronic CSCR patients (CSCR group), 15 (60%) of whom were male and 10 (40%) female. The mean age of the CSCR group was 43.4 ± 6.3 years. The control group consisted of 25 participants, 14 (56%) male and 11 (44%) female, with a mean age of 41.8 ± 5.3 years. There was no statistically significant difference between the two groups in

Table 1. Demographical characteristics of the participants in the CSCR and control groups.

	CSCR Group (n=25)	Control Group (n=25)	p value
Age, years, mean±SD	43.4±6.3	41.8±5.3	0.336*
Gender			
Male (n, %)	15, 60.0%	14, 56.0%	0.774**
Female (n, %)	10, 40.0%	11, 44.0%	

* Tested using Independent samples – t test ** Tested using Pearson's Chi – squared test CSCR: Central Serous Chorioretinopathy

Table 2. Comparison of the ASI-3, BAI, BDI scores between CSCR and control groups.

	CSCR Group (n=25)	Control Group (n=25)	p value
ASI-3, median [IQR]	22.0 [26.0]	12.0 [7.5]	0.015*
BAI, median [IQR]	9.0 [12.5]	5.0 [3.0]	0.013*
BDI, median [IQR]	7.0 [9.0]	4.0 [4.5]	<0.001*

* Tested using Mann-Whitney test **Bold:** statistically significant results **ASI-3:** Anxiety Sensitivity Index-3 **BAI:** Beck Anxiety Inventory **BDI:** Beck Depression Inventory

terms of mean age and sex (p=0.336 and p=0.774, respectively) (Table 1). The median disease duration in the CSCR group was 4.0 [4.0] years.

Based on the BDI scores, depression was detected in 11 (44%) patients in the CSCR group, while 14 (56%) had no depression. In the control group, 23 (92%) participants had no depression, and 2 (8%) had depression. The median BDI score was 7.0 [9.0] in the CSCR group and 4.0 [4.5] in the control group. The BDI score was statistically significantly higher in the CSCR group compared to the control group (p<0.001).

Evaluation of the BAI revealed anxiety in 13 (52%) patients in the CSCR group and no anxiety in 12 (48%). In the control group, 22 (88%) had no anxiety, while 3 (12%) had anxiety. The median BAI score was 9.0 [12.5] in the CSCR group and 5.0 [3.0] in the control group. The BAI score was statistically significantly higher in the CSCR group compared to the control group (p=0.013).

The median ASI-3 score was 22.0 [26.0] in the CSCR group and 12.0 [7.5] in the control group. The ASI-3 score was statistically significantly higher in the CSCR group compared to the control group (p=0.015) (Table 2).

DISCUSSION

Our study demonstrates that patients with CSCR exhibit higher levels of anxiety and depressive symptoms compared to healthy controls. These findings support the hypothesis that CSCR patients may experience increased psychological distress. This research contributes significantly to the literature by investigating the link between CSCR and psychological functioning, highlighting that chronic CSCR not only affects vision but also impacts quality of life through anxiety and depressive symptoms. This study may also enhance the understanding of the psychological processes involved in CSCR.

CSCR, the fourth most common maculopathy, is characterized by choroidal hyperpermeability and subsequent subretinal fluid accumulation (18). This condition can lead to temporary or irreversible vision loss due to neuronal tissue atrophy, in addition to symptoms like metamorphopsia, micropsia, hypermetropia, and dyschromatopsia. Although the exact etiology remains unknown, CSCR is considered a multifactorial disease (19). The most established and strongest risk factors are exogenous corticosteroid use and elevated endogenous cortisol levels (20,21). Other risk factors include sympathetic-parasympathetic imbalance, sleep disorders, uncontrolled hypertension, pregnancy, alcohol, and tobacco use (22).

The psychological characteristics of CSCR patients have become a frequent research topic in recent years. Yannuzzi, in 1987, hypothesized that individuals with "Type A personality" are at higher risk of developing CSCR (8). Numerous studies have evaluated psychopathological symptoms in CSCR patients. Conrad et al. found significantly higher emotional stress levels, measured by the Global Severity Index, in CSCR patients compared to healthy controls (23). Another study by Sahin et al. demonstrated more pronounced psychological symptoms and poorer quality of life in CSCR patients compared to healthy controls (24). Siguan and Aguilar found a higher likelihood of schizophrenic (84%), hysterical (83%), depressive (75%), psychopathic deviant (67%), and hypochondriacal (58%) tendencies in CSCR patients (25). Piskunowicz et al. observed higher insecurity, frustration, and anxiety levels in CSCR patients compared to healthy controls (26). These findings corroborate the results of our study.

However, a study by Kim YK et al. comparing acute and chronic CSCR patients found that anxiety, depression, and stress are associated with the active phase of CSCR but not the inactive phase. Their analysis linked acute CSCR with depression and chronic CSCR with stress (27). Contrary to this hypothesis, Tittl et al. reported a higher likelihood of anxiolytic

or antidepressant use in chronic CSCR patients compared to controls, but not in acute CSCR patients (28). Our study, unlike Kim YK et al.'s, found significantly higher depression scores in chronic CSCR patients, aligning with Tittl et al.'s hypothesis.

This study uniquely assesses depression and anxiety in chronic CSCR patients using scales not previously employed in this patient group. However, it has limitations, including a small sample size, the exclusion of acute CSCR patients due to their scarcity, its single-center design, and the lack of socio-economic and demographic data. Further research with larger sample sizes, including acute CSCR patients, is needed.

In conclusion, we found higher depression and anxiety scores in chronic CSCR patients compared to healthy controls. Like most previous studies, our findings suggest a clear association between psychological factors and CSCR. Healthcare professionals should incorporate psychosocial management alongside physical care in individualized, patient-centered, ethical, and constructive care plans for CSCR patients, considering the challenges that may arise during the long treatment process (29). Ophthalmologists should be mindful of the need for referrals to psychosocial support or interventions for CSCR patients.

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Address correspondence to: *Ali Osman Gundogan, Necmettin Erbakan University, Faculty of Medicine, Department of Ophthalmology, Konya, Türkiye*
e-mail: *aogundogan@hotmail.com*

REFERENCES

1. Liew G, Quin G, Gillies M, et al. Central serous chorioretinopathy: a review of epidemiology and pathophysiology. Clin Exp Ophthalmol. 2013;41(2):201-14. doi:10.1111/j.1442-9071.2012.02848.x.
2. Gilbert CM, Owens SL, Smith PD, et al. Long-term follow-up of central serous chorioretinopathy. Br J Ophthalmol. 1984;68(11):815-20. doi:10.1136/bjo.68.11.815.
3- Nicholson B, Noble J, Forooghian F, et al. Central serous chorioretinopathy: update on pathophysiology and treatment. Surv Ophthalmol. 2013;58(2):103-26. doi:10.1016/j.survophthal.2012.07.004.
4. Leveque TK, Yu L, Musch DC, et al. Central serous chorioretinopathy and risk for obstructive sleep apnea. Sleep Breath. 2007;11(4):253-57. doi:10.1007/s11325-007-0112-3.
5. Carvalho-Recchia CA, Yannuzzi LA, Negrão S, et al. Corticosteroids and central serous chorioretinopathy. Ophthalmology. 2002;109(10):1834-37. doi:10.1016/s0161-6420(02)01117-x.
6. Chumbley LC, Frank RN. Central serous retinopathy and pregnancy. Am J Ophthalmol. 1974;77(2):158-60. doi:10.1016/0002-9394(74)90667-9.
7. Haimovici R, Koh S, Gagnon DR, et al. Central Serous Chorioretinopathy Case-Control Study Group. Risk factors for central serous chorioretinopathy: a case-control study. Ophthalmology. 2004;111(2):244-49. doi:10.1016/j.ophtha.2003.09.024.
8. Yannuzzi LA. Type A behavior and central serous chorioretinopathy. Trans Am Ophthalmol Soc 1986;84:799–845.
9. Bazzazi N, Ahmadpanah M, Akbarzadeh S, et al. In patients suffering from idiopathic central serous chorioretinopathy, anxiety scores are higher than in healthy controls, but do not vary according to sex or repeated central serous chorioretinopathy. Neuropsychiatr Dis Treat. 2015;11:1131-36. doi:10.2147/NDT.S83216.
10. Yang L, Zhao Y, Wang Y, et al. The Effects of Psychological Stress on Depression. Curr Neuropharmacol. 2015;13(4):494-504. doi:10.2174/1570159x1304150831150507.
11. Chen YY, Huang LY, Liao WL, et al. Association between Central Serous Chorioretinopathy and Risk of Depression: A Population-Based Cohort Study. J Ophthalmol. 2019;2019:2749296. doi:10.1155/2019/2749296.
12. Beck AT, Ward CH, Mendelson M, et al. An inventory for measuring depression. Arch Gen Psychiatry. 1961;4:561–71. doi:10.1001/archpsyc.1961.01710120031004
13. Hisli N. Beck Depresyon Envanterinin geçerliği üzerine bir çalışma. Psikoloji Dergisi 1988;6:118-22.
14. Beck AT, Epstein N, Brown G, et al. An inventory for measuring clinical anxiety: psychometric properties. J Consult Clin Psychol. 1988;56(6):893-97. doi:10.1037//0022-006x.56.6.893.
15. Ulusoy M, Şahin N, Erkmen H. Turkish version of the Beck Anxiety Inventory: psychometric properties. J Cogn Psychother 1998;12:28-35
16. Taylor S, Zvolensky MJ, Cox BJ, et al. Robust dimensions of anxiety sensitivity: development and initial validation of the Anxiety Sensitivity Index-3. Psychol Assess. 2007;19(2):176-88. doi:10.1037/1040-3590.19.2.176.
17. Mantar A, Yemez B, Alkın T. Anksiyete Duyarliliği Indeksi-3'ün Türkçe Formunun Geçerlik ve Güvenilirlik Calişmasi [The validity and reliability of the Turkish version of the anxiety sensitivity index-3]. Turk Psikiyatri Derg 2010;21:225-34.
18. van Rijssen TJ, van Dijk EHC, Yzer S, et al. Central serous chorioretinopathy: Towards an evidence-based treatment guideline. Prog Retin Eye Res. 2019;73:100770. doi:10.1016/j.preteyeres.2019.07.003.
19. Kaye R, Chandra S, Sheth J, et al. Central serous chorioretinopathy: An update on risk factors, pathophysiology and imaging modalities. Prog Retin Eye Res. 2020;79:100865. doi:10.1016/j.preteyeres.2020.100865.
20. Rim TH, Kim HS, Kwak J, et al. Association of Corticosteroid Use With Incidence of Central Serous Chorioretinopathy in South Korea. JAMA Ophthalmol. 2018;136(10):1164-69. doi:10.1001/jamaophthalmol.2018.3293.
21. Garg SP, Dada T, Talwar D, et al. Endogenous cortisol profile in patients with central serous chorioretinopathy. Br J Ophthalmol. 1997;81(11):962-64. doi:10.1136/bjo.81.11.962.
22. Daruich A, Matet A, Dirani A, et al. Central serous chorioretinopathy: Recent findings and new physiopathology hypothesis. Prog Retin Eye Res. 2015;48:82-118. doi:10.1016/j.preteyeres.2015.05.003.
23. Conrad R, Geiser F, Kleiman A, et al. Temperament and character personality profile and illness-related stress in central serous chorioretinopathy. ScientificWorldJournal. 2014;2014:631687. doi:10.1155/2014/631687.
24. Sahin A, Bez Y, Kaya MC, et al. Psychological distress and poor quality of life in patients with central serous chorioretinopathy. Semin Ophthalmol. 2014;29(2):73-6. doi:10.3109/08820538.2013.793728

25. Siguan CS, Aguilar RN. Psychological profile of patients with central serous retinopathy. Philipp J Ophthalmol 2014;39:16–20.
26. Piskunowicz M, Jaracz M, Lesiewska H, et al. Temperament profile in patients with central serous chorioretinopathy: a case-control study. Eur J Ophthalmol. 2014;24(3):392-95. doi:10.5301/ejo.5000377.
27. Kim YK, Woo SJ, Park KH, et al. Association of Central Serous Chorioretinopathy with Psychosocial Factors is Dependent on Its Phase and Subtype. Korean J Ophthalmol. 2018;32(4):281-9. doi:10.3341/kjo.2017.0144.
28. Tittl MK, Spaide RF, Wong D, et al. Systemic findings associated with central serous chorioretinopathy. Am J Ophthalmol. 1999;128(1):63-8. doi:10.1016/s0002-9394(99)00075-6.
29. Kocaman Yıldırım N. Psikososyal bakımda onkoloji hemşireliği İç: Can G. Onkoloji Hemşireliği. Nobel Tıp Kitabevleri İstanbul 2015, 1043-63.

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OPEN ARAŞTIRMA MAKALESİ / RESEARCH ARTICLE

Comparison of Pediatric Retrograde Intrarenal Surgery Outcomes in Less than 2 cm Single Stones: Lower Pole and Other Localizations

İki cm'den Küçük Tek Taşlarda Pediatrik Retrograd İntrarenal Cerrahi Sonuçlarının Karşılaştırılması: Alt Kutup ve Diğer Lokalizasyonlar

Muzaffer Tansel Kilinc[1], Mehmet Mesut Piskin[2], Omer Faruk Cavdar[2], Bilal Gunes[2], Mehmet Serkan Ozkent[1]

[1] Konya City Hospital, Department of Urology, Konya, Türkiye
[2]Necmettin Erbakan University, Medical Faculty,Department of Urology, Konya, Türkiye

ÖZET

Amaç: Çalışmamızın amacı 2 cm'den küçük tek taşlarda alt pol lokalizasyonunun diğer lokalizasyonlara kıyasla pediatrik retrograd intrarenal cerrahi (RIRS) sonuçları üzerindeki etkisini araştırmaktır.

Gereç ve Yöntemler: Ocak 2021 ile Haziran 2024 arasında bir üniversite hastanesinde RIRS uygulanan hastaların verileri retrospektif olarak analiz edildi. Çalışmaya 2 cm'den küçük, tek taşı olan ve verilerine ulaşılabilen, 18 yaş altı 69 hasta dahil edildi. Hastalar böbrek taşı lokalizasyonuna göre iki gruba ayrıldı: alt pol (Grup 1) ve diğer lokalizasyonlar (Grup 2). Her iki grupta hastaların demografik verileri, klinik özellikleri, taşla ilgili verileri, perioperatif ve postoperatif verileri istatistiksel olarak karşılaştırıldı.

Bulgular: Çalışmaya ortalama yaşı 7±4.4 (1-17) yıl ve ortalama taş boyutu 11±3.3 (5-20) mm olan 69 hasta dahil edildi. Grup 1'de 21 hasta ve Grup 2'de 48 hasta vardı. Her iki gruptaki hastaların demografik verileri ve klinik özellikleri benzerdi. Grupların taş boyutu, lokalizasyonu ve dansitesi benzerdi (sırasıyla p=0.58, 0.58 ve 0.63). Grup 1'de prestenting oranı Grup 2'ye göre istatistiksel olarak anlamlı derecede daha yüksekti (%76.2 vs %50, p=0.04). Gruplar arasında access sheath kullanımı, operasyon süresi, floroskopi süresi, 1. gün ve 3. aydaki taşsızlık oranı veya ek prosedürler açısından istatistiksel olarak anlamlı bir fark saptanmadı (sırasıyla p=0.69, 0.95, 0.60, 0.97, 0.27 ve 0.28). Komplikasyon oranları her iki grupta benzerdi (p=0.28). Hastaların hiçbirinde yüksek dereceli veya anesteziyle ilişkili komplikasyon gözlenmedi.

Sonuç: Alt pol lokalizasyonu 2 cm'den küçük tek taşlarda prestenting oranı hariç cerrahi parametreleri etkilememektedir. Pediatrik popülasyonda prestenting uygulamasının genel anestezi altında yapıldığı göz önüne alındığında, alt pol taşları anestezi seanslarının sayısını, radyasyon maruziyetini ve hastane yatışlarını artırabilir.

Anahtar Kelimeler: Alt pol, böbrek taşları, pediatrik RIRS, RIRS sonuçları

ABSTRACT

Objective: Our study aimed to investigate the effect of lower pole localization in solitary stones smaller than 2 cm on pediatric retrograde intrarenal surgery (RIRS) outcomes compared to other localizations.

Materials and Methods: Data from patients who underwent RIRS in a university hospital between January 2021 and June 2024 were retrospectively analyzed. The study included 69 patients under 18 years of age with single stones less than 2 cm and whose data were available. Patients were divided into two groups according to kidney stone localization: lower pole (Group 1) and other localizations (Group 2). Demographic data, clinical characteristics, stone-related data, and perioperative and postoperative data of the patients were statistically compared in both groups.

Results: The study enrolled 69 patients with a mean age of 7±4.4 (1-17) years and a mean stone size of 11±3.3 (5-20) mm. There were 21 patients in Group 1 and 48 patients in Group 2. The patient's demographic data and clinical characteristics in both groups were similar. The groups' stone size, side, and density were similar (p=0.58, 0.58, and 0.63, respectively). The prestenting rate was statistically significantly higher in Group 1 than in Group 2 (76.2% vs 50%, p=0.04). No statistically significant difference was detected between the groups in access sheath use, operation time, fluoroscopy time, the stone-free rate on 1st day and 3rd month, or auxiliary procedures (p=0.69, 0.95, 0.60, 0.97, 0.27, and 0.28, respectively). The complication rates were similar in both groups (p=0.28). No high-grade or anesthesia-related complications were observed in any of the patients.

Conclusion: The lower pole localization does not affect surgical parameters, except for the prestenting rate, in single stones smaller than 2 cm. Considering that prestenting is performed under general anesthesia in the pediatric population, lower pole stones may increase the number of anesthesia sessions, radiation exposure, and hospitalizations.

Keywords: Lower Pole, renal stones, pediatric RIRS, RIRS outcomes

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Sorumlu Yazar/Corresponding Author: Muzaffer Tansel Kilinc, Konya City Hospital, Department of Urology, Konya, Türkiye
e-mail: m.tanselkilinc@gmail.com

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INTRODUCTION

Pediatric stone disease is a significant health problem that is endemic in Turkey and has an increasing incidence worldwide (1). The main reasons for this increase are changes in dietary habits, increased carbohydrate consumption, and a sedentary lifestyle (2). The higher recurrence rates compared to the adult population highlight the determination of underlying metabolic problems, preventive measures, and complete stone removal as the most critical steps in management (3).

Extracorporeal shockwave lithotripsy (ESWL) remains a critically important noninvasive treatment option for treating pediatric kidney stones <2 cm (4). In case of ESWL failure or the presence of unfavorable factors for ESWL (narrow infundibulum, long calyx, hars stone), retrograde intrarenal surgery (RIRS) with a flexible ureterorenoscope stands out as a minimally invasive treatment option (4). Technological advances have led to the emergence of flexible ureterorenoscopes with narrower calibers, better image quality, and greater flexion-deflexion capacity, making RIRS more common in the pediatric population for <2 cm kidney stones (5).

RIRS is an endourological modality with a stone-free rate ranging from 60% to 100% and a 10% to 20% complication rate (6, 7). The most important factors affecting success are stone size, surgeon experience, multiple localizations, the harsh chemical structure of the stone, and differences in the anatomical structure of the calyces (8, 9). The debate over whether stone localization affects the outcomes is a current issue.

Lower pole localization may affect RIRS results because it reduces the deflexion capacity of the laser fiber and makes access to the stone difficult (10, 11). However, some data also show that localization doesn't change the results of RIRS in children. This might be because more new, flexible ureterorenoscopes with smaller diameters are being used (12). The current literature contains limited and contradictory data investigating the effect of stone localization on pediatric RIRS results. Our study aimed to investigate the effect of lower pole localization in solitary stones smaller than 2 cm on pediatric RIRS outcomes compared to other localizations.

MATERIALS and METHODS

Patients:

Data from patients who underwent RIRS in a university hospital between January 2021 and June 2024 were retrospectively analyzed. The study included 69 patients under 18 years of age with single stones less than 2 cm and whose data were available. Patients with multiple stones, urinary tract infections, and those who underwent other surgery simultaneously with RIRS were excluded from the study.

Patient's demographic data, clinical data (comorbidity, American Society of Anesthesiologists score, kidney or urinary tract anomaly, creatinine levels, hemoglobin levels), stone-related data (localization, size, side, density), perioperative data (prestenting, use of access sheath, operation time, fluoroscopy time), and postoperative data (postoperative stenting, stone-free rates on the postoperative first day and third months, hospital stay, need for auxiliary procedures, complications) were analyzed. Preoperative low-dose non-contrast computed tomography was used to evaluate the stone characteristics.

Patients were divided into two groups according to kidney stone localization: lower pole (Group 1) and other localizations (Group 2). The investigated parameters were compared statistically between both groups. Ethical approval was obtained before the study (No:2024/5148).

Surgical Procedure:

All procedures were performed by a single surgeon under general anesthesia in the lithotomy position. The surgery was started by placing the guide wire into the renal pelvis with a 4.5/6.5 Fr fiber ureterorenoscope under direct vision. The surgeon determined the decision for prestenting, use of access sheath, and postoperative stenting. In cases where access sheath was used, 9.5/11 Fr size was preferred.

The RIRS was performed with a 7.5 Fr flexible ureteroscope. Lithotripsy was performed with 270 nm holmium: YAG laser fiber at 0.5–1 Joule, 5–12 Hertz settings. A combination of fragmenting, dusting, and pop-dusting techniques was employed based on stone characteristics during each surgery. Repositioning with a basket did not perform any of the patients. The stone-free rate was evaluated by perioperative ureterorenoscopy and postoperative ultrasonography and was accepted as fragments <3 mm (13). Patients were followed up with ultrasound and kidney ureter bladder (KUB) graphy on the 1st postoperative day and with urinalysis, serum creatinine levels, and ultrasound at the 3rd month.

Statistical Analysis:

A statistical software package program was utilized for statistical analysis. Descriptive analysis was performed on the statistics of all numerical data with mean, standard deviation, minimum, and maximum values. Hospitalization time was expressed as the median value due to the standard deviation rate. Distribution was analyzed depending on normality using either the Student's T-test or Mann–Whitney U test. Categorical data were compared using Fisher's exact test. The Wilcoxon signed-rank test was used to compare the dependent samples. A mixed ANOVA test was used to compare the preoperative and postoperative creatinine and hemoglobin levels. A "p" value < 0.05 was accepted as statistically significant.

RESULTS

The study enrolled 69 patients with a mean age of 7±4.4 (1-17) years and a mean stone size of 11±3.3 (5-20) mm. There were 21 patients in Group 1 and 48 patients in Group 2. In Group 2, 12 (25%) patients had middle calyx stones, 7 (14.6%) patients had upper calyx stones, and 29 (60.4%) patients had renal pelvis stones.

Demographic and clinical characteristics of patients were similar in both groups (Table 1). No kidney or urinary tract anomaly was detected in Group 1. In Group 2, two patients had mild ureteropelvic junction obstruction, and one had horseshoe kidney (p=0.24). No statistically significant difference was detected within the groups' preoperative and postoperative hemoglobin and creatinine levels (p>0.05).

Table 1. Demographic and clinical characteristics of patients

	Group 1 (n=21)	Group 2 (n=48)	p
Age (years)	7.8±4.1 (3-16)	6.6±4.6 (1-17)	0.33
Gender (F/M)	12/9	23/25	0.55
Weight (kg)	28.1±12.2 (13-50)	24.8±11.8 (9-50)	0.30
Height (cm)	114±16 (94-142)	109±18 (74-145)	0.23
Comorbidity	1 ASD	1 VSD	0.32
ASA Score			
1	10	24	
2	10	23	0.92
3	1	1	
Kidney or urinary tract anomaly (n/%)	0 (0)	3 (6.3)	0.24
Preoperative creatinine (mg/dl)	0.5±0.1 (0.3-0.8)	0.5±0.2 (0.2-1.9)	0.70
Postoperative creatinine (mg/dl)	0.5±0.1 (0.2-0.8)	0.57±0.3 (0.2-1.9)	0.47
Preoperative hemoglobin (g/dl)	12.6±1.4 (10-14.9)	12.1±1.4 (9-15.9)	0.21
Postoperative hemoglobin (g/dl)	12.8±1.9 (10.2-16.1)	12.4±1.5 (9.4-15.8)	0.15

ASA: American Society of Anesthesiologists score, ASD: atrial septal defect VSD: ventricular septal defect

In addition, the mixed ANOVA test detected no statistically significant difference in creatinine (p=0.22) and hemoglobin (p=0.76) levels. The groups' stone size, side, and density were similar (p=0.58, 0.58, and 0.63, respectively). The prestenting rate was statistically significantly higher in Group 1 than in Group 2 (76.2% vs 50%, p=0.04). The access sheath use rate was similar (p=0.69, Table 2).

In Group 1, the mean operation time and fluoroscopy time were higher. However, this difference was not statistically significant (p=0.95 and p=0.60). Stone-free rate (SFR) on 1st day and 3rd month was lower in Group 1 than in Group 2 (81% vs 81.3%, 85.7% vs 93.8%). However, the difference was not vital to generate statistical significance (p=0.97 and 0.27). The rate of auxiliary procedures required to achieve the SFR in the 3rd month was 19% in Group 1 and 14.5% in Group 2 (p=0.28, Table 2).

Patients were discharged after a median of 2 (1-3) days of hospitalization. The total complication rate was 14.4%. Complication rates were similar between groups, and no high-grade complications were observed in any patient (p=0.28). In Group 1, two patients had grade 1 complications (stent discomfort), and one patient had grade 2 complications (urinary infection). In Group 2, five patients had grade 1 (three stent discomforts, two fevers), and two had grade 2 (urinary infection) complications (Table 2). No long-term complications (such as ureteral stenosis, vesicoureteral reflux, or recurrent urinary tract infection) were observed during the follow-up period.

Table 2. Perioperative and postoperative data of patients

	Group 1 (n=21)	Group 2 (n=48)	p
Stone size (mm)	11.3±3.5 (7-20)	10.8±3.3 (5-20)	0.58
Stone side (R/L)	12/9	24/24	0.58
Stone density (HU)	914±189 (500-1280)	951±327 (300-1677)	0.63
Prestenting (n/%)	16 (76.2)	24 (50)	0.04
Access sheath (n/%)	6 (28.6)	16 (33)	0.69
Operation time (min)	66.1±19 (30-95)	65.8±23.3 (25-140)	0.95
Fluoroscopy time (sec)	10.7±2.7 (7-15)	10.3±3.3 (6-25)	0.60
Postoperative stenting (n/%)	13 (61.9)	36 (75)	0.27
Stone-free rate on 1st day (n/%)	17 (81)	39 (81.3)	0.97
Stone-free rate on 3rd month (n/%)	18 (85.7)	45 (93.8)	0.27
Hospitalization time (day)	2±2.1 (1-10)	2.6±2.7 (1-15)	0.39
Auxiliary procedures			0.28
ESWL	1	3	
URS	1	2	
RIRS	2	4	
Complication (Clavien-Dindo grade)			0.36
1	2 (9.5)	5 (10.4)	
2	1 (4.7)	2 (4.1)	

ESWL: Extracorporeal Shock Wave Lithotripsy, HU: Hounsfield Unit, RIRS: Retrograde Intrarenal Surgery, URS: Ureterorenoscopy

DISCUSSION

The current study showed that lower pole localization increases the prestenting rate during RIRS of solitary pediatric kidney stones smaller than 2 cm. However, no difference was observed in other surgical parameters such as operative time, fluoroscopy time, stone-free rate, and complications. Since prestenting is performed under general anesthesia in the pediatric population, the possibility of requiring multiple sessions in the treatment of lower pole stones with flexible ureteroscopy and the possible clinical consequences of this should be considered.

Technological innovations in endourology have brought about major changes in the treatment of pediatric kidney stones. ESWL and RIRS have become the most preferred treatment methods for kidney stones smaller than 2 cm (14). ESWL is the first-line safe and effective treatment option for ≤2cm kidney stones (4). However, the need for repeated sessions for complete stone-free status increased general anesthesia and radiation exposure in pediatric patients. In cases such as increasing stone size, multiple localization, and the presence of unfavorable factors for ESWL, RIRS stands out as a minimally invasive treatment option. In addition, improved image quality, deflection capacity, and advances in laser technology make RIRS more popular in pediatric kidney stones ≤2 cm (5).

Pediatric RIRS requires reaching the renal pelvis, which has less capacity than adults, through a narrow ureter and performing lithotripsy using the maneuverability of the flexible ureterorenoscope in this limited area. There are different data in the literature regarding the factors affecting pediatric RIRS results for general reasons, such as the different technical features of flexible ureterorenoscopes, surgeon experience, and age differences of the patient population included in the studies. Lower pole localization is also a factor in solitary stones, and contradictory data exist about whether it affects the RIRS results (15).

Cannon et al. reported in their study that lower pole localization significantly reduced SFR, especially in larger than 15 mm, when RIRS was not as common as it is today (16). Similarly, in their study, including adult and pediatric patients, Özkent et al. reported that lower pole localization significantly reduced SFR (11). It has also been stated that lower pole localization reduces SFR in multiple large stones (17). The main reasons why lower pole localization affects SFR are unfavorable anatomy, narrow infundibulopelvic angle, and laser fiber decreasing the deflection capacity of the flexible ureterorenoscope (11, 18). However, on the contrary, essential data in the literature shows that lower pole localization does not affect SFR in pediatric RIRS.

A study using two different calibers of ureterorenoscopy stated that lower pole localization did not affect SFR (12). Kaygısız et al. reported that lower pole localization did not affect the SFR in single kidney stones smaller than 2 cm, similar to our data (19). Some studies have revealed a similar situation. Unsal et al. reported that localization did not affect the results of RIRS in their studies, which included infants and preschool-age children, and Azili et al. reported that localization did not affect the results of RIRS in their studies, which included mostly children with staghorn stones (20, 21). The most important focus of the studies indicating that stone localization does not affect SFR has been the increase in maneuverability of flexible ureterorenoscopes with technological developments (12).

We believe that the most important reasons stone localization did not affect RIRS outcomes except for prestenting in our study are improvement in image quality and increase in flexion-deflexion capacity with the developments in endourology. The study included up-to-date patient data, which led us to reach this opinion. Another reason may be that a single experienced surgeon operates on patients. The most important advantages of experience that will improve RIRS outcomes are developing tips and tricks and reflexive surgical skills (22). In this way, surgical gains that provide access to all localizations, including the lower pole, may contribute to RIRS results.

The ureter is narrower in caliber in pediatric patients than in adult patients, so retrograde access may be more difficult during RIRS. Balloon dilatation, hydrodilatation, and passive dilatation with a double J stent (prestenting) techniques can be used to overcome this difficulty (5, 23). Conflicting recommendations exist on which technique to use. However, concerns that it may increase the incidence of ureteral complications and vesicoureteral reflux have led us to move away from active balloon dilation. Approximately 58% of our patients underwent prestenting. This rate varies between 38% and 100% in the literature (8, 16, 20, 24).

The high rate of prestenting lower pole stones in our study may be due to two reasons. Lower pole localization complicates ESWL and reduces SFR (25). This may have led to the prioritization of RIRS to provide SFR in lower pole stones. Concerns about the low efficacy of ESWL may lead to a greater preference for prestenting to increase retrograde access to the kidney. Another reason for the higher prestenting rate in lower pole stones may be these patients' incidental narrower ureteral caliber. The fact that ureteral caliber was not measured in the patients included in the study makes it impossible to present objective data regarding this hypothesis.

Considering that double J stents are placed under general anesthesia in pediatric patients, the clinical consequences of higher prestenting rates in lower pole stones become important. Increased anesthesia complications and radiation exposure due to repeated sessions are situations that should be taken into consideration in lower pole stones. It has also been reported that recurrent urological surgeries increase parenteral anxiety levels (26). This may lead to treatment noncompliance and an increase in medicolegal problems. Parents of patients with lower pole stones should be adequately informed about the increased prestenting risk and cumulative general anesthesia risks.

When we evaluated our other findings, we found that lower pole localization statistically insignificantly increases operation time, fluoroscopy time, and auxiliary procedures, decreasing the SFR on the first day and third month. However, since more patients may make this difference statistically

significant, caution is required in lower pole RIRS. The fact that complication rates in both groups were similar to those in the literature indicates that pediatric RIRS can be safely applied in all localizations (27).

