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Turkish Journal of COLORECTAL DISEASE



Aims and Scope

Turkish Journal of Colorectal Disease is an official journal of the Turkish Society of Colon and Rectal Surgery to provide epidemiologic, pathologic, diagnostic and therapeutic studies relevant to the management of small intestine, colon, rectum, anus and pelvic floor diseases. It was launched in 1991. Although there were temporary interruptions in the publication of the journal due to various challenges, the Turkish Journal of Colorectal Disease has been published continually from 2007 to the present. It is published quarterly (March, June, September and December) as hardcopy and an electronic journal at <http://www.turkishjcrd.com/>. The target audience of Turkish Journal of Colorectal Disease includes surgeons, pathologists, oncologists, gastroenterologists and health professionals caring for patients with a disease of the colon and rectum.

The Turkish name of the journal was formerly Kolon ve Rektum Hastalıkları Dergisi and the English name of the journal was formerly Journal of Diseases of the Colon and Rectum.

Turkish Journal of Colorectal Disease is indexed in TÜBİTAK/ULAKBİM, Directory of Open Access Journals (DOAJ), British Library, ProQuest, Root Indexing, Ideallonline, Gale/Cengage Learning, Index Copernicus, Turkish Citation Index, Hinari, GOALI, ARDI, OARE, J-GATE and TürkMedline.

The aim of Turkish Journal of Colorectal Disease is to publish original research papers of the highest scientific and clinical value at an international level. Furthermore, review articles, case reports, technical notes, letters to the editor, editorial comments, educational contributions and congress/meeting announcements are released.

Turkish Journal of Colorectal Disease is an independent open access peer-reviewed international journal printed in Turkish and English languages. Manuscripts are reviewed in accordance with "double-blind peer review" process for both referees and authors. The Editorial Board of the Turkish Journal of Colorectal Disease endorses the editorial policy statements approved by the WAME Board of Directors. The journal is in compliance with the uniform requirements for manuscripts submitted to biomedical journals published by the International Committee of Medical Journal Editors (NEJM 1997;336:309-315, updated 2001).

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Turkish Journal of COLORECTAL DISEASE



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Derginin Türkçe eski adı; Kolon ve Rektum Hastalıkları Dergisi ve İngilizce eski adı; Journal of Diseases of the Colon and Rectum'dur.

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Turkish Journal of Colorectal Disease follows the "Uniform Requirements for Manuscripts Submitted to Biomedical Journals" (International Committee of Medical Journal Editors: Br Med J 1988;296:401-5).

Upon submission of the manuscript, authors are to indicate the type of trial/research and statistical applications following "Guidelines for statistical reporting in articles for medical journals: amplifications and explanations" (Bailar JC III, Mosteller F. Ann Intern Med 1988;108:266-73).

Preparation of research articles, systematic reviews and meta-analyses must comply with study design guidelines:

CONSORT statement for randomized controlled trials (Moher D, Schultz KF, Altman D, for the CONSORT Group. The CONSORT statement revised recommendations for improving the quality of reports of parallel group randomized trials. JAMA 2001; 285:1987-91) (<http://www.consort-statement.org/>);

PRISMA statement of preferred reporting items for systematic reviews and meta-analyses (Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 2009; 6(7): e1000097.) (<http://www.prisma-statement.org/>);

STARD checklist for the reporting of studies of diagnostic accuracy (Bossuyt PM, Reitsma JB, Bruns DE, Gatsonis CA,

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Glasziou PP, Irwig LM, et al., for the STARD Group. Towards complete and accurate reporting of studies of diagnostic accuracy: the STARD initiative. *Ann Intern Med* 2003;138:40-4. (<http://www.stard-statement.org/>);

STROBE statement, a checklist of items that should be included in reports of observational studies (<http://www.strobe-statement.org/>);

MOOSE guidelines for meta-analysis and systemic reviews of observational studies (Stroup DF, Berlin JA, Morton SC, et al. Meta-analysis of observational studies in epidemiology: a proposal for reporting Meta-analysis of observational Studies in Epidemiology (MOOSE) group. *JAMA* 2000; 283: 2008-12).

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Use tab stops or other commands for indents, not the space bar.

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Results: What were the main findings?

Conclusion: What are the main conclusions or implications of the study?

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Example: 1. Dilaveris P, Batchvarov V, Gialafos J, Malik M. Comparison of different methods for manual P wave duration measurement in 12-lead electrocardiograms. *Pacing Clin Electrophysiol* 1999;22:1532-1538.

Book chapter; Last name(s) of the author(s) and initials, chapter title, book editors, book title, edition, place of publication, date of publication and inclusive page numbers of the extract cited.

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Example: 1. Schwartz PJ, Priori SG, Napolitano C. The Long QT Syndrome. In: Zipes DP, Jalife J, eds. Cardiac Electrophysiology. From Cell to Bedside. Philadelphia; WB Saunders Co. 2000:597-615.

Tables: All tables are to be numbered using Arabic numerals. Tables should always be cited in text in consecutive numerical order. For each table, please supply a table caption (title) explaining the components of the table. Identify any previously published material by giving the original source in the form of a reference at the end of the table caption. Footnotes to tables should be indicated by superscript lower-case letters (or asterisks for significance values and other statistical data) and included beneath the table body.

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Case Reports

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Article length: Not to exceed 1000 words.

Reference Number: Not to exceed 15 references.

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Abstract: An unstructured abstract that summarizes the case.

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Case Report: This section describes the case in detail, including the initial diagnosis and outcome.

Discussion: This section should include a brief review of the relevant literature and how the presented case furthers our understanding to the disease process.

References: See under 'References' above.

Acknowledgments.

Tables and figures.

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Method

Comparison with other methods: advantages and disadvantages, difficulties and complications.

References, in Vancouver style (see under 'References' above).

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Tables and figures: Including legends.

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Video Article

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Yazarlara Bilgi

GENEL BİLGİ

Türk Kolon ve Rektum Hastalıkları Dergisi, Türk Kolon ve Rektum Cerrahisi Derneği'nin dergisidir. Derginin misyonu; ince bağırsak, kolon, rektum, anüs ve pelvik taban bozuklukları hakkındaki bilgiye katkı sağlamaktır. Dergi daha önce başka bir yerde yayınlanmamış olması koşuluyla, derginin kapsamı ile ilgili ve talep üzerine yazılan derleme makaleleri, araştırma makaleleri, kısa raporlar ve editöre mektuplar ve olgu sunumlarını yayınlamaktadır. Randomize, kohort, kesitsel ve vaka kontrol çalışmaları gibi temel bilim yazılarına öncelik verilir. Alanında bilinen uzmanlarca talep üzerine yazılan derlemeler dikkate alınacaktır.

Yazılar ICMJE yönergelerine göre (<http://www.icmje.org/>) hazırlanmalıdır. Tüm yazılar dergi tarafından benimsenen stile uygunluk sağlamak için editöryal kontrol ve düzeltmelere tabi tutulmaktadır. Derginin çift kör bir değerlendirme sistemi vardır. Değerlendirilen ve kabul edilen yayınlar Türkçeden İngilizceye veya İngilizceden Türkçeye derginin profesyonel çeviri hizmeti aracılığıyla tercüme edilir. Yayınlanmadan önce, çeviriler onay veya düzeltme istekleri için yazarlara gönderilir ve 7 gün içinde geri dönüş talep edilir. Bu süre içinde yanıt alınmazsa, çeviri kontrol ve yayın kurulu tarafından onaylanır.

Kabul edilen yayınlar hem Türkçe hem de İngilizce olarak yayınlanır.

Türk Kolon ve Rektum Hastalıkları Dergisi'ne gönderilen tüm yayınlar 'iThenticate' yazılımı kullanılarak intihal açısından taranır. İntihal saptanan durumlarda yayın iade veya reddedilir.

Türk Kolon ve Rektum Hastalıkları Dergisi, makale gönderme veya işlem ücreti adı altında herhangi bir ücret talep etmemektedir.

Türk Kolon ve Rektum Hastalıkları Dergisi'nin kısaltması "TJCD"dir, ancak, refere edildiğinde "Turk J Colorectal Dis" olarak kullanılmalıdır.

YAYIN POLİTİKASI

Tüm makaleler bilimsel katkıları, özgünlük ve içerikleri açısından bilimsel komite tarafından değerlendirilecektir. Yazarlar verilerinin doğruluğundan sorumludurlar. Dergi gerekli gördüğü yerlerde dil ve uygun değişiklik yapma hakkını saklı tutar. Gereğinde makale revizyon için yazara gönderilir. Dergide basılan yayının mali haline gelir ve telif hakkı "Türk Kolon ve Rektum Hastalıkları Dergisi" adına alınmış olur. Daha önce herhangi bir dilde yayınlanmış makaleler dergide yayınlanmak üzere kabul edilmeyecektir. Yazarlar bir başka dergide yayınlanmak üzere olan makaleyi teslim edemez. Tüm değişiklikler, yazar ve yayıncının yazılı izni alındıktan sonra yapılacaktır. Tüm makalelerin tam metinleri derginin www.journalagent.com/krhd web sitesinden indirilebilir.

YAZAR KILAVUZU

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Makale Gönderilirken Sunulması Gereken Formlar:

Telif Hakkı Devir Bildirimi

Yayınlann bilimsel ve etik sorumluluğu yazarlarına aittir. Yazıların telif hakkı ise Türk Kolon ve Rektum Hastalıkları Dergisi'ne aittir. Yazarlar yayınlann doğruluk ve içeriğinden ve kaynakların doğruluğundan sorumludur. Yayınlanmak üzere gönderilen tüm yayınlara Telif Hakkı Devir Formu (telif hakkı transferi) eşlik etmelidir. Tüm yazarlar tarafından imzalanarak gönderilen bu form ile yazarlar, ilgili yayının ve içerdiği datanın başka bir yayın organına gönderilmediğini veya başka bir dergide yayınlanmadığını beyan ederler. Ayrıca bu belge yazarların bilimsel katkı ve tüm sorumluluklarının ifadesidir.

Açıklama Bildirimi

Çıkar çatışmaları: Yazarlar, finansal, kurumsal, danışmanlık şeklinde ya da herhangi bir çıkar çatışmasına yol açabilecek başka ilişkiler de dahil olmak üzere yayındaki ilgili tüm olası çıkar çatışmalarını belirtmelidir. Herhangi bir çıkar çatışması yoksa da bu da açıkça belirtilmelidir. Tüm finansman kaynakları yazının içinde belirtilmelidir. Finansman kaynakları ve ilgili tüm çıkar çatışmaları yazının başlık sayfasında "Finansman ve Kaynak Çatışmaları:" başlığı ile yer almalıdır.

Üst Yazı

Yazarlar, yazının içinde malzemenin elektronik ortam da dahil olmak üzere herhangi bir başka bir yerde yayımlanmak üzere gönderilmediğini veya planlanmadığını üst yazıda belirtmelidir. Yine "Kurumsal Değerlendirme Kurulu" (KDK) onayı alınıp alınmadığı ve 2013 yılı Helsinki Bildirgesi'ne eşdeğer kılavuzların izlenip izlenmediği belirtilmelidir. Aksi takdirde, bir açıklama temin edilmelidir. Üst yazı; adres, telefon, faks ve ilgili yazının e-posta adresini içermelidir.

Makale Yazım Kuralları

Tüm makaleler online başvuru sistemi üzerinden teslim edilmelidir. Yazarlar web sitesi www.journalagent.com/krhd adresinde oturum açtıktan sonra internet üzerinden yazıların sunulmalıdır.

Makale gönderimi yapılırken sorumlu yazarın ORCID (Open Researcher ve Contributor ID) numarası belirtilmelidir. <http://orcid.org> adresinden ücretsiz olarak kayıt oluşturabilir.

Online Başvuru

Gecikmeyi önlemek ve hızlı hakemlik için sadece çevrim içi gönderimler kabul edilir. Yazılar word belgesi (*.doc) veya zengin metin biçimi (*.rtf) olarak hazırlanmalıdır. www.journalagent.com/krhd adresinde web oturumu açtıktan sonra "Makale gönder" ikonuna tıklayın. Tüm yazarlar, gerekli bilgileri sisteme girdikten sonra bir şifre ve bir kullanıcı adı alır. Kendi şifre ve kullanıcı adını ile makale gönderme sistemine kayıt olduktan sonra yazının işleme alınmasında bir gecikme olmaması için gerekli tüm bilgileri sağlamak için sistemin yönergelerini dikkatlice okuyunuz. Makaleyi ve tüm şekil, tablo ve ek dokümanları ekleyiniz. Ayrıca üst yazı ve "Telif Hakkı ve Finansal Durum" formunu ve yazının tipine göre aşağıda belirtilen kılavuzların kontrol listesini ekleyiniz.

Makale Hazırlama Kuralları

Türk Kolon ve Rektum Hastalıkları Dergisi "Biyomedikal Dergilere Gönderilen Makaleler için Gerekli Standartları" izler. (International Committee of Medical Journal Editors: Br Med J 1988; 296: 401-5).

Yazarlar yayınlannı gönderirken, çalışmalarının türünü ve uygulanan istatistik yöntemlerini "Tıbbi Dergilere Gönderilen Makaleler için İstatistiksel Raporlama Rehberi"ne uygun olarak belirtmelidir (Bailar JC III, Mosteller F. Ann Intern Med 1988;108:266-73).

Araştırma makalesi, sistematik değerlendirme ve meta-analiz hazırlanması aşağıdaki çalışma tasarımı kurallarına uymak zorundadır; (CONSORT statement for randomized controlled trials (Moher D, Schulz KF, Altman D, for the CONSORT Group).

Makale Hazırlama Kuralları

The CONSORT statement revised recommendations for improving the quality of reports of parallel group randomized trials. JAMA 2001; 285:1987-91) (<http://www.consort-statement.org/>);

PRISMA statement of preferred reporting items for systematic reviews and meta-analyses (Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 2009; 6(7): e1000097.) (<http://www.prisma-statement.org/>);

STARD checklist for the reporting of studies of diagnostic accuracy (Bossuyt PM, Reitsma JB, Bruns DE, Gatsonis CA, Glasziou PP, Irwig LM, et al., for the STARD Group. Towards complete and accurate reporting of studies of diagnostic accuracy: the STARD initiative. Ann Intern Med 2003;138:40-4) (<http://www.stard-statement.org/>);

STROBE statement, a checklist of items that should be included in reports of observational studies (<http://www.strobe-statement.org/>);

MOOSE guidelines for meta-analysis and systemic reviews of observational studies (Stroup DF, Berlin JA, Morton SC, et al. Meta-analysis of observational studies in epidemiology: a proposal for reporting Meta-analysis of observational Studies in Epidemiology (MOOSE) group. JAMA 2000; 283: 2008-12).

Metin Biçimlendirme

Yazılar Word programı ile hazırlanarak teslim edilmelidir.

- Metin için normal, düz yazı tipi kullanın (örneğin, 10 punto Times Roman).

- Sayfa numarası için otomatik sayfa numaralandırma işlevini kullanın.

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Yazarlara Bilgi

- Alan fonksiyonları kullanmayın.
- Girintiler için sekme durakları (Tab) kullanın, ara çubuğu ve diğer komutlar kullanmayın.
- Tablo yapmak için diğer işlevleri değil, elektronik tablo fonksiyonunu kullanın.
- Dosyamızı .docx formatında (Word 2007 veya üstü) ya da .doc formatında (eski Word sürümü) kaydedin.
- Giriş sayfası
- Tüm yazılar, makale türü ne olursa olsun, aşağıdakileri içeren bir başlık sayfası ile başlamalıdır:
- Makalenin başlığı;
- Makalenin kısa başlığı;
- Yazarların isimleri, isimlerinin baş harfleri ve her yazının akademik ünvanı;
- Her yazının görevi;
- Her yazının kurumu;
- Yazının adı ve e-posta adresi;
- Herhangi bir yazının olası bir çıkar çatışması olduğunu teyit eden bir ifade, aksi takdirde çatışma olmadığını belirten bir açıklama;
- Özet, kaynaklar, tablo ve şekiller hariç kelime sayısı;
- Varsa yayının yayınlanmış olduğu bilimsel toplantının tarihi, yeri ve varsa kongre özet kitabındaki özeti.

Makale Tipleri

Orijinal Makaleler

Bu kategori, klinik ve temel bilimlerde orijinal araştırmaları içerir. Yayın orijinal olmalı ve başka bir dergide yayınlanmış/gönderilmiş ya da kabul edilmiş olmamalıdır. Yazarlar, herhangi biri tarafından bir dergiye gönderilmiş, baskıda veya basılmış ilgili herhangi bir çalışmaya atıfta bulunmak istiyorlarsa açıkça atıfta bulunulmalı ve kaynak gösterilmelidir.

Tüm klinik çalışmalar, Uluslararası Tıp Dergisi Editörler Komitesince (ICMJE) kabul gören bir kayıt sistemine kayıtlı olmalıdır. Bunun için <http://www.icmje.org/faq.html> adresine müracaat edin. Randomize kontrollü çalışmaların yazarları da, www.consort-statement.org adresinden başvurulabilen CONSORT kılavuzuna uymalıdır ve yayınlarıyla birlikte CONSORT kontrol listesi ve akış diyagramı tebliğ edilmelidir. Akış şeması olarak www.consort-statement.org adresinde bulunan MS Word şablonunun kullanılması ve bunun yayının içinde bir alıntı veya bir figür olarak yerleştirilmesi gereklidir. Buna ek olarak, sunulan yayımlar her yayına spesifik verilen özel kayıt numarasını içermelidir.

Tüm yazarların, insan üzerindeki çalışmalar ve hayvan deneylerinde etik standartlara uymaları beklenmektedir. İnsan üzerindeki veya laboratuvar hayvanları içeren çalışmalarda, yazarların yayının Gereç ve Yöntem kısmında deney protokolünün ilgili kurumsal inceleme komitesi tarafından onaylandığını ve sorumlu devlet kurumu kurallarına uyduğunu açık bir dille açıklamaları gereklidir. İnsan üzerindeki çalışmalarda kurumsal inceleme kurulu onayına ek olarak, aydınlatılmış onam da bulunmalıdır.

Orijinal Makaleler (özet, kaynaklar, tablolar, rakamlar hariç) 3000 kelime ve dört figürü aşmamalıdır.

Orijinal Makaleler aşağıdaki gibi organize edilmelidir:

Özet: Özet 250 kelimeyi geçmemeli ve şunları içermelidir;

Amaç: Çalışmanın amacı nedir?

Yöntem: Kullanılan yöntem ve materyaller (örneğin hayvanlar) veya hastalar ya da konu (sağlıklı gönüllüler gibi) hakkında kısa bir açıklama içermelidir.

Bulgular: Ana bulgular nelerdir?

Sonuç: Çalışmanın ana sonuçları ve etkileri nelerdir?

Anahtar kelimeler: Özeti altında en az 3 anahtar kelime veriniz. Kısaltmalar anahtar kelime olarak kullanmayınız.

Giriş: Açık bir dille çalışmanın amaç ve gerekçesini belirtin ve çalışmanın arka planını açıklarken sadece en önemli kaynaklardan alıntı yapın.

Gereç ve Yöntem: Gözlemsel veya deneysel deneklerin (hastalar, deney hayvanları veya kontrol grupları dahil) seçim şeklini açıklayın. Deney protokolünün ilgili kurumsal inceleme komitesi tarafından onaylandığını ve ilgili devlet kurumu kurallarına uyduğunu açık bir dille açıklayın. İnsan çalışması durumunda, tüm şahısların aydınlatılmış onamlarının alındığını açık bir dille belirtin. Yöntem, cihaz ve türleri tanımlayın (Parantez içinde üretici firma adı ve adresi)** Uygulanmış olan tüm prosedürler, diğer çalışmacıların aynı deneyi tekrar edebilecekleri detay ve netlikte anlatılmalıdır. İstatistiksel yöntemler de dahil olmak üzere yerleşik ve yaygın olarak bilinen çalışma yöntemleri için kaynaklar belirtilmelidir. Yayınlanmış ancak yaygın olarak bilinmeyen yöntemler için ise kaynaklar ve kısa tanımlamalar verilmelidir. Kullanma sebepleri ve limitasyonları belirtilmelidir.

Bulgular: İstatistiksel yöntemlerle desteklenmiş bulgularınızı ayrıntılı olarak sunun. Şekil ve tablolar metni tekrar değil, takviye etmelidir. Verilerin hem metinde hem figür olarak verilmemesi gerekir. Metin veya figürden birisi olarak verilmesi yeterlidir. Sadece kendi önemli izlenimlerinizi belirtin. Kendi izlenimlerinizi diğerlerininle karşılaştırmayın. Bu tür karşılaştırma ve yorumlar tartışma bölümünde yapılmalıdır.

Tartışma: Bulgularınızın önem ve anlamını vurgulayın ancak bulgular kısmında verilenleri tekrarlamayın. Fikirlerinizi yalnızca bulgularınızla kanıtlayabildiklerinizle sınırlı tutun. Bulgularınızı diğerlerininle karşılaştırmayın. Bu bölümde yeni veriler bulunmamalıdır.

Teşekkür: Sadece çalışmaya ciddi katkılarda bulunmuş kişilere teşekkür edin. Yazarlar ismen teşekkür ettikleri herkesten yazılı izin almak zorundadır. Teşekkür kısmına "Yazarlarteşekkür eder" şeklinde başlayın.

Yazarlık ve Katkı Sağlayanlar: Dergi, biyomedikal dergilere gönderilen yayınlara yönelik ICMJE tavsiyelerini izler. Buna göre "yazarlık" aşağıdaki dört kritere dayalı olmalıdır:

Yazar;

- Yayının konsept veya dizaynına, çalışmanın verilerinin elde edilmesine, analizine ve yorumlanmasına önemli katkılar veren; ve

- İşi hazırlayan veya entelektüel içerik açısından eleştirel biçimde gözden geçiren; ve

- Yayınlanacak son şekli onaylayan; ve

- Çalışmanın her bir bölümünün doğruluğu ve bütünlüğü ile ilgili sorunları uygun bir şekilde inceleleyen ve çözüm sağlayan sorumlu kişidir.

Bu şartların hepsini sağlamayan diğer tüm katılımcılar yazar değil, "Teşekkür" bölümünde anılması gereken katkı sağlamış kişilerdir.

Kaynaklar: Kaynakları 1'den başlayarak Arap rakamları ve alfabetik sıra ile verin. Kaynak numaraları cümle sonunda noktadan sonra üstte küçük rakamlar şeklinde (superscript) yazılmalıdır. Kısaltmalar için gerekli standartları <http://www.bilimterimleri.com> adresinde bulunan Türk Bilim Terimleri Kılavuzu'ndan edinin.

Dergi başlıkları "Cumulated Index Medicus" kısaltmalarına uygun olmalıdır.

Dergiden: Yazar/yazarların soyadı ve adının ilk harfi, makale başlığı, dergi başlığı ve derginin özgün kısaltması, yayın tarihi, baskı, kapsayıcı sayfa numaralarını içermelidir.

Örneğin: 1. Dilaveris P, Batchvarov V, Gialafos J, Malik M. Comparison of different methods for manual P wave duration measurement in 12-lead electrocardiograms. Pacing Clin Electrophysiol 1999;22:1532-1538.

Kitap Bölümü: Yazar/yazarların soyadı ve adının ilk harfi, bölüm başlığı, kitap editörleri, kitap başlığı, basım, yayın yeri, yayın tarihi, kapsadığı sayfa numaralarını içermelidir

Örneğin: 1. Schwartz PJ, Priori SG, Napolitano C. The Long QT Syndrome. In: Zipes DP, Jalife J, eds. Cardiac Electrophysiology. From Cell to Bedside. Philadelphia; WB Saunders Co. 2000:597-615.

Tablolar: Tüm tablolar Arapça sayılarla numaralandırılmalıdır. Tüm tablolardan metin içerisinde numara sırası ile bahsedilmelidir. Her tablo için tablonun içeriği hakkında bilgi veren bir başlık verin. Başka yayından alıntı olan tüm tablolar tablonun alt kısmında kaynak olarak belirtin. Tabloda dipnotlar tablonun altında, üst karakter olarak küçük harflerle verilmelidir. İstatistiksel anlamı değerler ve diğer önemli istatistiksel değerler yıldız ile işaretlenmelidir.

Şekiller: Şekillerin "Windows" ile açılması gerekir. Renkli şekiller veya gri tonlu görüntüler en az 300 dpi olmalıdır. Şekiller ana metinden ayrı olarak ".tif", ".jpg" veya ".pdf" formatında kaydedilmelidir. Tüm şekil ayrı bir sayfada hazırlanmalı ve Arap rakamları ile numaralandırılmalıdır. Her şekilde kendisindeki işaret ve semboller açıklayan bir alt yazı olmalıdır. Şekil gönderme için yazardan hiçbir ek ücret alınmaz.

Ölçü Birimleri ve Kısaltmalar: Ölçü birimleri System International (SI) birimleri cinsinden olmalıdır. Kısaltmalardan başlıkta kaçınılmalıdır. Sadece standart kısaltmalar kullanın. Metinde kısaltma kullanılırsa ilk kullanıldığı yerde tanımlanmalıdır.

İzinler: Yazarlar yayınlara önceden başka bir yerde yayınlanmış şekil, tablo, ya da metin bölümleri dahil etmek isterlerse telif hakkı sahiplerinden izin alınması ve bu izin belgelerinin yayına beraber gönderilmeye gönderilmesi gerekmektedir. Böyle bir belgenin eşlik etmediği her materyalin yazara ait olduğu kabul edilecektir.

Davetli (Talep üzerine yazılan) Derlemeler

Özet uzunluğu: 250 kelimeyi aşmamalıdır.

Makale uzunluğu: 4000 kelimeyi aşmamalıdır.

Kaynak sayısı: 100 kaynağı aşmamalıdır.

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Yazarlara Bilgi

Derlemeler, üzerine konuyla ilgili yeni bir hipotez ya da çalışma oturtulabilecek bir sonuç içermelidir. Literatür taraması metodlarını veya kanıt düzeyi yöntemlerini yayınlamayın. Derleme makaleleri hazırlayacak yazarların ilgili konuda önceden araştırma makaleleri yayınlamış olması gerekir. Çalışmanın yeni ve önemli bulguları sonuç bölümünde vurgulanır ve yorumlanmalıdır. Derlemelerde maksimum iki yazar olmalıdır.

Olgu Sunumları

Özet uzunluğu: 100 kelimeyi aşmamalıdır.

Makale uzunluğu: 1000 kelimeyi aşmamalıdır.

Kaynak sayısı: 15 kaynağı aşmamalıdır.

Olgu Sunumları aşağıdaki gibi yapılandırılmalıdır:

Özet: Olguyu özetleyen bir yapılandırılmamış özet (gereç ve yöntem, bulgular, tartışma gibi bölümlerin olmadığı).

Giriş: Kısa bir giriş (tavsiye edilen uzunluk: 1-2 paragraf).

Olgu Sunumu: Bu bölümde ilk tanı ve sonuç da dahil olmak üzere olgu ayrıntılı olarak anlatılır.

Tartışma: Bu bölümde ilgili literatür kısaca gözden geçirilir ve sunulan olgunun, hastalığa bakışımızı ve yaklaşımımızı nasıl değiştirebileceği vurgulanır.

Kaynaklar: Vancouver tarzı, (yukarıda 'Kaynaklar' bölümüne bakınız).

Teşekkür

Tablolar ve şekiller

Teknik Notlar

Özet uzunluğu: 250 kelimeyi aşmamalıdır.

Makale uzunluğu: 1200 kelimeyi aşmamalıdır.

Kaynak Sayısı: 15 kaynağı aşmamalıdır.

Teknik Notlar, yeni bir cerrahi tekniğin açıklanmasını ve az sayıda olguda uygulanmasını içermektedir. Büyük bir atılım/değişikliği temsil eden bir tekniğin sunulması durumunda tek bir olgu yeterli olacaktır. Hastanın takip ve sonucu açıkça belirtilmelidir.

Teknik Notlar aşağıdaki gibi organize edilmelidir:

Özet: Aşağıdaki gibi yapılandırılmalıdır:

Amaç: Bu çalışmanın amacı nedir?

Yöntem: Kullanılan yöntemlerin, hastalar ya da sağlıklı gönüllülerin veya hayvanların tanımı, malzemeler hakkında kısa bir açıklama.

Bulgular: Ana bulgular nelerdir?

Sonuç: Bu çalışmanın ana sonuçları ve etkileri nelerdir?

Endikasyonları

Yöntem

Diğer yöntemlerle karşılaştırılması: Avantaj ve dezavantajları, zorluklar ve komplikasyonlar.

Kaynaklar: Vancouver tarzı (yukarıda 'Kaynaklar' bölümüne bakınız)

Teşekkür

Tablolar ve şekiller; alt yazıları dahil

Video Makale

Makale Uzunluğu: 500 kelimeyi aşmamalıdır.