Our study has several limitations. The retrospective design prevents the evaluation of the current RIRS criteria, such as removal, fragmentation, basketing, and operating rates. Another significant limitation is the lack of stone analysis data. However, the fact that stone densities were similar in both groups suggests that the chemical structure was also similar. Despite all these limitations, our study provides significant findings regarding the effects of stone localization on pediatric RIRS results. Our data should be supported with prospective randomized controlled studies.

CONCLUSION

Innovations in endourology, structural changes in flexible ureterorenoscopes, and increased surgical knowledge are increasing the popularity of pediatric RIRS. Although lower pole localization does not change SFR in single stones smaller than 2 cm, it is important because it affects factors such as prestenting rate, which will increase the number of anesthesia sessions, radiation exposure, and hospitalizations. The surgeons should inform the parents about this issue and plan the endourological procedure.

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Address correspondence to: *Muzaffer Tansel Kilinc, Department of Urology, Konya City Hospital, Konya, Türkiye*
e-mail: *m.tanselkilinc@gmail.com*

REFERENCES

1. Carmen Tong CM, Ellison JS, Tasian GE. Pediatric Stone Disease: Current Trends and Future Directions. Urol Clin North Am. 2023;50(3):465-75. doi: 10.1016/j.ucl.2023.04.009
2. Dwyer ME, Krambeck AE, Bergstralh EJ, et al. Temporal trends in incidence of kidney stones among children: A 25-year population based study. J Urol. 2012;188(1):247-52. doi: 10.1016/j.juro.2012.03.021
3. Servais A, Thomas K, Dello Strologo L, et al. Cystinuria: Clinical practice recommendation. Kidney Int. 2021;99(1):48-58. doi: 10.1016/j.kint.2020.06.035
4. Radmayr C, Bogaert G, Bujons A, et al. Guidelines Associates: Kennedy UK, Gnech M, Skott M, van Uitert A, Zachou A. Guidelines Office: Bezuidenhout C. Guidelines on Paediatric Urology 2024; ISBN 978-94-92671-23-3.
5. Sultan S, Aba Umer S, Ahmed B, et al. Update on Surgical Management of Pediatric Urolithiasis. Front Pediatr. 2019;7:252. doi: 10.3389/fped.2019.00252
6. Ishii H, Griffin S, Somani BK. Ureteroscopy for stone disease in the paediatric population: A systematic review. BJU Int. 2015;115(6):867-73. doi: 10.1111/bju.12927
7. He Q, Xiao K, Chen Y, et al. Which is the best treatment of pediatric upper urinary tract stones among extracorporeal shockwave lithotripsy, percutaneous nephrolithotomy and retrograde intrarenal surgery: A systematic review. BMC Urol. 2019;19(1):98. doi: 10.1186/s12894-019-0520-2
8. Halinski A, Steyaert H, Wojciech M, et al. Endourology Methods in Pediatric Population for Kidney Stones Located in Lower Calyx: FlexURS vs. Micro PCNL (MicroPERC®). Front Pediatr. 2021;9:640995. doi: 10.3389/fped.2021.640995
9. Quiroz Y, Somani BK, Tanidir Y, et al. Retrograde Intrarenal Surgery in Children: Evolution, Current Status, and Future Trends. J Endourol. 2022;36(12):1511-21. doi: 10.1089/end.2022.0160
10. Kilicarslan H, Kaynak Y, Kordan Y, et al. Unfavorable anatomical factors influencing the success of retrograde intrarenal surgery for lower pole renal calculi. Urol J. 2015;12(2):2065-68. doi: 10.22037/uj.v12i2.2730
11. Ozkent MS, Piskin MM, Balasar M, et al. Is Retrograde Intrarenal Surgery as Safe for Children as It Is for Adults? Urol Int. 2021;105(11-12):1039-45. doi: 10.1159/000517290
12. Kahraman O, Dogan HS, Asci A, et al. Factors associated with the stone-free status after retrograde intrarenal surgery in children. Int J Clin Pract. 2021;75(10):e14667. doi: 10.1111/ijcp.14667
13. Castellani D, Somani BK, Ferretti S, et al. Role of PreoperativeUreteral Stent on Outcomes of Retrograde Intra-Renal Surgery (RIRS) in Children. Results From a Comparative, Large, Multicenter Series. Urology. 2023;173:153-58. doi: 10.1016/j. urology.2022.11.019
14. Kumar A, Vasudeva P, Nanda B, et al. A Prospective Randomized Comparison Between Shock Wave Lithotripsy and Flexible Ureterorenoscopy for Lower Caliceal Stones ≤2 cm: A Single-Center Experience. J Endourol. 2015;29(5):575-79. doi: 10.1089/end.2013.0473
15. Juliebø-Jones P, Gauhar V, Lim EJ, et al. Outcomes and considerations for retrograde intrarenal surgery (RIRS) in the setting of multiple and large renal stones (>15 mm) in children: Findings from multicentre and real-world setting. BJUI Compass. 2024;5(6):558-63. doi: 10.1002/bco2.357
16. Cannon GM, Smaldone MC, Wu HY, et al. Ureteroscopic management of lower-pole stones in a pediatric population. J Endourol. 2007;21(10):1179-82. doi: 10.1089/end.2007.9911
17. Cohen J, Cohen S, Grasso M. Ureteropyeloscopic treatment of large, complex intrarenal and proximal ureteral calculi. BJU Int.2013;111(3 Pt B):E127-31. doi:10.1111j.1464-410X.2012.11352.x
18. Inoue T, Murota T, Okada S, et Influence of Pelvicaliceal Anatomy on Stone Clearance After Flexible Ureteroscopy and Holmium Laser Lithotripsy for Large Renal Stones. J Endourol. 2015;29(9):998-05. doi: 10.1089/end.2015.0071
19. Kaygısız O, Aydın YM, Turan L, et al. Factors Affecting Stone-freeness in the Initial Session of RIRS in Childhood Kidney Stones. J Urol Surg 2024;11(1):1-6. doi: 10.4274/jus.galenos.2023.2023.0005
20. Azili MN, Ozcan F, Tiryaki T. Retrograde intrarenal surgery for the treatment of renal stones in children: Factors influencing stone clearance and complications. J Pediatr Surg. 2014;49(7):1161-65. doi: 10.1016/j.jpedsurg.2013.12.023
21. Unsal A, Resorlu B. Retrograde intrarenal surgery in infants and preschool-age children. J Pediatr Surg. 2011;46(11):2195-99. doi: 10.1016/j.jpedsurg.2011.07.013
22. Kourmpetis V, Dekalo S, Levy N, et al. Toward Respiratory-Gated Retrograde Intrarenal Surgery: A Prospective Controlled Randomized Study. J Endourol. 2018;32(9):812-17. doi: 10.1089/end.2018.0231

23. Yuan Y, Liang YN, Li KF, et al. A meta-analysis: Retrograde intrarenal surgery vs. percutaneous nephrolithotomy in children. Front Pediatr. 2023;11:1086345. doi:10.3389/fped.2023.1086345

24. Berrettini A, Boeri L, Montanari E, et al. Retrograde intrarenal surgery using ureteral access sheaths is a safe and effective treatment for renal stones in children weighing <20 kg. J Pediatr Urol. 2018;14(1):59.e1-.e6. doi: 10.1016/j.jpurol.2017.09.011

25. Alzahrani MA, Alghuyaythat WKZ, Alsaadoon BMB, et al. Comparative efficacy of different surgical techniques for pediatric urolithiasis-a systematic review and meta-analysis. Transl Androl Urol. 2024;13(7):1127-44. doi: 10.21037/tau-23-676

26. Selvi I, Hajiyev P, Ekberli G, et al. The effects of primary and recurrent pediatric urological surgeries on parental anxiety levels. J Pediatr Urol. 2020;16(5):652.e1-.e9. doi: 10.1016/j.jpurol.2020.07.036

27. Yuruk E, Tuken M, Gonultas S, et al. Retrograde intrarenal surgery in the management of pediatric cystine stones. J Pediatr Urol. 2017;13(5):487.e1-.e5. doi: 10.1016/j.jpurol.2017.01.015

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OPEN ARAŞTIRMA MAKALESİ / RESEARCH ARTICLE

Factors Affecting the Prediction of Smoking Cessation Success in Patients Admitted to a Family Health Center

Aile Sağlığı Merkezine Başvuran Hastalarda Sigara Bırakma Başarı Öngörüsünü Etkileyen Faktörler

Aynur Yalcintas[1], Hatice Kucukceran[2]

[1]Karatay Family Health Center No. 09, Family Medicine, Konya, Türkiye
[2]Necmettin Erbakan University, Faculty of Medicine, Department of Family Medicine, Konya, Türkiye

ÖZET

Amaç: Sigara, neden olduğu hastalıklar ve ölümler nedeniyle önemli bir halk sağlığı sorunudur. Her klinik görüşmede sigara içme durumu sorgulanmalı ve sigara içen hastalara sigara bırakma önerilmelidir. Aile hekimleri, hastaların ilk temas noktası olmaları, bakımın sürekliliğini sağlamaları ve koruyucu sağlık hizmetlerine öncelik vermeleri nedeniyle tütün bağımlılığı ile mücadelede benzersiz bir konumdadır. Sunulan çalışmada aile sağlığı merkezine başvuran hastalarda sigara bırakma başarısının öngörülmesine etki eden faktörlerin araştırılması amaçlanmıştır.

Gereç ve Yöntemler: Tanımlayıcı tipteki çalışmanın evrenini Konya'nın Karatay ilçesine bağlı bir aile hekimliği birimine kayıtlı hastalar oluşturmaktadır. Gönüllülük esasına göre toplam 292 katılımcı tarafından doldurulan anket formlarının verileri analiz edildi. Anket formunda sosyo demografik özellikler, sigara kullanımı ile ilgili sorular, Fagerström Nikotin Bağımlılık Testi (FNBT) ve Sigara Bırakma Başarı Öngörüsü (SBBÖ) Ölçeği yer aldı.

Bulgular: Katılımcıların yaş ortalaması 33,11±12,42 (en düşük:18; en yüksek:72) yıl, %41,4'ü (n=121) yüksek derecede nikotin bağımlısı ve %57,5'ine (n=168) bir doktor tarafından sigarayı bırakmaları önerilmişti. SBBÖ Ölçeği toplam puan ortalaması 33,96±7,67 (en düşük:13; en yüksek:50) idi. Kadınlar, 45 yaş ve üzeri, evliler, çocuk sahibi olanlar, nikotin bağımlılığı düşük olanlar, daha önce sigarayı bırakmayı denemiş ve bir doktor tarafından sigarayı bırakması önerilmiş olan katılımcıların kendi kategorilerindeki ortalama puanları diğerlerine kıyasla istatistiksel olarak anlamlı derecede daha yüksekti (p<0,05). SBBÖ Ölçeği toplam puanı ile Fagerström Bağımlılık Testi toplam puanı arasında orta düzeyde negatif bir korelasyon bulunmuştur (r=-272; p=<0,001).

Sonuç: Katılımcıların sigara bırakma başarı öngörüsü puanları orta düzeyde bulunmuş olmasına rağmen, daha önce bir doktor tarafından bırakma tavsiyesi almış hastaların sigara bırakma başarısının daha yüksek olduğunun öngörülmesi önemli bir bulgudur. Sigara bırakma oranlarını artırmak için birinci basamak sağlık hizmetlerinin tütün kontrolünde aktif bir rol oynaması önemlidir.

Anahtar Kelimeler: Sigara bırakma, tütün bağımlılığı, birinci basamak hekimleri, aile hekimliği

ABSTRACT

Objective: Smoking status should be questioned in every clinical interview and smoking cessation should be recommended to patients who smoke. Family physicians are in a unique position in the fight against tobacco addiction because they are the first point of contact for patients, provide continuity of care and prioritise preventive health services. Our study aimed to investigate the factors affecting the prediction of smoking cessation success in patients applying to the family health centre.

Materials and Methods: Patients registered in the Family Medicine Department of Konya Karatay were the population of the descriptive study. The data of the questionnaire form completed by 292 participants on a voluntary basis were analyzed. The questionnaire included sociodemographic characteristics, questions about smoking, Fagerström Nicotine Dependence Test (FNDT) and Smoking Cessation Success Prediction Scale (SCSPS).

Results: The mean age of the participants was 33.11±12.42 (min:18; max:72) years, 41.4% (n=121) were highly nicotine dependent and 57.5% (n=168) had been advised to quit smoking by a doctor. The mean total score of the SCSPS was 33.96±7.67 (min:13; max:50). Participants who were female, aged 45 years or older, married, had children, had low nicotine dependence, had tried to quit smoking before and had been advised to quit smoking by a doctor had statistically significantly higher mean scores in their categories compared to others (p<0.05). A moderate negative correlation was found between the total score of the SCSPS and the Fagerström score (r=-272; p=<0.001).

Conclusion: Despite the moderate scores of the participants in predicting smoking cessation success, a significant finding indicates that patients who received prior medical advice to quit were more likely to achieve successful smoking cessation. It is important that primary health care services play an active role in tobacco control to increase smoking cessation rates.

Keywords: Smoking-cessation, tobacco dependence, primary care physicians, family practice

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Sorumlu Yazar/Corresponding Author: Aynur Yalcintas, Karatay Family Health Center No. 09, Family Medicine, Konya, Türkiye
e-mail: draynurerturk@hotmail.com

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INTRODUCTION

Tobacco addiction is the first cause of deaths from preventable diseases. Tobacco-related diseases kill more than 8 million people every year (1). According to projections for Turkey for the coming years, the prevalence of tobacco use is estimated to be 30.4%, 40.1% for men and 20.5% for women in 2025 (2). More than 60% of the world's 1.25 billion tobacco users (more than 750 million people) want to quit, but 70% do not have access to effective cessation services (3).

There is evidence showing that a timely intervention in tobacco addicts is effective in preventing tobacco-related diseases (4,5). More than 70% of smokers consult a physician for any reason every year and most of them report that they want to quit (6).

Family physicians, who provide primary health care services, are uniquely positioned to intervene in tobacco dependence due to their long-term relationships with patients and their role in disease prevention. In family health centres where preventive health services are a priority, helping a patient who smokes to quit smoking is the most effective intervention to reduce the risk of disease, disability and death. Evidence-based guidelines on the treatment of tobacco dependence also emphasize the important role of primary care physicians (7). It is recommended that physicians advise smokers to quit during routine examinations, advise and/or prescribe effective medications and refer them to smoking cessation centers (7,8).

Most smokers are aware of the harms of smoking and try to quit. However, many of them fail in quitting smoking. Professional help may be needed to reduce this failure (9). A person's own will, decision and willpower are the most important factors in the success of quitting smoking. The patient's desire to quit smoking can be achieved with the physician's advice to quit and motivational interview. Face-to-face discussions with doctors have been reported to double the quit rate (10). Other factors that are effective in the success of smoking cessation include gender, age, degree of addiction, psychological status, social support and presence of chronic diseases (11,12). Predicting patients with high quitting potential in primary care and directing them for professional help may contribute to more efficient use of health support and increase the success rates in smoking cessation centers. For these reasons, we aimed to investigate the factors that influence the prediction of smoking cessation success among patients attending family health centers.

MATERIALS AND METHODS

Type, location and population of the study

The population of the descriptive study consisted of 2276 people over 18 years of age registered in unit number 4222055 of the Konya Karatay Family Health Centre No: 09. Assuming a smoking prevalence of approximately 32%, the aim was to reach at least 292 people with a 95% confidence interval and 5% margin of error (13,14). Pregnant women, nursing mothers and the puerperium were excluded from the study. The study was explained to smokers over the age of 18 who presented to the outpatient clinic for any reason, and those who gave verbal consent, were literate and whose native language was Turkish were included in the study. The number of participants was reached in about one month (October 2024). The short information form prepared by the researchers, the Fagerström Nicotine Dependence Test (FNDT) and the Smoking Cessation Success Prediction Scale (SPSPS) were applied to the volunteer participants.

Information Form: The first part of this form, designed by the researchers, consists of socio-demographic information such as age, gender, education level, employment status, perceived income level, marital status and presence of chronic diseases. The second part includes information about smoking, such as the number of years of smoking, previous smoking cessation experience, status of receiving professional help, previous smoking cessation advice from a physician, etc.

Fagerström Nicotine Dependence Test (FNDT): The scale for measuring physical dependence on cigarettes was developed by Fagerström in 1989 (15). The Turkish study on the validity and reliability of the six-item scale was carried out by Uysal et al. in 2004 (16). The FNDT consists of six items and results in a score ranging from 0 to 10. A score below 6 points indicates low-moderate dependence, while a score of 6 points and above indicates severe dependence (16). In our study, Cronbach's Alpha coefficient was found to be 0.751.

Smoking Cessation Success Prediction Scale (SCSPS): It was developed by Aydemir et al. (11) in 2019. The scale is a five-point Likert type and consists of 10 items. The participants were expected to give the most appropriate answer to the questions scored as "Very Little", "Little", "Moderate", "A little bit" and "A lot". The scale has two sub-dimensions: "Determination and Readiness" and "Health Perception and Favorable Environment". The reliability of the scale, Cronbach's Alpha coefficient was found to be 0.782. The maximum score that can be obtained from the scale is 50 and the minimum score is 10. An increase in the scale score indicates that individuals will have a high prediction of success in smoking cessation (11). In our study, Cronbach's Alpha coefficient was found to be 0.830.

Ethical Permission of the Study: T.C. Necmettin Erbakan University Pharmaceuticals and Non-Medical Device Research Ethics Committee on 20.09.2024 with the board decision numbered 2024/5180.

Statistical Analysis

When the findings were obtained in our study were evaluated, 'SPSS (Statistical Package for Social Sciences) for Windows 20.0' was used for statistical analyses. Descriptive statistics were evaluated with number, percentage, mean and standard deviation. Chi-square test was used to compare categorical data. Normal distribution was assessed using the Kolmogorov-Smirnov test. Since quantitative data were normally distributed, Student-t test was used in binary groups and One-way Anova test was used in multiple groups. In cases where there was a difference between groups, significance was evaluated with Post-Hoc Tukey tests. $p<0.05$ was considered statistically significant. The relationships between the parameters were analyzed by Pearson correlation analysis. Correlation coefficient (r); 0.000-0.249 was considered as weak,

max:50). In the study, it was found that the mean scores of women were higher than men, those aged 45 years and over were higher than those younger, married people were higher than single people, and those with children were higher than those without children (p<0.05). In addition, participants with low nicotine dependence level, those who had tried to quit smoking before, and those who were advised by a physician to quit smoking had higher mean scores on the SCSPS than others within their categories and this difference was statistically significant (p<0.05). The comparison of the participants' socio-demographic and smoking-related characteristics with the SCSPS and its sub-dimensions is shown in Table 3.

The scores of the participants from the SCSPS and Fagerström test were evaluated by Pearson Correlation Analysis. A moderate negative correlation was found between the total score of the SCSPS and the Fagerström score (r=-0.272; p=<0.001).

DISCUSSION

Table 1. Distribution of Sociodemographic Characteristics of Participants

	n (%)
Gender	
Female	107 (36.6)
Male	185 (63.4)
Age	
Young adult (18-25 years)	49 (16.8)
Adult (26-44 years)	160 (54.8)
Middle age (45-59)	64 (21.9)
Elderly (60 years and over)	19 (6.5)
Education level	
Primary School	74 (25.3)
Middle School	91 (31.2)
High School	82 (28.1)
University	45 (15.4)
Employment status	
Working	176 (60.3)
Not working	116 (39.7)
Income status	
Income less than expenditure	67 (22.9)
Income matches expenditure	184 (63.0)
Income more than expenditure	41 (14.1)
Marital status	
Married	229 (78.4)
Single	63 (21.6)
Childbearing status	
There is	225 (77.1)
No	67 (22.9)
Number of children*	
A child	25 (11.1)
Two children	100 (44.4)
Three children and above	100 (44.4)
Presence of chronic disease	
There is	97 (33.2)
No	195 (66.8)
Total	292 (100)

*225 people responded.

Table 2. Distribution of Participants' Characteristics Regarding Smoking.

	n (%)
Duration of smoking (years)	
< 10 years	81 (27.7)
≥ 10 years	211 (72.3)
Amount of cigarette smoking (days/piece)	
< 10 pieces	93 (31.8)
≥ 10 pieces	199 (68.2)
Previous experience of quitting smoking	
Yes	161 (55.1)
No.	131 (44.9)
Previous professional support to quit smoking	
Yes	42 (14.4)
No.	250 (85.6)
Longest duration of smoking cessation*	
Less than 1 month	25 (15.5)
1 month to 1 year	119 (73.9)
More than 1 year	17 (10.6)
Previous recommendation to quit smoking by a physician	
Yes	168 (57.5)
No.	94 (32.2)
I don't remember	30 (10.3)
Nicotine dependence level (Fagerström score)	
Low-moderate dependency (<6 points)	171 (58.6)
High level of dependency (≥6 points)	121 (41.4)

*161 people responded.

0.250-0.499 as moderate, 0.500-0.749 as strong, 0.750-1.000 as very strong relationship.

RESULTS

The mean age of the 292 participants was 33.11±12.42 years (min:18; max:72) and 54.8% (n=160) were in the adult age group (26-44 years) according to the life cycle (17). 63.4% (n=185) of the participants were male, 15.4% (n=45) were university graduates, 60.3% (n=176) were employed, 63.0% (n=184) had equal income and expenses, 78.4% (n=229) were married and 44.4% (n=100) had two children. Of the 97 (33.2%) people with chronic diseases, 43.3% (n=42) had more than one chronic disease and 41.2% (n=39) had a lung-related disease. Table 1 shows the distribution of sociodemographic characteristics of the participants.

The median smoking duration of the participants was 12.5 (min: 0.5; max: 84) pack-years. There were 161 (55.1%) participants who had tried to quit smoking before and 42 (14.4%) had received professional support for smoking cessation. Of those who had previously tried to quit smoking, 10.6% (n=17) were able to quit smoking for more than one year and 57.5% (n=168) were advised to quit smoking by a physician. The mean Fagerström score of the participants was 4.42±2.9 (min:0; max:10) and 41.4% (n=121) had a high level of nicotine dependence. The distribution of the characteristics of the participants regarding smoking is shown in Table 2.

The mean score of the participants on the Smoking Cessation Success Prediction Scale was 33.96±7.67 (min:13;

Table 3. Comparison of Socio-Demographic and Smoking Characteristics of the Participants and Smoking Cessation Success Prediction Scale and Its Subscales

	Total score of SCSPS	Stability and readiness subscale score	Health perception and appropriate environment subscale score
	Mean±SD	Mean±SD	Mean±SD
Gender			
Female	35.28±7.45	19.76±4.39	15.51±3.68
Male	33.21±7.71	18.80±5.02	14.40±3.31
p*	0.026	0.101	0.009
Age			
18-25 yearsa	33.73±6.92	19.04±3.85	14.69±3.58
26-44 yearsb	33.03±7.96	18.66±5.03	14.37±3.65
45 years and overc	35.90±7.22	20.18±4.80	15.72±2.93
p**	0.016[bc]	0.065	0.012[bc]
Education level			
Secondary school and below	34.27±7.55	19.46±4.84	14.81
High School	32.82±8.13	18.32±4.88	14.50
University	34.93±7.12	19.55±4.52	15.37
p**	0.250	0.185	0.401
Employment status			
Working	33.41±8.05	18.94±5.20	14.47±3.54
Not working	34.81±6.99	19.48±4.16	15.32±3.36
p*	0.128	0.350	0.040
Income status			
Income less than expenditure	33.53±8.86	18.67±5.66	14.86±4.01
Income matches expenditure	33.86±7.22	19.07±4.46	14.78±3.33
Income more than expenditure	35.14±7.59	20.31±4.77	14.82±3.36
p**	0.547	0.212	0.987
Marital status			
Married	34.55±7.62	19.47±4.82	15.07±3.46
Single	31.85±7.54	18.00±4.65	13.85±3.43
p*	0.013	0.031	0.014
Childbearing status			
There is	34.51±7.45	19.48±4.70	15.03±3.39
No	32.13±8.16	18.05±5.06	14.07±3.73
p*	0.025	0.033	0.049
Number of children*			
A child	35.52±6.60	20.20±3.92	15.32±3.18
Two children	35.43±6.87	19.99±4.25	15.44±3.11
Three children and above	33.35±8.08	18.80±5.23	14.55±3.66
p**	0.110	0.146	0.162
Presence of chronic disease			
There is	35.80±7.71	18.65±4.60	15.63±3.32
No	33.05±7.50	20.16±5.04	14.40±3.50
p*	0.004	0.120	0.004
Duration of smoking			
< 10 years	33.86±8.31	19.17±4.79	14.69±3.90
≥ 10 years	34.00±7.42	19.15±4.83	14.85±3.32
p*	0.885	0.973	0.716
Amount of cigarette smoking			
< 10 pcs/day	36.61±7.81	20.97±4.83	15.63±3.54
≥ 10 pcs/day	32.73±7.30	18.30±4.57	14.42±3.40
p*	<0.001	<0.001	0.006
Previous experience of quitting smoking			
Yes	36.55±6.93	20.69±4.56	15.85±3.05
No.	30.79±7.35	17.26±4.45	13.52±3.57
p*	<0.001	<0,001	<0.001
Previous professional support to quit smoking			
Yes	35.64±7.75	20.02±5.13	15.61±3.39
No.	33.68±7.63	19.01±4.75	14.67±3.49
p*	0.127	0.209	0.105
Longest period of smoking cessation			
Less than 1 monthd	33.24±6.39	18.64±4.68 14.60±3.25	
1 month to 1 yeare	37.10±6.56	20.98±4.33 16.12±2.81	
More than 1 yearf	37.52±9.00	21.70±5.28 15.82±4.05	
p**	0.029[de]	0.050[de]	0.076
Previous recommendation to quit smoking by a physician			
Yesg	35.29±7.05	19.72±4.72	15.56±2.94
No.h	32.75±8.15	18.87±4.80	13.88±4.01
I don't rememberı	30.36±7.90	16.86±4.77	13.50±3.49
p**	0.025[gh] 0.003[gı]	0,007gı	<0.001gh 0.007[gı]
Nicotine dependence level (Fagerström score)			
Low-moderate dependency (<6 points)	35.38±7.77	20.19±4.83	15.18±3.67
High level of dependency (≥6 points)	31.96±7.08	17,68±4,41	14.28±3.15
p**	<0.001	<0.001	0.029

*Student T test was used ** One-Way ANOVA test was applied. When there was significance in the One-WayAnova test, significance was evaluated with the post hocTukey test.
pxy = significant between x and y options
SCSPS: Smoking Cessation Success Prediction scale

This study, in which the prediction of smoking cessation success of patients who applied to a family health center for any reason was examined with a measurement tool with proven validity and reliability, is important because it is one of the rare studies conducted in primary care.

Factors affecting smoking cessation success in our study were gender, age, marital status, having children, nicotine dependence level, having tried to quit smoking before and receiving smoking cessation advice from a physician.

There are different results in the literature regarding the

effect of gender on smoking cessation success. While some studies reported that men could quit smoking more easily, some studies showed that there was no difference according to gender (18,19,20). In our study, it is predicted that women may quit smoking more easily than men. This is only a prediction and in other studies, smoking cessation for at least one year in smoking cessation outpatient clinics is considered as success (18,19,20). Successful smoking cessation rates between men and women may vary according to the sociocultural environment and the time and place of the study (21).

Age is an effective factor in smoking cessation success. Previous studies have also shown that success in smoking cessation is directly proportional to age (21,22,23). Since the duration of smoking increases with age, the fact that the patient starts to feel the negative effects of smoking more especially after the age of 45 may be a source of motivation to quit smoking.

A physician's advice to quit smoking increases the success of smoking cessation (10,24). In our study, approximately six out of every 10 people remembered having been advised by a physician to quit smoking and it is predicted that those who received advice would have a higher quit success rate. In the tobacco dependence treatment guideline, it is a strong recommendation that healthcare professionals should give brief tobacco control advice ranging from 30 seconds to 3 minutes while providing any healthcare service (3). Therefore, it is a remarkable result that there were missed opportunities for some patients.

In our study, approximately 15% of the patients stated that they received professional help for smoking cessation. Öztürk et al. also found that 15% of research assistant physicians received professional help to quit smoking (25). According to WHO data, more than 60% of tobacco users want to quit, but 70% cannot access effective cessation services (3). We think that family physicians informing their patients about smoking cessation centers and identifying and directing patients who are likely to quit will increase the success rates in smoking cessation centers.

In our study, it was determined that the prediction of smoking cessation success of patients applying to the Family Health Center did not show a significant difference according to education level, employment status, income status, number of children, duration of smoking, status of receiving professional support to quit smoking before and presence of chronic disease. There are studies in the literature showing that smoking cessation success is not affected by education (20,26). Regarding the effect of chronic disease status on smoking cessation success, there are studies showing that those with chronic disease quit smoking more easily and their success is high (27,28), as well as studies showing that it has no effect (26,29). In support of our study, there are studies showing that smoking cessation success is not affected by smoking duration (30,31). Smoking cessation success is affected by many factors and the reason for the difference in study results may be due to the fact that they were conducted in different populations and in different places.

In our study, it was predicted that smoking cessation success would decrease as the level of nicotine dependence increased. In the literature, there are studies that support this result (32,33), as well as studies that found that smoking cessation success was not affected by the level of addiction (12,31).

There are studies similiar to ours and they were studied with different groups like COVID infections (34,35), like chronic lung disease (36,37), like pregnant women (38) and at Smoking Cessation Clinic (39). All these studies show that motivational interviewing is very effective on quitting smoking.

The limitation of our study is that it was conducted in a single family medicine unit and it is recommended that it be conducted in different regions and in larger sample groups in order to generalize it to the population. In addition, investigating the actual success rates of patients who are predicted to have high smoking cessation success after receiving professional support will support the scale to be more recommended in primary care practice.

CONCLUSION

The results of our study showed that the smoking cessation success prediction scores of patients who applied to the primary care center were at an intermediate level, but predicted that patients who were previously advised to quit by a physician would have a higher smoking cessation success. Combating tobacco addiction is a serious public health problem that many stakeholders should act together. Among these stakeholders, family physicians, who are in the group of healthcare professionals, have an important place in the fight against tobacco addiction as they are the first point of contact with the patient and provide continuous care. Determining the addiction level and smoking cessation success prediction of a patient who applies to primary care and smokes will both encourage the patient to quit and provide an opportunity to receive professional help. It is recommended that more studies should be conducted on combating tobacco addiction in primary care and family physicians should take a more active role in the fight against tobacco.

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Address correspondence to: *Aynur Yalcindag, Necmettin Erbakan University, Faculty of Medicine, Department of Family Medicine, Konya, Türkiye*
e-mail: *draynurerturk@hotmail.com*

REFERENCES

1. World Health Organization. Tobacco. [19.11.2024]. Available from: https://www.who.int/health-topics/tobacco#tab=tab_1
2. World Health Organization. Estimate of current tobacco use prevalence. [20.11.2024]. Available from: https://www.who.int/

data/gho/data/themes/topics/sdg-target-3_a-tobacco-control
3. World Health Organization. Releases first-ever clinical treatment guideline for tobacco cessation in adults. [19.11.2024]. Available from: https://www.who.int/news/item/02-07-2024-who-releases-first-ever-clinical-treatment-guideline-for-tobacco-cessation-in-adults
4. Critchley J, Capewell S. Smoking cessation for the secondary prevention of coronary heart disease. Cochrane Database Syst Rev. 2004;(1):CD003041. doi: 10.1002/14651858.
5. Matulewicz RS, Sherman S, Bjurlin MA. Smoking Cessation and Cancer Survivorship. JAMA. 2020;13;324(14):1475. doi: 10.1001/jama.2020.16277.
6. Clinical Practice Guideline Treating Tobacco Use and Dependence 2008 Update Panel, Liaisons, and Staff. A clinical practice guideline for treating tobacco use and dependence: 2008 update. A U.S. Public Health Service report. Am J Prev Med. 2008;35(2):158-76. doi: 10.1016/j.amepre.2008.04.009.
7. Verbiest M, Brakema E, Van der Kleij R, et al. National guidelines for smoking cessation in primary care: A literature review and evidence analysis. NPJ Prim Care Respir Med. 2017;20;27(1):2. doi: 10.1038/s41533-016-0004-8.
8. West R, McNeill A, Raw M. Smoking cessation guidelines for health professionals: An update. Health Education Authority. Thorax. 2000;55(12):987-99. doi: 10.1136/thorax.55.12.987.
9. Bardak F, Demir İ, Dinar C, et al. Farklı Değişim Aşamalarına Göre, Sigara İçme Davranışı ve Psikolojik Değişkenler Arasındaki İlişkinin İncelenmesi. Bağımlılık Dergisi. 2016;17(4):152-63.
10. Fidan F, Pala E, Ünlü M, et al. Sigara bırakmayı etkileyen faktörler ve uygulanan tedavilerin başarı oranları. Kocatepe Tıp Dergisi. 2005;6(3):27-34.
11. Aydemir Y, Doğu Ö, Dede C, et al. Sigara Bırakma Başarısı Öngörü Ölçeği: Geliştirme ve Geçerlik, Güvenirlik Çalışması. Addicta: The Turkish Journal on Addictions. 2019;6(2): 387-402. doi:10.15805/addicta.2019.6.2.0022
12. Berkeşoğlu Ç, Özgür ES, Demir AU. Sigara bırakma başarısını etkileyen faktörler. Mersin Üniversitesi Sağlık Bilimleri Dergisi. 2018;11(3):355-65. doi:10.26559/mersinsbd.473902
13. Tütün Kontrolü Strateji Belgesi ve Eylem Planı 2018-2023. [25.11.2024]. Available from: https://ika.org.tr/assets/upload/dosyalar/tutun-kontrolu-strateji-belgesi-ve-eylem-plani2018-2023.pdf
14. Sample Size Calculator Find Out The Sample Size. [25.11.2024]. Available from: https://www.calculator.net/sample-size-calculator.html?type=1&cl=95&ci=5&pp=32&ps=2276&x=Calculate
15. Fagerstrom KO, Schneider NG. Measuring nicotine dependence: a review of the Fagerstrom Tolerance Questionnaire. J Behav Med. 1989;12(2):159-82. doi: 10.1007/BF00846549.
16. Uysal MA, Kadakal F, Karşıdağ Ç, et al. Fagerstrom test for nicotine dependence: Reliability in a Turkish sample and factor analysis. Tuberk Toraks. 2004;(52):115-21.
17. Peng Y, Zhu Q, Wang B, et al. A cross-sectional study on interference control: age affects reactive control but not proactive control. PeerJ. 2020;(27);8:e8365. doi: 10.7717/peerj.8365.
18. Demir T, Tutluoğlu B, Koç N, et al. Sigara bırakma polikliniğimizin bir yıllık izlem sonuçları. Tüberküloz ve Toraks Dergisi 2004;(52):63-8.
19. Renaud JM, Halpern MT. Clinical management of smoking cessation: Patient factors affecting a reward-based approach. Patient Prefer Adherence. 2010;10(4):441-50. doi: 10.2147/PPA.S8913.
20. Salepçi B, Fidan A, Oruç Ö, et al. Sigara bırakma polikliniğimizde başarı oranları ve başarıda etkili faktörler. Tur Toraks Derg. 2005;(6):151-8.
21. Luu NM, Tran TTH, Luong NK, et al. Smoking Cessation, Quit Attempts and Predictive Factors among Vietnamese Adults in 2020. Asian Pac J Cancer Prev. 2023;1;24(5):1701-10. doi: 10.31557/APJCP.2023.24.5.1701.
22. Asi E, Gözüm S. Tütün Ürünlerine Yönelik Oluşturulan Politikalara Verilen Tepkiler ve Türkiye'deki Karşılığı. Anadolu Hemşirelik ve Sağlık Bilimleri Dergisi. 2020;23(2):319-30. doi: 10.17049/ataunihem.616471.
23. Kutluk T. Tütün Kontrolü müdahalelerin Etkin Uygulanması: Ulusal ve Uluslararası Tütün Kontrol Programları. Erdöl C, Ergüder T, editörler. Tütün ve Tütün Ürünlerinin Kullanımının Önlenmesi, Kontrolü ve Tedavisi. 1. Baskı. Ankara: Sağlık Bilimleri Üniversitesi Yayınları. 2021;61-8.
24. Bozkurt N, Bozkurt Aİ, Erdoğan A. Sigara bırakma/bıraktırmada en önemli sorun ne? Akd Med J. 2020;6(3):430-8. doi: 10.17954/amj.2020.2373
25. Ozturk O, Ozturk G, Yazicioglu B, et al. Smoking frequency, cessation knowledge; attitudes and beliefs among internal and surgery residents. J Exp Clin Med. 2015; 32(4): 171-5. doi: 10.5835/jecm.omu.32.04.006
26. Argüder E, Karalezli A, Hezer H, et al. Sigara bırakma başarısını etkileyen faktörler. Türk Toraks Dergisi. 2013;14(3):81-7. doi: 10.5152/ttd.2013.18
27. De Lemos JA, Blazing MA, Wiviott SD, et al. Early intensive vs a delayed conservative simvastatin strategy in patients with acute coronary syndromes: phase Z of the A to Z trial. JAMA. 2004;15;292(11):1307-16. doi: 10.1001/jama.292.11.1307
28. Ezzati M, Henley SJ, Lopez AD, et al. Role of smoking in global and regional cancer epidemiology: current patterns and data needs. Int J Cancer. 2005;10;116(6):963-71. doi: 10.1002/ijc.21100.
29. Önen ZP, Şen E, Gülbay BE, et al. Kardiyopulmoner hastalığı olanlarda sigaranın bırakılması. Anatolian Journal of Cardiology / Anadolu Kardiyoloji Dergisi. 2011;11(3).
30. Altın AÖ. Sigara Bırakma Polikliniğine Başvuran Hastalarda Sigara Bırakma Başarısını Etkileyen Faktörlerin Saptanması. İzmir. (dissertation). T.C. Dokuz Eylül Üniversitesi Tıp Fakültesi; 2019
31. Hoş B. Sigara Bırakma Polikliniği'ne Başvuran Hastaların Sigara Bırakma Başarı Öngörülerinin Belirlenmesi. İstanbul. (dissertation). T.C. Sağlık Bakanlığı Sağlık Bilimleri Üniversitesi Hamidiye Uluslararası Tıp Fakültesi Kartal Dr. Lütfi Kırdar Şehir Hastanesi;2021
32. Breslau N, Peterson EL. Smoking cessation in young adults: Age at initiation of cigarette smoking and other suspected influences. Am J Public Health. 1996;86(2):214-20. doi: 10.2105/ajph.86.2.214.
33. Kanatsız B, Başlılar Ş, Şaylan B, et al. Sigara Bırakma Başarısını Etkileyen Faktörler ve Medikal Tedavilerin Değerlendirilmesi. Euras J Fam Med. 2017;6(2):65-71.
34. Ergüden B, Aslan Y. Covıd-19 Pandemisinin Yetişkin Bireylerde Sigara Bırakma Başarı Öngörüsü Üzerindeki Etkisinin Değerlendirilmesi. İnönü Üniversitesi Sağlık Hizmetleri Meslek Yüksekokulu Dergisi. 2024;12(1):118-34. doi: 10.33715/inonusaglik.1378070
35. Kaya F, Tiryaki D, H, Selçuk E, B, et al. COVID-19 Pandemic and Motivation to Smoking Cessation Journal of MTU. 2024;3(1):14-21. doi: 10.58651/jomtu.1446249
36. Bardakcı M, I, Sumerkan M, Albayrak Ayhan G, et al. Comparison of Smoking Cessation Outcomes in Smokers With Chronic Obstructive Pulmonary Disease, Coronary Artery Disease, Asthma, and Healthy Smokers: A Prospective Study of 400 Participants.

Cureus 2024;16(12): e75095. doi:10.7759/cureus.75095
37. Fan M, Fang Y, J, Chen J, et al. Investigation of Smoking Cessation Status and Its Influencing Factors in Patients with Chronic Obstructive Pulmonary Disease. International Journal of Chronic Obstructive Pulmonary Disease 2024;(19):2763–73 doi:10.2147/ COPD.5482234
38. Mitta K, Tsakiridis I, Drizou S, et al. Smoking Status in Pregnancy: A Retrospective Analysis in Northern Greece. J. Clin. Med. 2025; (14); 431. doi:10.3390/ jcm14020431
39. Öztürk O, Yavuz E, Özdemir M, et al. Bir Aile Sağlığı Merkezi Bünyesinde Kurulan Sigara Bıraktırma Kliniğine Müracaat Eden Bireylerin Analizi. Bağımlılık Dergisi, 2023; 24(4):507-13 doi: 10.51982/bagimli.1264049

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ARAŞTIRMA MAKALESİ / RESEARCH ARTICLE

Comparison of Patients Undergoing Stripping, Endovenous Laser Ablation and Radiofrequency Ablation for Chronic Venous Insufficiency

Kronik Venöz Yetmezlikte Stripping, Endovenöz Lazer Ablasyon ve Radyofrekans Ablasyon Uygulanan Hastaların Karşılaştırılması

Abdullah Guner[1], Volkan Burak Taban[2], Serkan Yildirim[3], Yalcin Gunerhan[3], Yuksel Dereli[3]

[1]Konya City Hospital, Department of Cardıovascular Surgery, Konya, Türkiye
[2]Şırnak State Hospital, Cardiovascular Surgery, Şırnak, Türkiye
[3]Necmettin Erbakan University, Meram Faculty of Medicine, Department of Cardıovascular Surgery, Konya, Türkiye

ÖZET

Amaç: Alt ekstremitelerdeki kronik venöz yetmezlik (KVY) için çeşitli tedavi yöntemleri bulunmaktadır. Bu çalışmada, KVY tedavisi için uygulanan stripping, radyofrekans ablasyon (RFA) ve endovenöz lazer ablasyon (EVLA) yöntemlerini, postoperatif birinci yıldaki nüks, derin ven trombozu (DVT) ve flebit komplikasyonları açısından karşılaştırmayı amaçladık.

Gereç ve Yöntemler: Kliniğimize 2018 ile 2023 yılları arasında başvuran, vena saphena magna (VSM) çapı 5,5 mm üzerinde ve reflü süresi 0,5 sn üzerinde olan ve bu hastalara stripping, RFA veya EVLA uygulanan 442 hasta retrospektif olarak çalışmaya dahil edildi. Hastaların, postoperatif birinci yıldaki renkli doppler ultrasonografi (RDUSG) sonuçları incelendi. Daha önce KVY nedeniyle operasyon geçirmiş veya DVT öyküsü olan, 18 yaş altı, hamile ve/veya emziren hastalar ile periferik vasküler hastalık semptomları olan hastalar çalışmadan hariç tutuldu.

Bulgular: Çalışmaya dahil edilen hastaların ortalama yaşı 46±12.3 yıl olup, bunların 266'sı (%60.2) kadın ve 176'sı ise (%39.8) erkek cinsiyetteydi. Çalışmaya dahil edilen 143 hastaya stripping prosedürü, 179 hastaya RFA ve 120 hastaya EVLA işlemi uygulandı. Endovenöz lazer ablasyon uygulanan hastalarda flebit ve DVT insidansı daha yüksek bulunmasına rağmen, bu fark istatistiksel olarak anlamlı değildi (sırasıyla p=0.166, 0.252). Postoperatif 1. yılda operasyon tipine göre RDUSG'de saptanan nüks analizi yapıldığında, RFA ve EVLA arasında istatistiksel olarak anlamlı bir fark bulunmazken, stripping prosedüründe RFA ve EVLA'ya kıyasla istatistiksel olarak daha düşük nüks oranı gözlendi (sırasıyla p=0.035, 0.002).

Sonuç: Bu çalışma, prosedürler arasında DVT oranlarında anlamlı farklılıklar bulmamıştır, ancak sonuçlar, stripping işleminin bir yıl sonra RFA ve EVLA'ya kıyasla daha düşük flebit oranlarına ve önemli ölçüde daha az rekürrenslere sahip olduğunu ortaya koymaktadır.

Anahtar Kelimeler: Kronik venöz yetmezlik Stripping, Endovenöz lazer ablasyon, EVLA, Radyofrekans ablasyon, RFA

ABSTRACT

Objective: Chronic venous insufficiency (CVI) of the lower limbs is managed with various treatment options. This study aimed to compare the outcomes of stripping, radiofrequency ablation (RFA), and endovenous laser ablation (EVLA) regarding recurrence, deep vein thrombosis (DVT), and phlebitis within the first postoperative year.

Materials and Methods: We retrospectively analyzed 442 patients treated between 2018 and 2023, all presenting with a vena saphena magna (VSM) diameter exceeding 5.5 mm and reflux time over 0.5 seconds. Patients underwent either stripping, RFA, or EVLA. Postoperative outcomes were evaluated using color Doppler ultrasound (CDUSG).

Results: The average age of participants was 46 ± 12.3 years, with 266 (60.2%) females and 176 (39.8%) males. The number of patients per procedure was as follows: 143 for stripping, 179 for RFA, and 120 for EVLA. While phlebitis and DVT were more frequent in the EVLA group, the differences were not statistically significant (p=0.166 for phlebitis, p=0.252 for DVT). However, recurrence rates at one year showed that stripping resulted in significantly fewer recurrences than RFA and EVLA (p=0.035 and p=0.002, respectively).

Conclusion: This study did not find significant differences in DVT rates among the procedures, but the results reveal that stripping had lower phlebitis rates and significantly fewer recurrences compared to RFA and EVLA after one year.

Keywords: Chronic venous insufficiency, Stripping, Endovenous laser ablation, EVLA, Radiofrequency ablation RFA

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Sorumlu Yazar/Corresponding Author: Abdullah Guner, Konya City Hospital, Department of Cardıovascular Surgery, Konya, Türkiye
e-mail: guner_426@hotmail.com

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INTRODUCTION

Chronic venous insufficiency (CVI) primarily affects the veins in the lower extremities, manifesting through a range of clinical symptoms. These symptoms can either present as cosmetic concerns or progress into serious conditions like venous ulceration (1). Varicose veins, a common sign of CVI, increase with age and are found in approximately 9% of men and 6% of women (2). Vena saphena magna (VSM) insufficiency is the most frequent venous reflux, affecting about 70% of CVI patients (3). CVI prevalence varies widely, ranging from 1% to 40% in women and 1% to 27% in men (4). This variance often stems from inadequate detection and assessment of venous insufficiency signs (5).

Several risk factors contribute to CVI, including age, family history of venous insufficiency, pregnancy, obesity, smoking, and prior history of deep vein thrombosis (DVT) (6, 7). The Clinical Etiological Anatomical Pathophysiological (CEAP) classification system is widely used for the standardized assessment and classification of CVI (8).

Treatment options for CVI include conservative approaches, along with more traditional methods like ligation and stripping, which have been extensively used over time. However, recent technological advancements have introduced catheter-based treatments such as radiofrequency ablation (RFA) and endovenous laser ablation (EVLA), which offer quicker recovery times, improved cosmetic results, and increased patient comfort. Despite these benefits, each treatment should be evaluated in terms of its potential complications and outcomes in clinical practice. For instance, a 2019 study reported a case where a guidewire migrated within the saphenous vein following an RFA procedure, necessitating a hybrid treatment (9). Given these advantages and risks, this study aims to compare the effectiveness of stripping, EVLA, and RFA treatments, along with their associated complications and VSM-related recurrences, evaluated through color Doppler ultrasonography (CDUSG) after one year.

MATERIALS AND METHODS

Patients treated at Necmettin Erbakan University Cardiovascular Surgery Clinic from 2018 to 2023, diagnosed with chronic venous insufficiency and presenting with a vena saphena magna (VSM) diameter greater than 5.5 mm and a reflux time over 0.5 seconds, were included if they underwent elective surgery and were assessed using lower extremity color Doppler ultrasonography (CDUSG) within the first postoperative year. Exclusion criteria included pregnancy, breastfeeding, age under 18, insufficient follow-up data, or a history of symptomatic peripheral artery disease, deep vein thrombosis (DVT), or pulmonary embolism.

Data from 442 patients were retrospectively analyzed and divided into three groups based on the procedure: RFA (n=179), EVLA (n=120), and stripping (n=143). Demographic information, preoperative CEAP classification (Table 1), VSM diameter, reflux duration, and recurrence of VSM-related varices were assessed at the first postoperative year using CDUSG. Additionally, DVT status on the treated limb was recorded.

The study received ethical approval from the Ethics Committee (Approval Date: 05.07.2024, No: 2024/5061), and informed consent was obtained from all patients in accordance with the Declaration of Helsinki.

Procedures

For RFA and EVLA, tumescent anesthesia was prepared with 1 liter of isotonic NaCl solution, mixed with 2% lidocaine (50 ml), 10 mEq $NaHCO_3$, and 1 ml of 1:1000 adrenaline, cooled to +4ºC.

Stripping: Under general anesthesia, the VSM was located and exposed via a 2 cm incision near the ankle. A 3 cm incision was made in the inguinal region, and the VSM branches were ligated. Stripping was then performed using a stripper.

Radiofrequency Ablation (RFA): With Doppler guidance, VSM was punctured medial to the knee, and a 7F sheath was inserted (ClosureFast [Medtronic Inc, Minneapolis, MN]). A fiber catheter was advanced to 1 cm from the sapheno-femoral junction, and tumescent anesthesia was applied around the VSM. Ablation was done by delivering 10-40 watts of power at 120°C for 10 seconds, with 7 cm between treated segments.

Endovenous Laser Ablation (EVLA): Under Doppler guidance, VSM was punctured medial to the knee, and the fiber catheter was positioned 1 cm from the sapheno-femoral junction. Following tumescent anesthesia, 1470 nm wavelength, energy was applied at 12 watts (8 sec/cm) per vascular segment, with a mean energy of 100 joules.

For all procedures, prominent varicose veins were marked and excised. Parva ligation was performed via a 3 cm incision in the popliteal fossa, with the vena saphena parva located 1.5-2 cm distal to the junction and double ligated. Post-procedurally, VSM closure, deep femoral vein, and sapheno-femoral junction patency were confirmed with CDUSG. Compression therapy with 20-30 mmHg stockings was recommended for 90 days.

Statistical Analysis

Statistical evaluations were carried out using SPSS software (version 26.0, SPSS Inc., Chicago, IL, USA). Continuous data were expressed as means with standard deviations (SD), while categorical variables were presented as frequencies and percentages. To compare qualitative data, Pearson's chi-square test and Fisher's exact test were applied. A p-value of less than 0.05 was considered statistically significant. Fisher's exact post-hoc test was used to further analyze significant group differences.

RESULTS

The average age of the 442 patients in the study was 46±12.3 years. Among them, 266 (60.2%) were female and 176 (39.8%) were male. In terms of treatment distribution, 143 patients underwent stripping, 179 had RFA, and 120 received EVLA. Most patients in the stripping, RFA, and EVLA groups were classified as stage C3 according to the CEAP clinical system (42.65%, 42.50%, and 40.23%, respectively) (Table 2).

Patient characteristics by procedure type, including limb treated and additional pane/parva ligation (Table 3). One-year recurrence rates for DVT, phlebitis, and VSM-associated varicose

Table 1. CEAP clinical classification (8)

Clinical stage		Clinical Status
C0		No visible or palpable signs of venous disease
C1		Telangiectasia or reticular veins
C2		Varicose veins
	C2r	Recurrent varicose veins
C3		Edema
C4		Changes in skin and subcutaneous tissue due to CVI
	C4a	Pigmentation or eczema
	C4b	Lipodermatosclerosis or white atrophy
	C4c	Corona filebectatica
C5		Healed ulcer
C6		Active venous ulcer
	C6r	Recurrent venous ulcer

CVI= Chronic Venous Insufficiency

Table 2. CEAP classification and preoperative VSM diameters of the patients

	RFA, n (%)	EVLA, n (%)	Stripping n (%)
C2	62 (34,64)	28 (23,34)	29 (20,29)
C3	72 (40,23)	51 (42,50)	61 (42,65)
C4	41 (22,90)	33 (27,50)	41 (28,67)
C5	4 (2,23)	8 (6,66)	12 (8,39)
Total Number of Patients	179	120	143
VSM mean diameter, SD(mm)	9,12±3,16	8,96±2,76	8,73±2,54

n=Number of patients, SD=standard deviation, RFA=Radiofrequency Ablation, EVLA=Endovenous Laser Ablation, VSM=Vena Saphena Magna

Table 3. Descriptive data by patient groups

		RFA, n (%)	EVLA, n (%)	Stripping, n (%)
Processed Party	Right	64 (%35,8)	31 (%25,8)	54 (%37,8)
	Left	57 (%31,8)	48 (%40,0)	48 (%33,6)
	Bilateral	58 (%32,4)	41 (%34,2)	41 (%28,7)
Pache Excision Status	Positive	133 (%74,3)	73 (%60,8)	130 (%90,9)
	Negative	46 (%25,7)	47 (39,2)	13 (%9,1)
Parva Ligation Status	Positive	12 (%6,7)	5 (%4,2)	10 (%7)
	Negative	167 (%93,3)	115 (%95,8)	133 (%93)

n=Number of patients, RFA=Radiofrequency Ablation, EVLA=Endovenous Laser Ablation

Table 4. Recurrence percentages of patients according to the type of surgery

		RFA, n (%)	EVLA, n (%)	Stripping, n (%)	p*
Recurrence	Positive	15 (%8,4)	15 (%12,5)	4 (%2,8)	0,012
	Negative	164 (%91,6)	105 (87,5)	139 (%97,2)	
Phlebitis	Positive	1 (%0,6)	4 (%3,3)	2 (%1,4)	0,166
	Negative	178 (%99,4)	116 (%96,7)	141 (%98,6)	
DVT	Positive	1 (%0,6)	2 (%1,7)	0 (%0)	0,252
	Negative	178 (%99,4)	118 (%98,3)	143 (%100)	

*=Chi Square, RFA= Radiofrequency Ablation, EVLA=Endovenous Laser Ablation, DVT=Deep Vein Thrombosis

Table 5. Pairwise comparisons according to the procedures performed on the patients

	Recurrence Positive	Recurrence Negative	Total Recurrence Positive	Total Recurrence Negative	p*
RFA vs	15 (%8,4)	164 (%91,6)			
EVLA	15 (%12,5)	105 (87,5)	30 (%10)	269 (%90)	0,245
EVLA vs	15 (%12,5)	105 (87,5)			
Stripping	4 (%2,8)	139 (%97,2)	19 (%7,2)	244 (%92,8)	0,002
RFA vs	15 (%8,4)	164 (%91,6)			
Stripping	4 (%2,8)	139 (%97,2)	19 (%5,9)	303 (%94,1)	0,035

*=Chi Square post-hoc, RFA= Radiofrequency Ablation, EVLA=Endovenous Laser Ablation

veins, as evaluated by CDUSG (Table 4). Although phlebitis and DVT rates were higher in the EVLA group, the differences were not statistically significant (p=0.166 and p=0.252, respectively).

Cross-tab analyses revealed no significant recurrence rate differences between RFA and EVLA, while the stripping method showed statistically lower recurrence rates (Table 5).

DISCUSSION

There are several treatment options for CVI, and both patient preferences and disease severity play crucial roles in choosing the appropriate method. Among these options, catheter-based treatments and surgical stripping are widely used today. Recent trends have shown a shift towards catheter-based procedures in CVI treatment. In our study, we compared catheter-based treatments (RFA, EVLA) with surgical stripping.

Dermody et al. (10) conducted a meta-analysis of 17 randomized control trials involving approximately 2,300 participants. The average age was 47.5 years, and around 70% of the cohort were female. No significant differences were found in DVT incidence between patients who underwent stripping, RFA, or EVLA, with rates of 0.4%, 0.5%, and 0.7%, respectively. Phlebitis rates were significantly lower in the stripping group compared to RFA and EVLA (3%, 5.5%, and 5.6%, respectively, p=0.003). Similarly, in our study, the mean age was 46 years, with around 60% female participants. Our results also showed no significant differences in postoperative DVT rates among the three groups. Although our postoperative phlebitis rates for stripping, RFA, and EVLA were lower than those in Dermody's study (1.4%, 0.6%, and 3.3%, p=0.166), these differences were not statistically significant. We believe this discrepancy may be due to the smaller patient population in our study.

Rajendran, S. et al. (11) found that 55% of patients had preoperative CEAP clinical stage scores of C2 and C3, while 11% were classified as C4. Helmy ElKaffas, K et al. (12) found that C2 and C3 patients made up 83%, while 15% were C4. In our study, around 75% of patients fell into the C2 and C3 classifications, while 25% were classified as C4. The higher proportion of C4 patients in our study likely reflects the tendency of patients to delay seeking treatment, possibly due to low awareness or viewing venous disease as purely cosmetic.

Studies have reported varying postoperative recurrence rates for patients undergoing vena saphena parva ligation and/or stripping. Rashid HI et al. (13) reported a recurrence rate of approximately 30% one year after parva ligation or stripping, while Hong KP et al. (14) found this rate to be around 4%. In our study, parva ligation was performed on 27 patients, and no recurrence or neovascularization was detected at the one-year follow-up with CDUSG. We attribute this difference to preoperative marking of the popliteoparval junction with CDUSG and performing ligation 2 cm distal to the junction, as well as the small number of patients who underwent parva ligation in our study.

Postoperative recurrence rates vary across studies. In a randomized controlled trial by Biemans, A.A. et al. (15), the recurrence rates for EVLA and stripping after one year were 11.5% and 11.8%, respectively, with no statistically significant differences between the methods. Another study involving 180 patients found 5.5% recurrence for both RFA and stripping after two years (12). In another study, the recurrence rate after RFA applied to 1273 extremities was reported as 3.69% (16). Furthermore, in a systematic review published in 2023, it was observed that the average follow-up period ranged between 112 days and 5 years and recurrence, defined as the development of new varicose veins, ranged from 29.8-91% in stripping, 40-81.6% in EVLA and 67.0% in RFA (17). A ten-year follow-up randomized controlled study found recurrence rates of 27% for stripping and 56% for EVLA, a statistically significant difference (p=0.002) (18). In our study, recurrence rates for stripping, RFA, and EVLA were 2.8%, 8.4%, and 12.5%, respectively, with statistically significant differences (p=0.012). Subgroup analysis showed no significant difference between RFA and EVLA in terms of recurrence, while stripping had significantly lower recurrence rates than both (p=0.245, 0.035, 0.002, respectively). Recurrences following catheter-based procedures may be due to recanalization or reflux into an overlooked accessory saphenous vein (19), while stripping-related recurrences are often attributed to technical errors or neovascularization during long-term follow-up (20). We believe that the lower recurrence rates with stripping in our study reflect the technical success of the procedure.

Our study has several limitations. Firstly, the retrospective design introduces the potential for bias during data collection. Additionally, the one-year follow-up period limits our ability to assess long-term outcomes, and further studies with longer follow-up are needed to better understand the lasting effects of these treatments. Another limitation is the lack of clinical benefit analysis, which prevents a full assessment of the impact on patient quality of life. Finally, the smaller number of patients, especially in the EVLA group, limits the generalizability of our results. Future large-scale, prospective studies are essential for validating our findings.

CONCLUSION

In this study, we observed no significant difference in the incidence of deep vein thrombosis (DVT) between RFA, EVLA and stripping procedures. However, the development of phlebitis was significantly less frequent in the stripping group, which may indicate that stripping is relatively safer in terms of inflammatory complications.

The most significant finding was that stripping was associated with lower recurrence rates. Assessment using colour doppler ultrasonography (CDUSG) at one year postoperative follow-up showed that stripping was associated with lower recurrence rates than RFA and EVLA. This finding is in agreement with other studies indicating that stripping is still an effective treatment modality for the long-term resolution of venous insufficiency. Although RFA and EVLA are more popular due to their minimally invasive properties, our results suggest that stripping, although more invasive, provides a more durable outcome in terms of recurrence.

From a clinical point of view, factors such as patient preferences, severity of disease, cosmetic concerns and long-

term recurrence risks should be taken into consideration when choosing between these treatment options. Although catheter-based treatments, RFA and EVLA, continue to be widely used, stripping should not be ignored as an effective treatment alternative, especially in patients at high risk of recurrence.

The findings of our study emphasise the importance of careful evaluation of patient characteristics when choosing treatment. However, considering its limitations such as limited sample size and retrospective design, further studies with larger patient groups and long-term follow-up are required to fully evaluate the long-term efficacy of these treatments.

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Address correspondence to: *Abdullah Guner, Konya City Hospital, Department of Cardıovascular Surgery, Konya, Türkiye*
e-mail: *guner_426@hotmail.com*

REFERENCES

1. Baliyan V, Tajmir S, Hedgire SS, et al. Lower extremity venous reflux. Cardiovascular diagnosis and therapy. 2016;6(6):533. doi:10.21037/cdt.2016.11.14
2. Ruckley CV, Evans CJ, Allan PL, et al. Chronic venous insufficiency: Clinical and duplex correlations. The Edinburgh Vein Study of venous disorders in the general population. Journal of Vascular Surgery. 2002;36(3):520-5. doi:10.1067/mva.2002.126547
3. Labropoulos N, Leon M, Nicolaides AN, et al. Superficial venous insufficiency: Correlation of anatomic extent of reflux with clinical symptoms and signs. Journal of vascular surgery. 1994;20(6):953-8. doi:10.1016/0741-5214(94)90233-x
4. Lo YF, Yang CH, editors. Stripping and ligation of the saphenous vein. Seminars in cutaneous medicine and surgery; 2005. doi:10.1016/j.sder.2005.10.004
5. Eberhardt RT, Raffetto JD. Chronic venous insufficiency. Circulation. 2014;130(4):333-46. doi:10.1161/circulationaha113.006898
6. Fowkes F, Lee AJ, Evans C, et al. Lifestyle risk factors for lower limb venous reflux in the general population: Edinburgh Vein Study. International journal of epidemiology. 2001;30(4):846-52. doi:10.1093/ije/30.4.846
7. Park TY, Jung JW, Choi JC, et al. Epidemiological trend of pulmonary thromboembolism at a tertiary hospital in Korea. The Korean Journal of Internal Medicine. 2017;32(6):1037. doi:10.3904/kjim.2016.248
8. Lurie F, Passman M, Meisner M, et al. CEAP classification system and reporting standard, revision 2020. J Vasc Surg Venous Lymphat Disord. 2020;8(3):342-52. doi:10.1016/j.jvsv.2019.12.075
9. Işık M. Removal of the splitt guidewire forgotten during the treatment of varicose veins via radiofrequency ablation. Turkish Journal of Vascular Surgery. 2020;29(1). doi:10.9739/tjvs.2020.281
10. Dermody M, O'Donnell TF, Balk EM. Complications of endovenous ablation in randomized controlled trials. Journal of Vascular Surgery: Venous and Lymphatic Disorders. 2013;1(4):427-36. e1. doi:10.1016/j.jvsv.2013.04.007
11. Rajendran S, Nair HR, Thaikattil NJ. Ultrasound-assisted varicose vein surgery and endovenous laser ablation using 1470-nm laser for treatment of great saphenous vein incompetence has similar outcomes at 1 year in a single-center prospective randomized study. Journal of Vascular Surgery: Venous and Lymphatic Disorders. 2022;10(2):370-5. doi:10.1016/j.jvsv.2021.08.013
12. Helmy ElKaffas K, ElKashef O, ElBaz W. Great saphenous vein radiofrequency ablation versus standard stripping in the management of primary varicose veins-a randomized clinical trial. Angiology. 2011;62(1):49-54. doi:10.1177/0003319710380680
13. Rashid H, Ajeel A, Tyrrell MR. Persistent popliteal fossa reflux following saphenopopliteal disconnection. Journal of British Surgery. 2002;89(6):748-51. doi:10.1046/j.1365-2168.2002.02125.x
14. Hong KP. Midterm clinical outcomes after modified high ligation and segmental stripping of incompetent small saphenous veins. The Korean Journal of Thoracic and Cardiovascular Surgery. 2015;48(6):398. doi:10.5090/kjtcs.2015.48.6.398
15. Biemans AA, Kockaert M, Akkersdijk GP, et al. Comparing endovenous laser ablation, foam sclerotherapy, and conventional surgery for great saphenous varicose veins. Journal of vascular surgery. 2013;58(3):727-34. e1. doi:10.1016/j.jvs.2012.12.074
16. Jun J, Yoon M, Jung H, et al. Feasibility and Safety of Flush Endovenous Thermal Ablation of the Great Saphenous Vein with Consecutive Foam Sclerotherapy of Saphenofemoral Junction Tributaries: A Single-Center Experience. J Clin Med. 2024;13(23). doi:10.3390/jcm13237148
17. Miranda M, Sousa J, Mansilha A. PREVAIT after modern open surgery and endothermal ablation: A systematic review. Int Angiol. 2023;42(5):436-47. doi:10.23736/S0392-9590.23.05082-4
18. Eggen CA, Alozai T, Pronk P, et al. Ten-year follow-up of a randomized controlled trial comparing saphenofemoral ligation and stripping of the great saphenous vein with endovenous laser ablation (980 nm) using local tumescent anesthesia. Journal of Vascular Surgery: Venous and Lymphatic Disorders. 2022;10(3):646-53. e1. doi:10.1016/j.jvsv.2021.08.008
19. Rass K, Frings N, Glowacki P, et al. Same site recurrence is more frequent after endovenous laser ablation compared with high ligation and stripping of the great saphenous vein: 5 year results of a randomized clinical trial (RELACS Study). European Journal of Vascular and Endovascular Surgery. 2015;50(5):648-56. doi:10.1016/j.ejvs.2015.07.020
20. Dwerryhouse S, Davies B, Harradine K, et al. Stripping the long saphenous vein reduces the rate of reoperation for recurrent varicose veins: Five-year results of a randomized trial. J Vasc Surg. 1999;29(4):589-92. doi: 10.1016/s0741-5214(99)70302-2.