Kaynak Sayısı: 5 kaynağı aşmamalıdır.

Tanımı, uygulanan cerrahi tekniği ve sonucu açıklayarak olguyu kısaca özetleyiniz. Uygun şekilde adlandırılmış ve referans edilmiş video materyalleri ile tüm önemli noktaları, örneğin; yeni cerrahi tekniği, belirtiniz. Materyaller, yazarların cerrahi tekniğini anlattıkları veya karşılaştıkları ilginç vakalardan oluşmalıdır.

Teknik Gereklilikler: Veriler, makale yükleme sırasında diğer dosyalarla birlikte eklenmelidir. Video süresinin 10 dakikayı geçmemesi kaydıyla dosya boyutu maksimum 350 MB olmalı ve 'MOV, MPEG4, AVI, WMV, MPEGPS, FLV, 3GPP, WebM' formatlarından biri kullanılmalıdır. 100 MB'yi aşmayan video dokümanları sisteme yüklenebilir. Daha büyük video dokümanları için lütfen iletisim@galenos.com.tr adresinden bizimle iletişime geçiniz. Tüm video seslendirmeleri İngilizce olmalıdır. Video atıfları, Şekil veya Tablo atıfları ile aynı biçimde kullanılmalıdır. Örneğin; "...Bunu gerçekleştirmek için, yeni bir cerrahi teknik geliştirdik (Video 1)." Video materyallerinde isim ve kurumlar yer almamalıdır. Kabul edilen makalelerin video materyalleri online yayınlanacaktır.

Editöre Mektuplar

Makale uzunluğu: 500 kelimeyi aşmamalıdır.

Kaynak Sayısı: 10 kaynağı aşmamalıdır.

Türk Kolon ve Rektum Hastalıkları Dergisi'nde yayınlanan makaleler hakkında yorumlar memnuniyetle kabul edilir. Özet gerekli değildir, ancak lütfen kısa bir başlık ekleyiniz. Mektuplar bir şekil veya tablo içerebilir.

Editöryal Yorumlar

Makale uzunluğu: 1000 kelimeyi aşmamalıdır.

Kaynak Sayısı: 10 kaynağı aşmamalıdır.

Editöryal yorumlar sadece editör tarafından kaleme alınır. Editöryal yorumlarda aynı konu hakkında başka yerlerde yayınlanmış yazılar hakkında fikir veya yorumlar belirtilir. Tek bir yazar tercih edilir. Özet gerekli değildir, ancak lütfen kısa bir başlık ekleyiniz. Editöryal gönderimler revizyon/gözden geçirme talebine tabi tutulabilir. Editörler, metin stilini değiştirmeye hakkını saklı tutar.

Etik

Bu dergi, bilimsel kayıtların bütünlüğünü korumayı taahhüt etmektedir. Yayın Etik Komitesi (COPE) üyesi olarak, dergi olası olumsuz davranışlarla nasıl başa çıkılacağı konusunda Yayın Etik Komitesi (COPE) kılavuzlarını takip edecektir.

Yazarlar araştırma sonuçlarını yanlış sunmaktan; derginin güvenilirliğine, bilimsel yazarlık profesyonelliğine ve en sonunda tüm bilimsel çabalara zarar verebileceğinden dolayı, sakınmalıdır. Araştırma bütünlüğünün sürdürülmesi ve bunun sunumu, iyi bilimsel uygulama kurallarını takip ederek başarılıdır. Bu da şunları içerir:

- Yazılı eser değerlendirilmek üzere eş zamanlı birden fazla dergiye gönderilmemelidir.

- Yazılı eser daha önceki bir eserin geliştirilmesi olmadıkça, daha önce (kısmen ya da tamamen) yayınlanmamış olmalıdır. [Metnin yeniden kullanıldığı imasından kaçınmak için tekrar kullanılabilir materyallerde şeffaflık sağlayın ("self-plagiarism" kişinin kendinden intihali")].

- Tek bir çalışma; sunum miktarını arttırmak için birçok parçaya bölünmemeli ve zaman içinde aynı ya da çeşitli dergilere gönderilmemelidir. (örneğin "salam-yayınçılık" "salamizasyon").

- Veriler, sonuçlarınızı desteklemek için fabrikasyon (uydurma) ya da manüple edilmiş olmamalıdır.

- Yazarın kendine ait olmayan hiçbir veri, metin veya teori kendininmiş gibi sunulmamalıdır (intihal). Diğer eserlerin kullanımı, (eserin birebir kopyalanması, özetlenmesi ve/veya başka kelimeler kullanarak açıklanması da içeren) ya telif hakkı korunacak şekilde izin alınarak ya da tırnak işaretinde birebir kopyalanarak uygun onay ile kullanılmalıdır.

Önemli not; Türk Kolon ve Rektum Hastalıkları Dergisi intihal taramak için bir program (iThenticate) kullanmaktadır.

- Eser sunulmadan önce sorumlu makamlardan ve çalışmanın yapıldığı enstitü/kuruluşlardan-zimnen veya açıkça-onay alınmasının yanı sıra tüm yazarlardan açıkça onay alınmış olmalıdır.

- Sunulan eserde yazar olarak ismi olanların, bilimsel çalışmaya yeterince katkısı olmuş olmalıdır ve ortak mesuliyet ve sorumluluğu olmalıdır.

Bununla beraber:

- Yazarlık veya yazarların sıra değişiklikleri eserin kabulünden sonra yapılamaz

- Yazının revizyon aşamasında, yayın öncesi veya yayınlandıktan sonra yazar isim eklenmesi veya çıkarılması istemi; ciddi bir konudur ve geçerli sebepler olduğunda değerlendirilebilir. Yazar değişikliği gerekçesi; haklı gerekçeli, inandırıcı ve sadece tüm yazarların yazılı onayı alındıktan sonra; ve yeni/siliniş yazının rolü silme hakkında ikna edici ayrıntılı bir açıklama ile kabul edilebilir. Revizyon aşamasında değişiklik olması halinde, bir mektup revise edilmiş yayına eşlik etmelidir. Yayına kabul edildikten veya yayınlandıktan sonra değişiklik olması halinde, bu istek ve gerekli dokümantasyonun yayıncı yoluyla editöre gönderilmesi gerekmektedir. Gerek görüldüğünde bu isteğin gerçekleşmesi için daha fazla doküman talep edilebilir. Değişikliğin kabul veya red karar dergi editörü insiyatifindedir. Bu nedenle, yayının gönderilmesi aşamasında yazar/yazarlar; gönderecekleri ilgili yazar grubunun isim doğruluğundan sorumludur.

- Yazarlardan sonuçların geçerliliğini doğrulamak amacıyla verilerin ilgili belgelerinin istenmesi halinde bu verileri göndermek için hazır bulundurulmalıdır. Bunlar, ham veri, örnekler, kayıt vb. şeklinde olabilir.

Görevi kötüye kullanma ya da suistimal şüphesi halinde dergi COPE yönergeleri izleyerek bir soruşturma yürütecektir. Soruşturmanın ardından, iddia geçerli görünüyorsa, yazara sorunu gidermek için bir fırsat verilecektir.

Usulsüzlük, şüphe seviyesinde kaldığında; dergi editörü aşağıdaki yollardan birine başvurabilir;

- Makale halen şüpheli ise, reddedilip yazara iade edilebilir.

- Makale online yayınlanmış ise; hatanın mahiyetine bağlı olarak ya yazım hatası olarak kabul edilecek ya da daha ciddi durumlarda makale geri çekilecektir.

- Hatalı yayın ve geri çekme durumlarında açıklayıcı not yayınlanır ve yazının kurumu bilgilendirilir.

Turkish Journal of COLORECTAL DISEASE



Yazarlara Bilgi

İnsan ve Hayvan Araştırmaları

İnsan Hakları Beyannamesi

İnsan katılımlı araştırmalar: 1964 Helsinki Deklarasyonu'na ve sonrasında yayımlanan iyileştirici ilkelere uygun olmalıdır ve yazarlar tarafından kurumsal ve/veya ulusal etik kurul komitelerine başvurulup onay alınmış olduğu beyan edilmelidir.

Araştırmanın 1964 Helsinki Deklarasyonu veya kıyaslanabilir standartlara göre yürütülmesi ile ilgili şüphe durumunda, yazarlar bu durumun nedenlerini açıklamak zorundadır ve bağımsız etik kurulları veya diğer değerlendirme kurulları aracılığıyla şüphelerin giderilmesi gerekmektedir.

Aşağıda belirtilen durumlar yazı içerisinde "Kaynaklar" bölümünden önce yer almalıdır:

Etik Kurul Onayı: "Çalışmada insanlara uygulanan tüm prosedürler kurumsal ve ulusal araştırma kurullarının etik standartlarına, 1964 Helsinki Deklarasyonu'na ve sonrasında yayımlanan iyileştirici ilkelere uygun olmalıdır."

Retrospektif çalışmalarda, aşağıda belirtilen cümle yer almalıdır.

"Bu tür çalışmalarda yazılı onam gerekmemektedir."

Hayvan Hakları Beyannamesi

Araştırmalarda kullanılan hayvanların refahına saygı gösterilmelidir. Hayvan deneylerinde, yazarlar hayvanların bakımında ve kullanımında uluslararası, ulusal ve/veya kurumsal olarak oluşturulmuş kılavuzlara uymalıdır ve çalışmalar için kurumdaki veya çalışmanın yapıldığı veya yürütüldüğü merkezdeki (eğer böyle bir merkez varsa) Klinik Araştırmalar Etik Kurulundan onay alınmalıdır. Deneysel hayvan çalışmalarında "Guide for the care and use of laboratory animals" <http://oacu.od.nih.gov/regs/guide/guide.pdf> doğrultusunda hayvan haklarını koruduklarını belirtmeli ve kurumlarından etik kurul onay raporu almaldır.

Hayvanlar ile yürütülen çalışmalarda, aşağıda belirtilen durumlar yazı içerisinde 'Kaynaklar' bölümünden önce yer almalıdır:

Etik Kurul Onayı: "Hayvanların bakımı ve kullanımı ile ilgili olarak uluslararası, ulusal ve/veya kurumsal olarak oluşturulmuş tüm kılavuzlara uyulmuştur."

Eğer uygun bulduysa (komitenin bulunduğu merkezde): "Hayvan çalışmalarında yapılan tüm uygulamalar kurumsal veya çalışmanın yürütüldüğü merkez tarafından belirlenmiş etik kurallara uyumludur."

Eğer makale insan ya da hayvan katılımlı bir çalışma değilse, lütfen aşağıda yer alan uygun durumlardan birini seçiniz:

"Bu makalenin yazarları insan katılımlı bir çalışma olmadığını bildirmektedir."

"Bu makalenin yazarları çalışmada hayvan kullanılmadığını bildirmektedir."

"Bu makalenin yazarları insan katılımlı veya hayvan kullanılan bir çalışma olmadığını bildirmektedir."

Bilgilendirilmiş Onam

Bütün bireyler ihlal edilemeyecek kişisel haklara sahiptir. Çalışmada yer alan bireyler, elde edilen kişisel bilgilere, çalışmada geçen görüşmelere ve elde edilen fotoğraflara ne olacağı konusunda karar verebilmeye hakkına sahiptir. Bundan dolayı, çalışmaya dahil etmeden önce yazılı bilgilendirilmiş onam alınması önemlidir. Bilimsel olarak gerekli değilse ve

katılımcılardan (veya katılımcı yetkin değilse ebeveynlerinden veya velilerinden) basılması için yazılı onam alınmadysa, katılımcılara ait detaylar (isimleri, doğum günleri, kimlik numaraları ve diğer bilgileri) tanımlayıcı bilgilerini, fotoğraflarını ve genetik profillerini içerecek şekilde yazılı formda basılmamalıdır. Tam gizlilik sağlanmasının zor olduğu durumlarda, bilgilendirilmiş onam formu şüpheyi içerecek şekilde düzenlenmelidir. Örneğin fotoğrafla katılımcıların göz kısmının maskelenmesi gizlilik açısından yeterli olmayabilir. Eğer karakteristik özellikler gizlilik açısından değiştirilirse, örneğin genetik profile, yazı yapılan değişikliğin bilimsel olarak sorun oluşturmadığını emin olmalıdır.

Aşağıdaki ifade belirtilmelidir:

Bilgilendirilmiş Onam: "Çalışmadaki tüm katılımcılardan bilgilendirilmiş onam alınmıştır."

Eğer makalede katılımcıların tanımlayıcı bilgileri yer alacaksa, aşağıdaki ifade belirtilmelidir:

"Makalede kişisel bilgileri kullanılan tüm katılımcılardan ayrıca bilgilendirilmiş onam alınmıştır."

DEĞERLENDİRME SÜRECİ

Türk Kolon ve Rektum Hastalıkları Dergisi'ne gönderilen tüm yazılar, sisteme yüklendikten sonra ilk önce editöryal kurul tarafından derginin amaç ve hedeflerine uygunluk ve temel şartları sağlama yönünden değerlendirilecektir. Yazılar, konusunda uzman dergi hakemlerine değerlendirilmek üzere gönderilecektir. Tüm kabul edilen yazılar yayımlanmadan önce, istatistik ve İngiliz dili konusunda uzman editörler tarafından değerlendirilecektir. Sayfaların ilk gözden geçirilmesinden sonra, hakem yorumları ön karar vermek için Editör'e gönderilecektir. Bu aşamada, ilk değerlendirmede bulunanların düşüncesi doğrultusunda, yazı kabul edilebilir, reddedilebilir veya yazıda düzeltme yapılması istenebilir. İlk değerlendirme sonrasında değerli bulunan makaleler için genellikle düzeltme istenir. Düzeltilen makaleler ilk karardan sonraki 2 ay içerisinde tekrar dergiye gönderilmelidir. Süre uzatılma yardımcı editörden 2 aylık süre bitmeden en az 2 hafta önce talep edilmelidir. Türk Kolon ve Rektum Hastalıkları Dergisi tarafından, 2 aylık düzeltme süresi sona erdikten sonra, yazı kabul edilmeyecektir. Düzeltme yapılan yazılar sisteme tekrar yüklendikten sonra değerlendirilmek üzere (genellikle ilk değerlendirmeyi yapan hakeme) gönderilecektir. Sonuç olarak yayımlanma kararı verildikten sonra, baskı öncesi Teknik Editör tarafından son kez değerlendirilecektir ve iletişim kurulacak olan yazara gözden geçirme ve son düzenlemeleri yapmak üzere işaretlenmiş bir nüshası elektronik ortamda gönderilecektir.

DÜZELTME SONRASI GÖNDERİLMESİ

Revize edilmiş bir versiyonu gönderirken yazar, yorumcular tarafından ele alınan her konuyu ayrıntılı olarak açıklamalı ve nokta nokta ayrıntılı olarak "yorumlara yanıt" sunmalıdır ve ardından belgenin açıklanmış kopyası bulunmalıdır (her yorumcunun yorumu nerede bulunabilir, yazarın cevap ve satır numaraları gibi yazarın değişiklikler).

Bunun yanı sıra ana revize yazı, kabul mektubu tarihinden itibaren 30 gün içinde teslim edilmelidir. Yazının revize edilmiş versiyonunun tanınan süre içinde verilmemesi durumunda, revizyon seçeneği iptal edilebilir. Yazar(lar) ek sürenin gerekli olduğunu düşünüyorsa, ilk 30 günlük süre bitmeden, uzatmayı talep etmelidir.

İNGİLİZCE YAZIM

Tüm yazılar yayımlanmadan önce profesyonel olarak "English Language Editor" tarafından değerlendirilmektedir.

KABUL SONRASI

Tüm kabul edilen makaleler editörlerden biri tarafından teknik açıdan değerlendirilecektir. Teknik inceleme tamamlandıktan sonra, makale ilgili birime gönderilerek yaklaşık bir hafta içerisinde tamamen atıf yapılabilir "Kabul Edilmiş Makale" şeklinde online olarak yayımlanacaktır.

Telif Hakkının Devri

Yayımlayan dergiyeye (veya basım ve yayma haklarının ayrı olduğu yapılarla ayrı olarak) makalenin telif hakkının devri gerekmektedir. Telif yasalara gereği bilginin yayılması ve korunması daha güvenli olarak sağlanacaktır.

Resimler

Renkli çizimlerin yayımlanması ücretsizdir.

Basım Öncesi Son Kontrol (Proof Reading)

Amaç; dizgi kontrolünü sağlamak veya dönüştürme hatalarını fark etmek, bütünlük ve netlik açısından yazıyı, tabloları ve şekilleri kontrol etmektir. Yeni bulgu ekleme, değerlerde düzeltme, başlıkta ve yazarlarda önemli değişikliklere editör izni olmadan müsadde edilmemektedir.

Online olarak yayımlandıktan sonra yapılacak değişikliklerde, Erratum üzerinden form oluşturulup makaleye erişim sağlayacak bağlantı oluşturulması gerekmektedir.

ERKEN YAYIN

Kabul edilmiş yazının baskı için tümü hazırlanırken online olarak özet hali yayımlanır. Kabul edilen yazı kontrolden geçtikten sonra, yazarlar son düzeltmeleri yaptıktan sonra ve tüm değişiklikler yapıldıktan sonra yazı online olarak yayımlanacaktır. Bu aşamada yazıya DOI (Digital Object Identifier) numarası verilecektir. Her iki forma da www.journalagent.com/krhd adresinden ulaşılabilecektir. Kabul edilen yazının yazarları elektronik ortamdaki sayfaları çıktı olarak aldıktan sonra proofreading yapmak, tüm yazıyı, tabloları, şekilleri ve kaynakları kontrol etmekte sorumludur. Baskıda gecikme olmaması için 48 saat içinde sayfa kontrolleri yapılmış olmalıdır.

YAZIŞMA

Tüm yazışmalar dergi editöryal kuruluna ait aşağıdaki posta adresi veya e-mail adresi ile yapılacaktır.

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Editorial/Editöryal

Değerli meslektaşlarım,

Yeni bir bahar ayında sizlerle birlikte olmaktan mutluluk duymaktayım. Geçtiğimiz üç ay içinde neler oldu, hangi yenilikler gelişti. Bu konuda sizleri biraz aydınlatmak isterim.

Öncelikle bir önceki sayıda sizleri davet ettiğim, TKRCD'nin olağan seçimi gerçekleşti. Bu seçimde görevini tamamlayan kıymetli Sökmen, Sungurtekin, Yamaner, Hamzaoğlu ve Leventoğlu bayrağı Kuzu, Terzi, Baca, Öztürk ve Sücüllü'ye devrettiler. Geri kalan Karakayalı, Öncel, Balık ve ben deniz ise görevimize devam ediyoruz. Yeni TKRCD Yönetim Kurulu'nu tebrik ederiz.

Bu dönem dergi stratejimizde, dergimizi daha da ileriye götürecek bazı değişiklikler yapmaya karar verdik. Öncelikle derginin dünya çapında tanınırlığını ve atıf sayısını arttırmak için komşu ülkelerde bulunan Kolorektal Cerrahlarla daha sıkı bir temas içine girmeyi hedefledik. Bununla birlikte, özellikle Orta Asya ve Uzak Doğu ile daha yakın bir temasa girmeyi amaçlıyoruz. Bu bizim atıf indeksimizin artmasına neden olacaktır.

Öte yandan, dünyaca ünlü, kendi alanlarında "Otor" olarak kabul edilen kişilerden makale ve hakemlik taleplerimiz, olumlu yanıtlar aldı. Bu bizim için çok önemli bir gelişmedir.

Diğer bir sevindirici gelişme ise, dergimizin EMBASE indeksine kabul edildiğine dair haberimiz oldu. Böylelikle derginin kısa vadeli hedeflerimizin tümüne varmış olduk. Orta dönem vadelerimizden "PupMed" indeksine girmenin eşliğinde olduğumuzu da bildirmek isterim.

Bununla birlikte, bu sayıda çok önemli bir Otörün derlemesini okuyacaksınız. Prof Sugarbaker, ileri evre kolon kanserinde HIPEC ve Sitoredüktif tedavi stratejisinin sonuçlarını irdeleyen makalesini mutlaka okumanızı tavsiye ederim. Ayrıca dikkatinizi çekecek çok sayıda araştırma makalesi ve olgu sunumlarına da yer verdik. Yararlı olacağını umuyoruz.

Nihayet, TKRCD'nin en önemli etkinliklerinden birisi olan İlkbahar Sempozyumu, bu yıl 13-15 Mart tarihleri arasında İzmir Wyndham Otel'de gerçekleştirilecektir. Bu sempozyumda özellikle tartışılmayan, zorlu ve komplike olguların tartışılması amaçlandı. Aynı zamanda eş başkanlığını yaptığım bu sempozyuma özellikle gelmenizi tavsiye ederim.

Bir sonraki sayıda yeniden buluşmak dileğiyle...

Prof Dr. Tahsin Çolak

TKRH Dergisi Editörü

Dear Colleagues,

I am happy to be with you in a new spring. What happened in the past three months, what innovations have evolved! I would like to enlighten you a bit about this.

First of all, the usual selection of TSCRS, which I invited you in the previous issue, was realized. The precious Sökmen, Sungurtekin, Yamaner, Hamzaoğlu and Leventoğlu, who completed their duties, handed over the flag to Kuzu, Terzi, Baca, Öztürk and Sücüllü in this election. The others, Karakayalı, Öncel, and me, continue our duty. Congratulations to the new TSCRS Board of Directors.

In this period, we decided to make some changes in our journal strategy that will take our journal further. First of all, we aimed to have a closer contact with the Colorectal Surgeons in neighboring countries in order to increase the journal's worldwide recognition and number of citations. In addition, we aim to have a closer contact, especially with Central Asia and the Far East. This will cause our citation index to increase.

Moreover, our articles and reviewership requests from world-renowned people who are considered as "authority" in their fields received positive responses. This is a very important development for us.

Another pleasing development was the news that our journal was accepted to the EMBASE index. Thus, we have reached all of the journal's short-term goals. I would also like to inform you that we are on the verge of entering the "PupMed" index, which is one of our aims in the medium term.

Besides that, in this issue, you will read a very important review of an authority. I strongly recommend you read the article of Prof Sugarbaker, examining the results of HIPEC and Cytoreductive treatment strategy in advanced colon cancer. We also included many research articles and case reports that will attract your attention. We hope it will be useful.

Finally, the Spring Symposium, one of the most important events of TSCRS, will be held this year between 13 and 15 March at İzmir Wyndham Hotel. In this symposium, it was aimed to discuss difficult and complicated cases that were not particularly discussed. At the same time, I recommend you come to this symposium where I am the co-president.

Hope to meet again in the next issue...

Prof. Dr Tahsin Çolak

Editor-in-Chief for the Journal of TJCD

What to Do When A Patient Infected With COVID-19 Needs An Operation: A Pre-surgery, Peri-surgery and Post-surgery Guide

COVID-19 ile Enfekte Bir Hastasının Operasyona İhtiyacı Olduğunda Ne Yapmalıyız: Cerrahi Öncesi, Cerrahi Sırası ve Cerrahi Sonrası Rehberi

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ABSTRACT

The virus, called COVID-19, which has emerged in China in December 2019, has been known to spread through droplets and close contact, and has evolved into a pandemic today. It is also known that in all patients who have come into contact with COVID-19, the infection is not severe and may even occur without symptoms. There is no consensus yet on how to take measures to protect the patient and the surgeon in case of diseases requiring urgent or elective surgery, and how preoperative preparation, perioperative phase, and postoperative care should be performed. The aim of this study was to prepare a guide on how the surgeon should behave in patients whose operation is mandatory in light of the available data.

Keywords: COVID-19, corona SARS-CoV-2, surgery guidelines

ÖZ

Aralık 2019'da Çin'de orta çıkan damlacık ve yakın temas yoluyla yayıldığı bilinen COVID-19 olarak adlandırılan virüs hastalığı günümüzde pandemiye dönüşmüştür. COVID-19 ile temas etmiş hastaların tümünde enfeksiyonun şiddetli olmadığı ve hatta semptomsuz seyredebileceği de bilinmektedir. Bu kişilerde acil veya elektif cerrahi yapılmasını gerektiren hastalıklar olması durumunda hastayı ve cerrahı koruyacak önlemlerin nasıl alınması gerektiği, ameliyat öncesi hazırlık, perioperatif faz, ve postoperatif bakımın nasıl yapılması gerektiği konusunda henüz fikir birliği oluşmamıştır. Bu çalışmada elde edilen veriler ışığında operasyonu zorunlu olan hastalarda cerrahın nasıl davranması gerektiği konusunda bir kılavuz hazırlanması amaçlandı.

Anahtar Kelimeler: COVID-19, corona SARS-CoV-2, ameliyat kuralları

Introduction

It is known that an outbreak in the form of pneumonia of unknown origin has occurred in Wuhan in China's Hubei Province in December 2019, killing 213 of the 9720 infected people in China and spreading in 19 other countries, infecting 106 people by January 31, 2020.¹ The causative virus has been tentatively named "Severe Acute Respiratory Syndrome Coronavirus 2" (SARS-CoV-2) and finally named

"Coronavirus Disease 2019 (COVID-19) by the World Health Organization. The disease is most commonly seen between the ages of 30-79 years and the median age is in the range of 49-59 years. It has been found very rarely under the age of 15. In about half of people infected with COVID-19, non-serious or overlooked symptoms occur, while in the other half the main symptoms are fever, fatigue and dry cough, myalgia and dyspnea.^{2,3} About half of the patients



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have co-existing diseases such as hypertension, diabetes and cardiovascular disease.³ The most common laboratory findings are leukopenia and lymphopenia. Elevation in lactate dehydrogenase and creatinine kinase levels can also be seen. Half of the patients may have abnormal liver function test findings such as elevation in alanine aminotransferase or aspartate aminotransferase levels. In most patients, normal serum procalcitonin levels are observed, but C-reactive protein levels are higher than the normal range. D-Dimer is high in a third of patients.^{4,5}

The risk of respiratory failure requiring critical care support in patients infected with COVID-19 is significant and prioritized, so critical care and anesthesiology teams should be prepared for the treatment and ongoing care of patients infected with COVID-19.⁶

Although there are studies focusing on the epidemiology, pathophysiology and management, best practices and their effect on public health outcomes in COVID-19-infected patients; the algorithm for surgical treatment of COVID-19-infected patients is still seen as an insignificant, secondary health problem. In addition, while anesthesiologists provide guidance on the equipment and preservatives needed to protect themselves during intubation, we surgeons are still a little behind on this issue.⁷ However, there is a need for guidance on how to follow these patients in situations that require elective, emergency or mandatory surgery.

The SARS experiences of many countries, such as Canada, create optimal care conditions to keep health workers safe in intervening patients infected with COVID-19, while countries without SARS experience such as Turkey, it is indisputable that health workers will be at great risk in intervening patients infected with COVID-19. On the other hand, the fact that patients with no symptoms or mild symptoms are more easily able to contact health workers increases both the spread of the disease and the risk to health workers. It has been proven that New Corona virus pneumonia (NCP) can be transmitted from person to person and can cause hospital infection that seriously threatens surgical staff and inpatient staff.⁸ Ti LK et al.⁷ suggested an operating room (OR) protocol prepared for confirmed or suspected COVID-19 infected patients who came to their hospital for surgery. As they suggested an OR protocol for the preparation period, intraoperative and postoperative phases for the nurse in charge, surgical staff, surgical nurse, anesthesiologist, anesthesia technicians and OR technicians; "the surgeon" was not included in this protocol.

Although we have experience in surgical procedures in patients with hepatitis, cyst hydatid and HIV infection, we do not currently have any experience with COVID-19

infected patients. Protection of health workers, other patients and wards, perioperative treatment, measures for operating rooms and surgical instruments, and operational, perioperative and postoperative management should be defined and known in detail in case of emergency operation in patients with suspected or confirmed COVID-19 infection. This will give health workers, especially surgeons, both protection from the disease and legal advantage.

In this study, it was aimed to establish a guide for establishing optimum protection conditions that could be done before, during and after surgical intervention, as specialists of surgical branches and anesthesiologists were at great risk in the treatment of patients infected with COVID-19.

In patients with suspected or approved COVID-19 infection, it is obvious that a special procedure should be performed beginning from the entry of patients to the hospital until their discharge from hospital. It is possible to evaluate the process from the point of view of the surgeon in 3 sub-sections: Evaluation phase, perioperative phase, and postoperative phase.

Evaluation Phase

A patient with suspected or confirmed COVID-19 infection may come to the surgical service from an outpatient clinic or emergency department following normal procedures. In both cases, the first evaluation of such patients should be done in a protected area that is predetermined according to the protocols of your hospital. First of all, elective surgery and endoscopic procedures should be postponed. This minimizes the risk for both the patient and the medical team, while minimizing the exposure of beds, ventilators, personal protective equipment (PPE), health care providers and other patients. In cases requiring emergency surgery, it is important to evaluate the suspected and confirmed patients in 2 separate groups. Although the protective measures to be taken during the evaluation are similar, treatment options may vary.