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OPEN ARAŞTIRMA MAKALESİ / RESEARCH ARTICLE

Investigation of Morphine-Induced Dopamine Release in the Nucleus Accumbens by Fiber Photometry

Nucleus Accumbens'te Morfine Bağlı Dopamin Salınımının Fiber Fotometri ile Araştırılması

Yasin Ali Cimen[1], Selim Kutlu[2]

[1]Bezmialem Vakif University, Faculty of Medicine, Department of Physiology, Istanbul, Türkiye
[2]Necmettin Erbakan University, Faculty of Medicine, Department of Physiology, Konya, Türkiye

ÖZET

Amaç: Morfin, akut ve kronik ağrı tedavisinde sıklıkla kullanılan bir opiyattır. Nucleus accumbens (NAc) ödül yolunun en temel merkezidir. Bağımlılık gelişimi ve ödül yolağının aktif olması bölgedeki dopaminerjik aktivitenin değişimi ile ilişkilendirilmiştir. Ardışık morfin kullanımı ventral tegmental alandaki dopaminerjik nöronların aktivasyonu yoluyla nükleus akumbenste dopamin düzeylerini artırır. Son zamanlarda popüler olmaya başlayan fiber fotometri sistemiyle dopaminerjik sensörlerden hızlı, anlık, tekrarlanabilir ve in vivo dopaminerjik sinyal kaydı yapılmaktadır. Konuyla alakalı çeşitli çalışmalar olmasına rağmen mevcut çalışmalar sınırlıdır. Çalışmanın amacı, yüksek teknolojili fiber optik fotometri sistemi kullanarak morfin bağımlılığı ve yoksunluğu sırasında NAc'deki dopaminerjik sinyalleri dopaminerjik sensör (GRABDA) vasıtasıyla araştırmaktır.

Gereç ve Yöntemler: Erkek Wistar sıçanlar morfin (M) ve morfin+nalokson (M+N) olmak üzere iki gruba ayrılmıştır. Fiber fotometri kaydı için tüm hayvanların sağ NAc bölgesine GRABDA enjekte edilmiştir. GRABDA, yapısında dopamin reseptörü 2'ye (DRD2) dayalı bir tanıma alanı içerir. Bu alana dopamin bağlandığında sensördeki yeşil floresan protein aktive olur. Oluşan floresan değişim, bölgedeki dopaminerjik aktiviteyi ve sinyal iletimini yansıtır. Daha sonra aynı bölgeye bir fiber optik kablo diş çimentosu ile sabitlenmiştir. 15 günlük dinlendirmenin ardından, 5 gün boyunca 10mg/kg morfin intraperitoneal olarak enjekte edilmiştir. Son enjeksiyondan sonra M+N grubuna 3mg/kg nalokson enjekte edilmiştir. Dopaminerjik sinyali ifade eden ortalama ΔF/F (%) değerleri, fiber fotometrik kayıtlar toplandıktan sonra Python ile hesaplanmıştır. ΔF/F (%) değeri, DRD2 reseptörlerine dopamin bağlanma düzeyini, normalize ederek yüzdelik olarak ifade eder. İstatistiksel karşılaştırmalar karma-ANOVA testi ve post-hoc karşılaştırmalar tahmini marjinal ortalamalar kullanılarak yapıldı.

Bulgular: M grubunun ΔF/F (%) değerleri morfin enjeksiyonu ile başlangıca kıyasla artmıştır ($p<0.05$). Nalokson enjeksiyonları sonucunda, M+N grubunun ΔF/F (%) değerleri M grubuna kıyasla önemli ölçüde azalmıştır ($p<0.05$). Morfin bağımlılığı NAc dopaminerjik sinyalini artırır. Nalokson bu artışı baskılar.

Sonuç: NAc'deki dopaminerjik aktivitenin yeni biyosensörlerle fiber fotometri ile saptanması, sıvı kromatografisi gibi eski tekniklerden daha etkili kanıt sağlama potansiyeline sahiptir. Konunun daha iyi anlaşılması için spesifik nöronal ve bölgesel çalışmalara ihtiyaç vardır.

Anahtar Kelimeler: Bağımlılık, dopamin, fiber fotometri, GRAB sensörleri, morfin, nalokson, sıçan.

ABSTRACT

Objective: Morphine is an opiate frequently used in the management of acute and chronic pain. Sequential use of morphine increases dopamine levels in the nucleus accumbens (NAc) through activation of dopaminergic neurons in the ventral tegmental area. The aim of the study was to investigate dopaminergic signals in the NAc during morphine dependence and withdrawal using fiber photometry system with dopaminergic sensor (GRABDA).

Materials and Methods: Male Wistar rats were divided into two groups as morphine (M) and morphine+naloxone (M+N). GRABDA was injected into the right NAc region. GRABDA contains a recognition domain based on the dopamine receptor 2 (DRD2) in its structure. When dopamine binds to this domain, the green fluorescent protein in the sensor is activated. The resulting fluorescence change reflects dopaminergic activity and signal transmission in the region. Afterwards, a fiber optic cable was fixed to NAc. After 15 days of rest, 10mg/kg morphine was injected intraperitoneally for 5 days. 3mg/kg naloxone was injected into the M+N group after the last injection. Average ΔF/F (%) values expressing dopaminergic signalling were calculated with Python after collecting fiber photometric records. The ΔF/F (%) value expresses the normalised level of dopamine binding to DRD2 receptors as a percentage. Statistical comparisons were made using a mixed-ANOVA test and post-hoc comparisons were made using estimated marginal means.

Results: The ΔF/F (%) values of the M and M+N groups increased with morphine injection compared to baseline period ($p<0.05$). As a result of naloxone injections, the ΔF/F (%) values of the M+N group significantly decreased compared to the M group ($p<0.05$). Morphine addiction increases dopaminergic signalling in the NAc, while naloxone suppresses this effect.

Conclusions: Fiber photometry with a novel biosensors enables more efficient detection of dopaminergic activity compared to older methods such as liquid chromatography. Further studies are needed for a better understanding of specific neuronal and regional processes.

Keywords: Addiction, dopamine, fiber photometry, GRAB sensors, morphine, naloxone, rat.

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Sorumlu Yazar/Corresponding Author: Yasin Ali Cimen, Bezmialem Vakif University, Faculty of Medicine, Department of Physiology, Istanbul, Türkiye
e-mail: yasin.alicimen@gmail.com

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INTRODUCTION

Morphine is an opiate widely used in chronic and acute pain management (1). The development of dependence may often limit morphine usage in many clinical cases. The drug addiction can cause social and financial problems worldwide (2, 3). Five types of opioid receptor have been discovered: mμ (MOR), kappa, delta, nociception and zeta (4). It's reported that opiates' habit-forming effects in the ventral tegmental area are mediated by mu and delta opioids receptors (5). Main effects of morphine are mediated through activation of the MOR, as the analgesic, rewarding and withdrawal aversive effects of morphine are abolished in MOR-deficient mice (6, 7). Naloxone is often used to reverse the clinically disabling effects of opioid overdose. Naloxone blocks the effects of opioids on their receptors by acting as a competitive antagonist of MORs. It has been widely used to induce withdrawal symptoms in rodents and to induce a withdrawal syndrome that produces adverse, stress-like states (8).

The nucleus accumbens (NAc) contains a high density of opioid receptors (9, 10). Morphine increases MOR-mediated dopamine release in the NAc (11). MOR agonists induce dopamine release in both core and shell areas of the NAc (12). MOR regulates dopamine release through disinhibition via GABA'ergic interneurons in the ventral tegmental area (VTA) (13). Dopaminergic projection to the NAc from VTA is the primary fundamental signalling circuit in opiate addiction (14). In addition, all drugs that cause addiction are known to increase dopaminergic activity in the NAc (15).

Dopamine is significantly implicated in the integration of reward and addiction mechanisms (16). In the human adult brain, dopaminergic neurons are found in the mesencephalon, diencephalon, and olfactory bulb. These neurones are most abundant in the ventral region of the mesencephalon, VTA and retrobulbar area (17). Dopaminergic neurons in the brain have four main pathways to the target areas. These mesolimbic, nigrostriatal, mesocortical and tuberoinfundibular system pathways play roles in integration of central motor coordination and several limbic functions such as some central mechanisms related to feeding, reward mechanisms, creation of attention and consciousness and some processes of learning (18). The mesolimbic dopaminergic system is vital for the behavioural changes caused by drug abuse (19). Dopamine exerts its diverse physiological effects by binding to five different G protein-coupled receptor subtypes (DRD1-5) (20). DRD1 and DRD5 receptors exert mainly stimulatory effects through activation of adenylate cyclase and elevation of intracellular levels of cyclic AMP (cAMP) (21). DRD2, DRD3 and DRD4 are generally inhibitory. They inhibit adenylate cyclase and reduce cAMP levels (22). Antagonists of the DRD1 and DRD2 receptors inhibit the reinstatement of cocaine seeking in rats (23). Dopamine levels in the NAc are increased after systemic injection of morphine, and pre-treatment with MOR or DRD1 receptor antagonists blocks the morphine-induced effects (24).

Although morphine dependence and NAc dopamine activity have been investigated in many studies (25-27), there is still a deficiency in this regard. Especially in recent years, fiber photometry and genetically encoded sensors have revolutionized in vivo studies on this subject. Therefore, our aim in this study is to examine NAc dopaminergic activity in morphine dependence in detail against time with fiber photometry in vivo. In addition, we aimed to investigate the time dependent change of NAc dopaminergic activity in morphine withdrawal modelling with naloxone in vivo.

MATERIALS AND METHODS

Twelve adults male Wistar rats weighing 300-350 g were used in the experiments. The animals were kept in plastic cages (temperature 22 ± 2°C) with food and tap water, and a 12-h light/dark cycle.

Virus Injection and Ferrule Implantation

Animals were anesthetized with a combination of ketamine and xylazine (80 mg/kg and 10 mg/kg, respectively) by intraperitoneally and their heads were shaved. Betadine and 70% ethanol were used to sterilize the surgical field. Animals were placed in a stereotaxic device with two ear bars and dental fixation. Terramycin cream was applied to the eyes of the rats to protect them from possible infections and to prevent dry eyes. The stereotaxic coordinates of the NAc region were determined from the rat brain atlas and the projection point on the bone tissue was marked. This pinpoint area was precisely drilled with a dentist's round and made suitable for intracerebral injection. Approximately 0.5 μL units/rat of pAAV-hsyn-GRAB_DA2m (GRABDA2m; Addgene #140553) was injected into the right NAc shell region of rats (bregma 1.70 mm, lateral + 0.80 mm and ventral - 7.0 mm from the brain surface) with a Hamilton syringe. A period of 10 minutes was allowed for the virus to diffuse into the area and the syringe was gently removed from the site after injection. Two small screws were implanted in order to fix the dental cement to the skull. Afterwards, an optical cable (400 μm diameter aperture; FP400URT Multimode, NA 0.50; Thorlabs) was placed in the previously prepared ferrules (SFLC440-10 with 400 μm diameter aperture, 6.4 mm length; Thorlabs) to target the NAc. After the ferrules were placed, the skull was covered with dental acrylic and the surgical procedure was completed. The rats were allowed to beg for two weeks to recover and for the virus to infect the area. Thus, dopaminergic receptors in the NAc region were labelled with green fluorescent protein (GFP). Rats that did not regain their preoperative body weight during this period were not used in subsequent experiments. The rats were randomly divided into two groups as morphine (M) and morphine+naloxone group (M+N). All animals were administered morphine (10 mg/kg) intraperitoneally between 09:00-10:00 every morning for 5 days. On the fifth day, morphine groups were injected with saline 15 minutes after morphine injection. On the fifth day, naloxone (3 mg/kg) was injected into the naloxone groups 15 minutes after morphine injection.

This study was approved by the Necmettin Erbakan University KONUDAM Experimental Medicine Application and Research Center Animal Experiments Local Ethics Committee (Ethics Number: 033-2021). Experimental studies

were conducted in the laboratories of the Experimental Medicine Application and Research Center. Animal rights are protected within the scope of the 'Guide for the Care and Use of Laboratory Animals'.

Fiber Photometry Recording and Analysis

Fiber photometry recordings were performed while the rats were free to move in their cages. The recordings were collected with a fiber photometry system (BFMC6; Doric Lenses) that transmits 405 nm as the control signal and 470 nm as the genetically encoded sensor signal to a fiber optic cable coupled to the fiber cannula.

Thomas Akam's open access GitHub library "Photometry data preprocessing" was used for fiber photometry analysis in our study (28). Briefly, raw signal data of 405nm control and 470nm GRABDA2m signals were acquired. To reduce high-frequency noise, the signals were low-pass filtered using a zero-phase filter with a cut-off frequency of 10Hz. The effects of photobleaching were removed with a double exponential fit and a 0.001 high-pass filter. Motion correction was applied to the signals. For normalization, ΔF/F was calculated as signal changes (ΔF) divided by initial fluorescence (F). The change in ΔF/F (%) was calculated according to the percentage of ΔF/F.

Brain Slice Imaging

Brains were fixed in 4% paraformaldehyde. Total brains were then cut into 70 um pieces in PBS using a vibratome. The sections placed in the wells were imaged with a Cell Discoverer 7 fluorescence microscope (Carl Zeiss, Germany). Histological verification was performed at the end of the experiments, and sterotaxic treatments that did not reach the shell region of the NAc were not included in the groups.

Statistical analysis

Statistical comparisons were made using a mixed-ANOVA test and post-hoc comparisons were made using estimated marginal means. All data were statistically analyzed with IBM SPSS 22 software and presented as mean ± standard error of the means (mean ± SEM). $p<0.05$ was accepted as significant.

RESULTS

We demonstrated that the injection of the dopamine sensor and the fiber optic cable was in the NAc region by photographing brain sections under an immunofluorescence microscope (Figure 1).

To determine the dynamics of dopaminergic activity, we performed in vivo fiber photometry recording from the rat right NAc shell region infected with pAAV-hsyn-GRAB_DA2m. To better understand the effect of morphine withdrawal, we first obtained a baseline recording (baseline period). Then we continued to record the effects of morphine administration (morphine period). Finally, we injected saline in the M group and naloxone in the M+N group and continued recording (saline or naloxone period). We completed the fiber photometry recording in 3 periods for a total of 25 minutes (Figure 2A). Fiber photometry recording in groups is shown in the heat map graph (Figure 2B).

We recorded baseline fiber photometric values for 5 min to detect dopaminergic activity in the NAc region before morphine injection of the animals. There was no significant difference in baseline period mean ΔF/F (%) between M and M+N groups (Figure 3).

There was no statistically significant difference between the mean ΔF/F (%) values of the M and M+N groups during the morphine period ($p>0.05$, Figure 4).

During the saline or naloxone period, the mean ΔF/F (%) values

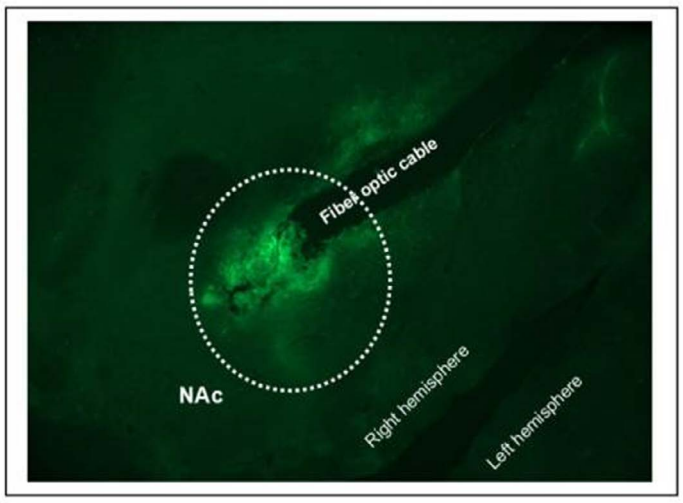

Figure 1. Microscopic image of injected GRABDA viruses and fiber optic ferule in NAc region. Rat brain section were visualized with immunofluorescence microscopy. Green color indicates GFP originating from GRABDA sensors. Abbreviations: NAc, Nucleous accumbens.

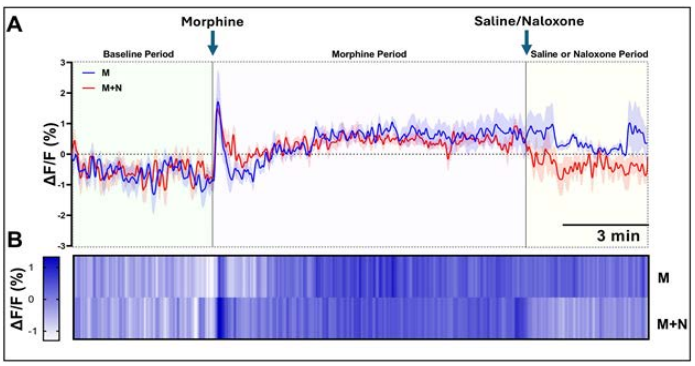

Figure 2. GRABDA sensor-induced ΔF/F (%) change over time in the NAc region according to groups. A, The mean ΔF/F (%) of the M group is shown as mean (blue trace) ± SEM (blue shading); the mean ΔF/F of the M+N group is shown as mean (red trace) ± SEM (red shading). B, The mean ΔF/F (%) of the M and M+N groups is shown as a heatmap plot. Abbreviations: M, morphine group; M+N, morphine+naloxone group.

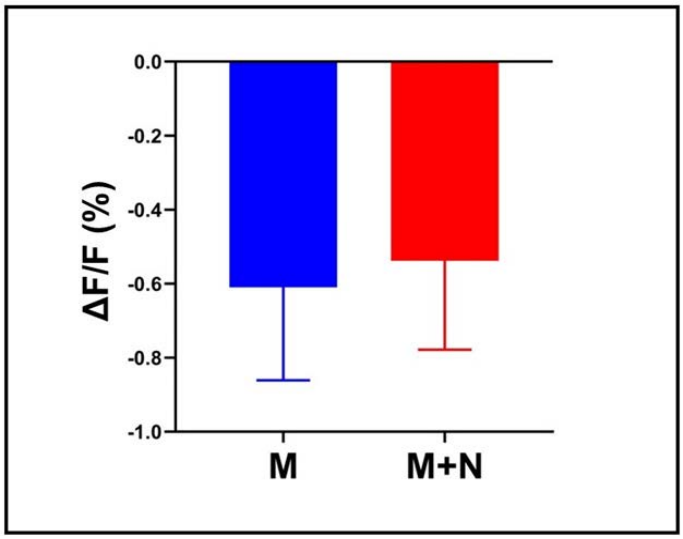

Figure 3. Comparison of NAc ΔF/F (%) baseline period data between groups.
Bar graph comparison of the mean ΔF/F (%) of the M and M+N groups during the baseline period. Data are expressed as mean ± SEM. Abbreviations: M, morphine group; M+N, morphine+naloxone group.

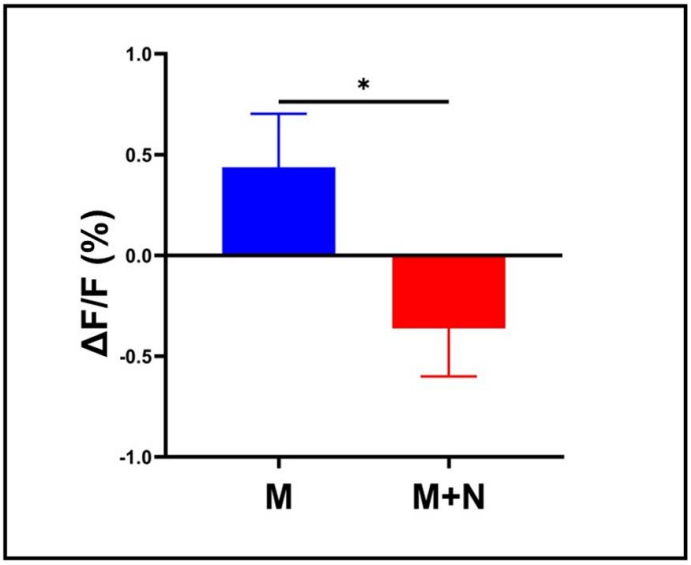

Figure 5. Comparison of mean ΔF/F (%) values after saline or naloxone injection between groups.
Average ΔF/F (%) comparison of the M and M+N groups during the saline or naloxone period. Data are expressed as mean ± SEM. *p<0.05 indicate significant difference between groups. Abbreviations: M, Morphine group; M+N, Morphine+Naloxone group.

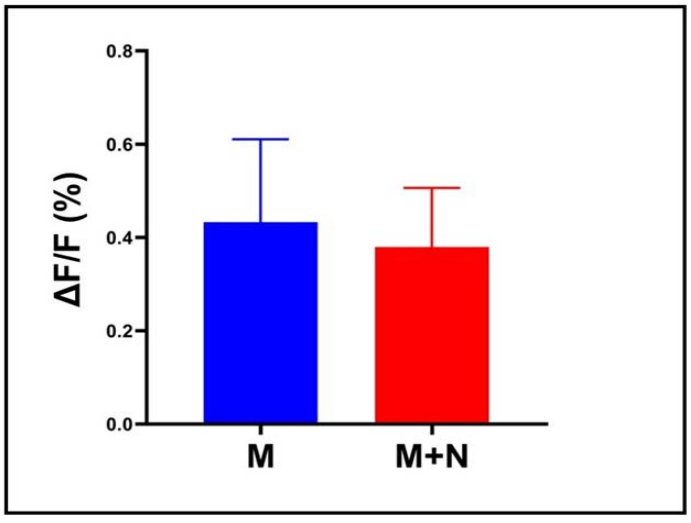

Figure 4. Comparison of mean ΔF/F (%) values of morphine period between groups.
Average ΔF/F (%) comparison of the M and M+N groups during the morphine period. Data are expressed as mean ± SEM. Abbreviations: M, morphine group; M+N, morphine+naloxone group.

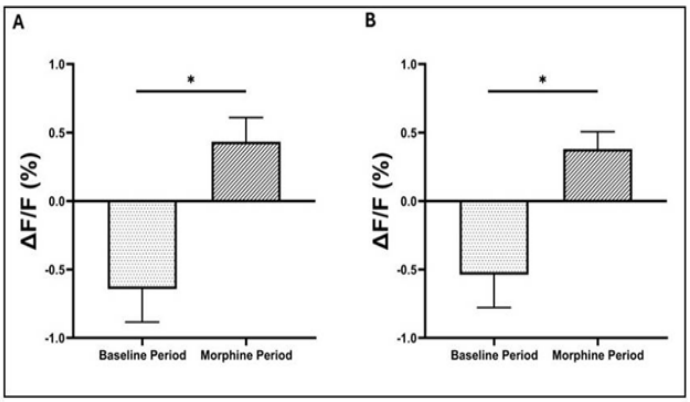

Figure 6. Comparison of mean ΔF/F (%) values of baseline and morphine periods in the M and M+N group.
Comparison of mean ΔF/F (%) values in the baseline and morphine periods of the M (A) and M+N (B) groups. Data are expressed as mean ± SEM. *p<0.05 indicate significant difference between groups. Abbreviations: M, morphine group; M+N, Morphine+Naloxone group.

of the naloxone-injected M+N group were significantly lower than those of the saline-injected M group ($p<0.05$, Figure 5).

When we compared the changes in dopaminergic activity in both M and M+N groups during basal and morphine periods, it was observed that the mean ΔF/F (%) value during morphine period was higher than basal period ($p<0.05$, Figure 6A, B).

DISCUSSION

Morphine injected systemically or into the VTA has been shown to increase the firing rate of dopamine neurons in anaesthetised animals (29, 30). This finding are supported by ex vivo studies showing that MOR agonists directly activate dopamine neurons in the VTA (31). MOR activation causes increased dopamine release by suppressing GABA release in the VTA (32, 33). Increased dopamine in the NAc can potentiate reward responses by activating DRD1 receptors, while its binding to DRD2 receptors can modulate the activity of medium spiny neurons (MSNs) (34). MSNs, which make up 95% of the NAc, can express DRD1 or DRD2 dopamine receptors (35, 36). Furthermore, by expressing MOR, these cells can be directly modulated by opioids such as morphine (37). Morphine injection has been shown to differentially alter excitatory glutamatergic activity in the NAc, D1R-MSNs and D2R-MSNs (38). In addition, it has been reported that dendritic spines of NAc DRD1-MSNs and DRD2-MSNs show distinct plasticity with chronic cocaine exposure (39). NAc dopamine activity during morphine withdrawal has also been assessed in several studies. The effects of morphine withdrawal in the NAc were found to be a consequence of alterations in dopamine neuron firing in the VTA (40). Opioid withdrawal also upregulates c-Fos activity in GABAergic VTA neurones (41). The near-complete disappearance of dopamine release in the NAc during withdrawal has been associated with the cessation of sustained stimulation of high-affinity, inhibitory DRD2 (42). The findings suggest that dopaminergic receptors, particularly DRD2, are actively involved in morphine dependence and withdrawal.

Immediate and highly sensitive detection of the dopaminergic VTA-NAc circuit, which forms the basis of drug addiction processes, using the newly developed fiber photometry technique has the potential to be a new research area for studies in this field. Our GRABDA fiber photometry measurements allow us to directly detect changes in dopamine binding to DRD2-MSNs during morphine dependence. Consequently, we are able to examine in greater detail the effects of morphine on the dopaminergic system and the relevance of DRD2 signalling in the NAc to addiction in vivo.

For the past 40 years, researchers have been using animal models to develop behavioural models of addiction and to try to understand the reward mechanisms (43). In these studies, the challenge is to measure dopamine in densely and sparsely innervated regions and to correlate dopamine levels in vivo with behavioural outcomes of interest. Reliable and accurate determination of dopamine levels in vitro or in vivo experiments is often closely related to efficient analytical techniques. In vivo measurements of dopamine concentration have been addressed using classical analytical chemistry techniques such as high-performance liquid chromatography with electrochemical detector system combined with micro dialysis. However, there are limitations that can make long-term measurements with sufficient spatio-temporal resolution and specificity relatively difficult.

Recently, scientists have developed genetically encoded dopamine sensors that overcome some of these technical hurdles. GRABDA sensors take part of the DRD2 receptor (the third intracellular loop, ICL3) and attach a fluorescent protein (cpEGFP) to it. When dopamine binds to the sensory receptor, a structural change takes place. This change affects cpEGFP and produces a fluorescent signal. This process allows the concentration of dopamine to be measured in real time (44, 45). GRABDA biosensors are now superior to chromatographic assays in many ways due to their fast data transfer, their ability to provide instantaneous measurements, the almost unlimited reproducibility of measurements and there in vivo usability (44). Whilst cerebrospinal fluid samples obtained by micro dialysis are typically reflective of a time frame ranging from minutes to hours (46), GRABDA biosensors signals facilitate real-time monitoring of neurochemical changes at the millisecond level. This fluorescence signal in GRABDA biosensors is recorded in vivo by a fiber photometry system (47).

In the present study, it was initially determined that the administration of morphine resulted in a significant augmentation in dopaminergic activity within the nucleus accumbens. This high dopamine level persisted for 20 minutes after morphine injection. A further salient finding was that naloxone significantly reduced morphine-induced dopamine levels. These results suggest that the combined use of GRABDA and a fiber photometry system is a highly effective method for monitoring dopaminergic signalling, especially the association of DRD2 receptors with addiction. The analysis of dopaminergic activity in the central nervous system was performed sensitively and efficiently in this study using a fiber photometer system and GRABDA biosensors. The findings of this study may prove to be of significant value in guiding future research endeavours focused on dopaminergic activation or inhibition in the NAc, particularly in the context of exploring novel therapeutic interventions for morphine addiction.

The analysis of dopamine by chromatography does not allow to follow a temporally continuous process. It can only determine the instantaneous concentration, which reflects the concentration of the sample obtained from the collection of a microdialysis sample of at least 10 minutes. It therefore does not reflect instantaneous changes in dopamine levels in brain tissue. Fiber photometry, on the other hand, offers the unique advantage of monitoring instantaneous changes in dopamine levels over a long period of time, with recordings taken at least 10 times per second. Thus, compared to chromatographic analysis, fiber photometry provides much clearer and more valuable findings in determining the effects of candidate molecules on dopamine levels. In this respect, it can be argued that research on the combination of biosensors and fiber photometry is much more effective in in vivo translational

research related to neuropsychopathologies.

CONCLUSION

This study demonstrates that morphine dependence significantly enhances dopaminergic activity in the nucleus accumbens, as observed through fiber photometry. Naloxone administration effectively suppresses this increase, highlighting its potential role in modulating dopaminergic signalling during withdrawal. The use of a novel biosensor for real-time detection provides a more precise and reliable method compared to traditional techniques, offering valuable insights for understanding addiction mechanisms and developing therapeutic strategies.

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Address correspondence to: *Yasin Ali Cimen, Bezmialem Vakif University, Faculty of Medicine, Department of Physiology, Istanbul, Türkiye*
e-mail: *yasin.alicimen@gmail.com*

REFERENCES

1. Carroll IR, Angst MS and Clark DJ, Management of perioperative pain in patients chronically consuming opioids. Regional Anesthesia & Pain Medicine, 2004; 29(6):576-91. doi. org/10.1016/j.rapm.2004.06.009.
2. Haghparast A, Khani A, Naderi N, et al. Repeated administration of nicotine attenuates the development of morphine tolerance and dependence in mice. Pharmacology Biochemistry and Behavior, 2008;88(4):385-92. doi.org/10.1016/j.pbb.2007.09.010.
3. Bart G, Maintenance medication for opiate addiction: The foundation of recovery. Journal of addictive diseases, 2012; 31(3):207-25. doi.org/10.1080/10550887.2012.694598.
4. Dhaliwal A, Gupta M. Physiology, opioid receptor. StatPearls Publishing, Treasure Island, 2019.
5. Devine DP and Wise RA, Self-administration of morphine, DAMGO, and DPDPE into the ventral tegmental area of rats. Journal of Neuroscience, 1994;14(4):1978-84. doi:10.1523/JNEUROSCI.14-04-01978.1994.
6. Matthes HW, Maldonado R, Simonin F, et al. Loss of morphine-induced analgesia, reward effect and withdrawal symptoms in mice lacking the μ-opioid-receptor gene. Nature, 1996; 383(6603):819-23. doi.org/10.1038/383819a0.
7. Sora I, Takahashi N, Funada M, et al. Opiate receptor knockout mice define μ receptor roles in endogenous nociceptive responses and morphine-induced analgesia. Proceedings of the National Academy of Sciences, 1997;94(4):1544-9. doi. org/10.1073/pnas.94.4.1544.
8. Schulteis G, Heyser C and Koob G, Differential expression of response-disruptive and somatic indices of opiate withdrawal during the initiation and development of opiate dependence. Behavioural pharmacology, 1999;10(3):235-42.
9. Massaly N, Copits BA, Wilson-Poe AR, et al. Pain-induced negative affect is mediated via recruitment of the nucleus accumbens kappa opioid system. Neuron, 2019; 102(3):564-73. e6. doi:10.1016/j. neuron.2019.02.029.
10. Li C, Sugam JA, Lowery-Gionta EG, et al. Mu opioid receptor modulation of dopamine neurons in the periaqueductal gray/dorsal raphe: A role in regulation of pain. Neuropsychopharmacology, 2016;41(8):2122-32. doi. org/10.1038/npp.2016.12.
11. Kuo CC, Shen H, Harvey BK, et al. Differential modulation of methamphetamine-mediated behavioral sensitization by overexpression of Mu opioid receptors in nucleus accumbens and ventral tegmental area. Psychopharmacology, 2016;233(4), 661-72. doi.org/10.1007/s00213-015-4134-4.
12. Spanagel R, Herz A and Shippenberg TS, The effects of opioid peptides on dopamine release in the nucleus accumbens: An in vivo microdialysis study. Journal of neurochemistry, 1990; 55(5):1734-40. doi.org/10.1111/j.1471-4159.1990. tb04963.x.
13. Jalabert M, Bourdy R, Courtin J, et al., Neuronal circuits underlying acute morphine action on dopamine neurons. Proceedings of the national academy of sciences, 2011;108(39):16446-50. doi.org/10.1073/pnas.1105418108.
14. Yun IA, Wakabayashi KT, Fields HL, et al. The ventral tegmental area is required for the behavioral and nucleus accumbens neuronal firing responses to incentive cues. Journal of Neuroscience, 2004; 24(12):2923-33.
15. Koob GF, Neural mechanisms of drug reinforcement. Annals of the new York Academy of Sciences, 1992; 654:171-91. doi. org/10.1111/j.1749-6632.1992.tb25966.x.
16. Nicola S, Taha S, Kim S, et al. Nucleus accumbens dopamine release is necessary and sufficient to promote the behavioral response to reward-predictive cues. Neuroscience, 2005;135(4):1025-33. doi.org/10.1016/j.neuroscience.2005.06.088.
17. Björklund A and Dunnett SB, Dopamine neuron systems in the brain: An update. Trends in neurosciences, 2007; 30(5):194-202. doi:10.1016/j.tins.2007.03.006.
18. Snyder SH, Taylor KM, Coyle JT, et al. The role of brain dopamine in behavioral regulation and the actions of psychotropic drugs. American Journal of Psychiatry, 1970;127(2):199-07. doi. org/10.1176/ajp.127.2.199.
19. Wise RA, Brain reward circuitry: Insights from unsensed incentives. Neuron, 2002; 36(2):229-40.
20. Missale C, Nash SR, Robinson SW, et al. Dopamine receptors: From structure to function. Physiological reviews, 1998. https:// doi.org/10.1152/physrev.1998.78.1.189.
21. Undieh AS, Pharmacology of signaling induced by dopamine D1-like receptor activation. Pharmacology & therapeutics, 2010; 128(1):37-60. doi.org/10.1016/j.pharmthera.2010.05.003.
22. Channer B, Matt SM, Nickoloff-Bybel E A, et al. Dopamine, immunity, and disease. Pharmacological reviews, 2023; 75(1):62-158. doi.org/10.1124/pharmrev.122.000618.
23. Gilbert JG, Newman AH, Gardner EL, et al. Acute administration of SB-277011A, NGB 2904, or BP 897 inhibits cocaine cue-induced reinstatement of drug-seeking behavior in rats: Role of dopamine D3 receptors. Synapse, 2005; 57(1):17-28. doi. org/10.1002/syn.20152.
24. Longoni R, Spina L and Di Chiara G, Dopaminergic D-1 receptors: Essential role in morphine-induced hypermotility.

Psychopharmacology, 1987; 93:401-2.
25. Di Chiara G and Imperato A, Drugs abused by humans preferentially increase synaptic dopamine concentrations in the mesolimbic system of freely moving rats. Proceedings of the National Academy of Sciences, 1988; 85(14):5274-78. doi.org/10.1073/pnas.85.14.5274.
26. Shahani P, Abolghasemi H, Abtin S, et al. The interaction effects between opioidergic and D1-like dopamine receptors in the nucleus accumbens on pain-related behaviors in the animal model of acute pain. Pharmacology Biochemistry and Behavior, 2025; 246:173911. doi.org/10.1016/j.pbb.2024.173911.
27. Sohn M, Nassef MT, Champagnol-Di Liberti C, et al. Manipulating ΔFOSB in D1-Type Medium Spiny Neurons of the Nucleus Accumbens Reshapes Whole-Brain Functional Connectivity. Biological psychiatry, 2024; 95(3):266-74. https://doi.org/10.1016/j.biopsych.2023.07.013.
28. Blanco-Pozo M, Akam T and Walton ME, Dopamine-independent state inference mediates expert reward guided decision making. bioRxiv, 2021:2021.06. 25.449995. doi.org/10.1101/2021.06.25.449995.
29. Spanagel R, Herz A and Shippenberg TS, Opposing tonically active endogenous opioid systems modulate the mesolimbic dopaminergic pathway. Proceedings of the National Academy of Sciences, 1992;89(6):2046-50. doi.org/10.1073/pnas.89.6.2046.
30. Chefer VI, Kieffer BL and Shippenberg TS, Basal and morphine-evoked dopaminergic neurotransmission in the nucleus accumbens of MOR-and DOR-knockout mice. European Journal of Neuroscience, 2003;18(7):1915-22. doi.org/10.1046/ j.1460-9568.2003.02912.x.
31. Johnson S and North R, Opioids excite dopamine neurons by hyperpolarization of local interneurons. Journal of neuroscience, 1992; 12(2):483-8. doi.org/10.1523/JNEUROSCI.12-02-00483.1992.
32. Matsui A, Jarvie BC, Robinson BG, et al. Separate GABA afferents to dopamine neurons mediate acute action of opioids, development of tolerance, and expression of withdrawal. Neuron, 2014; 82(6):1346-56. doi:10.1016/j.neuron.2014.04.030.
33. Matsui A and Williams JT, Opioid-sensitive GABA inputs from rostromedial tegmental nucleus synapse onto midbrain dopamine neurons. Journal of Neuroscience, 2011; 31(48):17729-35.
34. Tye KM and Deisseroth K, Optogenetic investigation of neural circuits underlying brain disease in animal models. Nature Reviews Neuroscience, 2012; 13(4):251-66.
35. Tejeda HA, Wu J, Kornspun AR, et al. Pathway-and cell-specific kappa-opioid receptor modulation of excitation-inhibition balance differentially gates D1 and D2 accumbens neuron activity. Neuron, 2017; 93(1):147-63. doi:10.1016/j.neuron.2016.12.005.
36. Wall NR, De La Parra M, Callaway EM, et al. Differential innervation of direct-and indirect-pathway striatal projection neurons. Neuron, 2013;79(2):347-60. doi:10.1016/j.neuron.2013.05.014.
37. Trieu BH, Remmers BC, Toddes C, et al., Angiotensin-converting enzyme gates brain circuit–specific plasticity via an endogenous opioid. Science, 2022; 375(6585):1177-82. doi:10.1126/science. abl5130.
38. Graziane NM, Sun S, Wright WJ, et al. Opposing mechanisms mediate morphine-and cocaine-induced generation of silent synapses. Nature neuroscience, 2016; 19(7):915-25.
39. MacAskill AF, Little JP, Cassel JM, et al. Subcellular connectivity underlies pathway-specific signaling in the nucleus accumbens. Nature neuroscience, 2012; 15(12):1624-6.
40. Williams JT, Christie MJ and Manzoni O, Cellular and synaptic adaptations mediating opioid dependence. Physiological reviews, 2001; 81(1):299-343.
41. Bagley EE, Hacker J, Chefer VI, et al., Drug-induced GABA transporter currents enhance GABA release to induce opioid withdrawal behaviors. Nature neuroscience, 2011;14(12):1548-54.
42. Richfield EK, Penney JB and Young AB, Anatomical and affinity state comparisons between dopamine D1 and D2 receptors in the rat central nervous system. Neuroscience, 1989;30(3):767-77.
43. Arias-Carrión O, Stamelou M, Murillo-Rodríguez E, et al. Dopaminergic reward system: A short integrative review. International archives of medicine, 2010; 3(1):24. doi:10.1186/1755- 7682-3-24.
44. Sun F, Zeng J, Jing M, et al. A genetically encoded fluorescent sensor enables rapid and specific detection of dopamine in flies, fish, and mice. Cell, 2018; 174(2):481-496. e19. doi:10.1016/j. cell.2018.06.042.
45. Beaulieu J-M, Gainetdinov RR and Sibley DR, The physiology, signaling, and pharmacology of dopamine receptors. Pharmacological reviews, 2011;63(1):182-17. doi.org/10.1124/pr.110.002642.
46. Chefer VI, Thompson AC, Zapata A, et al. Overview of brain microdialysis. Current protocols in neuroscience, 2009; 47(1):7-1.
47. Kielbinski M and Bernacka J, Fiber photometry in neuroscience research: Principles, applications, and future directions. Pharmacological Reports, 2024;76(6):1242-55. doi.org/10.1007/s43440-024-00646-w.

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A Comparative Analysis of Large Language Models in Managing Disorders of Sex Development: Evaluation Based on Clinical Guidelines

Cinsiyet Gelişim Bozukluklarının Yönetiminde Büyük Dil Modellerinin Karşılaştırmalı Analizi: Klinik Kılavuzlara Dayalı Bir Değerlendirme

Saime Sundus Uygun[1], Fatma Ozcan Siki[2]

[1]Selcuk University, Faculty of Medicine, Department of Naonatology, Konya, Türkiye
[2]Selcuk University, Faculty of Medicine, Department of Pediatric Surgery, Konya, Türkiye

ÖZET

Amaç: Bu çalışma, günümüzde yaygın olarak kullanılan iki yapay zekâ tabanlı sohbet sistemi olan ChatGPT ve Bing AI'nin, Türk Neonatoloji Derneği tarafından yayımlanan Cinsiyet Gelişim Bozuklukları kılavuzunda yer alan klinik önerilerle uyum düzeylerini karşılaştırmayı amaçlamaktadır.

Gereç ve Yöntemler: Türk Neonatoloji Derneği Cinsiyet Gelişim Bozuklukları kılavuzuna dayalı olarak hazırlanmış 40 sorudan oluşan standart bir değerlendirme seti kullanılmıştır. Sorular, klinik karar verme süreçlerini yansıtan altı ana kategori altında gruplandırılmış ve tamamı hem ChatGPT hem de Bing AI'ya yöneltilmiştir. Tüm sorular yazılı metin formatında iletilmiştir. Yanıtlar, kılavuzla uyum açısından biri neonatoloji, diğeri çocuk cerrahisi uzmanı olmak üzere iki bağımsız uzman tarafından 5 puanlık Likert ölçeği ile değerlendirilmiştir. Her kategori için ChatGPT ve Bing AI'nin ortalama puanları hesaplanmış, bu puanlar arasındaki fark Wilcoxon işaretli sıra testi ile istatistiksel olarak karşılaştırılmıştır.

Bulgular: ChatGPT, altı kategorinin tamamında Türk Neonatoloji Derneği'nin Cinsiyet Gelişim Bozuklukları kılavuzu ile yüksek düzeyde uyum göstermiştir (ortalama puan: 4,88). Buna karşın, Bing AI bazı kategorilerde daha düşük uyum sergilemiştir (ortalama puan: 3,25). İki sistem arasındaki ortalama puan farkları tüm kategorilerde istatistiksel olarak anlamlı bulunmuştur ($p<0,05$). Özellikle tanı süreci/laboratuvar testleri ve tedavide multidisipliner yaklaşım kategorilerinde Bing AI'nın performansı belirgin şekilde düşüktür.

Sonuç: ChatGPT, Cinsiyet Gelişim Bozuklukları konusunda kılavuz temelli klinik destek sağlama açısından Bing AI'ya göre daha yüksek doğruluk ve tutarlılık göstermiştir. Güncel klinik kılavuzlarla uyumlu yapay zekâ destekli sistemlerin kullanımı, karmaşık ve multidisipliner karar verme süreçlerinde hekimleri destekleme potansiyeline sahiptir. Bu nedenle, klinik uygulamalarda kullanılacak yapay zekâ araçlarının seçimi, bu tür sistematik değerlendirmelere dayanmalıdır. Güvenilir yapay zekâ tabanlı sistemler, hasta yönetiminde klinisyenlere önemli katkılar sağlayabilir.

Anahtar Kelimeler: Büyük Dil Modelleri, Cinsiyet Gelişim Bozuklukları, Yapay Zekâ, Neonatoloji, Karar Destek Sistemleri

ABSTRACT

Objective: This study aims to compare the guideline compliance of two widely used AI-based chatbot systems, ChatGPT and Bing AI, with the clinical recommendations outlined in the Disorders of Sex Development (DSD) guideline published by the Turkish Neonatal Society.

Materials and Methods: A standardized evaluation set comprising 40 questions based on the DSD guideline was utilized. The questions were grouped under six main categories reflecting clinical decision-making processes and were presented to both ChatGPT and Bing AI. Responses were scored on a 5-point Likert scale by two independent experts, assessing their alignment with the guideline. Mean scores were calculated for each category, and statistical comparisons were made using the Wilcoxon signed-rank test.

Results: ChatGPT demonstrated high consistency with the guideline across all categories (mean score: 4.88), while Bing AI showed lower compliance in several areas (mean score: 3.25). The differences in scores between the two systems were statistically significant across all categories ($p < 0.05$), with Bing AI performing particularly poorly in the areas of diagnosis/laboratory testing and multidisciplinary approach.

Conclusion: ChatGPT demonstrated higher accuracy and consistency than Bing AI in providing guideline-based clinical support regarding DSD. The use of AI-supported systems aligned with current guidelines holds significant potential in supporting complex, multidisciplinary decision-making processes. Therefore, the selection of AI tools in clinical settings should be informed by such systematic evaluations.

Keywords: Large Language Models, Disorders of Sex Development, Artificial Intelligence, Neonatology, Decision Support Systems

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Sorumlu Yazar/Corresponding Author: Saime Sundus Uygun, Selcuk University, Faculty of Medicine, Department of Naonatology, Konya, Türkiye
e-mail: uygunsaime@hotmail.com

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INTRODUCTION

Disorders of Sex Development (DSD) represent a group of rare but clinically complex conditions in which chromosomal, gonadal, and anatomical sex do not align. The diagnostic and management process typically begins immediately after birth and requires a multidisciplinary approach that incorporates not only physical findings but also genetic, hormonal, radiological, and ethical evaluations. These cases often create significant psychosocial pressure for both families and healthcare providers, particularly in terms of diagnosis and gender assignment. For this reason, the diagnosis and management of DSD must be conducted in strict accordance with up-to-date clinical guidelines (1–4).

In recent years, the use of artificial intelligence (AI) applications in the healthcare field has rapidly increased, emerging as valuable tools in clinical decision support. Among these, large language model (LLM)-based chatbots have gained attention for their potential to provide rapid and easily accessible medical information. However, the degree to which these systems offer recommendations and answers that align with evidence-based clinical guidelines remains a matter of concern (5).

Several studies have investigated the guideline compliance of popular chatbots such as ChatGPT and Bing AI across different medical disciplines (6,7). This study aims to systematically evaluate the responses of these two AI systems—both built on LLMs—to questions derived from the Turkish Neonatal Society's clinical guideline for the management of DSD. In doing so, the study not only tests the accuracy of these technological tools but also provides insight into their suitability as future clinical decision support systems.

MATERIALS AND METHODS

In this study, a standardized evaluation set consisting of 40 questions was developed based on the clinical guideline titled "Clinical Approach to Disorders of Sex Development" published by the Turkish Neonatal Society. The questions were categorized into six thematic domains that reflect the diagnostic and management steps outlined in the guideline:

1. Definition and Classification (Questions 1–5)
2. Postnatal Evaluation (Questions 6–12)
3. Diagnostic Process and Laboratory Testing (Questions 13–22)
4. Decision-Making and Multidisciplinary Approach (Questions 23–30)
5. Family Counseling and Social Considerations (Questions 31–35)
6. Outcomes and Recommendations (Questions 36–40)

Both AI systems—ChatGPT and Bing AI—were tested separately using this set of questions. All items were presented in identical format and sequence to each system via written input. The responses were independently evaluated by two experts (a pediatric surgeon and a neonatologist) for their compliance with the guideline.

Each response was scored using a 5-point Likert scale as follows:

Score	***Description***
5	Complete alignment with the guideline
4	Largely consistent – minor omissions
3	Moderate alignment – key omissions present
2	Low consistency – significant contradictions
1	No alignment – incorrect or irrelevant answer

Following evaluation, mean scores were calculated for both AI systems across all questions. Additionally, subgroup analyses were conducted to assess the average score within each thematic category.

Each response was independently scored by two clinicians (a pediatric surgeon and a neonatologist). The final score was calculated as the average of the two ratings. To assess inter-rater reliability, the intraclass correlation coefficient (ICC) was computed, revealing excellent agreement (ICC = 0.91).

Statistical Analysis

Since the distribution of scores did not meet the assumption of normality, the Wilcoxon signed-rank test was used to compare the paired scores of ChatGPT and Bing AI across the questions. Mean scores were also analyzed separately for each category, and a significance threshold of $p < 0.05$ was applied.

The Wilcoxon signed-rank test was chosen because each question was answered by both AI systems under identical conditions, and their paired scores were evaluated by the same raters. As the data are dependent, a paired non-parametric test was appropriate.

To further illustrate the comparative performance of the two systems, a summary table and a bar chart were generated to display average scores by category. Data analysis was conducted using Python, and visualizations were created with the matplotlib library.

RESULTS

The comparison of both AI systems revealed that ChatGPT exhibited high consistency with the national DSD guideline across all categories, with an overall mean score of 4.88 out of 5. In contrast, Bing AI demonstrated lower levels of compliance, with an overall mean score of 3.25. The group-based analysis showed that ChatGPT consistently outperformed Bing AI in every thematic category.

The Wilcoxon signed-rank test revealed statistically significant differences in mean scores between ChatGPT and Bing AI for all six categories ($p < 0.05$). The most prominent discrepancies were observed in the "Diagnostic Process and Laboratory Testing" and "Decision-Making and Multidisciplinary Approach" categories, where Bing AI performed notably poorly. A total score of 195 was calculated for ChatGPT across all 40 questions, whereas Bing AI received a cumulative score of 130. This substantial difference supports the conclusion that ChatGPT provides more guideline-consistent responses and may be better suited as a clinical decision support tool in the context of DSD.

Details of the category-based performance and statistical

Table 1. Statistical Comparison of AI Responses According to the National DSD Guideline

Category	chatGPT Mean Score	Bing AI Mean Score	Wilcoxon p-value
Definition and Clasification	5±0.00	3,4±0.18	0,0431
Postnatal Evaluation	5±0.00	3,29±0.22	0,0277
Diagnosis and Laboratory	4,8±0.12	2,9±0.15	0,0078
Desicion and Multidisciplinary	5±0.00	3,13±0.16	0,0123
Family and Social Approach	4,8±0.11	3,2±0.18	0,0417
Outcomes and Recommendations	5±0.00	3,2±0.14	0,0346

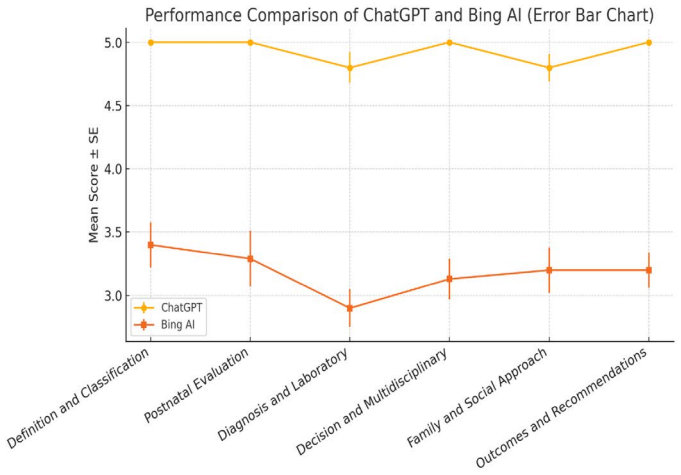

Figure 1. Comparative Analysis of ChatGPT and Bing AI Performance by Category

analysis are presented in Table 1, and a visual comparison of mean scores is provided in Figure 1.

DISCUSSION

Technological advancements in recent years have led to the widespread use of online resources for accessing medical information. The integration of artificial intelligence (AI) into these platforms has further accelerated this trend, making information retrieval more accessible for both physicians and patients. However, uncertainties remain regarding the clinical effectiveness and reliability of AI-based chatbots in healthcare settings. In this study, we evaluated the responses of two popular AI chatbot systems—ChatGPT and Bing AI—on the complex and multidisciplinary topic of Disorders of Sex Development (DSD) in newborns, by assessing their alignment with the guideline published by the Turkish Neonatal Society. ChatGPT demonstrated superior performance, particularly in categories involving diagnostic processes, laboratory testing, and multidisciplinary planning. This suggests that ChatGPT may have been trained with more comprehensive medical datasets.

Previous studies have reported similar findings. For example, ChatGPT has been shown to outperform Bing AI in the accuracy and comprehensiveness of information provided on topics such as prostate cancer (6) and microbiology (8). In the pediatric domain, studies have shown that ChatGPT demonstrated higher compliance with guidelines for conditions such as vesicoureteral reflux (VUR), while Bing AI often omitted critical elements (9). In another comparison of four AI systems, all models demonstrated guideline adherence for VUR; however, consistency varied across platforms (10). Additionally, ChatGPT was found to make more frequent and accurate references to scientific sources in pediatric urology evaluations (7).

In thyroid nodule management, ChatGPT provided consistent answers across different time points, suggesting temporal stability in its clinical guidance (11), which is a valuable feature for reliability. On the other hand, Bing AI's performance has been reported as more variable and limited, particularly in areas such as urolithiasis, where it failed to provide adequate references or comprehensive guideline-based answers (12,13). These findings align with the outcomes of our study. A similar trend has been observed in other medical disciplines. For instance, in obesity surgery, ChatGPT was more successful in identifying appropriate surgical options (14), and in gastroenterology, it was found to have a high informative capacity, though some limitations were also noted (15). Large language models have also been shown to provide higher-quality recommendations in managing complex, multidisciplinary cases (16). Given that DSD management inherently requires multidisciplinary collaboration, ChatGPT's consistent and evidence-based responses support its potential role in assisting clinical decision-making.

Nonetheless, several studies have also highlighted limitations of AI systems, such as delays in incorporating the latest guideline updates, lack of patient-specific personalization, and ethical decision-making challenges (15,17). Some of these limitations were also partially observed in our study, where both systems occasionally offered vague or superficial responses. A key strength of our study is the use of a double-blind evaluation design, in which both AI systems were assessed under identical conditions by two independent experts. However, one limitation is that only text-based responses were evaluated; visual or interactive capabilities of the systems were not included in the assessment.

CONCLUSION

In today's healthcare landscape, rapid access to medical information is essential; however, it is equally important that

such information is accurate, evidence-based, and personalized. Within this context, ChatGPT demonstrated notable superiority over Bing AI in terms of guideline adherence and consistency, particularly in domains requiring multidisciplinary coordination. These findings highlight ChatGPT's potential utility in clinical education, family counseling, and decision-support systems.

Nevertheless, it remains critical that AI systems maintain alignment with the most recent clinical guidelines, exhibit ethical sensitivity, and operate under expert supervision. As artificial intelligence continues to integrate into healthcare practice, the evaluation and selection of these systems should rely on structured, guideline-based analyses. Future studies involving diverse clinical guidelines and larger datasets will be instrumental in enhancing the reliability, standardization, and clinical integration of AI-supported tools. In this regard, guideline-oriented AI evaluations may represent a new paradigm for medical education and patient management.

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Address correspondence to: *Saime Sundus Uygun, Selcuk University, Faculty of Medicine, Department of Naonatology, Konya, Türkiye*
e-mail: *uygunsaime@hotmail.com*

REFERENCES

1. Özalp Kızılay D, Özen S. Current diagnostic approaches in the genetic diagnosis of disorders of sex development. J Clin Res Pediatr Endocrinol. 2024;16(4):401-10. doi: 10.4274/jcrpe.galenos.2024.2024-3-3.
2. Yavas AZ, Guran T. Diagnosis and management of non-CAH 46,XX disorders/differences in sex development. Front Endocrinol (Lausanne). 2024;15:1354759. doi: 10.3389/fendo.2024.1354759.
3. Ndoye NA, Diallo BA, Sylla M, et al. Ovotesticular disorders of sexual development: Diagnostic, therapeutic, and evolutionary aspects. J Pediatr Surg. 2025;60(4):162187. doi: 10.1016/j.jpedsurg.2025.162187
4. Khorashad BS, Goodarzi H, Greenfield D, et al. Recommendations for 46,XY disorders/differences of sex development across two decades: Insights from North American pediatric endocrinologists and urologists. Arch Sex Behav. 2024;53(8):2939-56. doi.org/10.1007/s10508-024-02942-1
5. Altıntaş E, Kılıç R, Gürlek C, et al. Comparative analysis of artificial intelligence chatbot recommendations for urolithiasis management: A study of EAU guideline compliance. Fr J Urol. 2024;34(7-8):102666. doi: 10.1016/j.fjurol.2024.102666
6. Alasker A, Alsalamah S, Alshathri N, et al. Performance of large language models (LLMs) in providing prostate cancer information. BMC Urol 24, 177 (2024). doi:10.1186/s12894-024-01570-0.
7. Caglar U, Tunç F, Özen B, et al. Evaluating the performance of ChatGPT in answering questions related to pediatric urology. J Pediatr Urol. 2024;20(1):26.e1-5. doi: 10.1016/j.jpurol.2023.08.003.
8. Ranjan J, Gupta A, Mehta S, et al. Assessment of artificial intelligence platforms with regard to medical microbiology knowledge: An analysis of ChatGPT and Gemini. Cureus. 2024;16(5):e60675. doi: 10.7759/cureus.60675.
9. Akyol Onder EN, Ensari E, Ertan P. ChatGPT-4o's performance on pediatric vesicoureteral reflux. J Pediatr Urol. 2025 Apr;21(2):504-09. doi: 10.1016/j.jpurol.2024.12.002.
10. Sarikaya M, Ozcan Siki F, Ciftci I. Use of artificial intelligence in vesicoureteral reflux disease: A comparative study of guideline compliance. J Clin Med. 2025 Mar 30;14(7):2378. doi: 10.3390/jcm14072378.
11. Deniz MS, Guler BY. Assessment of ChatGPT's adherence to ETA-thyroid nodule management guideline over two different time intervals 14 days apart: In binary and multiple-choice queries. Endocrine. 2024;85(2):794-02. doi: 10.1007/s12020-024-03750-2.
12. Cakir H, Kaya Z, Tunçer M, et al. Evaluating the performance of ChatGPT in answering questions related to urolithiasis. Int Urol Nephrol. 2024;56(1):17-21. doi: 10.1007/s11255-023-03773-0
13. Cil G, Dogan K. The efficacy of artificial intelligence in urology: A detailed analysis of kidney stone-related queries. World J Urol. 2024;42(1):158. doi: 10.1007/s00345-024-04847-z.
14. Lee Y, Tessier L, Brar K, et al. Performance of artificial intelligence in bariatric surgery: Comparative analysis of ChatGPT-4, Bing, and Bard in the American Society for Metabolic and Bariatric Surgery textbook of bariatric surgery questions. Surg Obes Relat Dis. 2024;20(7):609-13. doi: 10.1016/j.soard.2024.04.014.
15. Klang E, Sourosh A, Nadkarni GN, et al. Evaluating the role of ChatGPT in gastroenterology: A comprehensive systematic review of applications, benefits, and limitations. Therap Adv Gastroenterol. 2023;16:17562848231218618. doi: 10.1177/17562848231218618.
16. Ríos-Hoyo A, Shan NL, Li A, et al. Evaluation of large language models as a diagnostic aid for complex medical cases. Front Med (Lausanne). 2024 Jun 20;11:1380148. doi: 10.3389/fmed.2024.1380148.
17. Lopez-Gonzalez R, Sanchez-Cordero S, Pujol-Gebellí J, et al. Evaluation of the Impact of ChatGPT on the Selection of Surgical Technique in Bariatric Surgery. Obes Surg. 2025 Jan;35(1):19-24. doi: 10.1007/s11695-024-07279-1.

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Clinical and Pathological Analysis of Non-Epithelial Tumours of the Genitourinary System: A Single Centre Experience

Genitoüriner Sistemin Epitelyal Olmayan Tümörlerinin Klinik ve Patolojik Analizi: Tek Merkez Deneyimi

Sevda Dalar[1], Gulsum Ceren Civcan[1], Esma Cinar[1], Birgul Tok[1], Ilkay Cinar[1], Ozge Aydin[1], Hulya Oksuz Kabadayi[1], Kivanc Yilmaz[2], Demet Sengul[1]

[1]Giresun Training and Research Hospital, Department of Pathology, Giresun, Turkiye
[2]Samsun Training and Research Hospital, Department of Pathology, Samsun, Turkiye

ÖZET

Amaç: Genitoüriner sistem tümörlerinin çoğunluğu epitelyal kökenli iken, epitelyal olmayan tümörler genitoüriner sistemde izlenen tümörlerin yalnızca küçük bir bölümünü temsil eder. Bu çalışmada, bu nadir tümörlere yönelik tanı yaklaşımına katkıda bulunmayı ve bunların hasta prognozu üzerindeki etkilerine dikkat çekmeyi amaçladık.

Gereç ve Yöntemler: 2021-2023 yılları arasında genitoüriner sistem biyopsisi yapılan hastaların hasta kayıtlarına hastane veri tabanından ulaşıldı. Histopatolojik değerlendirmeye göre epitelyal tümör veya non-neoplastik doku tanısı konulan hastalar çalışma dışı bırakıldı. Epitelyal olmayan tümör tanısı almış hastaların demografik bilgilerine hastane veri tabanından, tümörle ilgili verilere ise patoloji raporlarından ulaşıldı.

Bulgular: Belirtilen dönemde, genitoüriner sistemde epitelyal olmayan tümör tanısı almış 20 vaka tespit edildi. Vakaların çoğu erkek hastalardan oluşmaktaydı. En sık görülen tümör lokalizasyon yeri böbrekti. Vakalar arasında 11 hastaya kötü huylu tümör tanısı konuldu, 9 hastaya ise iyi huylu tümör tanısı konuldu. Leiomyosarkom en sık görülen kötü huylu tümör olarak izlenirken, anjiyomyolipom en sık görülen iyi huylu tümördü. Diğer malign tümörler arasında rabdomyosarkom, liposarkom, andiferansiye pleomorfik sarkom, paraganglioma, malign soliter fibröz tümör ve diffüz büyük B hücreli lenfoma yer almaktaydı. İyi huylu epitelyal olmayan tümörler arasında ise anjiyoleiomyoma, schwannoma, renomedüller interstisyel hücreli tümör, leiomyoma ve anjiyofibrom mevcuttu. İyi huylu tümörü olan hastalara parsiyel rezeksiyon, transüretral rezeksiyon, eksizyonel biyopsi gibi cerrahi işlemler uygulanırken, kötü huylu tümörü olan hastalara radikal rezeksiyon, parsiyel rezeksiyon, trucut biyopsi ve transüretral rezeksiyon işlemleri uygulandı. Çalışma periyodunun sonunda (1 ila 38 ay arasında), iyi huylu tümör tanısı alan tüm hastalar hayattaydı, kötü huylu tümörü olan üç hasta ise hayatını kaybetmişti.

Sonuç: Genitoüriner sistemde, epitelyal olmayan tümörler nadir olarak izlenir ve geniş bir histolojik çeşitlilik gösterir. Kesin tanı histopatolojik incelemeye dayanır. Bu nadir tümörler için doğru tanı ve doğru tedavi stratejisi hastanın sağ kalımını önemli ölçüde değiştirir.

Anahtar Kelimeler: Genitoüriner sistem, epitelyal olmayan tümörler, malign, benign

ABSTRACT

Objective: While the majority of tumours in the genitourinary system originate from epithelial origin, non-epithelial tumours constitute only a minor subset. This study was conducted to improve diagnostic approaches for these rare tumours and to emphasize their impact on patient outcomes.

Materials and Methods: The patient records of patients who underwent genitourinary system biopsy between 2021 and 2023 were accessed from the hospital database. Patients diagnosed as epithelial tumour or non-neoplastic tissue according to histopathological evaluation were excluded from the study. Demographic data of patients diagnosed with non-epithelial tumours were obtained from the hospital database and tumour-related data were obtained from pathology reports.

Results: During the specified period, a total of 20 patients were identified, most of whom were male. The kidney was the most frequently affected site. Malignant tumours were diagnosed in 11 patients, and benign tumours in 9. Leiomyosarcoma was the most common malignant tumour, while angiomyolipoma was the most frequently observed benign tumour. Other malignant tumours included rhabdomyosarcoma, liposarcoma, undifferentiated pleomorphic sarcoma, paraganglioma, malignant solitary fibrous tumour, and diffuse large B-cell lymphoma. Benign tumours included angioleiomyoma, schwannoma, renomedullary interstitial cell tumour, leiomyoma, and angiofibroma. Surgical procedures varied depending on tumour type and included excisional biopsy, partial resection, and radical resection. During the follow-up period (ranging from 1 to 38 months), survival was achieved in all patients with benign tumours, whereas three patients with malignant tumours died.