The following suggested path can be followed in the initial evaluation of the patient.

Preliminary evaluation:

- The patient's file should be examined in a safe area before contact with the patient. In this examination, previously recorded medical history, tests such as CT imaging that have been done, should be evaluated.
- The patient is reviewed with other intervening doctors, information is obtained from the family in terms of other aspects not reflected in the patient's medical history and all these data are recorded.

Preparation for Examination

- After that, the first thing to do is to go to the area near the room where PPE will be worn, along with doctors, nurses and assistants, to examine the patient. All items must be left in a safe area, hair must be collected, the top of the uniform must be tucked into the trousers. The shoes should also be made of sterilizable material that covers the feet and ankles exactly, such as boots, without holes and if possible, and the pants' legs should be inserted into the boot. After preparation, a cap covering the head and neck, protective mask, inner gloves, apron, outer gloves are worn, followed by glasses or face protective transparent barrier is worn. After the preparation is completed, the room is entered from its clean entrance and the patient is reached by following the shortest path without touching the items in the room.

Examination

- Anamnesis: The patient may not know who you are because of the PPE you wear. It is therefore recommended that you introduce yourself. Anamnesis should not be kept long due to the discomfort of the environment, should be clear and concise.
- Physical examination: Routine standards should be done. Due to the noise of the environment and isolations, most of the time there may not be auscultation. Standard equipment (sterile gloves, lubricants, gauze, etc.) can be used when there is a surgical wound or mucosa that needs to be evaluated or rectal examination that needs to be performed.

Leaving the Room

- Since the area where the patient is examined is considered to be a contaminated area, after the examination, we should go to the exit section where the auxiliary team is waiting for us. We have to wash hands with antiseptic without removing anything and then remove PPE with the help of a support team. We often wash our hands

with virucidal products. Especially caution should be exercised because contamination may be most common in this area.

Consultation

- When the cleaning process is complete, the treatment protocol is determined by consulting with the other doctors involved in the case and the result is notified to the family by telephone. The goal here is to have as little contact as possible.

Consent

- Everything that is done must be written and recorded on the computer on a regular basis. However, signed consent may not be obtained for security reasons.

On the other hand, surgery should not be delayed until diagnostic tests for COVID-19 are concluded if undiagnosed but suspicious patients are to undergo elective surgery.^{6,7} Patients with COVID-19 infection who need surgery will follow the same protocols as any other patient. In such cases, the rational use of available resources should be prioritized and both stigma of patients and the occurrence of unnecessary alarm situations should be avoided

Perioperative Phase

• Before Surgery

In patients with confirmed or suspected COVID-19 infection, all operating room personnel are required to wear PPE under their surgical dress to prevent contamination. PPE is essential for all interventions requiring close contact, such as surgical intervention, intubation, regional anesthesia, cannulation or catheterization. It is essential that all personnel and surgeons are trained to prevent contamination during the wearing and removal of these PPEs (Table 1).

There are different types of PPE, but the basic equipment needed to perform a surgical intervention can be summarized as follows:

Table 1: Personal protective equipment usage when intervening COVID-19 infected patients⁸

3 rd level protection	<ul style="list-style-type: none"> • Disposable surgical cap • Protective medical mask (N95) • Work clothes • Disposable protective suit • Disposable latex gloves • Protective glasses • All face respiratory protective equipment or motorized air purifying respirator 	<ul style="list-style-type: none"> • Should be used during operations such as tracheal intubation, tracheotomy, bronchofibroscope, gastroenterological endoscopy in patients with suspected or confirmed COVID-19 infection because these patients may spray or splash respiratory secretion, blood or body fluid • Should be used when medical personnel perform surgery or autopsy on the suspected or confirmed patient • Should be used by personnel when performing COVID-19 NAT
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1. Waterproof Apron
 2. Mask: Traditional surgical mask does not provide protection if aerosols are present. N95 or FFP2/FFP3 type masks are required.
 3. Glasses or face protective transparent barrier. But if the procedure produces aerosols, full-size barrier eye coverage is required. If not, just a partial barrier may be enough to prevent splashing or direct contamination.
 4. Latex gloves
 5. It is recommended that all long-haired staff hold their hair under the bonnet and, if they have a beard, they should cut to make masks comfortable to sit.
 6. Shoes must be without holes and cover the whole foot. Sterile rubber boots should be worn if possible
 7. After these preparations, standard sterile surgical aprons should be worn. Before surgical gloves are worn, the lower gloves should be washed with virucidal agents or alcohol.
- Since the mortality risks of COVID-19 infected patients who are diagnosed in preoperative period and need to be taken to emergency surgery are very high, the patients and their families should be informed about this. During the outbreak, the same OR and the same anesthesia device should be used in the operations of COVID-19 infected patients.⁶

The surgical team to make contact with critically ill patients with confirmed or suspected COVID-19 infection should use a properly tested N95 respiratory mask, eye protection, full face cover, liquid-resistant apron, long boots and rubber gloves (Picture 1).⁶ Longer-sleeved gloves are preferred to prevent glove slip. Alternatively, vertical tape strips may be used to help secure the gloves to the dress.⁶ The use of new type surgical gloves or synthetic gloves with disinfectant

agent between the two layers may provide disinfection (G-VIR) in case of puncture. It is also recommended to use such gloves.⁹ Jumpsuits with an integrated headgear can simplify the substrate worn, but product selection must be assessed for ease of removal to prevent contamination during removal.

• Surgery

On the other hand, it is still debatable whether the surgical procedure to be applied to these patients should be performed with laparoscopic or conventional methods. As is known, the experiences so far are early results from case reports or case series. Therefore, according to the low level evidences, the risk of viral contamination that may occur with aerosol effect of the gas used in laparoscopic surgery or surgical smoke should be taken into consideration while surgical team's contact with the patient's fluids and tissues increases with conventional method. On the other hand, laparoscopic operations create a physiological functional barrier between the surgeon and the disease because the abdomen is not opened, reducing exposure to the disease and cross infections. On the other hand, it may be necessary to avoid prolonged laparoscopic operations. Constant pressure insufflators can be used to reduce the aerosol effect of insufflation, and central aspirator systems must be used to drain the smoke. Although these characteristics of coronavirus are unknown, it has been determined that other viruses, such as Hepatitis B virus, can be found in surgical smoke formed during laparoscopy. For laparoscopic procedures, the use of CO₂ filters for aerosolized particles should be strongly considered. Yu GY et al.¹⁰ have shown that SARS-Cov-2 is transmitted by droplet and contact



Figure 1: Personal protective equipment. “WaxRS, ChristianMD. Practical recommendations for critical care and anesthesiology teams caring for novel coronavirus (2019-nCoV) patients. *Can J Anaesth.* 2020 Feb 12. doi: 10.1007/s12630-020-01591-x”.⁶

paths, but fecal-oral and aerosol paths can not be ignored. Also, it has been shown that laparoscopic surgery operations can be performed in patients with colon cancer infected with COVID-19, but the necessity of managing laparoscopic gases is emphasized and NOSES and TaTME operations are recommended to be performed carefully during the epidemic period.¹⁰ Luo Y et al. published a paper called the “Renji Experience”. That article stated that although colorectal surgery was not a priority in the fight against COVID-19, there might be a need to treat colon cancer and the highest level of protection for patients and their families, the health of medical personnel and other patients, and the safety of wards and hospitals could be provided in such a case.¹¹ In that study, it was stated that diagnosis and treatment of COVID-19 infected patients with colorectal cancer should not just be done by routine departments and should be conducted by a multidisciplinary team including departments of respiratory diseases and infectious diseases. It was stated that colonoscopy was inadvisable except in emergency and life threatening situations (bleeding, obstruction, foreign bodies, etc.), because it might cause cross-infection in patients and other health care workers and that even in these cases colonoscopy should not be performed and surgery should be the first preferred. It was also stated that COVID-19 infected patients with colorectal cancer should be placed in the isolation room with separate medical devices and that negative pressure rooms (below 5 PA) should be prepared and that all disposable medical products, body fluids and feces should be disposed of after surgery according to standard medical waste protocol and that after surgery, health workers were told to be taken for observation and isolated for 14 days.^{10,11} On the other hand, Chen YH et al.¹² stated that surgical operation should be reduced to a minimal level to prevent cross-infection in this special period and that surgical interventions for benign tumors should be postponed and that multidisciplinary treatment and non-surgical anti-tumor treatment should be chosen with a higher priority for malignant tumors, and that neoadjuvant therapy was highly recommended to the advanced stage cancers of the gastrointestinal tract meeting the criteria of NCCN guideline, and that in patients with a malignant tumor causing obstruction in gastric or esophagogastric junction could be managed with gastric tube decompression or stent placement to alleviate symptoms, and that transnasal enteral feeding tube intubation/percutaneous endoscopic gastrostomy could be used to provide enteral nutrition, and that stent placement for colorectal malignancy leading to simple

bowel obstruction could not only help you avoid emergency surgery, but also could provide a high success rate for future surgery, and that transcatheter arterial embolization could be an alternative choice to treat bleeding gastrointestinal tumors, and that emergency surgery could be a necessity in case of uncontrolled bleeding, blockage, or failure to other alternative treatments.¹² All invasive interventions should be performed in a designated isolation area. Protective enterostomy is a preferred method in lower digestive system surgery.¹²

In addition, it is still unknown how the intraoperative and postoperative wastes of these patients (including aspirator content, organs, feces, urine, used surgical materials) will be disposed of. It is also not known how to send the tissue samples that come out during surgery to pathology and how they will be subjected to a procedure in pathology, how to protect the pathologists and how to store the preparations. However, standard practices are recommended for these wastes.

After Surgery

Disinfection procedures for the isolation area such as the OR during the post-operative period are detailed in the “Covid-19 Prevention and Treatment Manual” prepared by CAI Hongliu et al.⁸ Accordingly;

For the disinfection of floor and wall; 1) Visible contamination must be completely removed before disinfection; blood and body fluids cleaning procedures should be followed; 2) The floor and walls should be disinfected with a disinfectant containing 1000 mg/L chlorine via floor mopping, spraying or cleaning; 3) It should be ensured that disinfection was performed for at least 30 minutes; 4) The disinfection process should be done three times a day and the procedure must be repeated in case of contamination.⁸

For the disinfection of object surfaces; 1) Visible contamination must be completely removed before disinfection; blood and body fluids cleaning procedures should be followed; 2) The surfaces of objects should be wiped with cloths containing disinfectants of 1000 mg/L chlorine and it should be rinsed with clean water after 30 minutes. The disinfection procedure should be performed three times a day (should be repeated when contamination is suspected); 3) First clean areas, then more contaminated areas should be wiped. First the surfaces of objects which are not frequently touched should be wiped and then the surfaces of frequently touched objects should be wiped (when the surface of an object is cleaned, replace the used wiper with a new one).⁸

For Air disinfection; 1) Plasma air sterilizers can be used for air disinfection in environments where humans are present and can be operated continuously; 2) If plasma air sterilizers are not available, an ultraviolet lamp should be used for 1 hour at a time. This should be done three times a day.⁸

For removal of faeces and sewage water; 1) Fecal matter and sewage system should be disinfected by purifying with disinfectant containing chlorine before it is sent to the drainage system (active chlorine should be more than 40 mg/L for the first application.). Ensure that the disinfection time is at least 1.5 hours; 2) The total residual chlorine concentration in the disinfected sewage system should reach 10 mg/L.⁸

Protection Against Spill of Blood and Fluids of The Patients with COVID-19 infection⁸;

In case of a small amount (10 mL) of blood or body fluid is spilled; 1) Option 1: Spills must be carefully covered with disinfectant wipes containing chlorine (containing 5000 mg/L effective chlorine) and cleared, then the surfaces of the objects should be cleared with disinfectant wipes containing chlorine (containing 500 mg/L effective chlorine) for the second time with; 2) Option 2: Spills should be carefully eliminated with disposable absorbent materials such as gauze, wipe, etc. soaked in disinfectant solution containing 5000 mg/L chlorine.⁸

In case of a large amount (>10 mL) of blood or body fluid is spilled; 1) first, place signs that indicate the presence of a spill; 2) apply clearing procedures described below in option 1 or 2: Option 1: Put a clean and absorbent towel on spills for 30 minutes (towels must contain peroxyacetic acid, which can absorb liquid up to 1 L) and clean the contaminated area after removing contaminated substances. Option 2: Completely cover the spill with disinfectant powder or bleach powder containing water-absorbing ingredients, or completely cover it with disposable water-absorbing materials. Then pour disinfectant containing 10,000 mg/L chlorine into the water-absorbing material (or cover it with a dry towel which will undergo high-level disinfection). Wait for at least 30 minutes before carefully removing the spill. 3) fecal matter, secretions, vomiting etc. taken from patients should be collected in special containers and should be disinfected for 2 hours with 20,000 mg/L chlorine-containing disinfectant (1:2 pouring/disinfectant); 4) after removing the spill, disinfect the surfaces of the contaminated environment or objects; 5) containers containing infected materials should be cleaned with a disinfectant containing 5,000 mg/l active chlorine for 30 minutes; 6) collected infected substances must be disposed of as medical waste; 7) used products

should be placed in double layer medical waste bags and disposed of.⁸

For decontamination of reusable medical devices; 1) Keep the device for at least 30 minutes in disinfectant containing 1000 mg/L chlorine if there is no visible contamination; 2) if there is visible contamination, keep the device for at least 30 minutes in disinfectant containing 5000 mg/L chlorine; 3) after drying, package the devices, close them completely and send them to the disinfection center.⁸

There is no guide on how to transport pathology preparations, how to process them, how to protect pathologists and how to store preparations. It has been suggested that a runner must be present outside the OR, and that such personnel must provide medicines or equipment when needed, or that they are required for arterial blood gas or frozen section operations.^{6,7} Staff leaving the OR throw away their used gowns and gloves in the entrance room and perform hand hygiene before leaving the entrance room.^{6,8} At the end of the surgery, one of the most important phases is for the team to remove their clothes before leaving the operating room to prevent contamination. At this stage, the team should move away from the patient with slow movements, avoid contact with each other. They should help each other during dressing and the basic principles of contamination prevention should be followed. Frequently the hands should be washed with virucidal agents or alcohol. The clothes should be in the dirty room or in the same OR at a remote point and, if possible, right next to the OR door. For this reason, ORs with large or sufficient space should be preferred to minimize contact.⁸

Postoperative Phase

Patients who do not require postoperative ICU care are kept in the operating room until complete recovery.⁶ After the OR personnel send the patient back to the service, a minimum of one hour is required between cases to clean all contaminated surfaces, screens, keyboards, cables, monitors and anesthesiology machine. Products not used in surgery should be considered infected. All staff are also required to shower before continuing their duties. Decontamination of OR should be provided by vaporizer using hydrogen peroxide.^{6,7}

Airflow in hospital wards can significantly affect the risk of nosocomial transmission of certain coronavirus strains, such as SARS.¹⁴ During the previous SARS outbreak, hospital administrations modified existing hospital systems to create negative airflow isolation rooms. In some cases, all intensive care units were converted into negative pressure/

airflow services instead of individual patient rooms. These strategies used during the SARS experience can be replicated if necessary when managing 2019-nCoV outbreak scenarios, with local operational limitations and capabilities in mind.

After the OR, patients should be monitored and treated in isolated intensive care units or in isolated rooms in accordance with hospital protocols. The basic rules mentioned above should be followed when taking care of the patients. On the other hand, it is debatable whether treatment for COVID-19 should be given during postoperative follow-up, besides giving disease-specific treatments. Since postoperative respiratory problems are more frequent than usual in these patients, a multidisciplinary approach with anesthesiologist and chest diseases specialist is required. If COVID-19 infection has not been proven in patients, there is no need to provide specific treatment for Coronavirus in these patients. Treatment should be administered as it is done to other patients.⁶ However, if patients have a confirmed diagnosis of COVID-19 infection, treatment for the coronavirus may be given. There is no consensus on the treatment to be given and the treatment is updated daily. Since the side effects and efficacy of the treatments are not certain, at least oral consent should be obtained from the patient before starting the treatment. Hydroxychloroquine, lopinavir/ritonavir are treatments currently used.¹⁵ Only hydroxychloroquine should be used in elderly patients using multidrugs. However, this medication should be avoided in case of liver disease.¹⁵ In addition to these treatments in patients with severe infection, Interferon/Tocilizumab may be added to treatment.¹⁶ Remdesavir may also have a role in the treatment.¹⁷ Oxygen therapy and N-acetylcysteine should also be given. Drugs that alter function and expression of angiotensin converting enzyme 2 (ACE-2) are being evaluated. However, corticosteroid therapy should be avoided. Although there is no conclusive evidence, NSAIDs such as ibuprofen are not recommended because they can worsen the disease. In the case of intrabdominal infection, it is not recommended to change the protocol applied in the treatment of intrabdominal infection.

In countries such as Turkey which are new to COVID-19; health care services, health centers, intensive care units and ORs should be reviewed. Each section should create its own protocol and guide and while doing this; protocols, algorithms, and guides that have been created by countries such as Canada which has the SARS experience should be taken into account. We believe that we will be able to overcome this outbreak by ensuring the health of

the patients infected with COVID-19 and the safety of the medical staff who encounter these patients.

Peer-review: Internally peer reviewed.

Authorship Contributions

Concept: E.K., T.Ç., Design: E.K., T.Ç., Data Collection or Processing: E.K., T.Ç., Analysis or Interpretation: E.K., T.Ç., Literature Search: E.K., T.Ç., Writing: E.K., T.Ç.

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Cytoreductive Surgery for Advanced Colon Cancer

İleri Kolon Kanseri için Sitoredüktif Cerrahi

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ABSTRACT

Peritoneal metastases from appendiceal and colorectal cancer continue to be a major threat to a favorable outcome with treatment. Reliable treatment strategies for the management of appendiceal and colorectal cancer start with the complete surgical removal of the disease. The surgical technology to accomplish this goal in patients with peritoneal metastases was reviewed. Electrosurgical dissection techniques and wide open exposure of the abdomen and pelvis were described. Five peritoneal stripping (peritonectomy) procedures were presented and integrated with visceral resections that may be required. Techniques to remove cancer nodules from small bowel and small bowel mesentery were itemized. Technology for complete resection of peritoneal metastases from patients with appendiceal and colorectal cancer was described and it can improve treatment outcomes for these patients.

Keywords: Peritoneal metastases, peritonectomy, cytoreductive surgery, electrosurgery, intraperitoneal chemotherapy

ÖZ

Apendiks ve kolorektal kanserden peritoneal metastazlar, tedavi ile olumlu bir sonuç alınması için büyük bir tehdit olmaya devam etmektedir. Apendiks ve kolorektal kanserin yönetimi için güvenilir tedavi stratejileri, hastalığın tamamen cerrahi olarak çıkarılması ile başlar. Bu çalışmada peritoneal metastazı olan hastalarda bu amaca ulaşmak için kullanılan cerrahi teknoloji gözden geçirilmiştir. Elektrocerrahi diseksiyon teknikleri ile birlikte karın ve pelvisin detaylı ve açık bir şekilde ekspoz edilmesi tanımlandı. Beş periton sıyırma (peritonektomi) prosedürü sunuldu ve gerekli olabilecek viseral rezeksiyonlarla entegre edildi. İnce barsaktan ve ince barsak mezenterinden kanser nodüllerini çıkarma teknikleri verildi. Apendiks ve kolorektal kanseri olan hastalardan periton metastazlarının tam rezeksiyonu için teknoloji tanımlandı.

Anahtar Kelimeler: Periton metastazı, peritonektomi, sitoredüktif cerrahi, elektrocerrahi, intraperitoneal kemoterapi

Introduction

As cancer surgery expanded in the midst of a technological revolution in patient care, this discipline accepted responsibilities not only for the resection of primary tumor but also for the surgical management of metastatic disease. Aggressive management strategies to bring about long-term survival to patients with peritoneal surface malignancy have been pioneered by our group.^{1,2} Successful treatment of abdominal and pelvic malignancies that disseminate to peritoneal surfaces has resulted from extensive experience with appendiceal cancer. Appendiceal cancer became the paradigm for successful treatment of peritoneal metastases

(PM).^{3,4} This review presents the concepts for and the technique of cytoreduction that optimally prepares the patient for chemotherapy used in the operating room with hyperthermia with acceptable morbidity and mortality.

Principles of Management

The successful treatment of peritoneal surface malignancy requires a comprehensive management plan that utilizes cytoreductive surgery (CRS) and perioperative chemotherapy. In addition, proper patient selection is mandatory. Complete resection of all visible malignancy is essential for the treatment of peritoneal surface malignancy to result in long-term survival. Up to five peritonectomy



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procedures may be required.⁵ The visceral resections and parietal peritonectomy procedures that one must utilize to adequately resect all visible evidence of disease are shown in Table 1. Their utilization depends on the distribution and extent of invasion of the malignancy disseminated within the peritoneal space. Normal peritoneum is not excised, only that which is implanted by cancer.

Peritonectomy Procedures and Visceral Resections

Rationale for Peritonectomy Procedures and Visceral Resections

Peritonectomy procedures are necessary if one is to successfully treat peritoneal surface malignancies with curative intent. Peritonectomy procedures are used in the areas of visible cancer progression in an attempt to leave the patient with only microscopic residual disease. Isolated tumor nodules on parietal peritoneum may be removed using electroevaporation. Involvement of the visceral peritoneum frequently requires the resection of a portion of the stomach, small intestine, or colorectum. Layering of cancer on a peritoneal surface or a portion of the bowel requires peritonectomy or bowel resection for complete removal.

Locations of Peritoneal Surface Malignancy

Peritoneal metastases, especially mucinous carcinomatosis, tend to involve the visceral peritoneum in greatest volume at three anatomic sites.⁶ These are sites where the bowel is anchored to the retroperitoneum and peristalsis causes less motion of the visceral peritoneal surface. The rectosigmoid colon, as it emerges from the pelvis, is a non-mobile portion of the bowel. Also, it is located in a dependent site and therefore is frequently layered by peritoneal metastases. Usually, a complete pelvic peritonectomy requires stripping of the pelvic sidewalls, the peritoneum overlying the bladder, the cul-de-sac, and resection of the rectosigmoid colon. The ileocecal valve is another area where there is limited mobility. Resection of the terminal ileum and a small portion of the right colon is often necessary. A final site often requiring resection is the antrum of the stomach which is fixed to the retroperitoneum at the pylorus. Tumor coming into the foramen of Winslow accumulates in the subpyloric

space and may cause intestinal obstruction as a result of gastric outlet obstruction.⁷ Large volumes of tumor in the lesser omentum combined with disease in the subpyloric space may cause a confluence of disease that requires a total gastrectomy for complete cytoreduction.

Electroevaporative Surgery

In order to adequately perform peritonectomy, the surgeon must use electrosurgery.⁸ The electrosurgical handpiece uses a ball tip that allows the tissue surfaces beneath the peritonectomy to be contoured (Valleylab, Boulder, CO). The smooth surface is then able to be resurfaced by peritoneum (Figure 1). Peritonectomies and visceral resections using traditional scissor and knife dissection will unnecessarily disseminate a large number of tumor cells within the abdomen. High voltage electrosurgery leaves a margin of heat necrosis that is devoid of viable malignant cells. Not only does electroevaporation of tumor and normal tissue at the margins of resection minimize the likelihood of persistent disease, but also it minimizes blood loss. In the absence of electrosurgery, profuse bleeding from stripped peritoneal surfaces may occur.

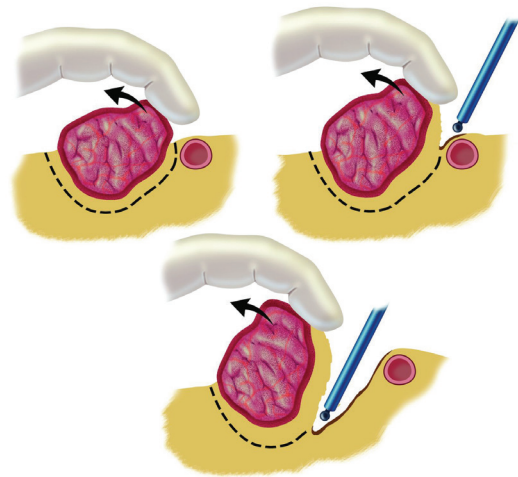


Figure 1. Ball-tipped electrosurgery is used to dissect and simultaneously provide small vessel hemostasis. Frequent room temperature saline irrigation is needed to prevent heat damage to tubular structures. A margin of heat necrosis from electrosurgical dissection at high voltage helps to prevent local recurrence. Smoke evacuation is required to prevent environmental contamination (From reference 5 with permission)

Table 1. Peritonectomy procedures and resections that are combined to complete a cytoreduction procedure

Peritonectomy	Resections
Anterior parietal peritonectomy	Old abdominal incisions, umbilicus and epigastric fat pad
Left upper quadrant peritonectomy	Greater omentectomy and spleen
Right upper quadrant peritonectomy	Tumor on Glisson's capsule of the liver
Pelvic peritonectomy	Uterus, ovaries and rectosigmoid colon
Omental bursectomy	Gallbladder and lesser omentum

Abdominal Exposure

The abdominal cavity is opened through a midline incision from the xiphoid to the pubis. The old abdominal incision is widely excised including the umbilicus. The skin edges are secured by heavy sutures to the self-retaining retractor. Traction on the edges of the abdominal incision elevates the structures of the abdominal wall to facilitate their accurate dissection (Figure 2). Strong elevation of abdominal wall helps to avoid damage to bowel loops that are adherent to the anterior abdominal wall.^{9,10} Generous abdominal exposure is achieved through the use of a Thompson Self-Retaining Retractor (Thompson Surgical Instruments, Inc., Traverse City, MI).

Total Anterior Parietal Peritonectomy

As the peritoneum is dissected away from the posterior rectus sheath, a single entry into the peritoneal cavity in the upper portion of the incision (peritoneal window) allows the surgeon to assess the requirement for a complete parietal peritonectomy (Figure 3). If cancer nodules are palpated on the parietal peritoneum, a complete dissection may be indicated to achieve a complete cytoreduction. If the parietal peritoneum is not involved by PM, except for the small defect in the peritoneum required for this peritoneal exploration, the remainder of the peritoneum is maintained intact.

The self-retaining retraction system is steadily advanced along the anterior abdominal wall. This optimizes the broad traction at the point of dissection of the peritoneum from its underlying tissues. The dissecting tool is the ball tip, and smoke evacuation is used continuously.¹¹ It is most adherent directly overlying the transversus muscle. In some instances, dissection from inferior to superior aspects of the abdominal

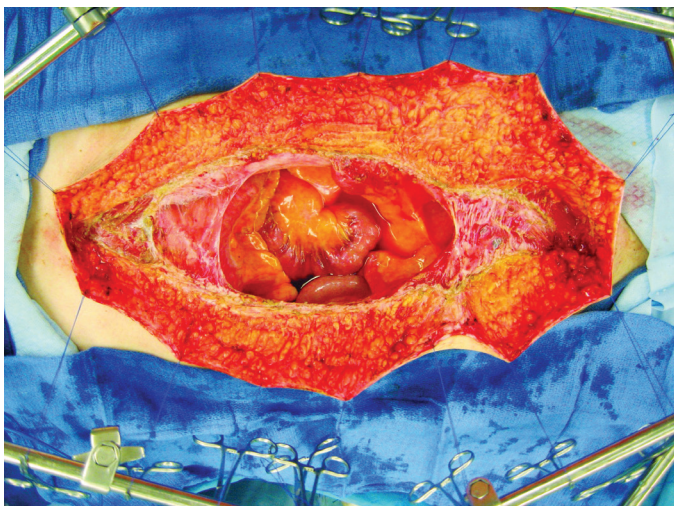


Figure 2. Elevation of the edges of the abdominal incision. Skin traction on a self-retaining retractor facilitates dissection of abdominal wall structures and minimizes the likelihood of damage to bowel loops adherent to the abdominal wall (From reference 5 with permission)

wall facilitates clearing in this area. The dissection blends in with the right and left subphrenic peritonectomy superiorly and with the complete pelvic peritonectomy inferiorly. As the dissection proceeds beyond the peritoneum overlying the paracolic sulcus (line of Toldt), the dissection becomes more rapid with the loose connections of the peritoneum at this anatomic site.

Left Subphrenic Peritonectomy

The peritonectomy procedures are greatly facilitated by the self-retaining retractor that provides continuous exposure of all quadrants of the abdomen including the pelvis. The epigastric fat and peritoneum at the edge of the abdominal incision are stripped off the posterior rectus sheath. Strong traction is exerted on the tumor specimen throughout the left upper quadrant in order to separate tumor from the diaphragmatic muscle, the left adrenal gland, and the superior half of the perirenal fat. The splenic flexure of the colon is severed from the left abdominal gutter and moved medially by dividing the peritoneum along Toldt's line. Dissection beneath the hemidiaphragm muscle must be performed with ball-tipped electrosurgery, not by blunt dissection (Figure 4). Numerous blood vessels between the diaphragm muscle and its peritoneal surface must be visualized and individually electrocoagulated before their transection or unnecessary bleeding will occur as the severed blood vessels retract into the muscle of the diaphragm. The plane of dissection is defined using ball-tipped electrosurgery on pure cut, but all blood vessels are electrocoagulated before their division.

Greater Omentectomy and Possible Splenectomy

To free the mid-abdomen of a large volume of tumor, the greater omentectomy-splenectomy is performed. The

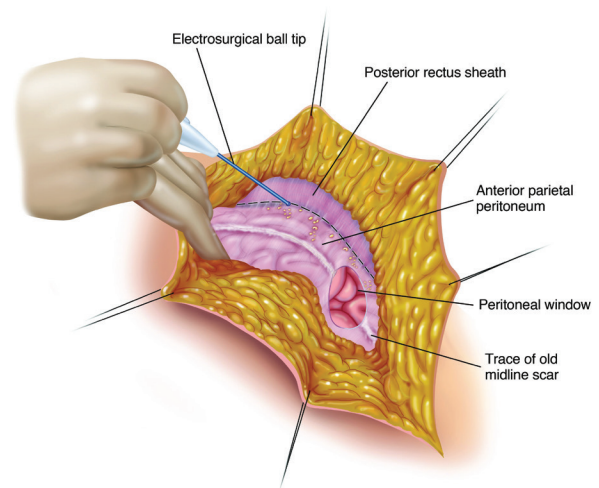


Figure 3. Peritoneal window is necessary to assess the need for total anterior parietal peritonectomy (From reference 5 with permission)

greater omentum is elevated and then separated from the transverse colon using electrocautery. This dissection continues beneath the peritoneum that covers the transverse mesocolon in order to expose the lower border of the pancreas. The branches of the gastroepiploic arcade to the greater curvature of the stomach are ligated in continuity and then divided.

Because the left upper quadrant peritonectomy has been completed, the structures deep beneath the left hemidiaphragm can be elevated. Therefore, under direct vision, the short gastric vessels are transected. With traction on the spleen, the peritoneum superior to the pancreas may be stripped from the gland bluntly or by using electrocautery. If the peritoneum covering the pancreas is free of cancer implants, it remains intact. The splenic artery and vein at the tail of the pancreas are ligated in continuity and proximally suture ligated. Great care is taken not to traumatize the body or tail of the pancreas.

Right Subphrenic Peritonectomy

Peritoneum is stripped from beneath the right posterior rectus sheath to begin the peritonectomy in the right upper quadrant of the abdomen. Strong traction on the specimen is used to elevate the hemidiaphragm into the operative field. Again, ball-tipped electrocautery on pure cut is used to dissect at the interface of tumor and normal tissue. Coagulation current is used to divide the blood vessels between the diaphragm and peritoneum as they are encountered and before they bleed.

Stripping of Tumor from Glisson's Capsule

The stripping of tumor from the right hemidiaphragm continues until the bare area of the liver is encountered.

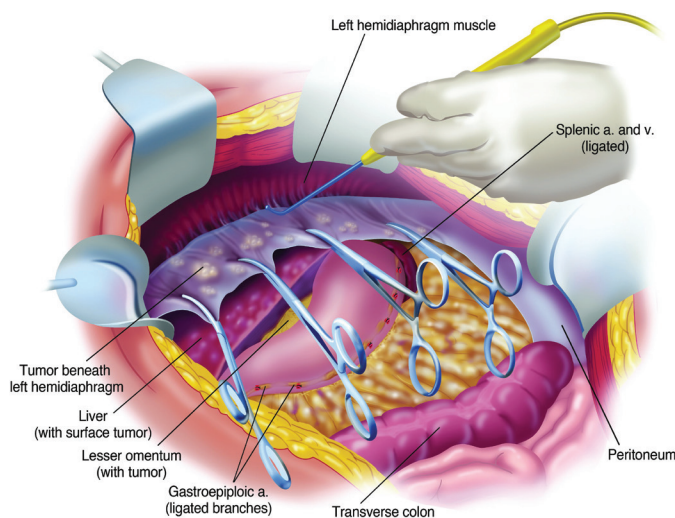


Figure 4. Peritoneal stripping of the undersurface of the left diaphragm (From reference 5 with permission)

At that point, tumor on the superior surface of the liver is electroevaporated until the liver surface is cleared (Figure 5). With ball-tipped electroevaporative dissection, a thick layer of tumor may be bloodlessly lifted off the liver surface by moving beneath Glisson's capsule (high voltage pure cut electrocautery dissection). Isolated patches of tumor on the liver surface are electroevaporated with the distal 2 cm of the ball tip bent and stripped of insulation ("hockey-stick" configuration). Ball-tipped electrocautery is also used to extirpate tumor from attachments of the falciform ligament and round ligament.

Tumor from beneath the right hemidiaphragm, from the right subhepatic space, and from the surface of the liver forms an envelope as it is removed *en bloc*. The dissection is greatly facilitated if the tumor specimen is maintained intact. The dissection continues laterally on the right to encounter the perirenal fat covering the right kidney. Also, the right adrenal gland is visualized and carefully avoided as tumor is stripped from the right subhepatic space. As the peritoneal reflection at the posterior aspect of the liver is divided, care is taken not to traumatize the vena cava or to disrupt the caudate lobe veins that pass between the vena cava and segment 1 of the liver.

Lesser Omentectomy and Cholecystectomy with Stripping of the Hepatoduodenal Ligament

The gallbladder is removed in a routine fashion from its fundus toward the cystic artery and cystic duct. These structures are ligated and divided. The hepatoduodenal ligament is characteristically heavily layered with tumor. After dividing the peritoneal reflection onto the liver, the cancerous tissue that coats the porta hepatis is bluntly stripped using Russian forceps from the base of the

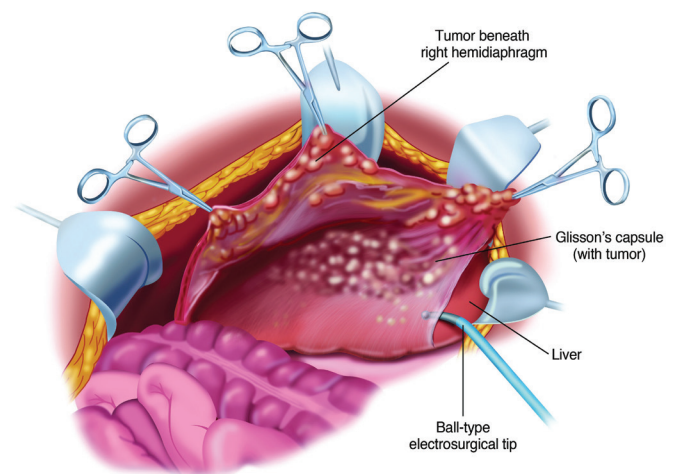


Figure 5. Electroevaporation of tumor from the liver surface with resection of Glisson's capsule (From reference 5 with permission)

gallbladder bed toward the duodenum. The right gastric artery going to the lesser omental arcade is preserved (Figure 6). To continue resection of the lesser omentum, the surgeon separates the gastrohepatic ligament from the fissure that divides liver segments 2 and 3 from segment 1. Ball-tipped electrocautery is used to electroevaporate tumor from the surface of the caudate process. Care is taken not to traumatize the anterior surface of the caudate process, for this can result in excessive and needless blood loss. The segmental blood supply to the caudate lobe is located on the anterior surface of this segment of the liver, and hemorrhage may occur with only superficial trauma. Also, care must be taken to avoid an accessory left hepatic artery that may arise from the left gastric artery and cross through the hepatogastric fissure. If the artery is embedded in tumor or its preservation occludes clear exposure of the omental bursa, the artery is ligated as it enters the liver parenchyma. It is resected as part of the hepatogastric ligament.

Circumferential Resection of the Hepatogastric Ligament and Lesser Omental Fat by Digital Dissection

The triangular ligament of the left lobe of the liver was resected in performing the left subphrenic peritonectomy. This completed, the left lateral segment of the liver is retracted left to right to expose the hepatogastric ligament in its entirety. A circumferential electrocautery release of this ligament (lesser omentum) from the fissure between liver segments 2 and 3, and the left caudate lobe, and from the arcade of right gastric artery to left gastric artery along the lesser curvature of the stomach is required. After electrocauterizing the peritoneum on the lesser curvature of the stomach, digital dissection with extreme pressure from the surgeon's thumb and index finger

separates lesser omental fat and tumor from the vascular arcade. As much of the anterior vagus nerve is spared as is possible. The tumor and fatty tissue surrounding the right and left gastric arteries are split away from the vascular arcade. In this manner, the specimen is centralized over the major branches of the left gastric artery. With strong traction on the specimen, the lesser omentum is released from the left gastric artery and vein.

Stripping of the Floor of the Omental Bursa

A Dever retractor or the assistant's fingertips beneath the left caudate lobe are positioned to expose the entire floor of the omental bursa (Figure 7). Further electrocautery of tumor from the caudate process of the left caudate lobe of the liver may be necessary to achieve this exposure. Ball-tip electrocautery is used to cautiously divide the peritoneal reflection of the liver onto the left side of the subhepatic vena cava. After the peritoneum is divided, Russian forceps assist in a blunt stripping of the peritoneum from the superior recess of the omental bursa, from the crus of the right hemidiaphragm, and from beneath the portal vein. Electrocautery of tumor from the shelf of the liver parenchyma beneath the portal vein that connects right and left aspects of the caudate lobe may be required. Care is taken while stripping the floor of the omental bursa to stay superficial to the right phrenic artery.

In some patients, a large volume of tumor on the posterior aspect of the hepatoduodenal ligament may be difficult to visualize. A 1/2 inch Penrose drain placed around the portal triad may allow improved visualization beneath these structures. Using Russian forceps tearing away the peritoneum beneath the porta hepatis may be necessary under direct visualization.

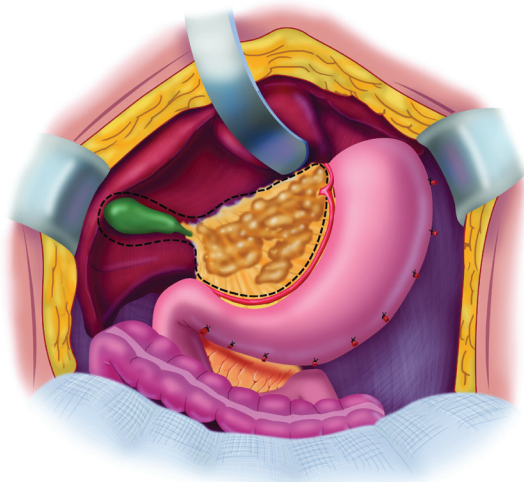


Figure 6. Lesser omentectomy and cholecystectomy with stripping of the anterior and posterior (if necessary) aspect of the hepatoduodenal ligament (From reference 5 with permission)

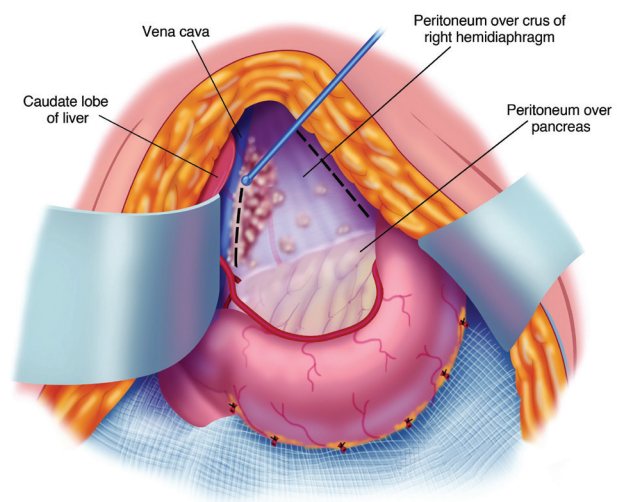


Figure 7. Stripping of the omental bursa after dividing the peritoneal reflection between the left caudate lobe and superior vena cava (From reference 5 with permission)

Complete Pelvic Peritonectomy

The tumor-bearing peritoneum is stripped from the posterior surface of the lower abdominal incision, exposing the rectus muscle. After dissecting generously the peritoneum on the right and left sides of the bladder, the urachus is localized and placed on strong traction using a Babcock clamp. The peritoneum with the underlying fatty tissues is stripped away from the surface of the bladder. Broad traction on the entire anterior parietal peritoneal surface and frequent saline irrigation clears the point for tissue transection that is precisely located between the bladder musculature and its adherent fatty tissue with the peritoneum. The inferior limit of dissection is the cervix in the female or the seminal vesicles in the male.

The peritoneal incision around the pelvis is connected to the peritoneal incisions of the right and left paracolic sulci (Figure 8). In the female, the round ligaments are divided as they enter the internal inguinal ring. The right and left ureters are identified and preserved. In women, the right and left ovarian veins are ligated at the level of the lower pole of the kidney and divided. A linear stapler is used to divide the sigmoid colon just above the limits of the pelvic tumor. The vascular supply of the distal portion of the bowel is traced back to its origin on the aorta. The inferior mesenteric artery is ligated, suture ligated and divided. This allows one to pack all the viscera, including the proximal sigmoid colon, in the upper abdomen.

Resection of Rectosigmoid Colon and Cul-de-Sac of Douglas

Electrosurgery is used to dissect at the limits of the mesorectum. The surgeon works in a centripetal fashion.

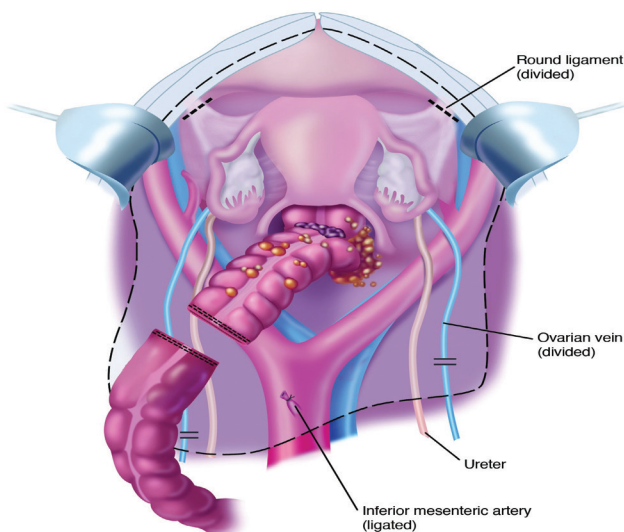


Figure 8. The complete pelvic peritonectomy includes the uterus and ovaries, rectosigmoid colon and pelvic peritoneum (From reference 5 with permission)

Extraperitoneal ligation of the uterine arteries is performed just above the ureter and close to the base of the bladder. The bladder is dissected away from the cervix and the vagina is entered. The vaginal cuff anterior and posterior to the cervix is transected using electrosurgery, and the rectovaginal septum is exposed. The perirectal fat is divided beneath the peritoneal reflection so that all tumor that occupies the cul-de-sac is removed intact with the specimen. The rectal musculature is skeletonized using electrosurgery so that a stapler can be used to close off the rectal stump.

Vaginal Closure and Low Colorectal Anastomosis

One of the few suture repairs performed prior to the intraoperative chemotherapy is the closure of the vaginal cuff. If one fails to close the vaginal cuff, chemotherapy solution will leak from the vagina. The circular stapled colorectal anastomosis occurs after the intraoperative chemotherapy has been completed. A circular stapling device is passed into the rectum, and the trochar penetrates the staple line. A purse-string applier is used to secure the staple anvil in the distal descending colon. The body of the circular stapler and anvil are mated, and the stapler is activated to complete the low colorectal anastomosis.

Optimization of Cytoreduction of Small Bowel and Its Mesentery

The peritonectomy procedures using high-voltage electrosurgery have been applied to the cytoreduction of parietal peritoneal surface malignancy. However, the electrosurgical techniques used in the peritonectomy procedures are not appropriate for the treatment of tumor nodules involving the small bowel. Only a very limited use of electrosurgery on the small bowel itself is possible in order to avoid postoperative fistula. In contrast, small bowel mesentery is an anatomic site for safe use of electroevaporation of cancer nodules.

Five Types of Small Bowel Involvement by Cancer

CRS with perioperative chemotherapy has been most commonly used for the management of mucinous appendiceal neoplasms but they have been successfully applied to other tumors, especially colon cancer and diffuse malignant peritoneal mesothelioma. The histological features and the depth of invasion of these different tumors into the bowel wall are not uniform. Based on the extent of the invasion, the size of the tumor nodule and its anatomic location on the bowel wall, small bowel involvement is classified into five types¹²:

Type 1. Non-invasive nodules.

Type 2. Small invasive nodules on the anti-mesenteric portion of the small bowel.

Type 3. Moderate size invasive nodules on the anti-mesenteric portion of the small bowel.

Type 4. All sizes of invasive nodules at the junction of the small bowel and its mesentery.

Type 5. Large invasive nodules.

Techniques Used in Cytoreduction of the Small Bowel

Type 1. Non-invasive nodules: This type of small bowel involvement involves minute nodules of aggressive histology that have not invaded past the peritoneum because of their small size. It would also include large non-invasive nodules of diffuse peritoneal adenomucinosis or nuclear grade I peritoneal mesothelioma.^{13,14} The curved Mayo scissors are used to trim these non-invasive nodules from the surface of the small bowel; this results in a localized removal of peritoneum. Larger nodules are frequently scissor-dissected in a piecemeal fashion to avoid damage to the deeper layers of the bowel wall. Considerable skill acquired over time may be needed to avoid damage to the muscularis propria of the bowel (Figure 9). There is usually no need for seromuscular repair.

Type 2. Small invasive nodules on the anti-mesenteric portion of the small bowel: These invasive nodules do not separate from the muscular layer of the small bowel and a partial thickness resection is required. The seromuscular layer is resected leaving mucosa and submucosa intact. This resection is usually performed with a curved Mayo scissor but occasionally it may be performed by pure cut electrosurgery with frequent irrigation to cool the resection site. Scissor or knife dissection is preferred. The seromuscular layer is repaired by suture plication after the intraoperative chemotherapy is completed (Figure 10).

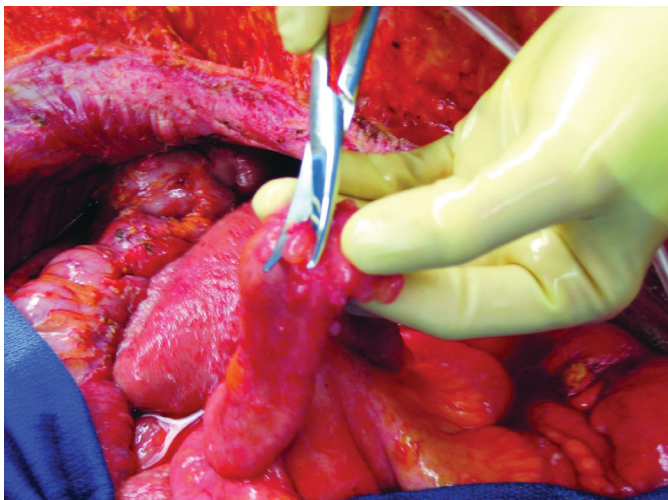


Figure 9. Type 1 - non-invasive tumor nodules are usually resectable using a curved Mayo scissor (From reference 5 with permission)

Type 3. Moderate size invasive nodules on the anti-mesenteric portion of the small bowel: In contrast to small invasive nodules in this location, larger nodules require a full thickness elliptical resection of the anti-mesenteric portion of the bowel wall. The closure is performed in two layers and at two different times. The first layer is a full thickness closure using absorbable suture. One suture starts at each corner of the defect and the sutures are then tied at the mid-portion of the resection. Following the POC, the defect is closed with a second layer of non-absorbable plication sutures (Figure 11).

Type 4. Small invasive nodules at the junction of the small bowel and its mesentery: These nodules can sometimes be removed by a localized removal with electrosurgery if sufficiently small and if the vascular supply to the segment of bowel is not compromised. A two-layer repair follows this localized resection. More often, these nodules are removed, and the incidence of fistula is reduced by a segmental small bowel resection with end-to-end hand-sewn anastomosis (Figure 12).

Type 5. Large invasive nodules: These lesions require a segmental small bowel resection with generous proximal and distal margins on the bowel wall and on the mesentery. The segment of small bowel and a portion of its mesentery are resected. The bowel is divided and closed using a linear cutter/stapler. The HIPEC is completed prior to a two-layer hand-sewn anastomosis (Figure 12).

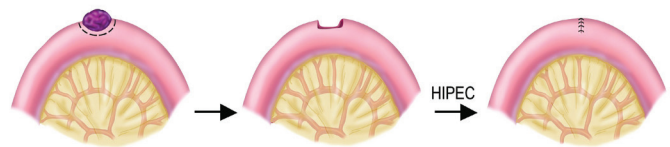


Figure 10. Type 2 - small invasive tumor nodules on the anti-mesenteric portion of the small bowel are resected along with the seromuscular layer. Hyperthermic intraperitoneal chemotherapy is administered prior to suture plication of the defect (From reference 5 with permission)

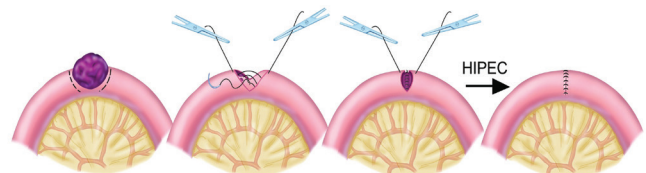


Figure 11. Type 3 - moderate sized invasive nodules on the anti-mesenteric portion of the small bowel are resected with a full thickness ellipse. Stay sutures elevate the portion of bowel to be resected. A full thickness closure with absorbable, running suture allows hyperthermic intraperitoneal chemotherapy to be given. After the intraperitoneal chemotherapy, a second layer of non-absorbable interrupted sutures is used to plicate the seromuscular layer (From reference 5 with permission)

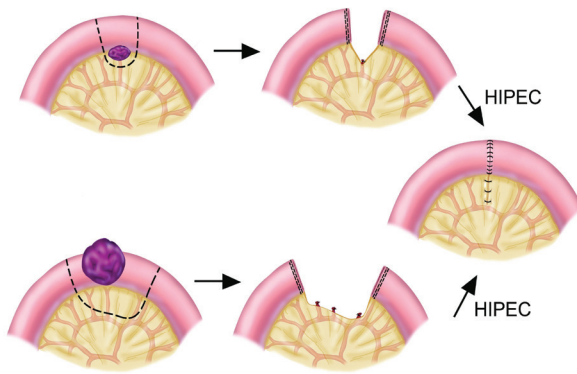


Figure 12. Small invasive nodules at the junction of the small bowel and mesentery (Type 4) or large invasive nodules (Type 5) are resected with generous margins using a linear stapler. After hyperthermic intraperitoneal chemotherapy is complete, a two-layer anastomosis is performed (From reference 5 with permission)

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25 Carcinoid Tumor Cases Incidentally Detected After 4642 Appendectomies

4642 Apendektomi Sonrası İnsidental Olarak Saptanan 25 Karsinoid Tümör Olgusu

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ABSTRACT

Aim: This study aimed to retrospectively investigate 25 cases of carcinoid tumors in 4642 pathological examinations of patients who admitted to our clinic with acute appendicitis in a period of 6 years.

Method: 4642 appendectomy operations performed in Şanlıurfa Training and Research Hospital and Mehmet Akif İnan Training and Research Hospital between 2012 and 2019 were evaluated retrospectively. Data regarding age, sex, preoperative clinical findings, histopathological results, operation reports, follow-up period, and metastasis status were extracted from electronic records and reported.

Results: Based on the histopathological examination of 4642 patients admitted to the emergency department of two large hospitals of Şanlıurfa province, 25 patients were diagnosed with carcinoid tumors (neuroendocrine tumor). Thirteen of our patients were male and 12 of them were female. The mean age of our patients was 33.2 years. The mean follow-up period was 5-62 months. No distant metastasis was detected in any of the follow-ups of our patients who had histopathologically well-differentiated carcinoid tumors.

Conclusion: Carcinoid tumors are the most common tumors of the appendix, which are detected incidentally after an acute appendicitis operation. Since these tumors are rare, histopathological evaluation and postoperative follow-up are important. Though, in our study, it is not common in terms of rate, it is still important to follow up these cases since it is common in the young population, and there is a possibility of metastasis in advanced stages.

Keywords: Carcinoid tumor, appendix, incidental

ÖZ

Amaç: Çalışmamızın amacı kliniğimize 6 yıl içerisinde akut apandisit tanısı ile başvuran ve opere edilen 4642 patolojik incelemede bulunan 25 karsinoid tümör olgusunun retrospektif olarak incelenmesidir.

Yöntem: 2012 ile 2019 yılları arasında Şanlıurfa Eğitim ve Araştırma Hastanesi ve Mehmet Akif İnan Eğitim ve Araştırma Hastanesi'nde yapılan 4642 apendektomi operasyonu retrospektif olarak değerlendirildi. Yaş, cinsiyet, ameliyat öncesi klinik bulgular, histopatolojik sonuçlar, operasyon raporları, izlem süresi ve metastaz durumu elektronik ortamda incelenerek rapor edildi.

Bulgular: Şanlıurfa ilimizin iki büyük hastanesinde arasında acil servise başvuran ve apandektomi yapılan 4642 hastanın histopatolojik incelemesinde 25 hastaya karsinoid tümör (nöroendokrin tümör) tanısı konuldu. Hastalarımızdan 13'ü erkek 12 tanesi de bayan idi. Hastalarımızın yaş ortalaması 33,2 idi. Hastalarımızı ortalama takip süremiz 5-62 aydı. Histopatolojik olarak hepsinde iyi diferensiyeli karsinoid tümör rastlanan hastalarımızın takiplerinde hiçbirinde uzak metastaz tespit edilmemişti.

Sonuç: Karsinoid tümörler çoğunlukla akut apandisit operasyonu sonrasında insidental olarak saptanan ve apandiks en sık rastlanan tümörleridir. Bu tümörlerin az rastlanması nedeniyle histopatolojik değerlendirme ve operasyon sonrası takibi önem arz etmektedir. Bizim çalışmamızda oran olarak sık görülmesi bile genç popülasyonda sık görülmesi ve ileri evrelerde metastaz ihtimali nedeniyle bu olguların yakın takibi önemlidir.

Anahtar Kelimeler: Karsinoid tümör, apandiks, insidental



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Introduction

Appendiceal tumors are among the less common tumors and these lesions are usually incidentally noticed after appendectomy. The incidence rate varies between 0.9 and 1%.^{1,2} Carcinoid tumors, also called neuroendocrine tumors, account for more than 50% of appendix tumors. They are generally more common in children and young adults.^{3,4,5} They are usually located at the tip of the appendix and most of the appendix carcinoids are smaller than 1 cm and rarely more than 2 cm in diameter.⁶ Although they are not frequently encountered after appendectomy operations, considering the number of appendectomies performed, it is important to follow up these cases that every general surgeon may face. Characteristics of patients histopathologically diagnosed with appendiceal carcinoid tumors were evaluated.

Materials and Methods

25 cases of carcinoid tumors detected after 4642 appendectomy operations performed in two major clinics in Şanlıurfa, Şanlıurfa Training and Research Hospital and Mehmet Akif İnan Training and Research Hospital between 2012 and 2019 were reviewed. The research was conducted following the principles of “World Medical Association Declaration of Helsinki: Ethical Principles for Medical Research Involving Human Subjects”. Ethics committee approval was not received for this study because of its retrospective design. Informed consent was obtained from all patients. The age, sex, preoperative clinical findings, histopathological results, operation reports, follow-up period, and metastasis status of all cases were retrospectively analyzed thorough electronic records.

Statistical Analysis

Social Science Statistical Package (SPSS Inc., Chicago, IL, USA) software was used for bio-statistical analysis. When data were presented as mean values, standard deviation values were given and when they were presented as mean values, minimum (min) -maximum (max) values were indicated.