Conclusion: Non-epithelial tumours of the genitourinary system are rare and display significant histological heterogeneity. Definitive diagnosis relies on histopathological evaluation. Appropriate diagnostic and therapeutic strategies may significantly influence patient survival.

Keywords: Genitourinary system, non-epithelial tumours, malignant, benign

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Sorumlu Yazar/Corresponding Author: Sevda Dalar, Giresun Training and Research Hospital, Department of Pathology, Giresun, Turkiye
e-mail: sevda.dalar@giresun.edu.tr

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INTRODUCTION

Non-epithelial tumours of the genitourinary system (GUS) are considered diagnostically challenging due to their rarity and wide morphological spectrum (1,2). These tumours may arise in various anatomical locations within the GUS, including the kidneys, bladder, prostate, testes, and paratesticular region. In the existing literature, only individual case reports have been presented on this topic. Therefore, the objective of this study was to evaluate the clinical and histopathological features of non-epithelial tumours occurring in the GUS and to underline the diagnostic difficulties they may present.

MATERIALS AND METHODS

Patient records of those who underwent biopsy of the genitourinary system between 2021 and 2023 were accessed from the hospital database. Patients diagnosed with epithelial tumours or non-tumoral tissue based on histopathological evaluation were excluded from the study. Tumours located in the entire genitourinary system—including the kidney, ureter, bladder, prostate, urethra, testis, and paratesticular region—were included, while those originating from the female genital tract were excluded. As a result, twenty patients diagnosed with non-epithelial tumours of the genitourinary system were identified.

Demographic data such as age and gender were retrieved from hospital records. Tumour-related information, including histopathological diagnosis, tumour size, anatomical location, metastasis status at diagnosis, and details of surgical intervention, was extracted from pathology reports. All pathological specimens were re-evaluated. Postoperative follow-up was performed at regular intervals. Survival data were obtained from patient files. Basic statistical methods (means, percentages) were used for the analysis of variables such as age, gender, histopathological diagnosis, tumour size, and anatomical location. Ethical approval for the study was obtained from the local Clinical Research Ethics Committee on 17 July 2024 (approval number: 17.07.2024/08).

RESULTS

The demographic characteristics of the patients are summarized in Table 1. A majority of the patients were male (13; 65%), and the remaining were female (7; 35%). Tumours were diagnosed in adulthood in 18 cases, while 2 cases involved pediatric patients. The patients' ages ranged from 11 to 89 years, with a mean age of 53.1 years. Additionally, one patient was diagnosed with Von Hippel–Lindau syndrome (VHL). The kidney was identified as the most common tumour site, accounting for 35% of cases (7 patients). Other locations included the bladder (5 cases), paratesticular region (3 cases), testis (3 cases), prostate (1 case), and urethra (1 case). The mean tumour diameter was 6.71 cm. Benign tumours had an average size of 3.3 cm, whereas malignant tumours averaged 9.4 cm

Table 1. Clinical and pathological features of the patients

Patient No	Age	Sex	Tumor type	Diameter (cm)	Localization	Metastasis	Operation	Survival	Follow-up
1	89	M	Angioleiomyoma	1	Bladder	None	TUR	Alive	9
2	78	M	MSFT	16	Bladder	None	Partial cystectomy	Alive	21
3	53	M	Paraganglioma	0.7	Bladder	None	TUR	Alive	12
4	40	M	Leiomyosarcoma	6.9	Prostate	None	Trucut biopsy	Alive	9
5	69	F	AML	2.5	Kidney	None	Partial nephrectomy	Alive	18
6	52	F	AML	11	Kidney	None	Partial nephrectomy	Alive	38
7	23	M	Schwannoma	5	Paratesticular region	None	Excisional biopsy	Alive	25
8	37	M	RMICT	1.2	Kidney	None	Partial nephrectomy	Alive	27
9	45	F	AML	2.5	Kidney	None	Partial nephrectomy	Alive	34
10	63	F	Leiomyosarcoma	17	Kidney	None	Radical nephrectomy	Alive	10
11	69	M	UPS	8	Kidney	Present	Trucut biopsy	Ex	7
12	32	M	Leiomyoma	2.5	Kidney	None	Partial nephrectomy	Alive	26
13	76	M	Liposarcoma	10	Paratesticular region	None	Radical orchiectomy	Alive	7
14	11	M	Angiofibroma	3.3	Paratesticular region	None	Excisional biopsy	Alive	8
15	16	M	Rhabdomyosarcoma	7.2	Testis	None	Partial orchiectomy	Alive	19
16	73	M	Leiomyosarcoma	10	Testis	None	Radical orchiectomy	Alive	28
17	75	M	DLBCL	13	Testis	Present	Radical orchiectomy	Ex	1
18	80	F	UPS	10.5	Bladder	None	Radical cystectomy	Ex	2
19	43	F	Leiomyoma	1.5	Urethra	None	Excisional biopsy	Alive	24
20	39	F	Paraganglioma	4.4	Bladder	None	TUR	Alive	1

M: Male, F: Female, TUR: Transurethral resection, MSFT: Malignant solitary fibrous tumor, AML: Angiomyolipoma, RMICT: Renomedullary interstitial cell tumor, UPS: Undifferentiated pleomorphic sarcoma, DLBCL: Diffuse large B-cell lymphoma

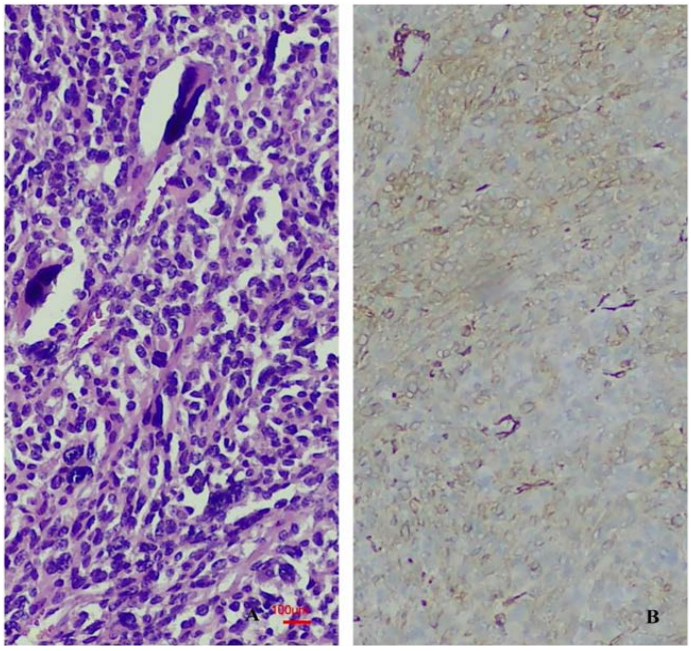

Figure 1. A) Leiomyosarcoma, composed of spindle-shaped smooth muscle cells, some of which have a bizarre appearance, HE x200. B) Positive staining of tumor cells with smooth muscle actin, SMA x200.

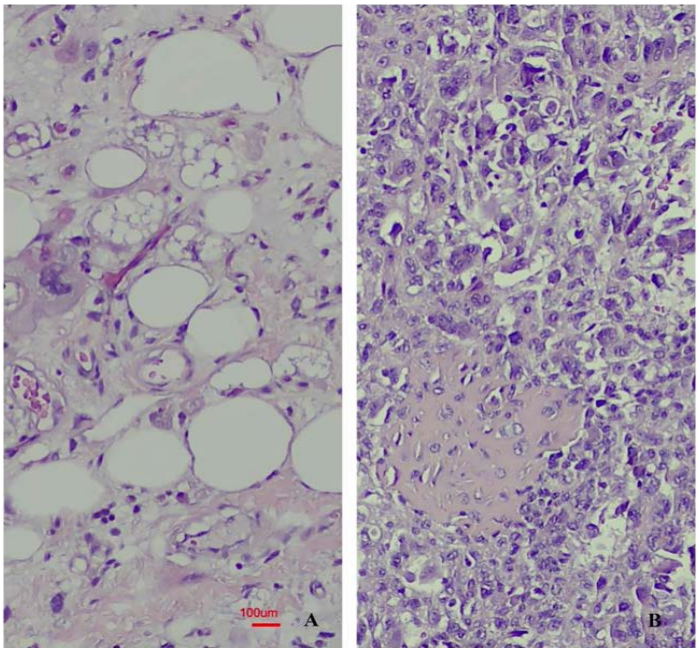

Figure 2. A) Areas of well-differentiated liposarcoma containing lipoblasts, HE x200. B) Dedifferentiated liposarcoma displaying regions of osteoblastic differentiation, HE x200.

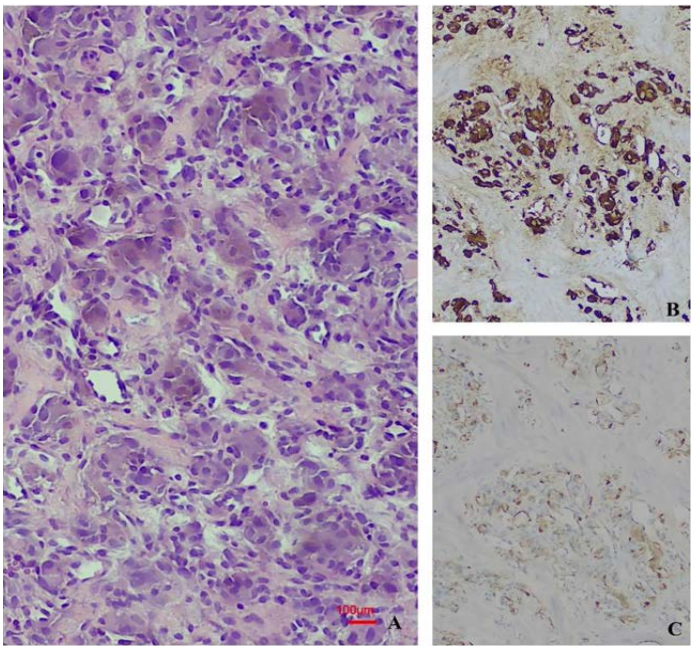

Figure 3. A) Paraganglioma exhibiting a nested pattern, HE x200. B) Neoplastic cells are positive for chromogranin A, x200. C) Sustentacular cells are positive for S100, x200.

in diameter. Of the total 20 patients, malignant tumours were diagnosed in 11 (55%) and benign tumours in 9 (45%).

Leiomyosarcoma was identified as the most common non-epithelial malignant tumour, accounting for 37.5% of all malignant cases (Figure 1). Other malignant tumours included rhabdomyosarcoma, liposarcoma (Figure 2), undifferentiated pleomorphic sarcoma, paraganglioma (Figure 3), malignant solitary fibrous tumour, and diffuse large B-cell lymphoma (DLBCL). Angiomyolipoma was the most frequently observed benign non-epithelial tumour, comprising 33.3% of benign cases (3 patients). Additional benign tumours included angioleiomyoma, schwannoma, renomedullary interstitial cell tumour, leiomyoma, and angiofibroma.

Among patients with benign tumours, partial resection was performed in 5 cases (55.5%), transurethral resection in 1 case, and excisional biopsy in 3 cases. In patients with malignant tumours, radical resection was conducted in 5 cases (45.4%), while partial resection, trucut biopsy, and transurethral resection were each performed in 2 cases. At the time of diagnosis, metastasis was present in 2 patients. The median follow-up period was 16.3 months. By the end of the follow-up (ranging from 1 to 38 months), all patients with benign tumours were alive, while 3 patients (27.3%) with malignant tumours had died.

DISCUSSION

Due to their rarity, non-epithelial tumours of the

genitourinary system (GUS) have primarily been reported in the literature through case reports or small series focused on specific organs (3–8). As a result of the limited number of comprehensive studies, data concerning their prevalence and incidence remain insufficient. In a study involving 48 cases of urological soft tissue sarcomas, the retroperitoneum was reported as the most frequent tumour location, with a male predominance and leiomyosarcoma being the most observed histological type. The average tumour diameter was noted as 9.5 cm (4). In the present study, most patients were male, the kidney was identified as the most frequent location, and leiomyosarcoma was the most common tumour type. The mean diameter of malignant tumours was found to be 9.4 cm. Another study analysing 28 bladder-based non-epithelial tumours reported 17 malignant and 11 benign cases. Small cell carcinoma and cavernous hemangioma were the most prevalent malignant and benign types, respectively (6). In the current series, paraganglioma was the most frequent malignant tumour in the bladder, while angioleiomyoma was the only benign tumour encountered in this site.

According to the World Health Organization (WHO) 5th edition classification of urinary and male genital tumours, non-epithelial tumours of the urogenital system are categorized as mesenchymal, hematolymphoid, melanocytic, and paragangliomas under neuroendocrine neoplasms. B-cell lymphomas and histiocytic tumours are classified within hematolymphoid neoplasms, whereas mucosal melanoma falls under melanocytic lesions (9). Mesenchymal tumours include fibroblastic, myofibroblastic, vascular, pericytic, smooth muscle, skeletal muscle tumours, and those of uncertain differentiation. Paragangliomas, as non-epithelial neuroendocrine tumours, are also classified under neuroendocrine neoplasms (9). Leiomyosarcoma has been identified as the most frequent histological subtype among non-epithelial tumours of the genitourinary tract (10). While commonly found in the retroperitoneum, its presence in the pelvis is less frequent. Within the GUS, these tumours are generally located in the bladder, prostate, and kidney, with primary paratesticular cases being extremely rare (11). In this study, leiomyosarcoma was the most prevalent histopathological diagnosis, with cases in the prostate, testis, and kidney.

Histologically, genitourinary leiomyosarcomas resemble those from other sites, consisting of intersecting fascicles of elongated spindle cells with blunt-ended nuclei. Well-differentiated tumours exhibit mild cytologic atypia and abundant eosinophilic cytoplasm, whereas poorly differentiated forms present with pleomorphism, necrosis, or increased mitotic activity (12). Adult genitourinary sarcomas are typically graded as low- or high-grade, with most leiomyosarcomas in the GUS—except those of the paratesticular region—being high-grade (13). These tumours generally show immunoreactivity for smooth muscle markers such as smooth muscle actin (SMA), desmin, h-caldesmon, and calponin, and are negative for S100. Embryonal rhabdomyosarcoma (ERMS) represents the most common urinary tract sarcoma in children, commonly affecting the urethra, bladder, and prostate (14). It is also the leading mesenchymal tumour of the paratestis in pediatric patients and may arise in the testicular parenchyma through somatic transformation of a teratoma (15). Although rare, renal involvement in children may occur through heterologous differentiation of Wilms tumour. In adults, bladder ERMS typically reflects sarcomatoid differentiation of urothelial carcinoma. In this series, ERMS was identified in an adolescent patient with testicular involvement.

ERMS displays variable cellularity, characterized by a range from spindle to fusiform cells within a loose myxoid stroma, with rhabdomyoblasts frequently present. In the botryoid subtype of ERMS, polypoid nodules with low cellular density are found near an epithelial surface, forming a dense layer of tumor cells known as the cambium layer. Alveolar RMS is composed of monomorphic round cells arranged in sheets or an alveolar pattern, separated by fibrous septa. Pleomorphic RMS features polygonal, round, and spindle-like cells with prominent nuclear pleomorphism. The spindle cell/sclerosing RMS subtype is defined by intersecting fascicles of monomorphic spindle cells in a dense, hyalinized matrix.
All rhabdomyosarcomas demonstrate skeletal muscle differentiation, with desmin positivity nearly universal and nuclear expression of myogenin and MYOD1 observed in most cases, albeit variably (16). Dedifferentiated liposarcoma (DDLPS) most commonly arises in the retroperitoneum but has also been documented in the spermatic cord, mediastinum, trunk, head, and neck. Within the GUS, case reports describe DDLPS in the paratesticular region and kidney (17,18). In the current case series, the tumour was located in the paratesticular area.

The histologic hallmark of DDLPS is an abrupt transition from an atypical lipomatous tumor/well-differentiated liposarcoma to a non-lipogenic, typically high-grade sarcoma. Dedifferentiated areas can display a variety of histologic patterns, most commonly resembling undifferentiated pleomorphic sarcoma or moderate to high-grade myxofibrosarcoma (19). Nearly all cases show diffuse nuclear expression of MDM2 and/or CDK4 (20). Undifferentiated sarcomas are rare and can appear in various anatomical sites without significant age or sex predilection. The pleomorphic subtype is more prevalent in older adults. In this study, such tumours were located in the kidney and bladder. These tumours lack distinct histological patterns and often exhibit pleomorphic multinucleated giant cells.

Solitary fibrous tumors (SFTs) of the GUS can arise in various anatomical sites, with cases reported in the kidney, urinary bladder, prostate, seminal vesicles, and penis. SFT is a fibroblastic tumor characterized by randomly arranged spindle cells in a "patternless" pattern with staghorn-like vascularization and defined by NAB2-STAT6 gene rearrangement. Immuno histochemically, most SFTs are positive for CD34 and STAT6, though PAX8 expression in some cases may lead to diagnostic confusion with sarcomatoid renal cell carcinoma, warranting consideration in the differential diagnosis of renal spindle cell tumors (21,22). Risk models based on factors such as patient age (≥ 55 years), mitotic rate (≥ 2 mitoses/mm^2), tumor size,

and presence of necrosis help estimate the risk of metastasis (23). In the current series, the SFT was in the bladder and classified as malignant based on risk stratification.

Paragangliomas (PGLs) are neuroendocrine neoplasms typically found in the retroperitoneum, pelvis, or bladder wall, associated with paraganglia presence. In the GUS, PGLs are infrequently observed in locations such as the prostate, seminal vesicles, kidneys, and paratestis. A significant proportion of PGLs 30-40% in adults and a higher percentage in children are linked to inherited conditions. Indicators such as young age, multiple tumors, and extra-adrenal tumors suggest the possibility of a germline mutation (24). PGLs display a distinctive Zellballen growth pattern, consisting of nests separated by a fibrovascular network and supported by sustentacular cells. Some PGLs, particularly those with clear cytoplasm, may mimic carcinomas of the bladder, prostate, or kidney (25). They typically show strong positivity for neuroendocrine markers like synaptophysin and chromogranin A, with S100 staining in sustentacular cells, while most are negative for cytokeratin. In our cases, the tumors were located in the bladder, with one patient being monitored for VHL. DLBCL can develop in any part of the GUS, with the kidney being the most frequent site (26). It is more prevalent within the GUS compared to other lymphoma types yet constitutes less than 1% of all genitourinary tumors (27). There is a slight male predominance in the incidence of primary genitourinary lymphomas (26).

DLBCL constitutes a morphologically and immuno phenotypically diverse group of aggressive lymphomas. It is characterised by sheets of large lymphoid cells with varying numbers of small lymphocytes, histiocytes, and other inflammatory elements. The tumour cells may exhibit centroblast or immunoblast features and can demonstrate variable pleomorphism (28). Among benign tumours of the GUS, a wide variety of histogenetic origins are observed, including cellular angiofibroma, hemangioma, glomus tumour, myointimoma, myopericytoma, PEComa, and leiomyoma. In addition to the general non-epithelial tumours encountered throughout the GUS, certain organs harbour specific tumour types. For instance, the kidney may host unique entities such as renomedullary interstitial cell tumour, juxtaglomerular cell tumour, and ossifying renal tumour of infancy.

This study was limited to cases from a single institution over a defined period. Expanding the study across multiple centres or extending the timeframe could potentially uncover additional mesenchymal tumours. For optimal patient care, it is crucial to maintain awareness of the morphological features of rare tumours and remain informed about emerging entities, even if direct morphological familiarity is lacking.

CONCLUSION

In addition to the numerous epithelial tumours, a broad spectrum of less common non-epithelial tumours can be encountered in the genitourinary tract. Accurate identification of these lesions is of critical importance, as it directly influences treatment protocols, surgical planning, and prognosis. A definitive diagnosis must be established through histopathological examination.

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Address correspondence to: *Sevda Dalar, Giresun Training and Research Hospital, Department of Pathology, Giresun, Turkiye*
e-mail: *sevda.dalar@giresun.edu.tr*

REFERENCES

1. Siegel R, Ward E, Brawley O, et al. Cancer statistics, 2011. CA Cancer J Clin 2011;61:212-36. doi: 10.3322/caac.20121.
2. Jemal A, Murray T, Ward E, et al. Cancer statistics, 2005. CA Cancer J Clin 2005;55:10-30. doi: 10.3322/canjclin.55.1.10.
3. Hatfield BS, Mochel MC, Smith SC. Mesenchymal Neoplasms of the Genitourinary System: A Selected Review with Recent Advances in Clinical, Diagnostic, and Molecular Findings. Surg Pathol Clin 2018;11:837-76. doi: 10.1016/j.path.2018.07.008.
4. Lee G, Lee SY, Seo S, et al. Prognostic factors and clinical outcomes of urological soft tissue sarcomas. Korean J Urol 2011;52:669-73. doi: 10.4111/kju.2011.52.10.669.
5. Shabaik A. Nonepithelial tumors and tumor-like lesions of the prostate gland. Crit Rev Clin Lab Sci 2003;40:429-72. doi: 10.1080/10408360390247823.
6. Xu AX, Wang XX, Hong BF, et al. Non-epithelial tissue tumors of the urinary bladder. Zhonghua Wai Ke Za Zhi 2003;41:530-3.
7. Paner GP, Aron M, Hansel DE, et al. Non-epithelial neoplasms of the prostate. Histopathology 2012;60:166-86. doi: 10.1111/j.1365-2559.2011.04020.x.
8. Galli L, Marcelli G. A proposito dei tumori non epiteliali della prostate. Arch Ital Urol Nefrol 1969;42:465-77.
9. WHO Classification of Tumours Editorial Board. Urinary and male genital tumours. Lyon (France): International Agency for Research on Cancer; 2022.
10. Urasaki T, Nakano K, Tomomatsu J, et al. Adult genitourinary sarcoma: The era of optional chemotherapeutic agents for soft tissue sarcoma. Int J Urol 2021;28:91-7. doi: 10.1111/iju.14417.
11. Dotan ZA, Tal R, Golijanin D, et al. Adult genitourinary sarcoma: the 25-year Memorial Sloan-Kettering experience. J Urol 2006;176:2033-8; discussion 2038-9. doi: 10.1016/j.juro.2006.07.021.
12. Bajaj G, Tirumani H, Whisman MK, et al. Comprehensive Review of Abdominopelvic Mesenchymal Tumors with Radiologic Pathologic Correlation and Update on Current Treatment Guidelines - Part 1. Semin Ultrasound CT MR 2020;41:222-38. doi: 10.1053/j.sult.2020.01.002.
13. Wang X, Liu L, Tang H, et al. Twenty-five cases of adult prostate sarcoma treated at a high-volume institution from 1989 to 2009. Urology 2013;82:160-5. doi: 10.1016/j.urology.2013.01.034.
14. Leiner J, Le Loarer F. The current landscape of rhabdomyosarcomas: an update. Virchows Arch 2020;476:97-108. doi: 10.1007/s00428-019-02676-9.
15. Raney B, Anderson J, Arndt C, et al. Soft-Tissue Sarcoma Committee of The Children's Oncology Group, Arcadia, CA. Primary renal sarcomas in the Intergroup Rhabdomyosarcoma Study Group (IRSG) experience, 1972-2005: A report from the Children's Oncology Group. Pediatr Blood Cancer 2008;51:339-43. doi: 10.1002/pbc.21639.

16. Morotti RA, Nicol KK, Parham DM, et al. An immunohistochemical algorithm to facilitate diagnosis and subtyping of rhabdomyosarcoma: The Children's Oncology Group experience. Am J Surg Pathol 2006;30:962-8. doi: 10.1097/00000478-200608000-00005.
17. Baran O, Bozkurt U, Aykac A. Hydrocele with Paratesticular Liposarcoma. J Coll Physicians Surg Pak 2022;32:S1-S2. doi: 10.29271/jcpsp.2022.Supp1.S1.
18. Williams JP, Savage PT. Liposarcoma of kidney. Br J Surg 1958;46:225-31. doi: 10.1002/bjs.18004619706.
19. McCormick D, Mentzel T, Beham A, et al. Dedifferentiated liposarcoma. Clinicopathologic analysis of 32 cases suggesting a better prognostic subgroup among pleomorphic sarcomas. Am J Surg Pathol 1994;18:1213-23. doi: 10.1097/00000478-199412000-00004.
20. Dei Tos AP, Doglioni C, Piccinin S, et al. Molecular abnormalities of the p53 pathway in dedifferentiated liposarcoma. J Pathol 1997;181:8-13. doi: 10.1002/(SICI)1096-9896(199701)181:1<8::AID-PATH700>3.0.CO;2-#.
21. Kouba E, Simper NB, Chen S, et al. Solitary fibrous tumour of the genitourinary tract: a clinicopathological study of 11 cases and their association with the NAB2-STAT6 fusion gene. J Clin Pathol 2017;70:508-514. doi: 10.1136/jclinpath-2016-204088.
22. Ullman D, Gordetsky J, Siegal GP, et al. PAX8 Expression in Solitary Fibrous Tumor: A Potential Diagnostic Pitfall. Appl Immunohistochem Mol Morphol 2019;27:195-202. doi: 10.1097/PAI.0000000000000561.
23. Demicco EG, Park MS, Araujo DM, et al. Solitary fibrous tumor: a clinicopathological study of 110 cases and proposed risk assessment model. Mod Pathol 2012;25:1298-306. doi: 10.1038/modpathol.2012.83.
24. Neumann HP, Bausch B, McWhinney SR, et al. Germ-line mutations in nonsyndromic pheochromocytoma. N Engl J Med 2002;346:1459-66. doi: 10.1056/NEJMoa020152.
25. Zhou M, Epstein JI, Young RH. Paraganglioma of the urinary bladder: a lesion that may be misdiagnosed as urothelial carcinoma in transurethral resection specimens. Am J Surg Pathol 2004;28:94-100. doi: 10.1097/00000478-200401000-00011.
26. Schniederjan SD, Osunkoya AO. Lymphoid neoplasms of the urinary tract and male genital organs: a clinicopathological study of 40 cases. Mod Pathol 2009;22:1057-65. doi: 10.1038/modpathol.2009.65.
27. Lontos K, Tsagianni A, Msaouel P, et al. Primary Urinary Tract Lymphoma: Rare but Aggressive. Anticancer Res 2017;37:6989-95. doi: 10.21873/anticanres.12167.
28. Swerdlow SH, Campo E, Pileri SA, et al. The 2016 revision of the World Health Organization classification of lymphoid neoplasms. Blood 2016;127:2375-90. doi: 10.1182/blood-2016-01-643569.

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ARAŞTIRMA MAKALESİ / RESEARCH ARTICLE

Is Prenatal Sex Hormone Balance a Risk Factor for the Development of Hidradenitis Suppurativa?

Prenatal Sex Hormon Balansı Hidradenitis Suppurativa Gelişimi için Bir Risk Faktörü müdür?

Mustafa Esen[1], Abdullah Demirbas[2], Esin Diremsizoglu[2]

[1]Dicle University, Faculty of Medicine Hospital, Department of Dermatology, Diyarbakır, Türkiye
[2]Kocaeli University, Faculty of Medicine Hospital, Department of Dermatology, Kocaeli, Türkiye

ÖZET

Amaç: Hidradenitis suppurativa (HS), hormonal etkilerin de rol oynadığı karmaşık ve çok faktörlü bir patogeneze sahip, kronik, inflamatuvar özellik gösteren bir deri hastalığıdır. İkinci ve dördüncü parmak uzunluğu oranı (2D:4D), doğum öncesi androjen etkisinin güvenilir bir biyobelirteci olarak kabul edilmekte olup, HS gelişimine yatkınlıkta etkili olabilir. Bu çalışmada, HS hastalarında 2D:4D oranı ile hastalık varlığı ve klinik şiddeti arasındaki olası ilişki araştırılmıştır.

Gereç ve Yöntemler: Yaş ve cinsiyet açısından eşleştirilmiş 140 HS hastası ile 140 sağlıklı kontrolün dahil edildiği kesitsel bir çalışma yürütüldü. Klinik hastalık şiddeti Hurley evrelemesi, Modifiye Sartorius Skoru (MSS) ve Klinik Genel Değerlendirme (PGA) kullanılarak değerlendirildi. Parmak uzunlukları dijital kumpas aracılığıyla standartize şekilde ölçülerek her iki el için ayrı ayrı 2D:4D oranları hesaplandı.

Bulgular: HS hastalarının her iki el 2D:4D oranı, kontrol grubuna kıyasla anlamlı olarak daha düşüktü ($p < 0.001$). Kadınlarda hem sol hem de sağ el oranları daha düşüktü ($p < 0.001$), erkeklerde ise yalnızca sol el oranı farklıydı ($p = 0.038$). Kadın hastalarda sol el oranı ile Hurley evresi, Modifiye Sartorius Skoru ve PGA arasında anlamlı ilişkiler saptandı (tüm $p < 0.05$).

Sonuç: Özellikle kadın HS hastalarında görülen düşük 2D:4D oranları, doğum öncesi artmış androjen maruziyetini yansıtabilir ve hastalık şiddeti ile ilişkili olabilir. Bulgular, HS patogenezinde hormonal etkilerin rolünü desteklemektedir; ancak bu ilişkinin doğrulanması için doğrudan hormonal ölçümleri içeren ileriye dönük çalışmalara ihtiyaç vardır. Bulguların yorumu, çalışmanın kesitsel tasarımı ile sınırlıdır. Ayrıca, tek merkezli tasarım ve biyokimyasal hormon düzeylerinin ölçülmemiş olması, sonuçların genellenebilirliğini ve hastalık mekanizmasına yönelik yorumların gücünü kısmen kısıtlayabilir.

Anahtar Kelimeler: Hidradenitis suppurativa, parmak uzunluğu oranı, testosteron, östrojen, hastalık şiddeti

ABSTRACT

Objective: Hidradenitis Suppurativa (HS) is a chronic skin condition marked by inflammation and driven by diverse underlying mechanisms, including hormonal involvement. The second-to-fourth digit ratio (2D:4D) is an established marker of prenatal androgen exposure, which may contribute to HS susceptibility. The objective of this study was to explore the potential link between 2D:4D digit ratios and hidradenitis suppurativa, along with their correlation to disease severity.

Materials and Methods: A total of 140 HS cases and 140 healthy subjects matched by age and gender were enrolled in this cross-sectional investigation. Clinical severity was assessed using Hurley staging, the Modified Sartorius Score, and the Physician Global Assessment (PGA). Finger lengths were measured using a digital caliper, and 2D:4D ratios were calculated separately for each hand.

Results: HS patients had significantly lower 2D:4D ratios in both hands compared with controls ($p < 0.001$). In females, both left- and right-hand ratios were lower ($p < 0.001$), while in males only the left-hand ratio differed ($p = 0.038$). In female patients, the left-hand ratio correlated with disease severity measures, including Hurley stage, Modified Sartorius Score, and PGA (all $p < 0.05$).

Conclusion: Lower 2D:4D ratios, particularly in female HS patients, may reflect higher prenatal androgen exposure and be linked to greater disease severity. These findings support a possible hormonal contribution to HS pathogenesis, though confirmation in prospective studies with direct hormonal assessment is warranted. Interpretation is limited by the cross-sectional design. Additionally, the single-center setting and absence of biochemical hormone measurements may partly limit generalizability and the strength of disease mechanism–related interpretations.

Keywords: Hidradenitis suppurativa, finger length ratio, testosterone, estrogen, disease severity

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Sorumlu Yazar/Corresponding Author: Esin Diremsizoglu, Kocaeli University, Faculty of Medicine, Department of Dermatology, Kocaeli, Türkiye
e-mail: mdesinarslan@gmail.com

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INTRODUCTION

Hidradenitis suppurativa (HS) is a chronic inflammatory disorder of the follicular units, most often affecting apocrine-bearing flexural regions such as the axillae, groin, and perianal area. The disease typically develops after puberty, with a reported prevalence between 1% and 4% (1). Its etiopathogenesis is multifactorial, involving hormonal factors, immune dysregulation, genetic predisposition, mechanical stress, smoking, and other environmental triggers (2,3). Hormonal influences are supported by the higher prevalence of HS in women and by symptom fluctuations linked to hormonal changes, such as exacerbations during the luteal phase and improvement during pregnancy, possibly due to the protective effects of elevated estrogen (4). HS also shares pathogenic features with acne vulgaris, including androgen-dependent follicular keratinization, suggesting a role for androgens in disease development (5-10).

The second-to-fourth digit ratio (2D:4D), calculated as the length of the second finger divided by the fourth, is an established indirect marker of prenatal androgen exposure and demonstrates sexual dimorphism (11). Lower 2D:4D ratios are associated with higher prenatal androgen and lower estrogen exposure, whereas higher ratios correspond to the opposite hormonal profile (11-14). Previous studies have reported significantly lower 2D:4D ratios in patients with androgen-dependent dermatological disorders such as androgenetic alopecia, seborrheic dermatitis, and acne vulgaris compared to healthy controls, reinforcing the hormonal connection in these conditions (15-17). Despite the recognized role of androgens in HS, the relationship between prenatal androgen exposure, as indicated by the 2D:4D digit ratio, and HS has not been systematically evaluated. This study aimed to investigate the potential association between 2D:4D ratios and HS, as well as their relationship with disease severity, to clarify the contribution of prenatal hormonal factors to HS pathogenesis.

MATERIALS AND METHODS

This cross-sectional study included 140 patients aged 18 years or older diagnosed with hidradenitis suppurativa (HS) based on clinical criteria, and 140 age and gender matched healthy controls, recruited from the Dermatology Clinic of a tertiary hospital between May 2024 and March 2025. Controls were healthy individuals without dermatological diseases or significant chronic illnesses. Demographic data (age, gender, BMI, waist circumference), disease duration, Hurley stage, modified Sartorius score, Physician Global Assessment (PGA), presence of comorbidities, and family history were obtained by anamnesis and clinical examination. PGA severity was classified into four categories (mild, moderate, severe, and very severe) based on lesion counts and characteristics.

Finger measurements were taken from both hands. The lengths of the second (index) and fourth (ring) fingers were measured on the palmar surface from the proximal palmar crease to the fingertip, using a digital Vernier caliper with 0.01 mm precision. All measurements were performed directly on the skin (not via photographs) by the same investigator to minimize inter-observer variability. Intra- and inter-observer reliability testing for finger length measurements was not conducted. The second-to-fourth digit length ratio (2D:4D) was calculated separately for the left and right hands. Blood samples for inflammatory markers (CRP, ESR), metabolic parameters (fasting blood glucose, LDL, triglycerides), and biochemical markers (ALT, creatinine) were collected from venous blood into vacuum tubes containing ethylenediaminetetraacetic acid (Vacutainer, Becton Dickinson, Marseille, France). ABO and Rh blood types were determined using standard tube and gel methods.

Psychological parameters (stress, depression, sleep quality) were evaluated using validated scales: Perceived Stress Scale (PSS), Beck Depression Inventory (BDI), and Pittsburgh Sleep Quality Index (PSQI).

Statistical analysis

The analysis was performed using SPSS version 25.0 (IBM Corp.). To determine data normality, the Kolmogorov–Smirnov test was used. As the data were non-normally distributed, outcomes were presented as median and interquartile range. Group comparisons for continuous variables were performed using the Mann–Whitney U test, while categorical variables were compared using the Chi-square test. Values of $p < 0.05$ were deemed statistically significant.

Ethics Approval

In accordance with the Declaration of Helsinki, the study was ethically approved by the institutional review board (Decision No: 2024/187).

RESULTS

A total of 140 patients with hidradenitis suppurativa (HS) and 140 healthy controls were enrolled in the study. Median age was similar between groups (patients: 36.00 years; controls: 35.00 years, p=0.781), and the proportion of females was comparable between patients (60.71%) and controls (55.00%; p=0.334). Median disease duration was 10.00 years (IQR: 8.00–14.00), and according to Hurley staging, 55.71% had stage 1, 34.29% had stage 2, and 10.00% had stage 3 disease. Inflammatory markers (CRP, ESR), metabolic parameters (blood glucose, LDL cholesterol, triglycerides), and liver enzyme (ALT) were significantly higher among patients compared to controls (p<0.001). Psychological and quality-of-life scores, including Perceived Stress Scale (PSS, 18.83 vs. 13.18), Beck Depression Inventory (BDI, 33.89 vs. 23.72), and sleep quality scores (9.62 vs. 6.73), were significantly worse in patients than controls (p<0.001; Table 1).

Digit length measurements and their ratios showed significant differences between hidradenitis suppurativa (HS) patients and controls. HS patients had significantly shorter left-hand 2nd finger (67.40 mm vs. 70.00 mm, p<0.001) and right-hand 2nd finger lengths (68.30 mm vs. 71.85 mm, p<0.001). The left (0.94 vs. 0.99) and right (0.95 vs. 0.99) hand 2D:4D ratios were also significantly lower in patients compared to controls (p<0.001 for both; Table 2). Gender-based subgroup analyses showed that female HS patients had significantly shorter left-hand 2nd finger lengths compared to female controls

Table 1. Clinical and Demographic Characteristics of Patient and Control Groups

Variables	Control (n=140)	Patient (n=140)	p-value
Age, years (median [IQR])	35.00 [32.00–38.00]	36.00 [30.00–38.00]	0.781[a]
Gender, female, n (%)	77 (55.00%)	85 (60.71%)	0.334[b]
BMI, kg/m^2 (median [IQR])	27.77 [26.57–29.05]	27.99 [26.52–28.63]	0.344[a]
Waist circumference, cm (median [IQR])	94.00 [85.00–106.75]	95.00 [82.50–106.00]	0.832[a]
Disease duration, years (median [IQR])	—	10.00 [8.00–14.00]	—
Hurley staging, n (%)	—	Stage 1: 78 (55.71%)	
		Stage 2: 48 (34.29%)	
		Stage 3: 14 (10.00%)	—
Modified Sartorius score (median [IQR])	—	13.00 [8.00–24.00]	—
Physician global assessment, n (%)	—	Mild: 78 (55.71%)	
		Moderate: 48 (34.29%)	
		Severe: 7 (5.00%)	
		Very severe: 7 (5.00%)	—
Comorbidities, n (%)	—	None: 55 (39.29%)	
		Severe Acne: 63 (45.00%)	
		Pilonidal Sinus: 22 (15.71%)	—
Family history, n (%)	—	Yes: 38 (27.14%)	
		No: 102 (72.86%)	—
Smoking, n (%)	65 (46.43%)	77 (55.00%)	0.152[b]
Alcohol consumption, n (%)	57 (40.71%)	67 (47.86%)	0.230[b]
CRP, mg/L (median [IQR])	17.08 [8.95–24.20]	24.40 [12.86–34.43]	<0.001[a]
ESR, mm/h (median [IQR])	12.16 [5.22–20.80]	17.38 [7.46–29.66]	<0.001[a]
Blood glucose, mg/dL (median [IQR])	108.51 [77.62–126.84]	155.01 [110.91–181.20]	<0.001[a]
HDL, mg/dL (median [IQR])	62.50 [45.71–79.01]	52.09 [38.09–65.83]	<0.001[a]
LDL, mg/dL (median [IQR])	92.92 [73.95–107.55]	132.75 [105.64–153.56]	<0.001[a]
Triglyceride, mg/dL (median [IQR])	129.60 [80.79–180.06]	185.14 [115.95–254.91]	<0.001[a]
ALT, U/L (median [IQR])	28.54 [21.62–34.57]	40.77 [30.89–49.33]	<0.001[a]
Creatinine, mg/dL (median [IQR])	0.71 [0.50–0.86]	1.02 [0.72–1.23]	<0.001[a]
PSS score (median [IQR])	13.18 [5.95–20.67]	18.83 [8.88–29.49]	<0.001[a]
BDI score (median [IQR])	23.72 [11.45–35.56]	33.89 [16.35–50.80]	<0.001[a]
Sleep quality score (median [IQR])	6.73 [3.54–10.84]	9.62 [5.06–15.45]	<0.001[a]

BMI: Body Mass Index; CRP: C-reactive protein; ESR: Erythrocyte sedimentation rate; HDL: High-density lipoprotein; LDL: Low-density lipoprotein; ALT: Alanine aminotransferase; PSS: Perceived Stress Scale; BDI: Beck Depression Inventory; 2D:4D ratio: 2nd to 4th digit length ratio; [a]Mann–Whitney U test, [b]Chi-square test.

Table 2. Comparison of Digit Length Measurements and 2D:4D Ratios between Patient and Control Groups

Variables	Control (n=140)	Patient (n=140)	p-value
Left hand 2nd finger length, mm (median [IQR])	70.00 [67.00–73.73]	67.40 [63.60–71.85]	<0.001[a]
Left hand 4th finger length, mm (median [IQR])	71.10 [68.60–75.60]	72.23 [69.10–75.30]	0.244[a]
Left hand 2D:4D ratio (median [IQR])	0.99 [0.94–1.01]	0.94 [0.88–0.99]	<0.001[a]
Right hand 2nd finger length, mm (median [IQR])	71.85 [68.60–75.30]	68.30 [64.13–73.30]	<0.001[a]
Right hand 4th finger length, mm (median [IQR])	71.60 [68.40–76.20]	72.45 [69.80–75.40]	0.437[a]
Right hand 2D:4D ratio (median [IQR])	0.99 [0.98–1.01]	0.95 [0.90–0.98]	<0.001[a]

[a] Mann–Whitney U test, IQR: Interquartile range, 2D:4D ratios: Second-to-fourth digit length ratios

(median: 67.04 vs. 69.80 mm; p<0.001). Similarly, female HS patients exhibited significantly lower 2D:4D ratios for both left (0.91 vs. 0.96; p<0.001) and right hands (0.92 vs. 0.97; p<0.001). Among male participants, only the left-hand 2D:4D ratio was significantly different between patients and controls (patients: 0.97, controls: 0.97; p=0.038), whereas other digit length measurements and right-hand 2D:4D ratio showed no significant differences (Table 3).

Gender subgroup analyses among clinical parameters showed that male HS patients had a significantly higher BMI than female patients (28.20 vs. 27.64 kg/m^2, p=0.028). Disease severity was also greater in males, with a higher proportion classified as Hurley stage 3 (18.18% vs. 4.71%, p=0.034) and more severe disease according to the Physician Global Assessment (PGA) (p=0.047). There was no significant difference between males and females in disease duration (10.00 vs. 9.00 years, p=0.928), Modified Sartorius Scores (p=0.416), or family history of HS (30.91% vs. 24.71%, p=0.420) (Table 4).

Analysis of the relationship between 2D:4D ratios and clinical parameters in HS patients revealed significant correlations in females but not in males. In female patients, left-hand 2D:4D ratio showed a positive correlation with Hurley staging (ρ=0.236, p=0.029), Modified Sartorius Score (ρ=0.255, p=0.019), and Physician Global Assessment (ρ=0.236, p=0.029). Additionally, right-hand 2D:4D ratio was negatively correlated with family history (ρ=-0.234, p=0.031) (Table 5).

Table 3. Gender subgroup comparison of digit lengths and 2D:4D ratios in patients and controls

Variables	Females (Median, IQR)			Males (Median, IQR)		
	Controls (n=77)	Patients (n=85)	P-value[a]	Controls (n=63)	Patients (n=55)	P-value[a]
Left-hand 2D	69.80 [67.00–72.65]	66.40 [62.40–70.40]	<0.001	68.90 [66.04–72.43]	68.90 [66.05–72.85]	0.573
Left-hand 4D	71.90 [68.85–75.60]	72.70 [69.20–75.60]	0.061	72.35 [69.10–75.40]	72.10 [68.50–75.60]	0.882
Left-hand 2D:4D ratios	0.96 [0.89–1.01]	0.91 [0.87–0.96]	<0.001	0.97 [0.93–0.99]	0.97 [0.94–1.00]	0.038
Right-hand 2D	68.90 [66.43–73.55]	66.90 [63.60–71.40]	<0.001	71.70 [67.85–74.60]	71.70 [67.90–74.30]	0.895
Right-hand 4D	72.20 [69.80–75.45]	73.20 [70.20–75.40]	0.163	72.75 [68.40–76.80]	72.20 [68.70–75.90]	0.846
Right-hand 2D:4D ratios	0.97 [0.92–1.01]	0.92 [0.88–0.96]	<0.001	0.98 [0.96–1.00]	0.98 [0.95–1.00]	0.452

[a] Mann–Whitney U test, IQR: Interquartile range, 2D:4D ratios: Second-to-fourth digit length ratios

Table 4. Clinical Characteristics of Female and Male Patients with HS

Variables	Females	Males	p-value
BMI (kg/m^2) (Median [IQR])	27.64 [26.26–28.60]	28.20 [26.96–29.30]	0.028[a]
Disease duration (years) (Median [IQR])	9.00 [8.00–14.00]	10.00 [7.00–14.00]	0.928[a]
Hurley staging 1/2/3 (n, %)	50 (58.82%)/ 31 (36.47%)/ 4 (4.71%)	28 (50.91%)/ 17 (30.91%)/ 10 (18.18%)	0.034[b]
Modified Sartorius Score (Median [IQR])	13.00 [8.00–23.00]	16.00 [8.00–26.00]	0.416[a]
Physician Global Assessment Mild/ Modarete/Severe/Very Severe (n, %)	50 (58.82%)/ 31 (36.47%)/ 1 (1.18%)/ 3 (3.53%)	28 (50.91%)/ 17 (30.91%)/ 6 (10.91%)/ 4 (7.27%)	0.047[b]
Family History (Yes, n [%])	21 (24.71%)	17 (30.91%)	0.420[b]

[a] Mann-Whitney U test, [b] Chi-Square test, IQR: Interquartile range

Table 5. Relationship Between 2D:4D Ratios and Disease Parameters in HS Patients

Variables	Females		Males	
	Left-hand 2D:4D	Right-hand 2D:4D	Left-hand 2D:4D	Right-hand 2D:4D
BMI (kg/m^2)	-0.056	0.041	-0.240	-0.163
Disease duration (years)	0.070	-0.069	0.045	-0.258
Hurley staging	0.236*	-0.012	0.116	-0.034
Modified Sartorius Score	0.255*	-0.094	0.114	-0.105
Physician Global Assessment	0.236*	-0.011	0.103	-0.119
Family History	-0.165	-0.234*	0.159	-0.102

Spearman's correlation coefficients (ρ) are shown. *Statistically significant correlations at $p < 0.05$.

DISCUSSION

In this study, we explored the association between second-to-fourth digit length ratios (2D:4D), an indirect marker of prenatal androgen exposure, and hidradenitis suppurativa (HS). HS is known to predominantly affect women, often emerging after puberty, which suggests a hormonal influence on disease expression (2). The majority of our HS patients were female (60.71%), and overall, patients had a similar median age (36 years) and BMI (27.99 kg/m^2) compared to controls. However, gender subgroup analysis in patients revealed that male HS patients exhibited significantly higher BMI and greater disease severity, with a higher proportion classified as Hurley stage 3 and more severe disease according to PGA, consistent with previous studies indicating that male HS patients are more likely to present with severe disease (3).

The exact hormonal mechanisms underlying HS are not fully understood, but clinical observations suggest significant hormonal influences, as disease flares often occur during low-estrogen, high-androgen menstrual phases, whereas clinical improvements are noted during pregnancy when estrogen levels rise (4). Furthermore, androgen-mediated follicular hyperkeratinization, a key feature shared with acne vulgaris,

may contribute to follicular occlusion and inflammation in HS patients (5-10). Supporting the androgen connection, previous studies have demonstrated beneficial effects of antiandrogen therapy in some HS cases, reinforcing androgen involvement in HS pathogenesis (18-23).

Recent studies have identified an association between 2D:4D ratios and various androgen-affected dermatological conditions. Research on androgenetic alopecia (AGA) has shown significantly lower right-hand 2D:4D ratios in affected individuals compared to healthy controls, though no correlation was found with disease severity (24). Another study reported a significant reduction in the left-hand 2D:4D ratio in AGA patients, while no change was observed in the right hand (15). Similarly, studies on acne vulgaris have reported lower 2D:4D ratios in female patients, with an observed link between increased sebaceous secretion and lower digit ratios in acne-prone women (17,21). However, conflicting findings exist, as some studies found no significant differences in 2D:4D ratios between acne patients and controls or correlations with reproductive hormones (26). Additionally, it has been suggested that right-hand 2D:4D ratios may serve as a stronger indicator of prenatal androgen exposure than left-hand ratios, although other research highlights a greater genetic influence on left-hand digit ratios (27).

Our findings revealed significantly lower left- and right-hand 2D:4D ratios in HS patients compared to controls, suggesting higher prenatal androgen exposure as a potential risk factor for HS. Gender subgroup analyses further demonstrated significantly lower 2D:4D ratios in female HS patients compared to female controls, consistent with similar observations in other androgen-sensitive dermatological diseases such as acne vulgaris and androgenetic alopecia (15-17,24,25). These previous studies indicated that lower 2D:4D ratios were associated with increased androgen sensitivity and disease severity in female patients (24,25). Interestingly, in our male subgroup, only the left-hand 2D:4D ratio showed a statistically significant difference between patients and controls. The relatively weaker associations observed in male patients could be related to inherently higher androgen levels in males, which might mask subtle variations in digit ratios linked to prenatal exposure. Further analysis of the relationship between 2D:4D ratios and clinical parameters in HS patients revealed significant correlations in females but not in males. The left-hand 2D:4D ratio was positively correlated with Hurley staging, Modified Sartorius Score, and Physician Global Assessment, suggesting a link between prenatal androgen exposure and disease severity in female patients. Additionally, a negative correlation was observed between the right-hand 2D:4D ratio and family history, indicating individuals with a family history of HS might have been exposed to higher prenatal androgen levels, which could play a role in disease susceptibility.

In addition, our study emphasized systemic involvement in HS patients, who demonstrated significantly elevated inflammatory markers (CRP, ESR), metabolic disturbances (higher LDL cholesterol, triglycerides, and fasting glucose), and increased liver enzyme levels (ALT). These findings are consistent with previous studies showing systemic inflammatory and metabolic implications of HS (8,9). Moreover, psychological and sleep quality assessments (PSS, BDI, sleep quality scores) were significantly worse among HS patients, highlighting the substantial psychosocial burden and impaired quality of life associated with HS. This study is among the first to investigate the role of prenatal androgen exposure in HS pathogenesis using digit ratios. A recently published study in 2023, which included 80 HS patients and 70 controls, found no significant difference in 2D:4D ratios between HS patients and controls. Additionally, in male HS patients, both right- and left-hand 2D:4D ratios were correlated with age of disease onset, while in female patients, individual right 2D and 4D finger lengths, not the ratio, were correlated with DHEA-S levels (28). However, our larger sample size enabled subgroup analyses by gender, providing additional insights into the relationship between 2D:4D ratios and HS.

Our study has some limitations. The cross-sectional design limits causal interpretations of our results. Furthermore, direct hormonal levels were not assessed, preventing confirmation of current hormonal status associations. Intra- and inter-observer reliability testing for finger length measurements was not conducted, which may introduce potential measurement variability. Future prospective studies with larger sample sizes, comprehensive hormonal profiling, and advanced analytical models such as factorial ANOVA, multiple linear regression, and interaction modeling are needed to validate and expand upon these findings.

CONCLUSION

In conclusion, our findings suggest that lower 2D:4D ratios, particularly in female HS patients, may indicate higher prenatal androgen exposure, potentially contributing to disease susceptibility and severity. Additionally, the left-hand 2D:4D ratio correlated with disease severity in females, while a negative correlation between the right-hand 2D:4D ratio and family history suggests a possible genetic influence on hormonal factors in HS. Further research should focus on prospective hormonal profiling alongside digit ratios to clarify their predictive role and to better understand HS pathogenesis.

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Address correspondence to: *Esin Diremsizoglu, Kocaeli University, Faculty of Medicine, Department of Dermatology, Kocaeli, Türkiye*
e-mail: *mdesinarslan@gmail.com*

REFERENCES

1. Marzano AV, Chiricozzi A, Giovanardi G, et al. Creation of a severity index for hidradenitis suppurativa that includes a validated

quality-of-life measure: The HIDRAscore. J Eur Acad Dermatol Venereol. 2020;34(8):1815-21. doi:10.1111/jdv.16328
2. Napolitano M, Megna M, Timoshchuk EA, et al. Hidradenitis suppurativa: From pathogenesis to diagnosis and treatment. Clin Cosmet Investig Dermatol. 2017;10:105-15. doi:10.2147/CCID.S111019
3. Shih T, Seivright JR, McKenzie SA, et al. Gender differences in hidradenitis suppurativa characteristics: A retrospective cohort analysis. Int J Womens Dermatol. 2021;7(5 Suppl B):672-74. doi:10.1016/j.ijwd.2021.07.003
4. Riis PT, Ring HC, Themstrup L, et al. The role of androgens and estrogens in hidradenitis suppurativa: A systematic review. Acta Dermatovenerol Croat. 2016;24(4):239-49.
5. George R, Clarke S, Thiboutot D. Hormonal therapy for acne. Semin Cutan Med Surg. 2008;27(3):188-96. doi:10.1016/j.sder.2008.06.002
6. Frew JW. Hidradenitis suppurativa is an autoinflammatory keratinization disease: A review of the clinical, histologic, and molecular evidence. JAAD Int. 2020;1(1):62-72. doi:10.1016/j.jdin.2020.05.005
7. Gervásio CG, Bernuci MP, Silva-de-Sá MF, et al. The role of androgen hormones in early follicular development. ISRN Obstet Gynecol. 2014;2014:818010. doi:10.1155/2014/818010
8. Melnik BC. Linking diet to acne metabolomics, inflammation, and comedogenesis: An update. Clin Cosmet Investig Dermatol. 2015;8:371-88. doi:10.2147/CCID.S69135
9. Danby FW. Diet in the prevention of hidradenitis suppurativa (acne inversa). J Am Acad Dermatol. 2015;73(5 Suppl 1): S52-54. doi:10.1016/j.jaad.2015.07.042
10. Verma SS, Sharma K, Chhabra S. Pathogenesis of hidradenitis suppurativa: An immunological perspective. Indian J Dermatol. 2023;68(3):296-300. doi:10.4103/ijd.ijd_594_22
11. Manning JT. Resolving the role of prenatal sex steroids in the development of digit ratio. Proc Natl Acad Sci U S A. 2011;108(39):16143-44. doi:10.1073/pnas.1113312108
12. Lutchmaya S, Baron-Cohen S, Raggatt P, et al. 2nd to 4th digit ratios, fetal testosterone and estradiol. Early Hum Dev. 2004;77(1-2):23-28. doi:10.1016/j.earlhumdev.2003.12.002
13. Hisasue S, Sasaki S, Tsukamoto T, et al. The relationship between second-to-fourth digit ratio and female gender identity. J Sex Med. 2012;9(11):2903-10. doi:10.1111/j.1743-6109.2012.02815.x
14. Pennell LM, Galligan CL, Fish EN. Sex affects immunity. J Autoimmun. 2012;38(2-3):J282-91. doi:10.1016/j.jaut.2011.11.013
15. Unal M. Digit ratio 2D:4D is a possible indicator for androgenetic alopecia in males. J Cosmet Dermatol. 2018;17(3):545-48. doi:10.1111/jocd.12403
16. Islamoglu ZGK. Second-to-fourth digit ratio and seborrheic dermatitis in males: A cross-sectional study. An Bras Dermatol. 2019;94(3):327-30. doi:10.1590/abd1806-4841.20198578
17. Bilgiç O, Altinyazar C, Hira H, et al. Investigation of the association of the second-to-fourth digit ratio with skin sebum levels in females with acne vulgaris. Am J Clin Dermatol. 2015;16(6):559-64. doi:10.1007/s40257-015-0147-3
18. Ceruti JM, Leirós GJ, Balañá ME. Androgens and androgen receptor action in skin and hair follicles. Mol Cell Endocrinol. 2017;465:122-33. doi:10.1016/j.mce.2017.09.009
19. Barth JH, Layton AM, Cunliffe WJ. Endocrine factors in pre- and postmenopausal women with hidradenitis suppurativa. Br J Dermatol. 1996;134(6):1057-59. doi:10.1111/j.1365-2133.1996.tb07800.x
20. Jemec GB. Hidradenitis suppurativa. J Cutan Med Surg. 2003;7(1):47-56. doi:10.1007/s10227-002-2104-z
21. Palmer RA, Keefe M. Early-onset hidradenitis suppurativa. Clin Exp Dermatol. 2001;26(6):501-03. doi:10.1046/j.1365-2230.2001.00876.x
22. Lewis F, Messenger AG, Wales JK. Hidradenitis suppurativa as a presenting feature of premature adrenarche. Br J Dermatol. 1993;129(4):447-48. doi:10.1111/j.1365-2133.1993.tb03174.x
23. Farrell AM, Randall VA, Vafaee T, et al. Finasteride as a therapy for hidradenitis suppurativa. Br J Dermatol. 1999;141(6):1138-39. doi:10.1046/j.1365-2133.1999.03224.x
24. Bilgiç O, Altinyazar HC, Eryilmaz D, et al. Are 2D:4D finger-length ratios an indicator of androgenetic alopecia in males? An Bras Dermatol. 2016;91(2):156-59. doi:10.1590/abd1806-4841.20164622
25. Bilgiç O, Doğdu M, Islamoğlu GK, et al. The relationship between the second to fourth digit ratio and acne vulgaris. J Eur Acad Dermatol Venereol. 2014;28(10):1340-43. doi:10.1111/jdv.12287
26. Unal M, Urun Unal G, Balevi S, et al. The second to fourth digit ratio in acne vulgaris. Pediatr Dermatol. 2015;32(5):651-55. doi:10.1111/pde.12594
27. Gobrogge KL, Breedlove SM, Klump KL. Genetic and environmental influences on 2D:4D finger length ratios: A study of monozygotic and dizygotic male and female twins. Arch Sex Behav. 2008;37(1):112-18. doi:10.1007/s10508-007-9272-2
28. Gonulal M, Altıner D, Ozturk A, et al. The second to fourth digit ratio in the patients with hidradenitis suppurativa. J Izmir Med Fac. 2023;2(1):9-14. doi:10.57221/izmirtip.1216588

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OPEN ARAŞTIRMA MAKALESİ / RESEARCH ARTICLE

Azacitidine and Venetoclax Treatment in Acute Myeloid Leukemia: Real-Life Experience

Azasitidin ve Venetoklaks Tedavisi ile Akut Myeloid Lösemi: Gerçek Yaşam Deneyimi

Ozlem Beyler[1], Nida Akgul[2], Hulya Yilmaz Tekinhatun[1], Ali Dogan[2], Cengiz Demir[1]

[1]Gazi Yaşargil Training and Research Hospital, Department of Hematology Diyarbakır, Türkiye
[2]Van Yüzüncü Yıl University, Department of Hematology, Van, Türkiye

ÖZET

Amaç: Bu çalışma, yoğun kemoterapiye uygun olmayan yeni tanı almış akut myeloid lösemi (AML) hastalarında azasitidin-venetoklaks (AZA-VEN) tedavisinin gerçek yaşam koşullarındaki etkinliğini, güvenilirliğini ve sağkalım sonuçlarını değerlendirmeyi amaçlamıştır.

Gereç ve Yöntemler: İki merkezde 2022–2025 yılları arasında tedavi edilen 36 AML hastası retrospektif olarak analiz edildi. Veriler arasında demografik özellikler, tedavi döngüleri, doz ayarlamaları, yanıt oranları (tam remisyon, parsiyel remisyon, refrakter hastalık), hematolojik iyileşme, yan etkiler ve genel sağkalım yer aldı.

Bulgular: Ortanca yaş 66 (dağılım: 27–98) idi ve hastaların %61,1'i tam remisyon (CR) sağladı. Ortanca genel sağkalım (OS) 22 ay idi (95% GA: 13,1–30,9); ≥3 kür alan hastalarda sağkalım anlamlı olarak daha uzundu (23,7 aya karşılık 6,4 ay; p=0,031) ve erken nötrofil iyileşmesi gösterenlerde (>1000/µL, 7. gün itibariyle: 29,4 aya karşılık 13,7 ay; p=0,009) de benzer şekilde anlamlı fark mevcuttu. Grade 3 toksisite görülen hastalarda (%33,3) sağkalım daha kötüydü (6,4 aya karşılık Grade 2 için 22 ay; p=0,006). İnvaziv fungal enfeksiyona rastlanmadı.

Sonuç: AZA–VEN tedavisi, yoğun kemoterapiye uygun olmayan AML hastalarında etkili ve güvenli bir seçenek olup, sağkalım sonuçları büyük klinik çalışmalarla karşılaştırılabilir düzeydedir ve bazı yönlerden onlarla uyum göstermektedir. Bulgularımız, özellikle üç veya daha fazla kür tedavi alabilen hastalarda sağkalımın anlamlı şekilde uzadığını göstermiştir; bu durum, yan etkiler uygun biçimde yönetildiğinde tedavi sürekliliğinin önemini vurgulamaktadır. Çalışmamızda invaziv fungal enfeksiyonların hiç görülmemesi, literatürde bildirilen değişken oranlarla karşılaştırıldığında dikkat çekicidir ve uyguladığımız profilaksi stratejisinin olumlu katkı sağlamış olabileceğini düşündürmektedir. Ayrıca, kadın hastalarda gözlenen sağkalım avantajı kayda değer olmakla birlikte, dikkatle yorumlanmalı, hipotez oluşturucu bir bulgu olarak kabul edilmeli ve daha büyük, iyi tasarlanmış çalışmalarda doğrulanmalıdır.

Anahtar Kelimeler: Akut Miyeloid Lösemi, Azasitidin, Venetoklaks, Gerçek Yaşam Verileri, Sağkalım

ABSTRACT

Objective: This study evaluated the real-world efficacy, safety, and survival outcomes of azacitidine-venetoclax (AZA-VEN) therapy in newly diagnosed acute myeloid leukemia (AML) patients ineligible for intensive chemotherapy.

Materials and Methods: A retrospective analysis was conducted on 36 AML patients treated at two centers between 2022–2025. Data included demographics, treatment cycles, dose adjustments, response rates (complete remission, partial remission, refractory disease), hematologic recovery, side effects, and overall survival.

Results: The median age was 66 years (range: 27–98), with 61.1% achieving CR. Median OS (Overall Survival) was 22 months (95% CI: 13.1–30.9), significantly longer in patients receiving ≥3 cycles (23.7 vs. 6.4 months; p=0.031) and those with early neutrophil recovery (>1000/µL by day 7: 29.4 vs. 13.7 months; p=0.009). Grade 3 toxicity (33.3% of patients) correlated with poorer survival (6.4 vs. 22 months for Grade 2; p=0.006). No invasive fungal infections occurred.

Conclusion: AZA–VEN is effective and safe in chemotherapy-ineligible AML, providing survival outcomes that are comparable to, and in some aspects even consistent with, those observed in pivotal clinical trials. Our findings indicate that extended therapy, especially in patients who were able to continue for three or more cycles, was associated with a meaningful improvement in overall survival, thereby emphasizing the importance of maintaining treatment continuity whenever possible. The complete absence of invasive fungal infections in our cohort, in contrast to the variable rates reported in previous studies, suggests that our prophylaxis strategy may have contributed positively and could be of clinical relevance. In addition, the female survival advantage observed in our study, while noteworthy, should be interpreted with caution, considered as hypothesis-generating, and further validated in larger, well-designed studies.

Keywords: Acute myeloid leukemia, azacitidine, venetoclax, real-world data, survival

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Sorumlu Yazar/Corresponding Author: Ozlem Beyler, Gazi Yaşargil Training and Research Hospital, Department of Hematology, Diyarbakır, Türkiye
e-mail: drozlembeyler@gmail.com

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INTRODUCTION

Acute myeloid leukemia (AML) is an aggressive hematologic malignancy resulting from the malignant transformation of hematopoietic stem cells and characterized by abnormal proliferation of immature myeloid cells. AML is particularly more common in the elderly population, with a significant proportion of patients being 65 years or older at the time of diagnosis. The clinical course and prognosis of the disease depend on many factors, including genetic and molecular characteristics, cytogenetic changes, and the patient's overall performance status (1). The traditional treatment approach for AML involves intensive induction chemotherapy with the cytarabine- and anthracycline-based "7+3" regimen. Although this regimen provides high complete response rates in young and healthy patients, intensive chemotherapy may not be suitable for patients aged 65 and older due to myelosuppression and treatment-related complications. For this group of patients, low-intensity chemotherapy regimens and targeted therapies have come to the forefront (2).