Results

Thirteen of our patients were male and 12 were female. The mean age of our patients was 33.2 years (min-max=18-72). All of our patients were admitted to the emergency department for acute appendicitis and were operated for the diagnosis of acute appendicitis. As preoperative imaging examinations, 9 of our patients had ultrasonography (USG) and 10 had computed tomography (CT). 6 of our patients were operated with the preliminary diagnosis of acute appendicitis based on physical examination findings. The mean appendicitis

diameter of patients who had any imaging examinations was 9.4 mm (min-max=3-20 mm) (Table 1). All appendectomies performed in emergent setting. Symptoms such as diarrhea flushing in carcinoid syndrome were not apparent in our patients in the preoperative period. There were 2 patients with a tumor diameter greater than 20 mm and 8 patients with a tumor diameter of 10-20 mm, and 15 patients with a tumor diameter less than 10 mm. Two patients with a tumor diameter greater than 20 mm had undergone complementary right hemicolectomy, and tumor tissue was not found in the specimen examination afterward. Histopathologic examination revealed tumor localization in the distal appendix in 6 patients, proximal appendix in 18 patients; and in 1 patient multicentric mass was present in both distal and proximal appendix. No metastasis was detected in any of our patients. No complication was observed in the postoperative period during follow-up period of 42 months (min-max=5-62 months).

Discussion

Among the appendiceal malign tumors, carcinoid tumors are the most common.⁷ Apart from that, although rare, goblet cell carcinoma, lymphoma, mucocele, primary adenocarcinoma, and mucinous cystadenocarcinoma are also seen.^{8,9} In our study, the incidence of carcinoid tumors in patients with appendectomy was 0.53%. In the literature, rates on this subject range from 0.3% to 0.9% and are slightly more common in women.^{5,10} However, in our study, 13 of our patients were male and 12 were female. Appendiceal carcinoid tumor is most commonly detected between 38 and 49 years of age.¹¹ In our study, the mean age was 33.2 years and was lower than the literature. Appendiceal carcinoid tumors do not usually present with flushing and diarrhea-like symptoms which are signs of carcinoid syndrome. Carcinoid

Table 1. Clinical and demographic variables

Parameters	Cases (n, %)
Age, mean (SD)	33.3±17.5
Diameter/mm, mean (SD)	9.4±4.7
Follow-up/month, mean (SD)	49.90±24
Gender	
Male	13 (52%)
Female	12 (48%)
Tumor size	
<10 mm	8 (32%)
10-20 mm	15 (60%)
20>	2 (8%)

SD: Standard deviation

syndrome which occurs due to vasoactive amine release is usually seen due to liver metastases. Tumors presenting with an acute appendicitis-like condition are incidentally diagnosed in postoperative period based on histopathologic findings.¹² In our study, all of our patients were admitted to the emergency department with the diagnosis of acute appendicitis which is later confirmed histopathologically.

In our patients who presented with acute appendicitis in the preoperative period, no pathology other than appendicitis was suspected macroscopically in this period.¹³ In our study, the rate of appendiceal carcinoid tumors, most of which were smaller than 1 cm, was 56%. In the literature, this rate was reported as 80%. Tumors between 1 and 2 cm were 36% and tumors larger than 2 cm was 8%. In the literature, tumors of 1-2 cm were reported as 15% and tumors larger than 2 cm were reported as 5%. Metastasis in appendiceal carcinoids is usually seen in tumors over 2 cm, as a rare finding in.^{14,15,16,17} In the literature, rates up to 85% have been reported, but no patients with metastases were found in our study. Therefore, right hemicolectomy is recommended for the treatment of tumors larger than 2 cm due to the high probability of metastasis. Right hemicolectomy is recommended for treatment of cases with tumor size greater than 2 cm. In cases with tumor smaller than 1 cm, appendectomy is sufficient. Treatment in controversial cases with tumor size between 1 and 2 cm is under debate.

In such cases, including localized tumors at the base of the appendix, tumors with mucin production, tumors with high mitotic rate, childhood carcinoid tumors, serosa invasion, mesoappendix invasion, and lymphatic duct involvement, right hemicolectomy should be applied.^{16,18} While approximately 75% of appendiceal carcinoids are located proximal to the appendix, up to 10% are localized at the base. In our study, the tumor was at an apex in 17 (68%) patients and radix in 7 (28%) patients. One patient had a multicentric tumor at the base and proximal of the appendix (Table 2).

The rate of the synchronous or metachronous lesion was 13-33% in the follow-up examinations of diagnosed patients.^{13,16,17,19} This shows the importance of colonoscopy in patients with carcinoid tumors. In our study, none of our patients were detected to have colorectal cancer. Colonoscopy requirement was reported to our patients.

Table 2. Location of tumor in the appendix

	Male (n=4)	Female (n=4)
Localization		
Distal	4 (16%)	3 (12%)
Proximal	9 (36%)	8 (32%)
Distal + Proximal	0	1 (4%)

The efficacy of effective chemotherapy in cases with metastasis was reported as 40% and the efficacy of radiotherapy in selected cases was reported as 60%. The 5-year survival was reported as 81% in cases with local metastasis and as 31% in cases with distant metastasis.^{11,19,20}

Conclusion

In conclusion, appendiceal carcinoid tumors are usually incidentally detectable tumors.

Ethics

Ethics Committee Approval: Ethics committee approval was not received for this study because of its retrospective design.

Informed Consent: Informed consent was obtained from all patients.

Peer-review: Externally peer reviewed.

Authorship Contributions

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

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

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Sentinel Lymph Node Mapping in Colon Cancer Patients: Does Make A Sense?

Kolon Kanseri Hastalarında Sentinel Lenf Nodu Haritalandırması: Bir Anlamı Var Mı?

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ABSTRACT

Aim: Lymph node status in colon cancer (CC) is a major prognostic factor that determines the disease recurrence, survival, and the adjuvant treatment. Although sentinel lymph node (SLN) is an effective technique that improves pathologic assessment in breast cancer and melanoma, the feasibility and outcomes of SLN in CC is still controversial. Hence, we aimed to evaluate the sensitivity, specificity, and accuracy of SLN for determining lymph node status in CC.

Method: A total of 84 consecutive patients undergoing urgent or elective colectomy for colon cancer were enrolled in this prospective randomized study. *In vivo* SLN mapping with blue dye was used to evaluate the lymph node status. The sensitivity of the method was evaluated by comparing the pathologic condition of 3-4 blue dyed lymph nodes with final conventional pathologic assessment.

Results: The sensitivity of identification for SLN was low (61.54%) for predicting lymph node metastasis, false-negative rates were high (38.5%), specificity was 100%, the detection rate was 88.1%, the overall accuracy rate was 81.08% , negative predictive value 82.76%, and positive predictive value was 100% . No upstaging was determined in our study.

Conclusion: Considering our results, SLN mapping could not predict the nodal status with clinically acceptable accuracy despite a high detection rate. We emphasize that en bloc tumor resection with regional lymph node dissection is still the standard treatment for CC. SLN mapping should not alter the extent of the operation due to its low predictive value.

Keywords: Sentinel lymph node, colorectal cancer, staging, lymph node metastasis

ÖZ

Amaç: Kolorektal kanserlerde (CC) lenf nodu tutulumu, hastalığın nüksü, sağkalım ve adjuvan tedaviye karar vermede majör prognostik faktör olarak değerlendirilir. Sentinel lenf nodu (SLN) meme ve melanomada patolojik değerlendirmeyi güçlendiren etkili bir teknik olsa da CC'de halen tartışmalıdır. Bu nedenle, bu çalışmada SLN'nin CC'de lenf nodu durumunu değerlendirmesindeki duyarlılığı, özgülüğü ve doğruluğunu değerlendirmeyi amaçladık.

Yöntem: Bu prospektif randomize çalışmaya, kolorektal kanser nedeniyle acil veya elektif ameliyata alınacak olan ardışık 84 hasta dahil edildi. Lenf nodu durumunu değerlendirmek için "in vivo" mavi boya ile haritalama yöntemi kullanıldı. Yöntemin duyarlılığı mavi boya ile ilk boyanan 3-4 lenf nodunun nihai patoloji raporuyla karşılaştırılarak değerlendirildi.

Bulgular: SLN'nin metastatik lenf nodunu tahmin (%61,54) etmedeki belirleyiciliği az, yalancı-negatiflik oranı yüksek (%38,5), özgülüğü %100, tahmin oranı %88,1 idi. Genel doğruluğu %81,08, negatif tahmin değeri %82,76, pozitif tahmin değeri ise %100 idi. Bizim çalışmamızda olduğundan daha ileri (upstaging) bir evreleme yapılmadı.

Sonuç: Bu sonuçlar göz önünde bulundurulduğunda, SLN haritalaması, yüksek tespit oranına rağmen hastanın lenf nodu durumunu klinik olarak kabul edilebilir doğrulukla tahmin edemedi. Çalışmada bölgesel lenf nodu disseksiyonuyla birlikte yapılan "en bloc" tümör rezeksiyonunun CC'lerde halen standart tedavi yöntemi olduğunu vurgulamaktayız. SLN haritalaması düşük prediktif değerinden dolayı, operasyonun niteliğini değiştirmemelidir.

Anahtar Kelimeler: Sentinel lenf nodu, kolorektal kanser, evreleme, lenf nodu metastazı



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Introduction

Colorectal cancer is the most encountered malignancy in the gastrointestinal tract and second leading cause of death among all cancers. Survival after radical surgery is strongly associated with the stage of the disease including lymph node status. The existence of metastasis in the lymph nodes (LN) decreases 5-year survival at a rate of 20-30%.^{1,2}

In fact, extended dissection and careful examination of LN increase the possibility of detecting the nodal metastasis.³ As Goldstein et al.⁴ have stated there is a strong correlation between the number of dissected LN in the specimen and the rate of lymph node metastasis. HE- stained section and paraffin-embedded block is still the most performed method by pathologists to evaluate the LN of the specimen. However, this conventional histopathologic examination may sometimes underestimate the true incidence of lymph node involvement due to the failure of detecting occult nodal micrometastasis. Unfortunately, this lack of the examination may cause recurrence in approximately 20-30% of the patients with node-negative early stage disease.^{5,6} Recurrence is related to several factors including inadequate lymph node resection at the time of surgery, inadequate sampling of the involved LN within the resected specimen, and failure to identify small-volume occult metastasis on pathologic assessment (micrometastasis).⁷

The concept of lymphatic mapping is based on the principle that each anatomic site has specific lymphatic drainage to a designated lymph node. A cancer that has spread beyond the primary tumor site will drain through the regional lymphatic into this first lymph node or chain of lymph nodes, termed the sentinel lymph node (SLN).⁸ Detailed examination of every lymph node removed in a standard colon resection is generally labor-intensive and costly. However, SLN has a potential to obviate this obstacle by limiting the number of LN to be evaluated. Hence, this may allow the pathologist to perform a more detailed analysis on specific LN by serial sectioning, also immunohistochemical (IHC) staining to identify micrometastasis, as well. During the last two decades, lymphatic mapping and sentinel lymph node biopsy (SLNB) have gained popularity due to accurate staging of solid neoplasms especially in breast cancer and melanoma.^{9,10} Thus, this condition encourages the surgeons to improve the staging of gastrointestinal cancers and decision of adjuvant treatment. However, considering the results of several studies about SLNB, it is obvious that the debate about the feasibility and outcomes of the technique in colon cancer (CC) still continues. Hence, we conducted this study to evaluate the sensitivity, specificity, and accuracy of SLNB for determining lymph node status in patients undergoing surgery for colon cancer.

Patients and Methods

After obtaining our institution's ethics committee approval, the study was conducted in Mersin University Medical Faculty Training and Research Hospital, Department of General Surgery in a period between October 2010 and October 2011. A total of consecutive 100 patients undergoing urgent or elective colectomy for CC were enrolled in this study. Patients were excluded in cases of aged less than 18 years, American Society of Anesthesiologists (ASA) scores V, food allergy, receiving radiotherapy, previous colon resection for benign or malign disease, recurrence and distant metastasis. Hence, one patient with food allergy, 2 patients with previous colon resection, 3 patients with recurrence, 6 patients with distant metastasis, and 4 patients who rejected the study were excluded. Finally, the study included 84 patients. A written informed consent concerning the surgical risks was obtained from all patients.

Surgical Technique

All patients were prepared to surgery routinely. No bowel preparation was performed. A single dose of 1 g cefazolin sodium and metronidazole 0.5% 100 mL was applied for prophylaxis. All patients underwent radical open surgery according to the localization of the tumor (right/left hemicolectomy, anterior resection, subtotal colectomy) under general anesthesia. Patent blue was applied into the subserosal layer of the colon around the tumors for SLN mapping. Before resection, 2-4 mL of patent blue was injected with a distance of 1 cm to four quadrants of the tumor and waited for 10 minutes. The first stained three or four LN were accepted as SLN and marked with 2/0 silk suture. Subsequently, radical surgery was accomplished in accordance with oncological principles. The histopathological examination of the specimen was done after marking. Dyed LN were first evaluated with hematoxylin-eosin and if metastasis was not detected, IHC pancytokeratin was applied. Histopathological examination of the first dyed three or four LN was compared to the final pathologic examination of the specimen. Patients were evaluated with regard to their demographic characteristics and tumor localization. The specimen was evaluated with regard to the number of stained, metastatic, total resected LN and the compatibility with the final pathologic stage of the tumor.

Statistical Analysis

Statistical MedCalc 9.3.9.0 software was used for statistical analysis. In this study, we assumed at least one SLN to be dyed with the standard deviation of two, and a sample size was calculated so that at least 78 patients were needed to provide 0.05 α and 0.01 β error. Hence, considering the patients would be excluded during the study, the sample

size was accepted as 100 patients. The data obtained were summarized in a computerized spreadsheet and statistical analyses were performed by using SPSS 11.5 for Windows. Numerical data were presented as mean ± standart deviation and categorical data were expressed as number and percent (%). Sensitivity, specificity, detection rate, accuracy rate, false-negative rate, and positive-negative predictive value of the method were analyzed to evaluate the applicability of the procedure.

Results

A total of 84 patients including 40 (47.6%) male and 44 (52.4%) female with a median age of 64.5 (41-87) years were enrolled in the study. Fifty-four patients (64.3%) were ASA II, 28 (33.3%) were ASA III, and 2 (2.4%) were ASA IV. Twenty-two (26.2%) of the operations were urgent while 62 (73.8%) were elective. In our study, 44 (52.4%) patients underwent right or extended right hemicolectomy, 10 (11.9%) patients underwent left or extended left hemicolectomy, 28 (33.3%) patients underwent anterior resection, and 2 (2.4%) patients underwent subtotal colectomy. The histopathological examination of the specimen revealed adenocarcinoma (83.3%), mucinous carcinoma (14.3%), and neuroendocrine carcinoma (2.4%). The tumor localization was ceacum in 22 (26.2%), right

colon in 16 (19%), transverse colon in 8 (9.5%), left colon in 8 (9.5%), and sigmoid colon in 30 (35.7%) patients.

In this study, no staining was observed in 10 (11.9%) patients. However, one area in 2 (2.4%) patients, two areas in 2 (2.4%) patients, three areas in 58 (69%) patients and four areas in 12 (14.3%) patients were stained and marked. The presence of lymph node in all four of the marked areas was detected for 6 patients (7.1%), three marked areas with lymph node in 36 patients (42.9%), two marked areas with lymph node in 22 patients (26.2%), and one marked area with lymph node in 10 (11.9%) patients. The T staging of the tumor was pT2 in 10 (11.9%), pT3 in 56 (66.7%), and pT4 in 18 (21.4%) patients. The pathologic staging of resected LN was as follows: N0 in 54 (64.3%), N1 in 14 (16.7%), and N2 in 16 (19.0%) patients. An average of 24 (5-48) LN were removed in final pathology. There was no staining in 10 of 84 patients; however, at least one lymph node was stained in the rest of the patients. The distribution of the patients according to the stage of the tumor, number of dyed areas, lymph node status of the dyed area, number of dyed LN and metastasis in LN was summarized in Figure 1.

Finally, there was no metastasis in 58 (69%) patients with stained lymph nodes. Macrometastasis was detected in 26 (31%) patients. There were macrometastasis in stained lymph nodes (SLN) in 16 of these patients, and 10 (12%)

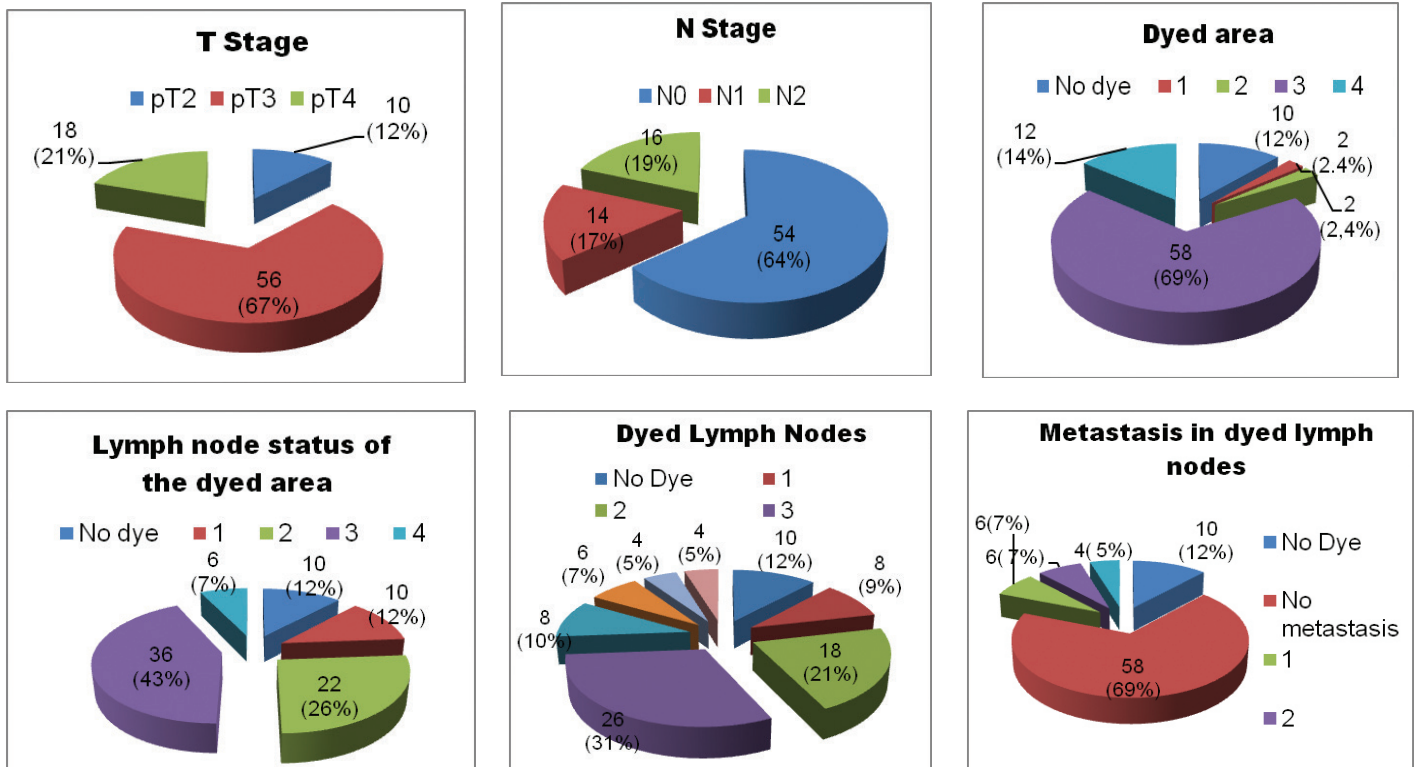


Figure 1. The distribution of the patients according to the stage of the tumor and pathologic assessment of the dyed lymph nodes

patients had macrometastases in undyed lymph nodes (non-SLN) (Figure 2).

The sensitivity of identification for SLN was low (61.54%) for predicting lymph node metastasis, false-negative rates were high (38.5%), specificity was 100%, the detection rate was 88.1%, the overall accuracy rate was 81.08% , negative predictive value was 82.76%, and positive predictive value was 100% (Table 1). Aberrant lymphatic drainage was not detected.

Discussion

Lymph node status in CC is a major prognostic factor that determines the disease recurrence, survival, and the adjuvant treatment.^{8,11,12,13,14} Disease recurrence still remains the most important problem after radical surgery likely due to inadequate lymph node dissection. The optimal number of LN required to accurately predicting lymph node negativity has been a point of debate. The view of identifying at least 12 LN in the specimen is considered proper for staging of CC by many clinicians. In contrast to

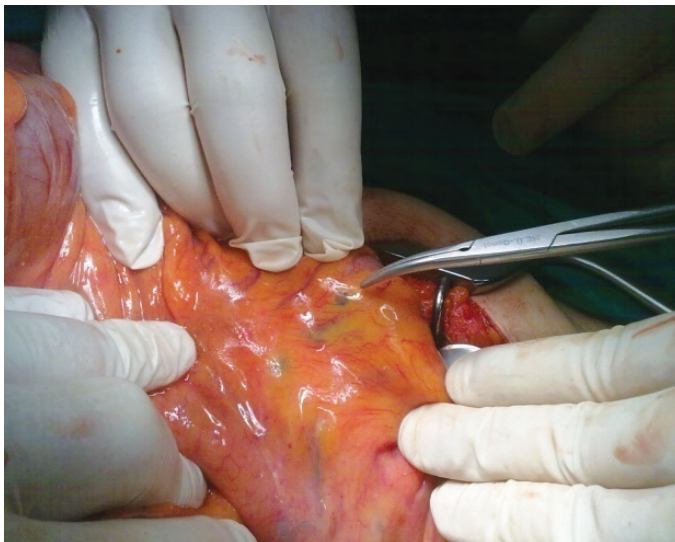


Figure 2. *In vivo* SLN mapping in CC (The tip of clamp reveals a blue dyed metastatic lymph node)

SLN: Sentinel lymph node, CC: Colon cancer

Table 1. The evaluation of SLN mapping in CC patients

Sensitivity	61.54% (40.57%-79.77%)
Specificity	100% (92.60%-100%)
Detection rate	88.1%
Overall accuracy rate	81.08 %
False negative rate	38.5 %
Positive predictive value	100 %
Negative predictive value	82.76 %

this view, survival is found to be strongly associated with the number of studied LN in recent studies.^{4,15} Hence, extended lymph node dissection (total mesocolic excision) (ELND) has been raised and better results have been obtained.^{15,16} Recently, SLN mapping has been tried to facilitate ELND and to improve staging accuracy in CC.^{12,13,14,17} However, notwithstanding our results, the feasibility of SLN in CC seems to be controversial and still remains to be defined. Hence, this study was planned.

The standard approach for lymph node evaluation in the specimen is based on manual dissection and histological evaluation of HE stained slides.¹⁸ Unfortunately, this conventional approach, especially by single section, allows analyzing only 1% of LN tissue and usually fails to identify micrometastasis. This leads to 70% of infiltrated LN that are smaller than 5 mm and with subcapsular location remain undetected. Unfortunately, this lack of the examination may cause recurrence in approximately 20-30% of the patients with node-negative early stage disease.⁷ Therefore, efforts have been made to improve pathologic staging of CC by identifying micrometastasis which is not detectable by conventional histopathologic techniques. Recently, SLN mapping in CC has been applied to enhance pathologic assessment.

SLN biopsy has been proposed as a simple, inexpensive and feasible method that allows accurate staging of CC in many studies with an advantage of short learning curve.¹² However, it is noteworthy that high variable rates of accuracy and sensitivity have been reported in the literature. Considering the results of SLN in CC, the detection rate and the false negative rate range from 59% to 99% and from 7,5 % to 60%, respectively.^{5,8,12,13,14,17,18,19,20} Among these studies, our results were consistent with the results of a multicenter study sponsored by "Cancer and Leukemia Group-B (CALGB)"²⁰ and S.J. Lim et al.⁸ demonstrated a sensitivity of 46%-41%, a false-negative rate of 54%-41%, and the overall accuracy rate of 80%-83%, respectively. According to our results, we emphasize that SLN mapping in CC could not predict node positivity due to its low sensitivity and high false negativity despite a high detection rate. However, our high false negative rate may be related to our high proportion of T3/T4 patients. In our opinion, the significant differences between these reports including our study are more likely due to inclusion criteria or skip metastasis. Furthermore, these results mainly depend on the experience of the team performing the procedure and the amount of infiltrated dye. It is notable that SLN mapping in CC surgery has to be assessed different from mapping in melanoma or breast cancer. Although the first dyed node has a prognostic importance in melanoma or breast cancer, in CC, the number of dyed LN retrieved from the specimen appears to

be important for targeted nodal assessment due to the watershed distribution of the colon's lymphatic basin.¹⁸ In other words, expectation from SLN mapping in CC is to help more accurate staging of stage II patients who have undetectable micrometastasis by conventional histopathologic techniques. At the beginning of our study, we expect to receive the same results from SLN mapping in CC, so that we enhance pathologic assessment of LN by HE and cytokeratin IHC stained step sections. However, our results did not support our hypothesis. Although Bembenek et al.²¹ detected micrometastasis or isolated tumor cells by examination of SLNB with IHC staining in 21% of node-negative patients and Sardón Ramos et al.¹³ received upstaging at a rate of 14% of the patients, no upstaging was determined in our study. Our results with IHC staining were compatible with the results of conventional examination. In our opinion, this finding is not associated with our technical error; it is more likely due to the majority of our patients with T3/T4 tumor. Because we believe that bulky tumor or invasion leads to obstruct the lymphatic channels, hence this disrupts proper dye spread via the lymphatic circulation.

Lymphatic drainage that extends beyond the planned resection margins may lead to skip metastasis so should be considered in disease recurrence. It is reported that skip metastasis is usually related to anatomic variations of lymphatic drainage pathways.^{13,18} Detecting this aberrant nodal dissemination beyond the limits of surgery has been advocated as another principal advantage of SLN mapping in CC, thus loco-regional recurrence may be prevented. Bilchik et al.²² have detected aberrant lymphatic pathways by SLN mapping in a majority of his patients. In another study, Coccetta et al.²³ detected the rate of skip metastasis as 20 % by SLN with IHC methods. However, no aberrant lymphatic pathways were detected in this study.

Conclusion

Although SLN mapping in CC surgery has been offered as a feasible method that allows accurate staging of CC, its clinical value should still be tested by large prospective studies. Considering our results, we suggested that SLN mapping could not predict the nodal status with clinically acceptable accuracy despite a high detection rate. Furthermore, we emphasize that en bloc tumor resection with regional lymph node dissection is still the standard treatment for CC. SLN mapping should not alter the extent of the operation due to its low predictive value. Surgeons should avoid conservative resection by relying on SLN results in CC surgery, which may lead to result under-treatment.

Ethics

Ethics Committee Approval: After obtaining our institution's ethics committee approval, the study was

conducted in Mersin University Medical Faculty Training and Research Hospital, Department of General Surgery in a period between October 2010 and October 2011.

Informed Consent: A written informed consent concerning the surgical risks was obtained from all patients.

Peer-review: Internally and externally peer reviewed.

Authorship Contributions

Surgical and Medical Practices: R.G., T.Ç., Ö.T., A.S., E.S., Concept: T.Ç., Design: Ö.T., Data Collection or Processing: R.G., Analysis or Interpretation: R.G., T.Ç., A.S., E.S., Literature Search: R.G., Ö.T., A.S., E.S., Writing: R.G., A.S.

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

Financial Disclosure: This prospective research was conducted in Mersin University Medical Faculty.

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Validity and Reliability of the Turkish Version of Pittman Ostomy Complication Severity Index

Pittman Ostomi Komplikasyon Şiddet İndeksi'nin Türkçe Geçerlilik ve Güvenilirliği

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ABSTRACT

Aim: This study aimed to investigate the reliability and validity of the Turkish version of the Pittman Ostomy Complication Severity index.

Method: This methodological research was carried out between January 1, 2017, and January 1, 2018, at the Stomatherapy Unit of a Health Practice and Research Center in the Western Black Sea Region. The sample of the study consisted of 90 patients with an ostomy who had colostomy and ileostomy for at least one month. Stoma Individual Follow-up Form and Pittman Ostomy Complication Severity Index form were used in the study. Preoperative demographic characteristics, stoma-related characteristics within the first 24 hours after surgery, and 30 days postoperatively were evaluated according to the Pittman Ostomy Complication Severity Index. SPSS 19.0 and Excel 2016 software were used for statistical analysis.

Results: The mean age of patients was 60.22±13.23 years. It was determined that 44.4% of the patients were women, and 55.6% were men. Of all patients, 90% were married, 71.1% were primary school graduates, and 41.1% were housewives. Translation-back translation was performed for the language validity of the index. Content validity was taken from 11 experts, and Content Validity Index was determined to be 0.95. Complication-related parameters for the construct validity of the index were calculated from the significance of the total score of the Pittman Ostomy Complication Severity index. The reliability of the Pittman Ostomy Complication Severity index was evaluated with the compliance between independent observers. The linguistic compliance, which was evaluated with the compliance between observers in expert opinions, was significant ($p<0.001$; Kendall's $W=0.131$; chi-square: 66.668). The content compliance, which was evaluated with the compliance between observers in expert opinions, was significant ($p<0.001$; Kendall's $W=0.132$; chi-square: 67.529).