In recent years, the use of targeted agents in AML treatment has brought about a significant shift. Venetoclax, a B-cell leukemia/lymphoma 2 (BCL-2) inhibitor, has emerged as an effective anti-leukemic agent by inducing apoptosis in leukemic cells. Its combination with hypomethylating agents (HMAs) such as azacitidine or decitabine provides an effective treatment option for newly diagnosed AML patients who are ineligible for intensive chemotherapy (3,4). Although azacitidine and venetoclax have become standard treatment in many centers today, significant differences are observed between real-world data and clinical trial results due to variations in practice.

In our study, we aimed to share our experience regarding the differences between real-life data and clinical trials in terms of treatment duration, side effect profile, and survival outcomes with azacitidine-venetoclax therapy.

MATERIALS AND METHODS

In this retrospective study, we included adult AML patients who were ineligible for intensive chemotherapy at diagnosis and were initiated on AZA-VEN therapy between January 2022 and May 2025 at Gazi Yaşargil Training and Research Hospital and Van Yüzüncü Yıl University Faculty of Medicine Hospital. Demographic data (age, sex), disease subtype, laboratory findings at diagnosis (WBC, hemoglobin, platelets, blast percentage), genetic/molecular characteristics, ECOG performance status, and whether AML was de novo or secondary were recorded. The treatment start date, venetoclax dose and possible dose reductions, side effects and their severity, bone marrow response after the first cycle, response status, and the number of cycles received during treatment were evaluated. Venetoclax dose adjustments due to drug side effects were documented. A history of invasive fungal infections and antifungal prophylaxis was investigated. Patients were regularly monitored during treatment, and the last follow-up date and survival status were included in the data. Our study has ethics committee approval dated 23/05/2025, numbered 497.

Statistical Analysis

Statistical analyses were performed using "IBM SPSS Statistics for Windows, Version 25.0 (Statistical Package for the Social Sciences, IBM Corp., Armonk, NY, USA)." Descriptive statistics were presented as n and % for categorical variables and as mean ± SD and median (min-max) for continuous variables. The Kaplan-Meier method was used to compare survival durations between clinical groups. A p-value <0.05 was considered statistically significant.

RESULTS

A total of 36 AML patients were included in this study. The mean age was 66.05 ± 14.75 years, with an age range of 27 to 98 years, and the median age was calculated as 66.0 years. Of the patients, 55.6% were over 60 years old, while 44.4% were 60 years or younger. The gender distribution showed that 38.1% were female and 61.1% were male. When the distribution of AML subtypes was evaluated, the most common was M1 subtype at 58.3%; other subtypes were M0 (8.3%), M2 (16.7%), M4 (8.3%), and M5 (8.3%). ECOG performance status assessment revealed that 16.6% of patients were ECOG 0, 41.7% were ECOG 1, and 41.7% were ECOG 2. Two patients were diagnosed with chronic myelomonocytic leukemia, one with prostate cancer, and one with secondary AML following ovarian cancer treatment. None of the patients had poor genetic risk. For venetoclax treatment doses, 400 mg was administered to 55.6% of patients, 100 mg to 19.4%, 200 mg to 16.7%, and 300 mg to 8.3%. The mean number of venetoclax cycles received by patients was 5.77 ± 3.57, with a median of 6 (1–12). Of the patients, 30.6% received 1–2 cycles, while 69.4% received 3 or more cycles. The mean day for neutrophil count to reach >500 cells/μL after treatment was 11.69 ± 14.86, and the rate of patients reaching this value by day 7 was recorded as 57.7%. The mean day for neutrophil count to reach >1000 cells/μL was 13.47 ± 13.98, and the rate of patients reaching this value by day 7 was calculated as 47.6%. The mean day for platelet count to reach >50,000/μL was 25.42 ± 12.84, with a median day of 27. At diagnosis, the mean bone marrow blast percentage was 54.27 ± 25.30, while the mean blast percentage after the first cycle was 10.11 ± 12.68. In the bone marrow evaluation after the first cycle, the rate of patients with blast count <5% was 61.1%, while the rate with ≥5% was 38.9%. In terms of treatment response, 61.1% of patients achieved complete remission, 33.3% achieved partial remission, and 5.6% were refractory. Among the side effects requiring venetoclax dose reduction, the most frequently reported was neutropenia at 62.5%, followed by abdominal pain at 25.0% and diarrhea at 12.5%. When the severity of side effects was examined, Grade 1 side effects were observed in 20.0% of patients, Grade 2 in 46.7%, and Grade 3 in 33.3%. The mean follow-up duration was 18.60 ± 17.74 months, with a median of 15 months (min: 2.77 – max: 97.73). Kaplan-Meier survival analysis revealed a median overall survival of 22.00 months for the entire patient group (95% CI: 13.09–30.90); the two-year survival rate was 43.0%, and the five-year survival rate was 27.9%. During the follow-up period, 52.8% of patients died

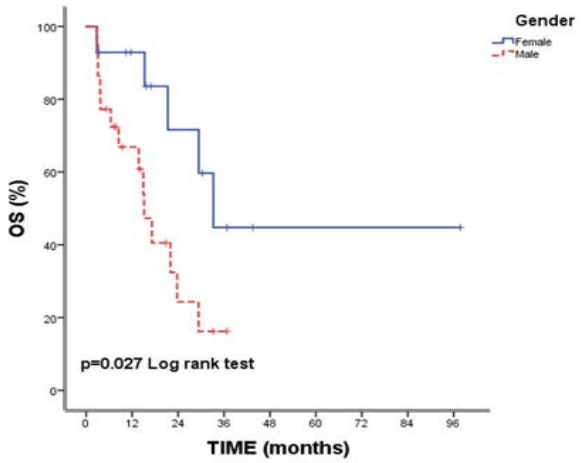

Figure 1. Overall survival (OS) according to gender. Median OS was 33.2 months for female patients and 15.1 months for male patients (p=0.027, Log-rank test).

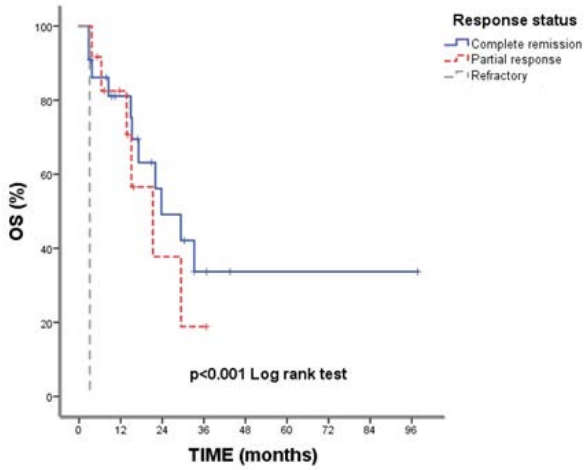

Figure 3. OS based on response status. Median OS was 23.73 months in complete remission, 21.26 months in partial response, and 3.06 months in refractory patients (p<0.001).

(exitus), while 47.2% survived. Significant survival differences were observed based on some variables. The median survival for female patients was 33.2 months, while for males it was 15.1 months, and the gender variable was found to be statistically significant (p=0.027) (Figure 1). The median survival of patients whose neutrophils reached >1000 cells/μL within 7 days after treatment was 29.43 months, while it was 13.73 months for those who reached this value on or after day 7, and the difference was statistically significant (p=0.009) (Figure 2). The median survival of patients who achieved complete remission was 23.73 months, while it was 21.26 months for those with partial response and only 3.06 months for refractory patients. The survival difference based on response status was statistically significant (p<0.001) (Figure 3). The median survival of patients who received ≥3 cycles of venetoclax treatment was 23.73 months, while it was 6.43 months for those who received only 1–2 cycles, and this difference was also significant (p=0.031) (Figure 4). When evaluated in terms of side effect severity, survival was 6.43 months in patients with Grade 3 side effects, 22.00 months in Grade 2, and 15.10

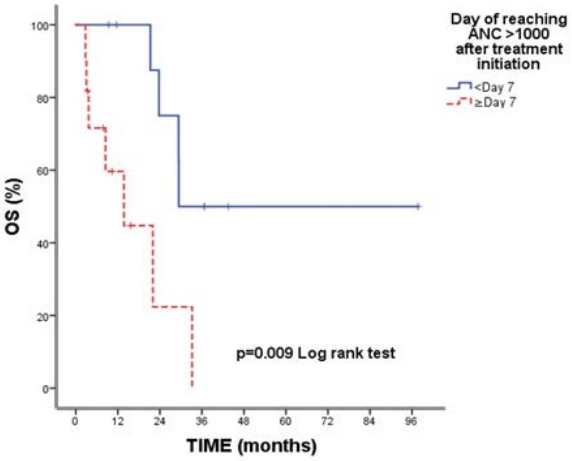

Figure 2. OS according to neutrophil recovery time. Patients who reached ANC >1000/μL before day 7 had significantly longer OS (29.43 vs. 13.73 months, p=0.009).

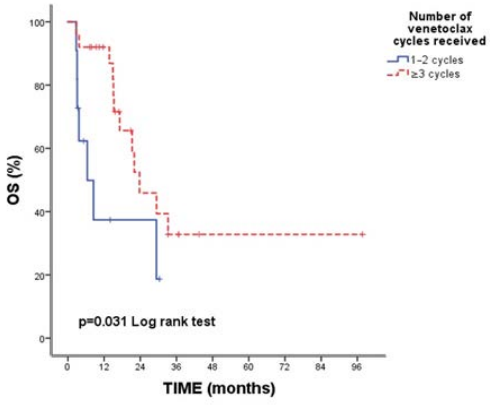

Figure 4. OS according to number of venetoclax cycles. Patients receiving ≥3 cycles had significantly better OS (23.73 vs. 6.43 months, p=0.031).

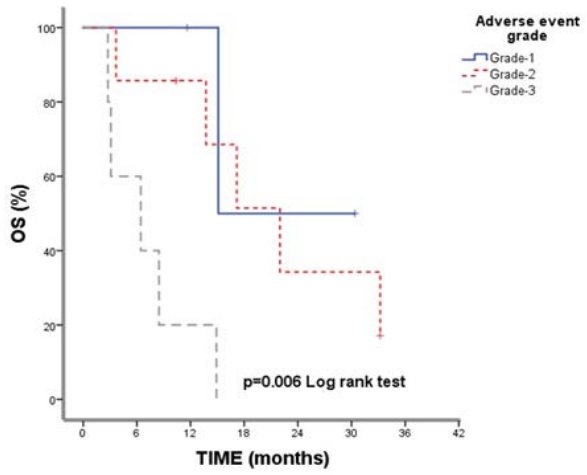

Figure 5. OS based on severity of adverse events. Median OS was 6.43 months for Grade 3, 22.00 months for Grade 2, and 15.10 months for Grade 1 (p=0.006).

months in Grade 1. The survival difference based on side effect severity was statistically significant (p=0.006) (Figure 5).

DISCUSSION

In this study, the efficacy and tolerability of AZA-VEN combination therapy in previously untreated AML patients under real-life conditions were evaluated. Due to the early achievement of response with AZA-VEN, response assessment was performed after the first cycle, in parallel with the literature (4). In the VIALE-A Phase III study, the complete response rates for azacitidine and venetoclax combination were 66.4%, and the median overall survival (OS) was reported as 14.7 months (4). In our patient group, the complete remission rate was 61.1%, and the median overall survival was calculated as 22.0 months. In addition to VIALE-A, the phase 3 VIALE-C trial evaluated venetoclax + low-dose cytarabine (LDAC) versus LDAC alone in chemotherapy-ineligible, newly diagnosed AML. VIALE-C improved response rates and showed a trend toward longer overall survival; in subsequent follow-up analyses, an OS benefit became more apparent with longer observation, although the primary OS endpoint was not met at the initial analysis due to limited follow-up time. These findings contextualize our results within the broader landscape of venetoclax-based, low-intensity regimens (5). These data support that the AZA-VEN combination is an effective alternative, especially for patients ineligible for intensive chemotherapy. Additionally, the finding that survival durations were consistent with or higher than the literature is important in demonstrating the feasibility and efficacy of this treatment in real-life conditions.

The effect of treatment duration and the number of cycles on OS has been reported to a limited extent in the literature. In the long-term follow-up of the VIALE-A study, it was reported that 76% of patients who achieved complete remission received ≥6 cycles of treatment, and this group had a survival advantage (6). In our study, the median OS was 23.73 months in patients who received ≥3 cycles, while it was 6.43 months in those who received only 1–2 cycles, and the difference was significant (p=0.031). This finding suggests the potential impact of treatment duration on survival. This situation indicates that treatment adherence may directly affect survival when hematologic side effects are controlled.

The effect of gender on survival has not been clearly demonstrated in the literature. In the multivariate analysis of the VIALE-A study, it was reported that gender did not have a significant effect on OS (6). In our study, however, the median OS was 33.2 months in female patients and 15.1 months in male patients, and the difference was statistically significant (p=0.027). It is thought that this difference is hypothesis-generating, considering the sample size and patient characteristics, and needs to be confirmed in larger series. Subgroup analyses, particularly considering parameters such as advanced age, comorbidities, and performance status, may provide a more accurate assessment of the effect of gender on survival.

When evaluated in terms of side effects, hematologic toxicities were significantly increased in patients treated with AZA-VEN. Neutropenia and thrombocytopenia were among the most commonly observed complications during treatment (6,7). In the VIALE-A study, Grade ≥3 neutropenia was reported in 43%, thrombocytopenia in 46%, and febrile neutropenia in 43% of patients (6). In our study, neutropenia (62.5%) was the most frequent reason for venetoclax dose reduction, and Grade-3 side effects were observed in 33.3%, Grade-2 in 46.7%, and Grade-1 in 20% of patients. Although the literature emphasizes that hematologic toxicities are common, studies analyzing survival differences based on side effect severity are limited. In the long-term follow-up of VIALE-A, deaths due to infections secondary to Grade 3–4 neutropenia were reported, but no direct association with survival was made (6). In our study, survival was 6.43 months in patients with Grade-3 side effects, 22.00 months in Grade-2, and 15.10 months in Grade-1, and the difference was significant (p=0.006). This finding suggests that timely and effective use of supportive treatments may have significant effects on survival. Additionally, considering the impact of side effect severity on treatment continuity, it is understood that dose modifications and G-CSF support should be planned on an individualized basis. Our findings are consistent with emerging Turkish real-world data reporting manageable toxicity and encouraging responses with AZA–VEN combinations in chemotherapy-ineligible AML (8).

Finally, as a notable finding in our study, no invasive fungal infections (IFI) developed in any of our patients. Reports in the literature regarding IFI frequency are conflicting, with rates ranging from 1% to 20% (9–12). The main factors influencing this include the duration of neutropenia, mucosal barrier integrity, degree of immune suppression, and antifungal prophylaxis use. Some studies found no significant difference despite prophylaxis use, while others advocated a risk-based approach (10–13). In our series, although some patients

received posaconazole and others did not, the absence of IFI is noteworthy in terms of the effectiveness of our infection management. This finding suggests that infections are shaped not only by prophylaxis but also by patient-specific risk factors, supporting the need for individualized antifungal prophylaxis decisions.

Our study has some limitations. First, the study was designed retrospectively, and patient data were obtained from past records. This increases the risk of missing data and potential bias. The limited sample size reduces the generalizability of subgroup analyses (e.g., survival differences by gender). Molecular and cytogenetic risk classifications were not evaluated in our study; however, notably, none of the patients had poor prognostic genetic/cytogenetic features. Another limitation is the absence of adverse-risk molecular/cytogenetic cases in our cohort. This may partly explain the relatively favorable survival we observed and should be considered when interpreting external generalizability. This may have contributed to the better response and survival rates observed.

On the other hand, the study also has strengths. Being derived from real-life data, it directly reflects the challenges encountered in clinical practice and patient management. The statistically significant association between side effect severity and survival is an original finding contributing to the literature. Additionally, the significant correlation between the number of treatment cycles and survival provides clinically relevant guidance for treatment planning. A notable aspect of the study is that the azacitidine-venetoclax combination was administered not only to elderly and comorbid patients but also to those aged ≤60 years. Of our patient group, 44.4% were under 60 years old, and significant treatment responses were achieved in these patients as well. This suggests that the regimen is effective and tolerable in younger patients and that patient selection should be based on biological suitability rather than age alone.

In conclusion, AZA-VEN therapy, supported by real-life data, offers a valuable treatment option for AML patients ineligible for intensive chemotherapy, with its demonstrated efficacy, manageable side effect profile, and survival advantage. Our findings highlight the importance of treatment duration, side effect management, and individualized supportive therapies, providing data that will contribute to clinical practice in these aspects.

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Address correspondence to: *Ozlem Beyler, Gazi Yaşargil Training and Research Hospital, Department of Hematology Diyarbakır, Türkiye*
e-mail: *drozlembeyler@gmail.com*

REFERENCES

1. Khoury JD, Solary E, Abla O, et al. The 5th edition of the World Health Organization Classification of Haematolymphoid Tumours: Myeloid and Histiocytic/Dendritic Neoplasms. Leukemia. 2022;36(7):1703-19. doi:10.1038/s41375-022-01613-1
2. Döhner H, Wei AH, Appelbaum FR, et al. Diagnosis and management of AML in adults: 2022 recommendations from an international expert panel on behalf of the ELN. Blood. 2022;140(12):1345-77. doi:10.1182/blood.2022016867
3. Maiti A, DiNardo CD, Wang SA, et al. Prognostic value of measurable residual disease after venetoclax and decitabine in acute myeloid leukemia. Blood Adv. 2021;5(7):1876-83. doi:10.1182/bloodadvances.2020003717
4. DiNardo CD, Jonas BA, Pullarkat V, et al. Azacitidine and Venetoclax in previously untreated acute myeloid leukemia. N Engl J Med. 2020;383(7):617-29. doi:10.1056/NEJMoa2012971
5. Wei AH, Panayiotidis P, Montesinos P, et al. 6-month follow-up of VIALE-C demonstrates improved and durable efficacy in patients with untreated AML ineligible for intensive chemotherapy (141/150). Blood Cancer J. 2021;11(10):163. doi:10.1038/s41408-021-00555-8
6. Pratz KW, Jonas BA, Pullarkat V, et al. Long-term follow-up of VIALE-A: Venetoclax and azacitidine in chemotherapy-ineligible untreated acute myeloid leukemia. Am J Hematol. 2024;99(4):615-24. doi:10.1002/ajh.27246
7. Rausch CR, DiNardo CD, Maiti A, et al. Duration of cytopenias with concomitant venetoclax and azole antifungals in acute myeloid leukemia. Cancer. 2021;127(14):2489-99. doi:10.1002/cncr.33508
8. Bulduk T, Cömert M, Kılıç E, et al. Real-life data of azacitidine-venetoclax combination in acute myeloid leukemia patients: A single center experience. J Health Sci Med. 2023;6(6):1237-43. doi:10.32322/jhsm.1359253
9. Pratz KW, Wei AH, Pollyea DA, et al. Management of neutropenia during venetoclax-based combination treatment in patients with newly diagnosed acute myeloid leukemia. Blood. 2019;134(Suppl 1):3897. doi:10.1182/blood-2019-124185
10. Weinbergerová B, Mayer J, Kabut T, et al. Fungal infection frequency in newly diagnosed acute myeloid leukaemia patients treated with venetoclax plus azacitidine with or without antifungal prophylaxis. Br J Haematol. 2024;205(5):1746-50. doi:10.1111/bjh.19670
11. On S, Rath CG, Lan M, et al. Characterisation of infections in patients with acute myeloid leukaemia receiving venetoclax and a hypomethylating agent. Br J Haematol. 2022;197(1):63-70. doi:10.1111/bjh.18051
12. Chen EC, Liu Y, Harris CE, et al. Outcomes of antifungal prophylaxis for newly diagnosed AML patients treated with a hypomethylating agent and venetoclax. Leuk Lymphoma. 2022;63(8):1934-41. doi:10.1080/10428194.2022.2047964
13. Jiwani S. An overview of EHA guidelines for the use of antifungal prophylactic agents in acute myeloid leukemia. Access link: https://aml-hub.com/medical-information/an-overview-of-eha-guidelines-for-the-use-of-antifungal-prophylactic-agents-in-acute-myeloid-leukemia. Accessed on: September 5, 2025.

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OLGU SUNUMU / CASE REPORT

Tracheal Diverticulum: A Case Series of Three Patients Presenting with Chronic Cough

Trakeal Divertikül: Kronik Öksürük ile Başvuran Üç Olgunun Sunumu

Abdurrahman Koc[1]

[1]Meram State Hospital, Department of Chest Diseases, Konya, Türkiye

ÖZET

Trakeal divertikül (TD), trakea duvarından posterolateral yönde gelişen, genellikle asemptomatik seyreden, nadir görülen bir solunum yolu anomalisi olup çoğu zaman tesadüfen saptanır. Ancak bazı olgularda kronik öksürük, tekrarlayan enfeksiyonlar veya hava yolu obstrüksiyonu gibi semptomlara yol açabilir. Bu çalışmada, kronik öksürük şikayeti ile başvuran üç erişkin hastada saptanan trakeal divertikül olguları sunulmuştur. Tüm hastalar bilgisayarlı toraks tomografisi ile değerlendirilmiş ve tüm hastalara bronkoskopi uygulanmıştır. Divertiküller sağ posterolateral trakea komşuluğunda yer almakta olup, semptomların hafif olması nedeniyle konservatif yaklaşım tercih edilmiştir. TD, nadir görülse de kronik öksürük şikayeti olan hastalarda ayırıcı tanıda göz önünde bulundurulmalı, BT ve bronkoskopi gibi görüntüleme yöntemleri ile tanı doğrulanmalıdır.

Anahtar Kelimeler: Bronkoskopi, kronik öksürük, toraks bilgisayarlı tomografi, trakeal divertikül

ABSTRACT

Tracheal diverticulum (TD) is a rare respiratory tract anomaly characterized by an outpouching from the posterolateral wall of the trachea. It is usually asymptomatic and often detected incidentally on imaging. However, in some cases, TD may lead to symptoms such as chronic cough, recurrent respiratory infections, or airway obstruction. In this case series, we present three adult patients who were evaluated for chronic cough and diagnosed with tracheal diverticulum. All patients underwent thoracic computed tomography (CT), and all of them also had bronchoscopy. The diverticula were located adjacent to the right posterolateral aspect of the trachea. Due to the mild nature of symptoms in all cases, a conservative treatment approach was preferred. Although TD is uncommon, it should be considered in the differential diagnosis of patients presenting with chronic cough, and the diagnosis should be confirmed using imaging methods such as CT and bronchoscopy.

Keywords: Bronchoscopy, chronic cough, thoracic computed tomography, tracheal diverticulum

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INTRODUCTION

Tracheal diverticulum is a rare anatomical anomaly defined as small, air-filled sacs developing from the posterolateral wall of the trachea (1,2). It is typically localized on the right posterolateral tracheal wall and is often incidentally discovered during thoracic CT examinations (2,3). However, large or infected diverticula can become clinically significant, causing symptoms such as chronic cough, sputum production, voice changes, or recurrent respiratory infections (4). It should be considered in the differential diagnosis of patients presenting with chronic cough and similar non-specific respiratory symptoms (4,5). Flexible bronchoscopy represents a valuable diagnostic approach in patients with chronic cough of undetermined etiology, as it enables visualization of anatomical and functional abnormalities and allows for culture and cellular analysis (6). This case series describes three adult patients presenting with chronic cough who were diagnosed with tracheal diverticulum, evaluating their clinical, radiological, and bronchoscopic characteristics, along with their management approaches.

CASE

Case 1: A 44-year-old female patient presented with a 15-year history of persistent dry cough. Physical examination and laboratory tests were unremarkable. Thoracic CT revealed a 1.5 × 1 cm diverticulum adjacent to the right posterolateral wall of the trachea. Bronchoscopy showed bulging of the posterior tracheal wall, but no distinct orifice was identified (Figure 1). Given the absence of risk factors, it was considered a congenital TD. The

Sorumlu Yazar/Corresponding Author: Abdurrahman Koc, Meram State Hospital, Department of Chest Diseases, Konya, Türkiye
e-mail: koc.abdurrahman@gmail.com

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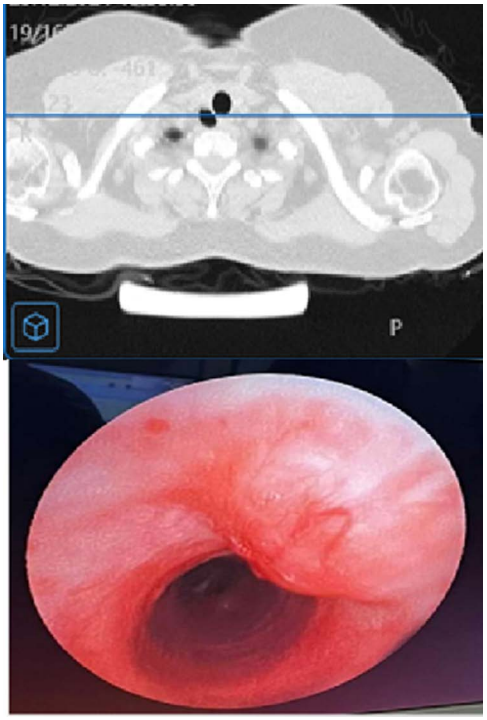

Figure 1. Axial thoracic computed tomography image demonstrating a tracheal diverticulum and bronchoscopic view showing bulging of the posterior tracheal wall (Case 1).

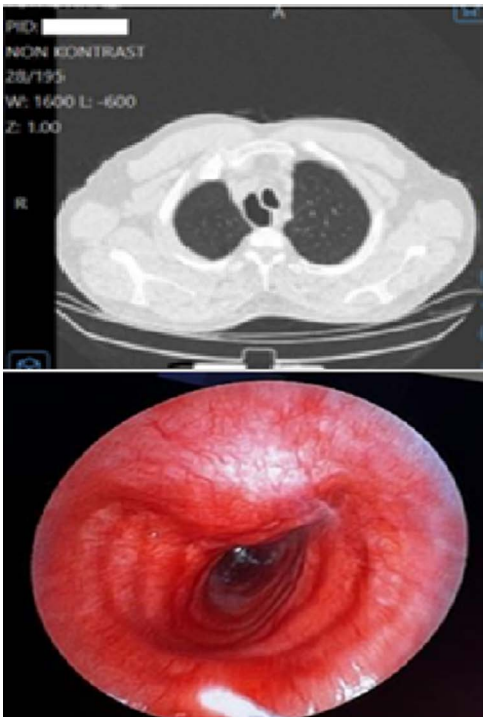

Figure 2. Axial thoracic computed tomography image demonstrating a tracheal diverticulum and bronchoscopic view showing bulging of the posterior tracheal wall (Case 2).

patient was started on conservative treatment, including proton pump inhibitors (PPI) and antacid therapy. Significant improvement in symptoms was noted at the first and third-month follow-up visits.

Case 2: A 67-year-old male patient with a 20 pack-year smoking history presented with a 5-year history of intermittent productive cough. Thoracic CT revealed a 36 × 27 mm diverticulum located on the right posterolateral tracheal wall. Bronchoscopy showed prominent bulging of the posterior wall (Figure 2). A conservative approach was preferred due to the mild nature of his symptoms. The patient was advised to quit smoking. Additionally, mucolytic therapy was initiated for symptoms consistent with chronic bronchitis, and long-acting bronchodilator treatment was prescribed for the mild obstructive impairment observed in pulmonary function tests. Symptom regression was observed at the first and third-month follow-up visits.

Case 3: A 43-year-old male patient, a farmer, with a 20 pack-year smoking history, presented with a 2-year history of cough and intermittent postnasal drip. Thoracic CT at the thoracic inlet level revealed a 19 × 16 mm diverticulum adjacent to the right posterolateral trachea. Bronchoscopy showed bulging of the posterior wall (Figure 3). The patient was started on a combination of antihistamines and a leukotriene antagonist. He was also advised to quit smoking. Significant improvement in symptoms was noted at the first and third-month follow-up visits.

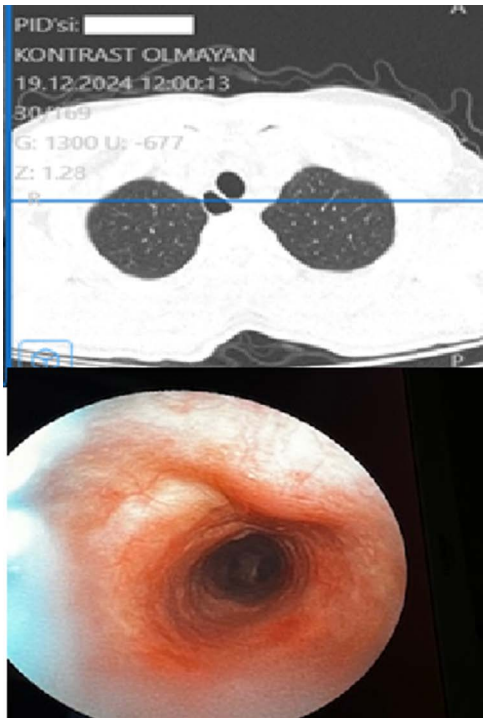

Figure 3. Axial thoracic computed tomography image demonstrating a tracheal diverticulum and bronchoscopic view showing bulging of the posterior tracheal wall (Case 3).

DISCUSSION

Tracheal diverticulum (TD) is defined as a rare but clinically significant airway anomaly, typically localized on the right posterolateral tracheal wall. TD is classified into two types: congenital and acquired. Congenital diverticula are generally narrow-necked, epithelium-lined pouches, whereas acquired diverticula have wider openings and are associated with a weakened tracheal wall (1). Computed tomography (CT) is the gold standard for diagnosing and anatomically evaluating TD. Specifically, thin-slice CT and multiplanar reconstructions clearly demonstrate the diverticulum's connection to the trachea and its location (2). Bronchoscopy is useful for directly assessing the connection between the tracheal lumen and the diverticulum; however, this connection may not always be detectable via bronchoscopy (3).

Although tracheal diverticula are often asymptomatic, they can lead to serious complications in some cases. Infected diverticula can result in recurrent bronchitis, pneumonia, productive cough, airway obstruction, and, rarely, mediastinitis. Furthermore, anesthesia-related complications such as diverticulum rupture and subcutaneous emphysema during intubation have been reported in the literature (2,4). Careful monitoring of patients is recommended given these risks. Conservative treatment (symptomatic approach, bronchodilators, antibiotics, physiotherapy, etc.) may be sufficient for patients with mild symptoms, whereas surgical resection should be considered in cases with severe symptoms or a risk of complications (5).

CONCLUSION

Tracheal diverticulum, though rare, should be considered in the differential diagnosis of patients presenting with non-specific respiratory complaints such as chronic cough. The diagnosis should be confirmed with thoracic CT and, if necessary, bronchoscopy. Treatment should be individualized based on the patient's symptoms. While successful outcomes can be achieved with conservative treatment, surgical intervention may also be preferred in certain situations. Early diagnosis and appropriate management can positively impact the patient's prognosis.

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Address correspondence to: *Abdurrahman Koc, Meram State Hospital, Department of Chest Diseases, Konya, Türkiye*
e-mail: *koc.abdurrahman@gmail.com*

REFERENCES

1. Soto-Hurtado EJ, Peñuela-Ruíz L, Rivera-Sánchez I, et al. Tracheal diverticulum: a review of the literature. Lung. 2006;184(6):303-7. doi: 10.1007/s00408-006-0010-7.
2. Tanrivermis Sayit A, Elmali M, Saglam D, et al. The diseases of airway-tracheal diverticulum: a review of the literature. J Thorac Dis. 2016;8(10):E1163-E1167. doi: 10.21037/jtd.2016.10.92.
3. Buterbaugh JE, Erly WK. Paratracheal air cysts: a common finding on routine CT examinations of the cervical spine and neck that may mimic pneumomediastinum in patients with traumatic injuries. AJNR Am J Neuroradiol. 2008;29(6):1218-21. doi: 10.3174/ajnr.A1058.
4. Takhar RP, Bunkar M, Jain S, et al. Tracheal diverticulum: an unusual cause of chronic cough and recurrent respiratory infections. Tuberk Toraks. 2016;64(1):77-82. doi: 10.5578/tt.9700.
5. Sagar AS, Tomeh C, Sagar D, et al. Bronchoscopic Management of Tracheal Diverticulum Using Argon Plasma Coagulation. Ann Am Thorac Soc. 2022;19(3):484-7. doi: 10.1513/AnnalsATS.202108-1001CC.
6. Pekcan S, Köse M, Kiper N, et al. Kronik öksürüklü çocuklarda fleksible bronkoskopi bulguları. Selcuk Tip Derg. 2008;24(4):183-9.