Conclusion: We showed that the Turkish version of the Ostomy Complication Severity index is a valid and reliable tool for evaluating the severity of complications in individuals with an ostomy. This index can also be used to identify and measure the severity of early complications in patients with an ostomy.

Keywords: Colostomy, ileostomy, complication, nursing care

ÖZ

Amaç: Bu çalışma Pittman Ostomi Komplikasyon Şiddet indeksinin Türkçe geçerliliğini ve güvenilirliğinin incelenmesi amacı ile yapıldı.

Yöntem: Metodolojik tipte olan bu araştırma, Batı Karadeniz Bölgesi'nde yer alan bir sağlık uygulama ve araştırma merkezinin stomaterapi ünitesinde 1 Ocak 2017-1 Ocak 2018 tarihleri arasında yürütüldü. Araştırmanın örneklemini en az bir aydır kolostomi ve ileostomiye sahip olan 90 ostomili birey oluşturdu. Araştırmada Stomalı Birey İzlem Formu ve Pittman Ostomi Komplikasyon Şiddet indeksi formu kullanıldı. Ameliyat öncesinde hastaların demografik özellikleri, ameliyattan sonraki ilk 24 saat içerisinde stoma ile ilgili özellikleri, ameliyattan 30 gün sonra ostomi bölgesi "Pittman Ostomi Komplikasyon Şiddet indeksi'ne" göre değerlendirildi. İstatistiksel analizlerinde SPSS 19,0 ve Excel 2016 paket programları kullanıldı.

Bulgular: Ostomili bireylerin yaş ortalamasının 60,22±13,23; %44,4'ü kadın, %55,6'sı erkek, %90'ının evli, %71,1'inin ilkökul mezunu, %41,1'inin ev hanımı olduğu belirlendi. İndeks dil geçerliliği için çeviri-geri çevirisi yapıldı. Kapsam geçerliliği için 11 uzmandan görüş alındı ve kapsam geçerliliği indeksinin 0,95 olduğu belirlendi. İndeks yapı geçerliliği için komplikasyonla ilişkili parametreler Pittman Ostomi Komplikasyon Şiddet indeksi toplam puan arasındaki anlamlılık hesaplandı. Pittman Ostomi Komplikasyon Şiddet indeksinin güvenilirliği bağımsız gözlemler arası uyum ile değerlendirildi. Uzman görüşlerinde gözlemler arasındaki uyum incelendiğinde dil bakımından uyum olduğu görüldü ($p<0,001$; Kendall's



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W=0,131; ki-kare=66,668). Uzman görüşlerinde gözlemciler arasındaki uyum değerlendirilmiş olup içerik bakımından uyum olduğu görüldü ($p<0,001$; Kendall's W=0,132; ki-kare=67,529).

Sonuç: Pittman Ostomi Komplikasyon Şiddet indeksinin Türkçe versiyonunun ostomili bireylerin komplikasyon şiddetini değerlendirmede geçerli ve güvenilir bir araç olduğunu göstermektedir. Ostomili bireyler de erken dönemde oluşan komplikasyonları tanımlamak ve şiddetini ölçmek için bu indeks kullanılabilir.

Anahtar Kelimeler: İleostomi, hemşirelik bakımı, kolostomi, komplikasyon

Introduction

The stoma that has been created to eliminate the underlying pathology and improve the patient's condition affects the whole life of the individuals. The stoma causes a variety of physiological, psychological, and social problems to the individual from the first time to the post-discharge period and thus adversely affects the adaptation process to life.¹ Despite the development of surgical methods and precautions taken, it is observed that the rate of complication development after stoma is high. Complications of the stoma may occur due to surgical intervention, underlying pathology, insufficient preoperative, and postoperative treatment and care.^{2,3,4}

Complications related to stoma can be a dull discomfort or a severe life-threatening problem. Complications are classified as early and late complications depending on the time of occurrence. It has been reported that early stoma complications are seen mainly in cases where the stoma region cannot be marked in emergency conditions or in case of technical errors. Ischemia and stoma necrosis, peristomal skin problems, and mucocutaneous separation develop in the early period. Late complications are usually seen in permanent stomas and can be listed as parastomal hernia, stomal prolapse, stenosis, and peristomal dermatitis.^{2,5,6} The incidence of stoma complications varies, and the rate is reported to be between 10% and 70%.^{7,8,9,10} It is stated that complication rates increase in emergency surgical procedures, and these rates are higher in individuals who do not have stoma sites marked than those who are marked.^{2,8,9} The incidence of stoma complications is related to the follow-up frequency of patients with a stoma, and the incidence of stoma complications decreases as the frequency of follow-up increases. Studies have reported a 6-fold reduction in the risk of complications associated with the care provided by the stoma team.^{11,12,13} The main goal of stoma care should be to support individuals with a stoma to adapt to the new lifestyle, to accept the image change in their body, and to be able to continue their life independently. Stoma and wound care nurses are responsible for the prevention and early recognition of complications and differentiating factors causing complications.¹⁴ Therefore, monitoring of complications is essential in terms of nursing care outcomes.

The tools with proven validity and reliability for the monitoring of stoma complications are limited in Turkey.³ The Pittman Ostomy Complicity Severity index (OCSI) was developed by Joyce Pittman to identify and assess the severity of complications during the follow-up period (30 days postoperatively) of patients with a stoma.⁴

This study aimed to evaluate the validity and reliability of the Turkish version of OCSI, which was prepared originally in English for patients with a stoma.

Materials and Methods

Type of research: Methodological research.

Time and Place of the Study: The research was conducted between January 1, 2017, and January 2018 at the Stomatherapy Unit of an Application and Research Center in the Western Black Sea Region. In the stomatherapy unit, training, counseling, and care services are provided to the individual with a stoma and his family by the researcher who has stomatherapy nursing certificate.

Population and Sample of the Study: The study population consisted of individuals who had colostomy and ileostomy for at least one month and who applied for treatment to the study centre during the study period. Inclusion criteria included being 18 years of age or older, having no hearing and speech problems, not having any cognitive problems preventing him/her from expressing himself/herself, having a stoma (colostomy, ileostomy) for one month (30 days), not having a psychiatric diagnosis and volunteering to participate in the study. One of the methods recommended in the determination of sample size in validity and reliability studies is the presence of at least 10 participants per item.¹⁵ In this research, this method was adopted, and 90 individuals with stoma were recruited.

Data Collection Tools

Stoma Follow-up Form and Turkish version of OCSI were used to collect data. This index is a tool used by the doctor or nurse to assess the individual with an ostomy.

Stoma Follow-up Form: This form, which was formed in accordance with the related literature¹⁶, included following data: The socio-demographic characteristics of the

individuals with stoma, being informed about stoma and surgery, and stoma site marking status in the preoperative period, chemotherapy/radiotherapy status and whether the surgery was urgent or planned, and surgery, type of stoma, duration of stoma, stoma region, stoma color, stoma moisture, stoma height, stoma shape, peristomal skin, stoma diameter, presence of baguette, presence of bleeding, mucocutaneous separation status in the postoperative period (within the first 24 hours), and whether there were stoma care-related impeding conditions.

Pittman Ostomy Complication Severity Index: OCSI was developed by Joyce Pittman in 2014 to assess the frequency and severity of early postoperative complications during follow-up (30 days postoperatively) in individuals with a stoma. The OCSI demonstrated acceptable evidence of content validity index [(CVI)=0.9], interrater reliability for individual items ($k=0.71-1.0$), and almost perfect agreement for total scores among raters ($ICC=0.991$, $p\leq 0.001$).⁴ This index evaluates leakage, peristomal irritant dermatitis, pain, bleeding in or around the stoma, stomal necrosis, stenosis, retraction, mucocutaneous separation, and hyperplasia. All complications are scored 0 to 3 (0=none, 1=mild, 2=moderate, 3=severe) with a Likert-like scale. The total score ranges between 0 and 27. Higher scores indicate more severe ostomy complications.⁴

Study Process

The original version of the index was obtained from Dr. Joyce Pittman by establishing communication via e-mail, and we gained permission for using a Turkish version of OSCI for a validity and reliability study. The following steps were taken in order to conduct the validity and reliability study of the scale with the patients in the study cohort:

- Language and content validity of the index were examined,
- For language validity, the index was translated from English to Turkish by two medical experts with extensive knowledge of English, and then translated from Turkish to English by one medical expert with extensive knowledge of English without seeing the original English version,
- 11 experts were consulted for content validity,
- The Turkish version of the index was finalized,
- Following finalizing the index after expert opinions, it was applied as pre-application to five individuals included in the study,
- Data were collected by face-to-face interview method and physical evaluation before and 30 days postoperatively from individuals who met the inclusion criteria.

Evaluation of Data

SPSS 19.0 and Excel 2016 software were used for statistical analysis. Descriptive data were shown with numbers,

percentage, mean, standard deviation, median, minimum, and maximum values. The suitability of continuous variables to normal distribution was examined by the Shapiro-Wilk test. Mann-Whitney U test and Kruskal-Wallis test were used for comparison of variables that did not meet normal distribution. The relationships between quantitative variables were analyzed by the Spearman correlation coefficient. Pearson chi-square test was used to compare qualitative variables between groups. The agreement between the expert opinions was examined by the Kendall W coefficient. $P<0.05$ was considered statistically significant.

Ethical Aspects of Study

Permission was granted from Joyce Pittman to use OCSI in the study. Permission was obtained from the Non-Interventional Clinical Research Ethics Committee of a University in the Western Black Sea Region (Date: 30.11.2016 No: 5/14). Written permission was obtained from the institution for the implementation of the study. The purpose of the study was explained by the researcher, and informed consent was obtained from the individuals willing to participate in the study.

Results

Evaluation of Descriptive Characteristics of Individuals with Stoma

The mean age of the participants was 60.22 ± 13.23 years, and the mean body mass index was 25.42 ± 7.5 . Of all participants, 55.6% were male, 71.1% were primary school graduates, 50% were retired, 90% were married, 93.3% had social insurance coverage, and 94.4% were living with their families. The medical diagnosis of patients was colon cancer in 35.6%, rectal cancer in 26.7%, and other malignancies and diseases in 37.8%. It was determined that 53.3% had a chronic disease, 74.4% had previous surgical operation, and 16.7% had a regular smoking habit (Table 1). It was determined that 58.9% of the stoma sites were marked before the surgery and that patients were informed about surgery. There were no impeding conditions to stoma care in all patients, and 15.6% of the patients received neoadjuvant therapy before surgery. It was found that 41.1% of the individuals in the study were operated urgently, and 58.9% of them were scheduled for surgery (Table 2).

In the evaluation results of individuals within the first 24 hours after surgery, it was found that 36.7% underwent colostomy, 37.8% underwent loop colostomy, 68.9% had a temporary stoma, and 58.9% had stoma in the left lower quadrant. It was determined that stoma color was pale pink in 63.3%, the stoma was moist in 96.7%, stoma height was

Table 1. Sociodemographic and clinical characteristics of individuals with a stoma

Variables	Mean	SD
Age	60.22	13.23
Body mass index	25.42	7.5
Gender	n	%
Female	40	44.4
Male	50	55.6
Education Level		
Not literate	7	7.8
Primary school	64	71.1
Middle School	12	13.3
High school and university	7	7.8
Profession		
Working	8	8.9
Retired	45	50
Housewife	37	41.1
Marital status		
Married	81	90
Single	9	10
Social insurance coverage		
Yes	84	93.3
No	6	6.7
Lives with		
Alone	5	5.6
Family	85	94.4
Diagnosis		
Colon cancer	32	35.6
Rectum cancer	24	26.6
Other malignancies and diseases (stomach cancer, Fournier gangrene, etc.)	34	37.8
Allergy		
Yes	4	4.4
No	86	95.6
Chronic disease status		
Yes	48	53.3
No	42	46.7
History of previous surgery		
Yes	67	74.4
No	23	25.6
Habits		
Smoking	15	16.7
Alcohol	2	2.2
No	73	81.1

SD: Standard deviation

Table 2. Preoperative evaluation of stoma

Conditions related to stoma	n	%
Informed about stoma		
Yes	53	58.9
No	37	41.1
Stoma marking		
Yes	53	58.9
No	37	41.1
Impeding factors to stoma care		
None	90	100
Chemotherapy status		
Neoadjuvant	14	15.6
Adjuvant	7	7.8
None	69	76.6
Type of surgery		
Urgent	37	41.1
Elective	53	58.9

prolapsed in 87.8%, the stoma was round in 73.3%, and peristomal skin was soft in 70%. The mean stoma diameter of the subjects was 43.93 ± 5.33 mm. In the first 24 hours postoperatively, all individuals in the study group were found to have no bleeding and mucocutaneous separation of the stoma (Table 3).

Language Validity of Pittman Ostomy Complication Severity Index

In order to determine the validity and reliability of OCSI, firstly, language validity studies were conducted. First, the index was translated from English to Turkish by two experts in the field of medicine. In the last step, the back-translation (Turkish to English) was performed by an expert in the field of medicine. The index was compared with the statements in the original form and presented to the expert opinion of 11 faculty members in the nursing and medical departments. Experts were asked to evaluate each item from 1 to 4 using a Likert-like scale for clarity of items [1= Major revision required (as suggested), 2= Minor revision required (as suggested), 3= Relevant, 4= Very relevant]. Following the recommendations of the experts, the scale items with a value of 1 and 2 were reviewed, and corrections were made, and the scale was finalized. When the analyzes of the scores given by the experts for OCSI language validity were evaluated, content validity ratio (CVR) was 0.59, and CVI was 0.954.

Content Validity of Pittman Ostomy Complication Severity Index

In the content validity study of the index, it was aimed to determine whether the items in the index were appropriate

Table 3. Evaluation results within the first 24 hours after surgery

Evaluation parameters	n	%
Surgery performed		
Low anterior resection	21	23.3
Ileostomy	13	14.4
Colostomy	33	36.7
Other	23	25.6
Stoma type		
End colostomy	22	24.4
Loop colostomy	34	37.8
End ileostomy	9	10.0
Loop ileostomy	25	27.8
Stoma duration		
Permanent	28	31.1
Temporary	62	68.9
Stoma site		
Left lower quadrant	53	58.9
Left upper quadrant	1	1.1
Right lower quadrant	36	40.0
Stoma color		
Pale pink	57	63.3
Reddish pink	33	36.7
Stoma moisture		
Moist	87	96.7
Dry	3	3.3
Stoma height		
Prolapsed	79	87.8
At the same level with skin	10	11.1
Retracted	1	1.1
Stoma shape		
Round	66	73.3
Oval	24	26.7
Parastomal skin		
Hard	27	30.0
Soft	63	70.0
Baguette		
Yes	14	15.6
No	76	84.4
Bleeding		
No	90	100
Mucocutaneous separation		
No	90	100
	Mean	± SD
Stoma radius	43.93	±5.33

SD: Standard deviation

for their purpose, whether they represented the content to be evaluated, whether they were related to the problem adopted and whether they contained different concepts outside the content. As for language validity, the same experts were asked to score by using a 4-point Likert-like scale. When the scores of experts given for OCSI content validity were analyzed, CVR was 0.59, and CVI was 0.971 (Table 4).

Reliability Analysis of Pittman Ostomy Complication Severity Index

The reliability of the index was evaluated by the agreement between the independent observers, and there was agreement in terms of language ($p < 0.001$; Kendall's $W = 0.131$; chi-square = 66.668) and content ($p < 0.001$; Kendall's $W = 0.132$; chi-square = 67.529).

Comparison of Socio-demographic and Clinical Characteristics of Patients with Total Score of Pittman Ostomy Complication Severity Index

When OCSI total score and sociodemographic and clinical characteristics of subjects were compared, the total OCSI score was significantly higher in the case of female gender ($p = 0.046$), stoma in the right lower quadrant ($p = 0.038$) and baguette ($p = 0.011$). It was found that the difference was not significant regarding the type of surgery, information about stoma, stoma marking, surgery performed, type of stoma, and duration of the stoma (Table 5).

Discussion

A stoma is opened in order to ensure the continuity of the system and improve the quality of life of individuals with problems related to the gastrointestinal system. It is a condition that both changes the lifestyles of individuals and affects the quality of their lives. It is essential to prevent complications in temporary or permanent stomas and to ensure that they do not adversely affect the quality of life. Although colon cancers are the most common cause of stoma, they can be created because of colon obstructions and diseases such as Fournier gangrene.^{6,17,18,19,20} In this study, the stoma was created due to colon and rectal cancer in the majority of patients. This is in parallel with the literature.

The validity and reliability of some tools have been made for the problems that patients with a stoma may experience in the long term. Often, these tools are intended to measure the quality of life of patients.^{17,21,22,23} However, valid tools for evaluating patient outcomes in the early postoperative period are very limited. In this study, it was evaluated whether or not the Turkish version of OCSI is a valid and reliable tool to follow up on the complications 30 days after stoma surgery.

Table 4. Content validity of Pittman Ostomy Complication Severity index




Items of Pittman Ostomy Complication Severity Index	Minimum, maximum item scores	Mean item score	Content validity ratio	Content validity index
Pittman Ostomy Complication Severity Index	3-4	3.91±0.30		
Complication	4-4	4.00±0.00		
0. None	4-4	4.00±0.00		
1. Mild	4-4	4.00±0.00		
2. Moderate	4-4	4.00±0.00	0.59	0.971
3. Severe	4-4	4.00±0.00		
Leakage	4-4	4.00±0.00		
0. None	4-4	4.00±0.00		
1. Approximately 1-2X / months	2-4	3.82±0.60		
2. Approximately 1-2X / weeks	2-4	3.82±0.60		
3. Approximately 1-2X / days	2-4	3.82±0.60		
Peristomal irritant dermatitis	4-4	4.00±0.00		
0. None	4-4	4.00±0.00		
1. Erythema or rash, but no skin loss. Skin intact.	3-4	3.82±0.40		
2. Rash with less than 50% peristomal skin loss	2-4	3.64±0.67		
3. More than 50% peristomal skin loss	2-4	3.55±0.69		
Pain	4-4	4.00±0.00		
0.0 	4-4	4.00±0.00		
1. 1,2,3 	4-4	4.00±0.00		
2. 4,5,6 	3-4	3.91±0.30		
3. 7,8,9,10 	3-4	3.91±0.30		
Bleeding	2-4	3.55±0.66		
0. None	4-4	4.00±0.00		
1. Superficial; easily stopped	3-4	3.91 ± 0.30		
2. Persistent bleeding requiring ten minutes or more pressure, silver nitrate, cauterization or hemostatic agent	3-4	3.64±0.50		
3. Bleeding requiring further medical intervention (sutures, transfusion)	3-4	3.73±0.47		
Stoma necrosis	3-4	3.91±0.30		
0. None	4-4	4.00±0.00		
1. Stoma Dusky	1-4	3.55±0.93		
2. Stoma ≤ 50% black	2-4	3.55±0.82		
3. Stoma >50% black/dry	3-4	3.91± 0.30		
Stoma stenosis	3-4	3.91±0.30		
0. None	4 - 4	4.00±0.00		
1. <5th digit diameter, No pain or discomfort, output normal	3-4	3.73±0.47		
2. <5th digit diameter, Ribbon-like output, occasional discomfort	3-4	3.64±0.50		

Table 4. continued

3. Unable to insert 5th digit, no output. Abdominal pain and distention.	3-4	3.82±0.40
Retraction	4-4	4.00±0.00
0. Stoma above skin	4-4	4.00±0.00
1. Stoma at skin level	4-4	4.00±0.00
2. Stoma below skin level	4-4	4.00±0.00
3. Stoma >2 cm below skin level or unable to see the stoma	4-4	4.00±0.00
Mucocutaneous separation	4-4	4.00±0.00
0. None	4-4	4.00±0.00
1. 1-49%	4-4	4.00±0.00
2. 50-74%	4-4	4.00±0.00
3. 75-100%	4-4	4.00±0.00
Hyperplasia	4-4	4.00±0.00
0. None	4-4	4.00±0.00
1. 1-49%	4-4	4.00±0.00
2. 50-74%	4-4	4.00±0.00
3. 75-100%	4-4	4.00±0.00

Table 5. Comparison of Sociodemographic and Clinical Characteristics of Patients with Ostomy with Total Score of Pittman Ostomy Complication Severity index

OCSI	n	Mean ± SD	p
Gender			
Female	40	1.65±1.87	0.046
Male	50	0.96±1.53	
Type of surgery			
Urgent	37	0.97±1.51	0.139
Elective	53	1.47±1.83	
Informed about stoma			
Yes	53	1.47±1.83	0.139
No	37	0.97±1.51	
Stoma marking			
Yes	53	1.47±1.83	0.139
No	37	0.97±1.51	
Surgery performed			
Low anterior resection	21	1.14±1.55	0.806
Ileostomy	13	1.46±1.45	
Colostomy	33	1.33±2.08	
Other	23	1.17±1.49	
Stoma type			
End colostomy	22	0.81±1.62	0.109
Loop colostomy	34	1.38±2.00	
End ileostomy	9	0.88±1.16	
Loop ileostomy	25	1.64±1.52	

Table 5. continued

Stoma duration			
Permanent	28	1.35±1.78	0.744
Temporary	62	1.22±1.70	
Stoma site			
Left lower quadrant	53	1.07±1.83	0.038
Left upper quadrant	1	-	
Right lower quadrant	36	1.44±1.42	
Baguette status			
No	14	2.28±1.93	0.011
Yes	76	1.07±1.62	

OCSI: Pittman Ostomy Complication Severity Index, SD: Standard deviation

While adapting a scale, it is necessary to investigate whether that scale is necessary for that society. The most important basic features sought in scales are validity and reliability. Reducing errors in both features can improve both the validity and reliability of the scale.²⁴ Validity is the ability of the scale to accurately measure the property it aims to measure without confusing it with other features. Since validity is the degree to which a scale serves the purpose for which it is used, the measurement validity will vary depending on the purpose for which the measurements to be obtained are used. The validity of a scale cannot be determined solely by itself. It also depends on the purpose

of use of the scale, the group to which it is applied, the way it is applied, and scoring. The validity of a scale is calculated by calculating the validity coefficient of that scale. This coefficient is the relationship between the values obtained from the scale and the values determined in accordance with the purpose of use of the scale. This value is between “-1.00” and “+1.00. The increased coefficient means that the scale serves the purpose more.²⁵ Content validity indicates whether the items of the scale are sufficient in terms of quality and quantity of the characteristics or behaviors that they want to measure. The agreement or disagreement between expert opinions, such as the comprehensibility of the items and their suitability to the intended audience, are used as a prediction for the validity of the content or construct.²⁶ Expert opinion is consulted to test face validity and content validity. The expert is asked to evaluate the items of the test in terms of content validity. Different methods can be used to evaluate expert opinion. The Lawshe technique is used to obtain opinions from a minimum of 5 and a maximum of 40 experts. The CVR is obtained by gathering expert opinions. The formula of CVR is $CVR=(Ne/N/2)-1$, in which the Ne is the number of experts indicating “essential” to an item, and N is the total number of experts who have expressed an opinion about an item.²⁷ The other method is the Davis technique. With this technique, expert opinions for each item are graded as a) very relevant, b) relevant but need minor revision, c) item need major revision, d) not relevant. With this technique, the number of experts choosing options (a) and (b) is divided by the total number of experts to CVI. CVI is obtained over the means of the items’ total CVR (26). In this study, the opinions of 11 experts were taken in terms of language and content. CVRs were calculated as a result of expert opinions. In terms of language and content validity, CVR was found to be 0.59. CVI was calculated as a result of expert opinions. CVI was 0.954 in language validity analysis and 0.971 in content validity analysis. In this sense, the index was found to be valid in terms of Turkish language and content.

Reliability is the ability of a scale to measure (error-free measurement) close to the actual size of the particular feature. In other words, reliability is the level of consistency between different measurement results of a scale. It is necessary to be confident that the data provided by the scale is stable and that the same results will be obtained in a second measurement for the same purpose. The unreliable scale is useless.²⁵ The Kendall’s W test, which is used to evaluate the similarity of the evaluation results of multiple observers evaluating the same subject, was used in the reliability analysis of the index. In order to see the agreement between the opinions of the experts, it was evaluated whether there is an agreement in terms of language and content. Kendall’s

W value of 0.131 in terms of language and 0.132 in terms of content confirmed that expert opinions were consistent and reliable.

A stoma can be created for any reason, either urgently or planned, and postoperative complications may occur, no matter how much precautions have been taken. Creating a stoma in an emergency setting increases the risk of peristomal complications, and the risk of complications increases by up to 18%.²⁸ In a prospective single-center study, including 192 patients, Parmar et al.¹¹ reported that 22% of patients developed complications after elective surgery and 46% after emergency surgery. Stoma site marking in the preoperative period facilitates compliance, improves quality of life, and reduces complication rates.⁸ The stoma site should be marked even in an emergency setting. The common recommendations of the American Society of Colon and Rectal Surgeons and Wound, Ostomy, and Continence Nurses Society are to mark the stoma site by the surgeon or stoma nurse before the surgical procedure in all individuals who will undergo bowel operation.^{29,30} If preoperative stoma site marking is not possible and the patient is obese, the stoma should be placed high above the abdomen from the subcostal region. This helps the patient to see the stoma more clearly.¹¹ In a study including 593 patients, Ratliff et al.³¹ reported that 95 of 292 individuals who were evaluated by the stoma nurse before surgery had postoperative complications, and 131 of 301 patients who had no preoperative evaluation were reported to have complications. Kozan and Gültekin³² found that the only factor that can be controlled in reducing the risk of parastomal hernia was the marking of the stoma site in the preoperative period. In this study, it was seen that all patients who underwent elective surgery (58.9%) were evaluated by the surgeon or stoma nurse, and the marking was performed, but that marking was not performed in emergency patients. Also, there was no significant difference in the severity of complications according to the type of surgery, information about stoma, stoma marking, surgery performed, type of stoma, and duration of the stoma. Risk factors for stoma complications include gender, body mass index, short mesentery, type of stoma, and abdominal features in the stoma site.^{8,9,10,11} In this study, it was found that the severity of complications was significantly higher in the female gender, stoma created in the right lower quadrant, and in the case of baguette. Although studies on gender are limited in the literature, the female gender is the predisposing factor in the parastomal hernia.^{32,33,34} The intestinal segment to be used for the stoma, age of the patient, the reason for the stoma, comorbid diseases, habits of the patient, and body structure are essential in determining the stoma site.³⁵ The type and location of the stoma directly affect the

complications, and the highest complication is seen in loop ileostomy.^{35,36,37} Another complication is retraction with a 6-10% incidence due to early removal of baguette used in loop stoma and intestinal dysfunction.⁷ A stoma is a very important condition that affects the life of individuals in physiological, psychological, and social aspects, so it is essential to pay attention to risk factors in order to avoid complications.

Conclusion

This study concluded that OCSI is a valid and reliable tool for assessing the severity of early complications of a stoma. As it is easy and practical to use, it guides health professionals in diagnosing and treating early complications. Accordingly, we recommend using this index in the follow-up of individuals with an ostomy.

Ethics

Ethics Committee Approval: Permission was obtained from the Non-Interventional Clinical Research Ethics Committee of a University in the Western Black Sea Region (Date: 30.11.2016 No: 5/14).

Informed Consent: The purpose of the study was explained by the researcher, and informed consent was obtained from the individuals willing to participate in the study.

Peer-review: Externally peer reviewed.

Authorship Contributions

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

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Appendix F: Pittman Ostomy Complication Severity Index (OCSI)

Time 2: 30 Days post surgery _____
Subject|

PITTMAN OSTOMY COMPLICATION SEVERITY INDEX					
For each item mark the score that corresponds to the description and mark in the Total column on the right. Then total all items for total score.					
Complication:	0-None ▼	1-Mild ▼	2-Moderate ▼	3-Severe ▼	Total
Leakage	None	Approx. 1-2x/mo	Approx. 1-2x/wk	Approx. 1-2x/day	
Peristomal Irritant Dermatitis	None	Mild- erythema or rash but no skin loss. Skin intact	Moderate- Rash with skin loss <50% peri-stoma	Severe- Skin loss >50% peri-stoma	
Pain	0 	1, 2, 3 	4, 5, 6 	7, 8, 9, 10 	
Bleeding-stoma or peristoma	None	Superficial; Stopped easily	Moderate-persistent bleeding requiring prolonged pressure ≥10 min, AgNO3, cauterization, or hemostatic agent	Severe-requiring advanced medical intervention (sutures, transfusion)	
Stomal Necrosis	None	Stoma dusky	Stoma black ≤ 50 % or greater	Stoma black/dry > 50%	
Stomal Stenosis	None	Stoma Os <5 th digit diameter, No pain or discomfort, Output normal	Stoma Os < 5 th digit diameter, Ribbon-like output, Occasional discomfort.	Unable to insert any digit into stoma os, No output x ≥6 hrs, Abd pain and distention.	
Retraction	Stoma above skin level	Stoma level with skin	Stoma below level of skin	Unable to see stoma Or Stoma >2cm below skin	
Mucocutaneous Separation	None	1%- 49%	50%-74%	75 %- 100%	
Hyperplasia	None	1%-49%	50%-74%	75%-100%	
Total					



Learning Curve at Laparoscopic Colorectal Surgery

Laparoskopik Kolorektal Cerrahide Öğrenme Eğrisi

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ABSTRACT

Aim: The learning curve at laparoscopic colorectal surgery is a long and laborious process. Therefore, despite its advantages, it cannot still be accepted as the gold standard procedure. The purpose of this study is to compare the effect of learning curve at laparoscopic colorectal surgeries performed beginning period and surgeries after getting experienced.

Method: All cases who underwent laparoscopic colorectal surgery in Adnan Menderes University Department of General Surgery between December 2014 and May 2019 were included in the study. The study was divided into two groups as the first time cases and the cases after the completion of the learning curve. The files of the cases were scanned and demographic data, types of operations, operation times, postoperative complications, oral intake times in the postoperative period, length of hospital stay, and number of extracted lymph nodes were recorded. The numbers of both groups were compared statistically.

Results: A total of 102 patients were included in this study and 71 (69.6%) of these patients were included in Group 1 and 31 (30.4%) of these patients were included in Group 2. In terms of the duration of operations, the mean duration of operation was 149.2±28.14 minutes in Group 1 and 87.16±13.98 minutes in Group 2 (p=0.001). There were no statistically significant differences in the duration of hospitalization and oral intake in the postoperative time in both groups. The number of extracted lymph nodes was 16.27±4.94 in Group 1 and 21.81±5.45 in Group 2 (p=0.001).

Conclusion: When experience increases in laparoscopic colorectal surgery, morbidity rate decreases and more complicated cases can be operated in a shorter time.

Keywords: Colorectal surgery, learning curve, laparoscopy

ÖZ

Amaç: Laparoskopik kolorektal cerrahide öğrenme eğrisi uzun ve zahmetli bir süreçtir. Bu sebeple birçok avantajına rağmen halen günümüzde altın standart olarak kabul edilememektedir. Bu çalışmadaki amacımız laparoskopik kolorektal cerrahideki öğrenme eğrisinin ilk başlangıcındaki ve tecrübe kazandıktan sonraki zamandaki ameliyatlar üzerine etkisinin karşılaştırılmasıdır.

Yöntem: Adnan Menderes Üniversitesi Kolorektal Bölümü'nde Aralık 2014- Mayıs 2019 tarihleri arasında laparoskopik kolorektal cerrahi uygulanmış tüm olgular çalışmaya dahil edildi. Çalışma, ilk başlanan olgular ve eğitim eğrisinin tamamlandığı olgular olarak 2 gruba ayrıldı. Olguların dosyaları taranıp demografik verileri, ameliyat çeşitleri, ameliyat süreleri, ameliyat sonrası gelişen komplikasyonlar, postoperatif dönemde oral alıma geçiş günleri, hastanede yatış süreleri, çıkartılan lenf nodu sayıları kaydedildi ve her iki grubun sayıları istatistiksel olarak karşılaştırıldı.

Bulgular: Çalışmaya toplam 102 hasta dahil edilmiş olup 71'i (%69,6) grup 1, 31'i ise (%30,4) grup 2'ye dahildir. Ameliyat sürelerine bakıldığında ise grup 1'de ortalama süre 149,2±28,14, grup 2'de ise 87,16±13,98 dakika bulunmuştur (p=0,001). Her iki grupta orala başlama ve hastanede yatış sürelerinde istatistiksel olarak anlamlı bir farklılık bulunmaz iken, çıkartılan lenf nodu sayısına bakıldığında grup 1'de 16,27±4,94, grup 2'de 21,81±5,45 olarak saptanmıştır (p=0,001).

Sonuç: Laparoskopik kolorektal cerrahide tecrübe arttıkça ameliyatta morbidite oranı azalmakta ve daha kısa sürede daha komplike olgular yapılabilmektedir.

Anahtar Kelimeler: Kolorektal cerrahi, öğrenme eğrisi, laparoskopi



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Introduction

Laparoscopic colorectal surgery has been evolving procedure since the early 1990s, especially with the development of laparoscopic staplers.^{1,2} As it is known, laparoscopic colorectal surgery is a procedure in which the duration of hospitalization is shorter compared to open surgery, the analgesic requirement in the postoperative period is less needed, better cosmetic results are obtained and the gastrointestinal system can work more quickly.³ However, despite the fact that colorectal surgery has many advantages and low morbidity rates, it is still not considered as the gold standard procedure among colorectal surgeons.⁴ One of the reasons for this is probably the fact that the learning curve is long and steep.⁵

The purpose of this study is to compare the effect of learning curve at laparoscopic colorectal surgery on the first time surgeries and surgeries after gaining experience.

Materials and Methods

All cases who underwent laparoscopic colorectal surgery in Adnan Mendres University Department of General Surgery between December 2014 and May 2019 were included in the study. This study was approved by local ethical committee. All cases were performed by the same general surgeon and his team.

The cases that were performed between December 2014 and January 2018 were evaluated as Group 1, and after gaining experience, the cases which were published in the literature between January 2018 and May 2019 were evaluated as group 2. The cases including conversion to open surgery were excluded from study. The files of the cases were scanned and demographic data, types of operations, operative times, postoperative complications, oral intake times in the postoperative period, length of hospital stay, and number of extracted lymph nodes were recorded. The numbers of both groups were compared statistically.

Statistical Analysis

SPSS 25 (IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp.) statistical package program was used to evaluate the data. Variables were expressed using mean \pm standard deviation, percentage and frequency values. Variables were evaluated (Shapiro Wilk and Levene test) after normalization, after homogeneity of variances was checked. In the analysis of data, student's t-tests were used for the comparison of two groups. When student's t-test did not provide preconditions, the Mann-Whitney U test was used. Categorical data were analysed by the Fisher's exact test and chi-square test. When the expected frequencies were less than 20%, the Monte Carlo Simulation method was used for the inclusion of

these frequencies in the analysis. The value of $p < 0.05$ was accepted as significant.

Results

A total of 102 patients were included in this study and 71 (69.6%) of these patients were included in group 1 and 31 (30.4%) were included in group 2. The mean age of group 1 was 68.76 ± 9.05 years, and the mean age of group 2 was 65.06 ± 12.52 years ($p = 0.001$). There were statistically no significant differences in the duration of hospitalization and oral intake in the postoperative time in both groups. The number of extracted lymph nodes was 16.27 ± 4.94 in group 1 and 21.81 ± 5.45 in group 2 ($p = 0.001$) (Table 1). In terms of the duration of operations, the mean duration of operation was 149.2 ± 28.14 minutes in group 1 and 87.16 ± 13.98 minutes in group 2 ($p = 0.001$).

Complications occurred in six patients. Five of these patients (83.3%) were in group 1 and one (16.7%) was in group 2 ($p = 0.689$). No complication was observed in 96 cases. Transrectal anterior resection was performed with natural orifice transluminal endoscopic surgery (NOTES) technique to a patient in group 2. No mortality was observed in both groups (Table 2).

Discussion

Advanced laparoscopic surgery has been used safely in many procedures recently but it is still not considered as the gold standard in colorectal surgery.^{6,7} One of the probable reasons for this is the fact that the learning curve is long and steep.⁵ The laparoscopic colorectal surgery, which is known to have more advantages than open surgery, provides significant benefit in obese, high ASA score and old patients.⁸

Because the learning curve in laparoscopic colorectal surgery is long and difficult, the benefit of simulation courses on cadavers and animals is quite good for the surgeon.⁹ COLOR is the most known one studied at laparoscopic colorectal surgery.¹⁰ In our country, it is thought that the initiatives and contributions of many associations and professional

Table 1. No mortality was observed in both groups

	Before n=71	After n=31	P
Age	68.76 \pm 9.05	65.06 \pm 12.52	0.100
Operation time	149.2 \pm 28.14	87.16 \pm 13.98	0.001**
Hospitalization	7.77 \pm 14.51	4.9 \pm 1.11	0.280
Oral intake	1.7 \pm 0.6	1.65 \pm 0.55	0.640
Lymph node	16.27 \pm 4.94	21.81 \pm 5.45	0.001**

** : $p < 0.01$

groups on this subject have important contributions to many young surgeons. Many publications and studies show that an experienced surgical team reduces operation time, conversion to open surgery and complication rate.¹¹ According to the study conducted by Li et al.¹², after 60-80 series on laparoscopic colorectal surgery, surgical acceleration, morbidity and decrease in complication were observed in cases. Simon et al.¹³ described this learning curve in 30-70 cases, while Bennet et al.¹⁴ described in 10-40 cases. In this study, after 70 cases, the duration of the operation

was shortened and the number of removed lymph nodes increased. There was no statistically significant difference in the complication rate.

In some studies, the rate of conversion from laparoscopic surgery to open surgery was 7-25% and in some studies, it was reported as 2-41%.^{15,16} In this study, the cases with conversion to open surgery from laparoscopic surgeries were excluded from the study because these data were not recorded. That is one of the important limitations of the study. In order to evaluate this study more meaningfully,

Table 2. Comparison of complications between the two groups

Before	After		Group	Total	p	
Gender	Male	n	46	18	64	0.518
		%	71.9%	28.1%	100.0%	
	Female	n	25	13	38	
		%	65.8%	34.2%	100.0%	
Disease type	Diverticulum	n	0	2	2	0.009**
		%	0.0%	100.0%	100.0%	
	Malignancy	n	71	27	98	
		%	72.4%	27.6%	100.0%	
	Polyp	n	0	2	2	
		%	0.0%	100.0%	100.0%	
Anatomic location	Abdominoperineal resection	n	4	1	5	0.94
		%	80.0%	20.0%	100.0%	
	Anterior resection	n	29	13	42	
		%	69.0%	31.0%	100.0%	
	Coloanal anastomosis	n	2	0	2	
		%	100.0%	0.0%	100.0%	
	Low anterior resection	n	18	9	27	
		%	66.7%	33.3%	100.0%	
Right colectomy	n	17	8	25		
	%	68.0%	32.0%	100.0%		
Complication	Subtotal colectomy	n	1	0	1	0.689
		%	100.0%	0.0%	100.0%	
	None	n	63	29	92	
		%	68.5%	31.5%	100.0%	
Detected	n	5	1	6		
	%	83.3%	16.7%	100.0%		
Total %	n	71	30	101		
	%	70.3%	29.7%	100.0%		

** : p<0.01

it is thought that prospective planning in a new beginning centre and the rates of conversion to open surgery from laparoscopic surgery should be included in these studies.

Patient selection is one of the most important factor when beginning laparoscopic colorectal surgery.¹⁷ Dinçler et al.¹⁸ suggest that the study curves should be started with sigmoid colectomies with no Body Mass index without comorbidity. It is stated that they can continue the series with more complicated and mixed cases in later periods. Especially when surgeons gain experience, they can also be more liberal in the use of laparoscopy in cases of diverticular disease and diverticulitis attack.¹⁹ In this study, there were no diverticular disease in group 1, and 2 patients in group 2 had diverticulitis. Again, expanding the policy of liberalism slightly, first NOTES transrectal anterior resection case was applied in Group 2.

Many studies in the literature show that intraoperative and postoperative complication rates in laparoscopic colorectal surgery decrease with increasing experience.^{20,21} In this study, it was observed that postoperative complication rate decreased as the experience increased but it was not statistically significant. Again, adequate oncologic lymphatic dissection was performed in both groups, but it was thought that total mesocolic and total mesorectal excision would be better with the increasing experience. As a result of this study, the learning curve in laparoscopic colorectal surgery is a long and time-consuming process, and with an increase in the experience of the surgeon, more complex cases can be coped with.

Study Limitations

Because of our patients' low number, we have to add our patients in our study. So, we cannot classify the patients for their surgery types.

Conclusion

With the increase experience of surgeon, more complicated cases can be operated in shorter time with low morbidity rate.

Ethics

Ethics Committee Approval: This study was approved by local ethical committee.

Informed Consent: Retrospective study.

Peer-review: Internally peer reviewed.

Authorship Contributions

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

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

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Our Colonoscopic Screening Results According to Risk Groups in Colorectal Cancers (Pilot Study)

Kolorektal Kanselerde Risk Gruplarına Göre Kolonoskopik Tarama Sonuçlarımız (Pilot Çalışma)

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ABSTRACT

Aim: Most of the colorectal cancers develop on a pre-existing polyp background. With the widespread use of screening tests, mortality of colorectal cancers has been shown to decrease. Our aim in this pilot study is to screen individuals according to risk groups in colorectal cancers and to obtain data that will lead in the establishment of community-based information and screening programs in this direction.

Method: Between October 2004 and February 2008, 358 people underwent colonoscopy for the purpose of screening. Individuals who had a family history of colorectal cancer or polyp, who had a history of colorectal polyps, and who were over the age of 40 years and wanted to voluntarily participate in the screening program although there were no risk factors were classified as average, low, medium and high risk groups. Individuals with a history of colorectal cancer and inflammatory bowel disease were excluded from the study.

Results: As a result of the screening, polyps were detected in 104 (29.1%) people, and masses with malignant appearance in 9 (2.5%) people. Histopathological evaluation revealed adenomatous polyp in 67 (18.7%) individuals, inflammatory polyp in 26 (7.3%) patients, malignant polyp in 11 (3.1%) patients, and invasive cancer in 9 (2.5%) patients (n=358).

Conclusion: Although the results of this pilot study do not reflect the whole society, the frequency of colorectal polyp and cancer is high in our country. In colorectal cancers, it is possible to cure the disease curatively with screening and early diagnosis before the development of cancer. In this regard, the society should be made more conscious and screening programs should be expanded.

Keywords: Colorectal cancers, screening, pilot study, colonoscopy

ÖZ

Amaç: Kolorektal kanserlerin büyük bir kısmı önceden var olan bir polip zemininde gelişir. Tarama testlerinin yaygın kullanımı ile kolorektal kanserlerin mortalitesinde azalma olduğu gösterilmiştir. Bu pilot çalışmada amacımız; kolorektal kanselerde risk gruplarına göre bireyleri taramak ve bu yönde toplum tabanlı bilgilendirme ve tarama programlarının oluşturulmasında öncülük edecek veriler elde etmektir.

Yöntem: Ekim 2004 ile Şubat 2008 tarihleri arasında 358 kişiye tarama amaçlı kolonoskopi yapıldı. Ailesinde kolorektal kanser veya polip hikayesi olan, kendisinde kolorektal polip hikayesi olan bireyler ve hiçbir risk faktörü olmadığı halde gönüllü olarak tarama programına katılmak isteyen 40 yaş üstü bireyler vasat, düşük, orta ve yüksek risk grubuna göre sınıflandırıldı. Daha önceden kolorektal kanser öyküsü, inflamatuvar barsak hastalığı olan bireyler çalışma dışında bırakıldı.

Bulgular: Tarama sonucunda 104 (%29,1) kişide polip, 9 (%2,5) kişide malign görünümlü kitle saptandı. Histopatolojik değerlendirme sonucunda; 67 (%18,7) kişide adenomatöz polip, 26 (%7,3) kişide inflamatuvar polip, 11 (%3,1) kişide malign polip ve 9 (%2,5) kişide invaziv kanser saptandı (n=358).

Sonuç: Bu pilot çalışmanın sonuçları toplumun genelini yansıtmasa da, ülkemizde kolorektal polip ve kanser sıklığı yüksektir. Kolorektal kanselerde, tarama ve erken tanı ile kanser gelişimi olmadan hastalığı küratif olarak tedavi etmek mümkündür. Bu konuda toplumun daha çok bilinçlendirilmesi ve tarama programlarının yaygınlaştırılması gerekmektedir.

Anahtar Kelimeler: Kolorektal kanserler, tarama, pilot çalışma, kolonoskopi



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Introduction

Colorectal cancers are the third most common cancer in the world and ranks 2nd in males and 3rd in females for cancer-related deaths.^{1,2} Life in colorectal cancers is closely related to the clinical and pathological stage of the disease at diagnosis. The 5-year survival rate of colorectal cancers varies as 90% in early diagnosed localized disease, 40-60% in regionally spreading disease and 6% in the presence of common metastasis.² This shows that if colorectal cancers are noticed and treated early, the death of many patients from this disease can be prevented.

The process of screening covers healthy individuals to undergo a check-up in order to prevent diseases before they develop, to catch them at an early stage and to treat them successfully. With the widespread use of screening tests, mortality of colorectal cancers has been shown to decrease. The majority of colorectal cancers develop on the background of a pre-existing polyp (adenoma). Based on the adenoma-carcinoma model defined by Vogelstein for the first time, clinical studies have shown that the progression from adenoma to invasive cancer covers a period of 8-10 years.³ In addition, the distribution of adenomas in the colorectum and the distribution of carcinoma have been shown to be parallel in the studies.^{4,5} In this long process, with the effective use of screening tests for colorectal cancers in the society, it will be possible to detect risky polyps before they overgrow and become cancer and to treat them at an early stage.

Although programs for screening and early diagnosis have been developed in recent years to inform our society about breast and cervical cancer in women and prostate cancer in men, it is very sad that many patients still die in our country due to colon and rectum cancers, which are completely curative with early diagnosis and treatment.

The frequency of colorectal cancer is extremely low between the ages of 20 and 39 years. It starts to increase significantly between the ages of 40 and 50 years and more than 90% of the cases occur after the age of 50 years.⁶ Many studies report that individuals with first-degree relatives who have a history of colorectal cancer also have an increased risk of developing this cancer compared to the normal population.^{7,8} Family cases constitute 10-30% of all colorectal cancers. In familial colorectal cancer cases, the risk is related to the age of the incidence of cancer in the family and the number of first degree relatives that are affected.⁹ To whom and when colorectal cancer screening tests are performed varies depending on the risk group in which the individuals are included. Many methods are used for screening in colorectal cancers. Colonoscopy is accepted by some authors as the gold standard in colorectal cancer screening programs. The

disadvantages of colonoscopy are that it requires complete bowel cleansing and sedation, person who will perform it should be educated and experienced, and it is expensive. However, if it is performed by people with sufficient experience and knowledge, it significantly reduces colorectal cancer mortality due to its high specificity and sensitivity, as it can evaluate the entire colon mucosa, remove the detected lesion, and take histopathological samples.^{10,11,12}

Our aim in this study is to screen individuals who are in the risk group for colorectal cancers and to provide early diagnosis and treatment to these individuals. Our aim is to obtain data that will lead the creation of community-based information and screening programs for individuals in the risk group as a result of this pilot study.

Material and Methods

Individuals who had a family history of colorectal cancer or polyp, who had a history of colorectal polyps, and who were over the age of 40 years and wanted to voluntarily participate in the screening program although there were no risk factors were classified as average, low, medium and high risk groups. Individuals with a history of colorectal cancer, hereditary colorectal cancer (HNPCC, FAP), or an inflammatory bowel disease were excluded from the study. The study was started on October 2004 and the study was carried out in the University Hospital General Surgery Department. Ethics committee approval was primarily received for the study. Within the framework of the study, information posters consisting of 4 parts and a brochure with 16 pages were prepared on an introductory basis for individuals (Figure 1, 2, 3, 4.) After obtaining the necessary permissions, the posters prepared were hung in the pre-determined places of the hospital. The relatives of colorectal cancer patients who received inpatient treatment in our hospital were interviewed, and they were given information about the screening program and they were recommended to participate in the screening program. In order to increase the interest in the screening program and to reach more individuals, informative meetings were held every month for primary care physicians in various regions of Ankara since the beginning of 2008. Written informed consents for the study were obtained from all individuals who participated in the study.

The study was done prospectively. Colonoscopy was performed as a screening method in 358 individuals who participated in the study. Colonoscopy was performed by appointment method at the Endoscopy Unit of University Hospital General Surgery Department. All individuals participating in the screening program were interviewed face-to-face and information was given about the procedure, and written informed consents were obtained from all

individuals. Diet, bowel cleansing and how to apply it before the procedure were told to individuals. It was also given to individuals in a written form. Sodium phosphate (fleet) oral suspension was used for colon cleansing.

During the procedure, Fujinon EC-450 WL5 and Olympus GIF-100 endoscope were used. On the day of the procedure, all individuals were monitored and the vascular access was opened and Midazolam (0.03-0.07 mg/kg) + Fentanyl (1-3 micrograms/kg) was administered as iv for premedication. Individuals who were detected to have polyp in colonoscopy underwent polypectomy in the same session or at a later session. No procedure-related complications (bleeding,

perforation) developed in any patient. The removed polyps were put into 10% formol and sent to the pathology department. After the procedure, all individuals were kept under surveillance in the recovery room for a certain period of time. In addition, due to the sedation applied, all

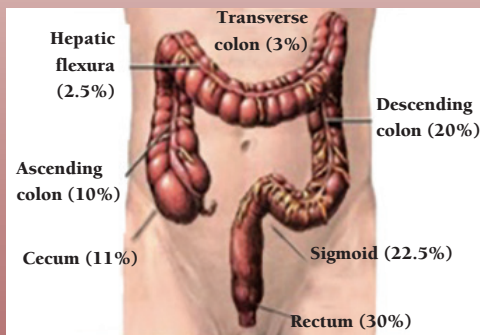
COLORECTAL CANCER IS A PREVENTABLE DISEASE.

Colorectal cancer is one of the most commonly seen cancers in our country.

The incidence of colorectal cancer in women and men is presented in the following table considering the statistics of Turkish Ministry of Health (2003).

Women	Men
1. Breast cancer	1. Lung cancer
2. Colorectal cancer	2. Gastric cancer
3. Gastric cancer	3. Colorectal cancer
	4. Urinary bladder cancer

REGIONS WHERE CANCER CAN DEVELOP IN THE COLON



Colorectal cancer is encountered more frequently in the regions close to the rectum.

WHAT ARE THE SYMPTOMS OF COLORECTAL CANCER?

- Rectal bleeding
- Blood in your stool
- Changes in your bowel habits
- Thinning of stool
- Diarrhea or constipation attacks
- Anemia, weakness and fatigue
- Bloating and too much gas
- Unexplained weight loss

Do you have one of these symptoms?

HOW CAN I PROTECT FROM COLORECTAL CANCER?

- Consume high-fiber foods (vegetables and fruit)
- Avoid red meat
- Avoid animal fat
- Do not consume snack food, eat regularly and adequately.
- Do not get weight
- Decrease alcohol consumption
- Do not smoke
- Do exercises

Can you do these items?

COLORECTAL CANCER IS A PREVENTABLE DISEASE.

The incidence of colorectal cancer is high in some individuals.

Therefore, we should know who are at risk !

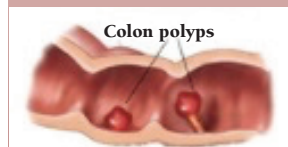
Who are at risk?

A personal or familial history of

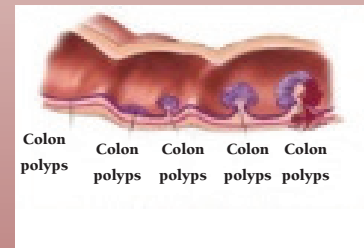
- colorectal cancer
- colorectal polyp
- Those older than 50 years
- Those having breast, cervical, and ovarian cancers
- Those having ulcerative colitis or Crohn disease (for longer than 10 years)

COLORECTAL CANCER MOSTLY ORIGINATE FROM POLYPS!

Polyps are the abnormal growths of the inner lining of the large intestine and its protruding into the colon.

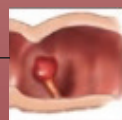


Transformation of polyp to cancer



View of polyps in the colon

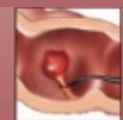
- Colorectal cancer develops in the polyps.
- Polyps usually do not present with a symptom.
- Some polyps do not transform into cancer.
- We cannot know which polyp will transform into cancer.
- Removal of polyps prevents cancer.
- It is necessary to remove the polyps.
- Patients whose polyps are removed should be followed up.
- Polyps can recur after removal.



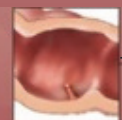
Polyp in the colon



Taking polyp into a noose



Cutting and removing polyp



Region where polyp is removed

The removal of polyps is performed during colonoscopy.

Scientific research have demonstrated that colorectal cancer CAN BE PREVENTED at the rate of 90% if polyps are detected before their being cancer and removed.

After the removal of polyps, they can recur.

These patients should be followed up by specialists regularly.

Figure 1. Information poster prepared for individuals emphasizing the importance of screening in colorectal cancers

Figure 2. Information poster prepared for individuals emphasizing the importance of screening in colorectal cancers.

individuals were warned (required not to drive for a certain period of time, to avoid works requiring attention) and sent to their homes.

Statistical Analysis

The data of all individuals participating in the study were recorded in the Microsoft Excel program and the statistical analysis of the data obtained was performed using the '11, 5' version of the software package 'SPSS for Windows'.

Results

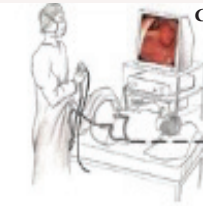
Between October 2004 and March 2008, 358 people underwent colonoscopy for screening at the Endoscopy Unit of University Hospital General Surgery Department. The mean age of the participants in the screening program was 49.4 ± 10.2 years and 53.4% were women. 288 (80.4%) of

these individuals were those aged 40 years and over. When the people participating in the screening were classified according to their risk groups; 86 (24%) people were in the average risk group, 125 (34.9%) were in the low risk group, 125 (34.9%) were in the middle risk group and 22 (6.1%) were in the high risk group.

COLORECTAL CANCER IS A PREVENTABLE DISEASE.
SCREENING TESTS CAN SAVE YOUR LIVES !


What are the screening tests?

- Guaiac-based fecal occult blood test
- Sigmoidoscopy and colonoscopy
- Virtual colonoscopy
- Colon radiography (medicated)




Colonoscopy procedure

Colonoscopy is performed with analgesic and sedative medications for patient not to feel pain.



Colon radiography (medicated)

The process of imaging polyps



WHEN TO PERFORM SCREENING TESTS?

When you do not have any problem
When you do not have any complaint
When everything is okay

HOW OFTEN TO PERFORM SCREENING TESTS

Colonoscopy every 10 years
Or
Guaiac-based fecal occult blood test every year and sigmoidoscopy every 5 years
Or
Colon radiography every 5-10 years

COLORECTAL CANCER IS A PREVENTABLE DISEASE.
Does hemorrhoid cause colorectal cancer?
NO, BUT
Hemorrhoid can present with symptoms like those in colorectal cancer.
When these symptoms are noticed, they should be evaluated by a specialist doctor.

Do you want to calculate your risk for colorectal cancer?

Question 1: Are you older than 50 years?
Yes No
-Age is the most important risk factor.
-40% of people older than 60 years have at least one polyp that can be transform into cancer.

Question 2: Do you have a history of the removal of polyp or cancer in your large intestine?
Yes No
- In those having a history of the removal of polyp or cancer in your large intestine, polyp can develop again at the rate of 50%.

Question 3: Do you have a familial history of colon polyps or cancer?
Yes No
- Colorectal cancer can sometimes be inherited?
- Ris is higher if you have a family member with colorectal cancer.

Question 4: do you have inflammatory bowel disease (ulcerative colitis and Crohn disease, for more than 10 years)?
Yes No

Question 5: Is there an evident change in your bowel habits?
Yes No
- Rectal bleeding and change in bowel habits are important findings and they should be investigated.

IF YOU ANSWER TO ONE OF THESE QUESTIONS IS YES, YOU ARE IN THE RISK GROUP !
BEING IN THE RISK GROUP DOES NOT MEAN YOU HAVE CANCER!
PERFORM SCREENING TESTS IN ORDER TO PREVENT FROM THE DISEASE!

Figure 3. Information poster prepared for individuals emphasizing the importance of screening in colorectal cancers.

Figure 4. Information poster prepared for individuals emphasizing the importance of screening in colorectal cancers.

At the end of the study, 104 (29.1%) individuals were found to have polyps and 9 (2.5%) people to have a mass suggesting malignancy, and biopsy was performed from them. 96 (26.8%) of 104 (29.1%) people who had polyps in the screening were over 40 years old (60% were male) (Table 1).

The demographic characteristics of the detected polyps were examined and the following results were obtained:

- Number of Polyps: Single polyp was found in 68 (19%) people, 2-4 polyps in 27 (7.5%) people and more than 4 polyps in 9 (2.6%) people.
- Polyp Size: The polyp size was below 1 cm in 81 (22.6%) people, 1-2 cm in 13 (3.6%) people and greater than 2 cm in 10 (2.9%) people.
- Type of Polyp: In people who had polyps, 61 (17.1%) of polyps were sessile and 43 (12%) were pedunculated.
- Localization of Polyps: Considering the localization of polyps in 104 people with polyps; it was observed that 23 (6.1%) polyp was located in the rectum, 53 (15.2%) were

in the left colon, 20 (5.6%) were in the right colon, and 8 (2.2%) were in the transverse colon.

Considering the localization distribution of 9 (2.5%) individuals with a malignant mass as a result of screening; it was observed that 3 lesions were located in the rectum, 5 were in the left colon and 1 was located in the cecum.

When screening results were evaluated according to risk groups, 34 (32.7%) of 104 (29.1%) individuals with polyp were in the average risk group, 34 (32.7%) were in the low risk group, 28 (27%) were in the medium risk group, and 8 (7.6%) were in the high risk group. Of the 9 (2.5%) people who were detected to have a mass as a result of screening, 4 were in the average risk group, 2 were in the low risk group and 3 were in the middle risk group (Table 2).

Histopathological evaluation revealed adenomatous polyp in 67 (18.7%) patients, inflammatory polyp in 26 (7.3%) patients, and malignant polyp in the remaining 11 (3.1%) patients. The pathology results of 9 (2.5%) individuals with a mass appearing as malignant were reported as cancer (Adenoca). Of the 9 (2.5%) mass lesions that were detected to have cancer as a result of pathology, 8 were located in the left colon and 1 in the right colon. As a result of pathology, 6 of 11 (3.1%) people who were found to have malignant polyps were treated surgically (stalk invasion, lymphovascular invasion) and carcinoma in situ was detected in 5 patients. No additional treatment was given to these people and follow-up was recommended. In addition, 9 (2.5%) people who were found to have cancer as a result of screening were treated surgically (Table 3). As a result of the pathological examination, 4 of these patients were in stage 2 and 5 in stage 3.

Table 1. Screening results in patients undergoing colonoscopy

Screening result	Patients (Total 358)	
	Number	%
No pathology	245	68,4
Polyp (+)	104	29,1
Above the age of 40 years	96	26,8
Below the age of 40 years	8	2,3
Malignant mass	9	2,5

Table 2. Screening results for colorectal cancer according to risk groups

Screening results according to risk groups	No pathology		Polyp		Malignant polyp		Cancer	
	Number	%	Number	%	Number	%	Number	%
- Average risk group (n=86)	48	55,8	27	31,4	7	8,1	4	4,7
-Low risk group (n=125)	89	71,2	30	24	4	3,2	2	1,6
-Moderate risk group (n=125)	94	75,2	28	22,4	0	0	3	2,4
-High risk group (n=22)	14	63,6	8	36,4	0	0	0	0

Table 3. Histopathological evaluation in patients with malign lesions and treatment modality

Pathology result	Treatment	
	Polypectomy	Surgery
Malign polyp (Carsinoma incitu)	5	-
Malign polyp (İnvazive cancer)	6	6
Mass (invazive cancer)	-	9

Discussion

According to the data of cancer registry center at the Ministry of Health in twelve provinces in 2007-2008, colorectal cancers rank 3rd among women with the rate of 7.8%, and 4th among men with the rate of 7.5%.² Around 1 million new cases of colorectal cancer are reported worldwide each year. Life in colorectal cancers is closely related to the clinical and pathological stage of the disease at the time of diagnosis. Epidemiological data show that studies to prevent or reduce the frequency of colorectal cancers should be increased. The incidence of colorectal cancer in the USA decreased significantly between 1992 and 1996 with the widespread use of screening tests and early detection and excision of colon polyps (2.1% /year).^{13,14} While early stage cancers constitute 30-40% of colorectal cancer cases in the USA, this rate is unfortunately very low in our country. In a study conducted in our country, between 1985 and 2001, 1771 patients who were operated with a diagnosis of colorectal cancer in a university hospital were retrospectively examined and the results of the study revealed that 82% of patients had advanced tumors.¹⁵ This clearly shows the importance of screening tests.

The majority of colorectal cancers develop on a pre-existing adenomatous polyp background. While the prevalence of adenomatous polyp is about 20-30% before the age of 40 years, it is 40-50% after the age of 60 years.^{5,6} Malignant polyps are encountered at the rate of 2-12% in colonoscopic polypectomies and at the rate of 4-9% in colorectal resection series.¹⁶ The risk of carcinoma in a polyp varies between 0.8 and 11%. Contrary to the general belief that the risk of malignancy in polyps smaller than 5 mm is almost nonexistent, 4% risk factors (>25 villous structure and severe dysplasia) for malignancy were detected in polyps smaller than 6mm and it was emphasized to treat all polyps regardless of their diameters in a study.¹⁷

Today, colonoscopy is accepted as the gold standard in colorectal cancer screening programs by most societies. In the colonoscopic screening study performed on 3196 asymptomatic individuals aged between 50 and 75 years old in America, it was stated that the cecum was reached at the rate of 97% and the procedure-related morbidity was very low (0.3%). In the individuals participating in the study, 38% polyp, 1.6% malignant polyps and 1% invasive cancer were detected, and 48 (2.7%) individuals with no lesions in the distal colon were found to have lesions in the proximal colon. At the end of the study, it was stated that sigmoidoscopy alone might be insufficient in colorectal cancer screening in terms of detecting proximal lesions.¹⁸

In our study, the rate of polyps in the general population was found to be 29.1%. 26.8% of these individuals were over

the age of 40 years and 2.3% were under the age of 40 years. As a result of the study, 3.1% malignant polyp and 2.5% cancer were detected in the entire population.

Colorectal cancers remain an important health problem for our country. Screening of asymptomatic individuals is of great importance since colon and rectum cancers are generally recognized in advanced stages in our country. Considering the durations of surgery, chemotherapy, radiotherapy, and hospital stay, and the periods when they fall behind in their works in patients with colorectal cancer diagnosed at advanced stage, it is inevitable that their medical expenses are much higher than those of the patients catching the disease in the early stages.

Considering all these data, in order to implement screening programs with broad participation, physicians who frequently encounter patients with colorectal cancer should be knowledgeable and sensitive in this regard. In a survey study conducted on 278 physicians to determine the approach of doctors to screening methods used in colorectal cancers, it has been revealed that even specialist physicians working at the branches most commonly encountering individuals having risk for colorectal cancer are negligent for various reasons in having a screening test for themselves or for their parents at risk.¹⁹

It is clear that this negligent behavior will increase to higher rates considering all physicians and candidates for physicians. It is imperative colorectal cancer screening programs to be implemented and at the same time, physicians and candidate physicians to be enlightened with more updated information. However, the results of this study do not fully reflect the distribution characteristics of colorectal polyp and colorectal cancer and their frequency in Turkish society. In order to obtain more satisfactory results, it will be more appropriate to carry out screening programs on a larger scale and in many centers and to evaluate the all results.

Ethic

Ethics Committee Approval: Ethics committee approval was primarily received for the study.

Informed Consent: The study was done prospectively.

Peer-review: Internally and externally peer reviewed.

Authorship Contributions

Surgical and Medical Practices: A.K., Consept: A.K., Design: A.K., O.Ş., Data Collection or Processing: O.Ş., Analysis or Interpretation: O.Ş., Literature Search: O.Ş., Writing: O.Ş.

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

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Clinical Value of Neutrophil/Lymphocyte Ratio in Predicting Postoperative Complications and Prognosis in Patients with Colorectal Cancer Undergoing Surgical Treatment

Nötrofil/Lenfosit Oranının Cerrahi Uygulanan Kolorektal Kanserli Hastalarda Postoperatif Komplikasyonları ve Prognozu Öngörebilmedeki Klinik Değeri

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ABSTRACT

Aim: Recently, the preoperative systemic inflammatory response has been reported to be a prognostic factor in patients with colorectal cancer (CRC). In this context, the preoperative neutrophil/lymphocyte ratio (NLR) has been proposed as a useful predictor of prognosis. In this study, we aimed to determine the clinical value and prognostic significance of neutrophil/lymphocyte ratio in predicting postoperative complications in patients undergoing surgical treatment for colorectal cancer.

Method: Patients who underwent surgical treatment for colorectal cancer between 2015-2019 were included in the study. group 1 (Low NLR) and group 2 (High NLR) were formed. Demographic and clinical characteristics, intraoperative and postoperative results, and mean survival were compared. The value of NLR in predicting postoperative complications at the determined cut-off value was examined.

Results: Patients were divided into two groups according to the cut-off value of 2.08. Group 1 consisted of 56 patients, and group 2 consisted of 223 patients. Male sex was dominant in both groups (60% vs 64%, $p=0.349$), while patients in group 2 received more neoadjuvant treatment (29.1% vs 12.5%, $p=0.007$). Intraoperative complication rates were similar (1.8% vs 4%, $p=0.369$), pathological grade ($p=0.031$), and stage ($p=0.113$) were similar. Postoperative complications were more common in group 2 (24.7% vs 10.7%, $p=0.015$). Total survival was shorter in group 2 (46 months vs. 52 months, $p=0.025$). At the determined cutoff value, NLR predicted postoperative complications with 22.94% specificity and 90.6% sensitivity.

Conclusion: High NLR was associated with postoperative complications and survival. Although it has a prognostic value, its value in predicting postoperative complications is limited and cannot be used alone.

Keywords: Colorectal cancer, neutrophil/lymphocyte ratio, prognosis

ÖZ

Amaç: Son zamanlarda, preoperatif sistemik enflamatuvar yanıtın kolorektal kanserli hastalarda (CRC) prognostik bir faktör olduğu bildirilmiştir. Bu bağlamda preoperatif nötrofil lenfosit oranı (NLO), prognoz için faydalı bir öngörü faktörü olarak öne sürülmüştür. Bu çalışmada nötrofil/lenfosit oranının kolorektal kanser nedeniyle cerrahi tedavi uygulanan hastalarda postoperatif komplikasyonları öngörebilmedeki klinik değerini ve prognostik önemini saptamayı amaçladık.

Yöntem: 2015-2019 yılları arasında kolorektal kanser nedeniyle cerrahi tedavi, uygulanan hastalar çalışmaya dahil edildi. Grup 1 (NLO düşük) ve grup 2 (NLO yüksek) olmak üzere iki grup oluşturuldu. Gruplarda hastaların demografik ve klinik özellikleri intraoperatif ve postoperatif sonuçlarını ortalama sağkalımları karşılaştırıldı. NLO belirlenen cut off değerinde postoperatif komplikasyonları öngörebilmedeki değerine bakıldı.

Bulgular: Hastalar 2,08 cut-off değerine göre iki gruba ayrıldı grup 1=56 hastadan grup 2=223 hastadan oluşuyordu Her iki grupta da erkek cinsiyet baskındı (%60 vs,%64 $p=0,349$), grup 2'deki hastalar daha çok neoadjuvant tedavi almıştı (%29,1 vs %12,5 $p=0,007$), intraoperatif komplikasyon



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oranları benzer (%1,8 vs %4 p=0,369), Patolojik grade p=0,031 ve evre p=0,131 benzerdi. Postoperatif komplikasyon grup 2'de daha sık görülmüştü (%24,7 vs %10,7 p=0,015) Toplam sağ kalım grup 2'de daha kısa (46 ay vs 52 ay p=0,025) belirlenen cut-off değerinde NLO %22,94 spesifite ve %90,6 sensitivite ile hastada postoperatif komplikasyonu ön görüyordu.

Sonuç: Yüksek NLO postoperatif komplikasyonlarla ve sağ kalımla ilişkiliydi. Prognostik değeri olmakla beraber postoperatif komplikasyonları tahmin etmedeki değeri kısıtlıdır ve tek başına kullanılamaz.

Anahtar Kelimeler: Kolorektal kanser, nötrofil/lenfosit oranı, prognoz

Introduction

Colorectal cancer (CRC) is the third most common type of cancer in men and the second most common type of cancer in women globally, according to the 2012 data of the International Cancer Agency.¹

It is important to investigate prognostic biological factors in CRC. The patient's outcome may be affected by tumor biology. Similar clinical or pathological characteristics often show different clinical outcomes. Although TNM classification is useful in classifying patients and choosing treatment, patients with the same stage may have different clinical outcomes. Therefore, it is important to detect molecular markers, especially in the selection of adjuvant or targeted therapy, in aggressive CRC.

Inflammation has been shown to play an important role in the pathogenesis and progression of CRC. Lab markers such as C-reactive protein, hypoalbuminemia, Glasgow Prognostic Score, white blood cell count, neutrophil/lymphocyte ratio, or platelet/lymphocyte ratio used to evaluate systemic inflammatory response have been studied as prognostic and predictive factors in various tumoral diseases.^{2,3,4,5} CRP, a marker of systemic inflammation, has been shown to be a prognostic factor in CRC patients.⁶

Neutrophil/lymphocyte ratio (NLR) is calculated by dividing neutrophil count by lymphocyte count in complete blood count and has been suggested to reflect the balance between pro-tumor inflammation and anti-tumor immune function, and its prognostic significance has been studied extensively in many solid tumors.⁷ NLR was reported to be an important prognostic factor in CRC patients.^{8,9}

However, inconsistent results also showed that NLR was not an independent prognostic factor for CRC in the Cox regression model of Wei et al.¹⁰ Therefore, the prognostic value of NLR in CRC is controversial.

The aim of this study was to determine the value of Neutrophil/Lymphocyte Ratio in predicting postoperative complications and prognosis in patients with CRC who underwent curative surgery.

Material and Methods

After obtaining permission from the Ethics Committee of Çukurova Faculty of Medicine dated 04.09.2019 and

numbered 91/29, 344 patients who underwent surgery for colorectal cancer between January 2015 and December 2018 were evaluated retrospectively. Patients who underwent palliative surgery, patients with metastatic disease, patients under the age of eighteen, pregnant patients, patients with chronic or hematological disease, steroid users, and patients whose records could not be reached were excluded from the study. The remaining 279 patients were included in the study.

The patients were divided into two groups according to the cut off value obtained from the ROC curve. Those lower than the cut off value of 2.08 were determined as group 1 (Low NLR), and those higher than 2.08 were determined as group 2 (High NLR). The relationship between NLR and clinicopathological parameters (age, sex, tumor stage, tumor markers, operation details, postoperative complications (clavien dindo 3 and above), wound site infection, intraabdominal abscess, evisceration, postoperative ileus, anastomotic leakage, reoperation, disease-free survival, median follow up) was statistically analyzed.

The criteria for discharge were meal tolerance without nausea or vomiting, defecation or stoma function, adequate pain control by oral analgesia, and independent mobilization.

Blood parameters were measured preoperatively. The total blood count was measured by an automated hematology analyzer (Roche Hitachi Cobas® 8000 Roche Diagnostics, Indianapolis, IN, USA). NLR was defined as the absolute neutrophil count divided by the absolute lymphocyte count.

Statistical Analysis

Data were analyzed using IBM SPSS Statistics for Windows, version 24 (IBM Corp., Armonk, N.Y., USA). In the evaluation of the study data, student's t-test was used for comparison of quantitative data as well as descriptive statistical methods [mean, standard deviation, median, frequency, ratio, minimum (min), maximum (max)], and Mann-Whitney U test was used for the evaluation of NLR which was not normally distributed. Pearson's chi-square test and Fisher's exact test were used to compare qualitative data, and logistic regression was used for multivariate evaluations. The patients were divided into two groups based on the presence of postoperative complications,

and receiver operating characteristic (ROC) analysis was performed according to these groups. Diagnostic accuracy was evaluated using ROC curve analysis. Kaplan-Meier and Log Rank tests were used for survival analysis. A p-value of <0.05 was considered statistically significant.

Results

In order to create a cut off value for NLR, ROC analysis and ROC curve were created. As a result of ROC analysis, the area under the ROC curve was calculated as 55.8%. According to the cut off value, if the NLR value is above 2.08, it is determined that the patient develops postoperative complications with 90.16% sensitivity and 22.94% specificity (Shown in Table 1 and Figure 1).

The patients were divided into two groups according to the cut off value of 2.08. Those lower than the cut off value of 2.08 were determined as group 1 (Low NLR), and it consisted of 56 patients, and those higher than 2.08 were determined as group 2 (High NLR) and it consisted of 223. There was no statistically significant difference between the groups in terms of mean age, sex, ASA scores, body mass index and tumor markers ($p>0.05$). The patients in group 2 received more neoadjuvant treatment (29% vs 12%, $p=0.007$). Demographic characteristics and preoperative findings of the patients are shown in Table 2.

The rate of laparoscopic surgery was similar between the groups (32.1% vs 42.6% $p=0.101$). Operation times were similar (168 vs 171 min, $p=0.592$). Intraoperative

complication rates were also similar (1.8% vs 4%, $p=0.369$). Intraoperative complications were ureteral injury, small bowel injury, and spleen injury. Additional non-tumor intervention rates were similar ($p=0.446$). Intraoperative features are given in Table 3.

When we looked at the pathological features of the tumors, histological types were similar ($p=0.166$). The rate of poorly differentiated tumors was higher in group 2 than in group 1 (21.5% vs. 8.9%, $p=0.031$). The distribution of the pathological stage was similar ($p=0.131$). When we evaluated the response to treatment in patients receiving neoadjuvant treatment, there was no difference between the groups ($p=0.439$). The pathological characteristics of the tumors are shown in Table 4.

Duration of the postoperative hospital stay was similar between the groups ($p=0.502$). Postoperative complications were higher in group 2 than group 1 (24.7% vs 10.7%, $p=0.015$). Intraoperative abdominal abscess and postoperative ileus were higher in group 2 ($p=0.034$; $p=0.050$, respectively). Wound infection, anastomotic leakage, and evisceration were similar ($p=0.456$, $p=0.426$ and $p=0.574$, respectively). There was no difference between the groups in terms of local recurrence and distant metastasis. Perioperative and postoperative clinical outcomes and oncological outcomes are shown in Table 5.

Total survival was lower in group 2 than in group 1 (46.87 months vs. 52.75 months, $p=0.025$). It is shown in Table 6 and Figure 2. Disease-free survival rates were similar in the groups (52.73 vs. 48.13 months, $p=0.073$). It is shown in Table 7 and Figure 3. Median follow up was 29.1 ± 13 (1-54) months.

Table 1. Proposed cut-off values for significant parameters in postoperative complications

	NLR
AUC	0.558
Cutoff	>2.08
Specificity	22.94
95%-CI (%)	17.5-29.1
Sensitive (%)	90.16
95%-CI (%)	79.8-96.3
PPV	24.7
NPV	89.3
+LR	1.17
-LR	0.43
p	0.154

AUC: Area under the curve, CI: Confidence interval, nLLR: Negative likelihood ratio, pLLR: Positive likelihood ratio, NLR: Neutrophil-to-lymphocyte ratio, NPV: Negative predictive value, PPV: Positive predictive value

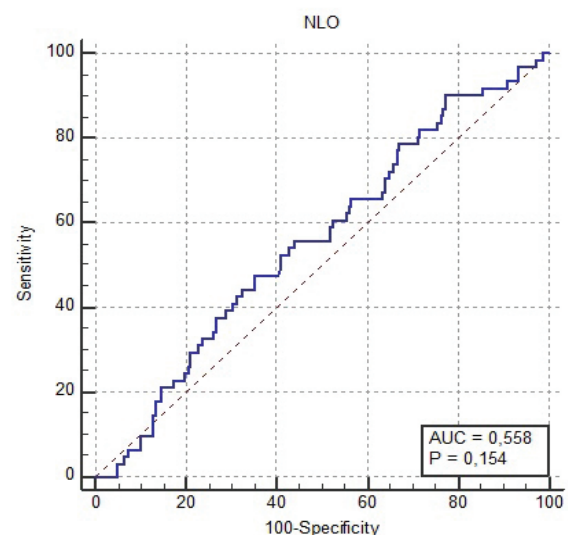


Figure 1. Receiver operating characteristic (ROC) curve analyses for postoperative complications

Table 2. Demographic characteristics and preoperative findings of the patients

		Low NLR n=56	High NLR n=223	p*
Age (Mean+SD) (Min-max)		59.60+11.71 29.0-83.0	61.91+12.21 20.0-107.0	0.205
Sex	Male	33 (60.0)	145 (64.7)	0.349
	Female	23 (40.0)	79 (35.3)	
ASA Score	1	24 (42.9)	111 (49.8)	0.633
	2	21 (37.5)	71 (31.8)	
	3	11 (19.6)	41 (18.4)	
BMI (Mean+SD) (Min-max)		27.17+5.66 19.8-50.0	26.13+4.30 18.0-51.0	0.131
CEA (Mean+SD) (Min-max)		6.46+14.63 0.0-77.0	5.54+12.28 0.0-146.0	0.631
Ca19.9 (Mean+SD) (Min-max)		93.59 +539.03 0.0-4036.0	33.75 +137.17 0.0-1760.0	0.139
Synchronous lesion		8 (14.3)	31 (13.9)	0.544
Neoadjuvant CRT (+)		7 (12.5)	65 (29.1)	0.007

ASA: American Society of Anaesthesiologists, BMI: Body mass index, CEA: Carcinoembryonic antigen; CRT: Chemoradiotherapy, NLR: Neutrophil/lymphocyte ratio

Table 3. Intraoperative features

		Low NLR n=56	High NLR n=223	p*
Emergency/Elective	Emergency	5 (8.9)	29 (13.0)	0.281
	Elective	51 (91.1)	194 (87.0)	
Operation type Laparoscopic	Conventional	38 (67.9)	128 (57.4)	0,101
	Laparoscopic	18 (32.1)	95 (42.6)	
Operation duration (min-max)		168.48+37.26 20-250	171.09+31.41 90-250	0.592
Intraoperative complication Yes	Cholecystectomy	0 (0.0)	4 (1.8)	0.446
	Bladder repair	1 (1.8)	1 (0.4)	
	Cystoscopy	0 (0.0)	1 (0.4)	
	Splenectomy	0 (0.0)	1 (0.4)	
	Splenectomy + distal pancreatectomy	1 (1.8)	0 (0.0)	
	Surrenal biopsy	0 (0.0)	1 (0.4)	
	TAH+BSO	0 (0.0)	1 (0.4)	
	Ureter repair	0 (0.0)	3 (1.3)	
	None	54 (96.4)	211 (94.6)	

TAH-BSO: Total abdominal hysterectomy + bilateral salpingoophorectomy, min: Minimum, max: Maximum, NLR: Neutrophil/lymphocyte ratio.

Table 4. Pathological characteristics

		Low NLR n=56	High NLR n=223	p*
Histological Type	Mucinous	6 (10.7)	45 (20.2)	0.166
	NOS	50 (89.3)	175 (78.5)	
	Signet ring	0 (0.0)	3 (1.3)	
Pathological grade	Poorly differentiated	5 (8.9)	48 (21.5)	0.031
	Mildly differentiated	16 (28.6)	75 (33.6)	
	Well differentiated	35 (62.5)	100 (44.8)	
Pathological stage	0	0 (0.0)	3 (1.3)	0.131
	1	13 (23.2)	41 (18.4)	
	2	0 (0.0)	1 (0.4)	
	2A	6 (10.7)	17 (7.6)	
	2B	10 (17.9)	66 (29.6)	
	2C	1 (1.8)	1 (0.4)	
	3A	4 (7.1)	10 (4.5)	
	3B	4 (7.1)	44 (19.7)	
	3C	4 (7.1)	40 (17.9)	
Treatment effect (only rectum)	Bad response	1 (25.0)	4 (8.3)	0.439
	Minimal response	1 (25.0)	9 (18.8)	
	Medium response	2 (50.0)	18 (37.5)	
	Full response	0 (0.0)	17 (35.4)	

NOS: Not otherwise specified, NLR: Neutrophil/lymphocyte ratio

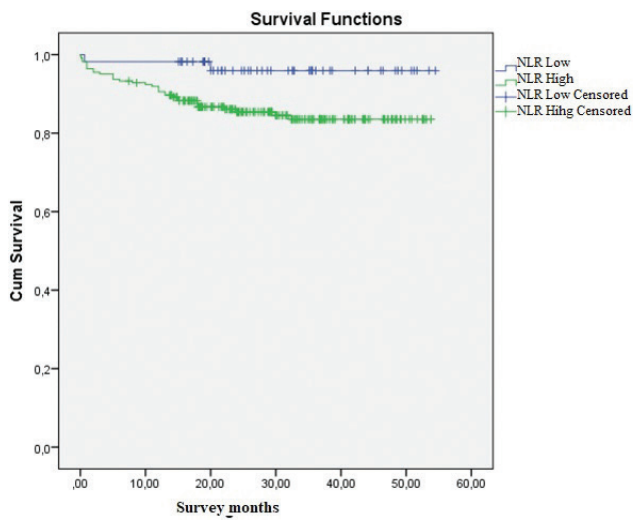


Figure 2. Total survival according to NLR groups
NLR: Neutrophil/lymphocyte ratio

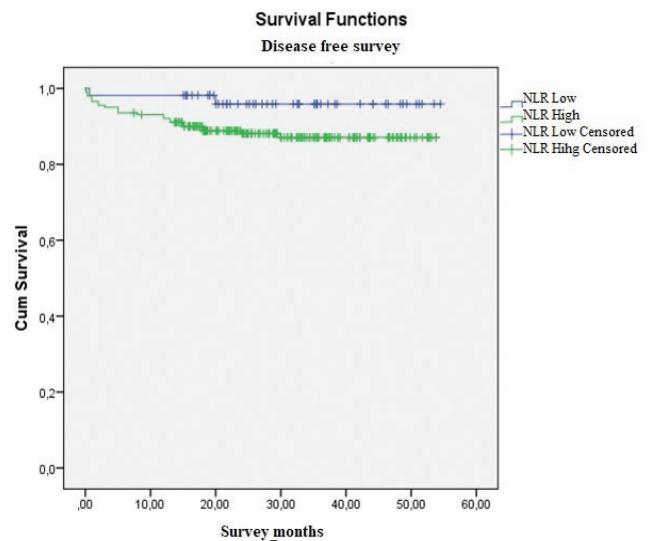


Figure 3. Disease-free survival according to NLR groups
NLR: Neutrophil/lymphocyte ratio

Table 5. Perioperative and postoperative clinical outcomes, oncological outcomes

		Low NLR n=56	High NLR n=223	p*
Postop hospitalization duration (mean + SD) (min-max)		10.05+6.69 4.0-40.0	9.32+7.34 1.0-75.0	0.502
Postoperative complication*		6 (10.7)	55 (24.7)	0.015
Wound site infection	Yes	7 (12.5)	32 (14.3)	0.456
	No	49 (87.5)	191 (85.7)	
Intraabdominal abscess	Yes	7 (12.5)	10 (4.5)	0.034
	No	49 (87.5)	213 (95.5)	
Evisceration	Yes	1 (1.8)	6 (2.7)	0.574
	No	55 (98.2)	217 (97.3)	
Ileus	Yes	2 (3.6)	26 (11.7)	0.050
	No	54 (96.4)	197 (88.3)	
Anastomotic leakage	Yes	2 (3.6)	5 (2.2)	0.426
	No	54 (96.4)	218 (97.8)	
Reoperation	Yes	3 (5.4)	12 (5.4)	0.647
	No	53 (94.6)	211 (94.6)	
Unplanned hospital readmission	Yes	6 (10.7)	31 (13.9)	0.352
	No	50 (89.3)	192 (86.1)	
Local recurrence	Yes	0 (0.0)	11 (4.9)	0.081
	No	56 (100.0)	212 (95.1)	
Distant organ metastasis	Yes	1 (1.8)	18 (8.1)	0.075
	No	55 (98.2)	205 (91.9)	

*Clavien dindo 3 and above, NLR: Neutrophil/lymphocyte ratio, SD: Standart deviation, min: Minimum, max: Maximum

Table 6. Total survival duration according to NLR groups

	Average (Mean + SD) (min-max)	P
NLR Group	Low NLR 52.75+1.22 50.361-55.142	0.025
	High NLR 46.87+1.12 44.68-49.07	

NLR: Neutrophil/lymphocyte ratio, SD: Standard deviation

Table 7. Disease-free survival duration according to NLR groups

	Average (Mean + SD) (min-max)	P
NLR Group	Low NLR 52.73+1.23 50.31-55.15	0.073
	High NLR 48.13+1.09 45.99-50.27	

NLR: Neutrophil/lymphocyte ratio, SD: Standard deviation, min: Minimum, max: Maximum

Discussion

In recent years, the relationship between inflammation and cancer has started to attract more attention and studies on the relationship between cancer and inflammation have been conducted. It has been shown that there is a significant relationship between systemic inflammation and relatively poor survival in various malignancies. Systemic inflammatory responses are thought to play a role in tumor progression

by inducing angiogenesis and inhibiting apoptosis and DNA damage, tumor proliferation, and metastasis.^{3,11,12} In addition to the high-risk factors associated with different tumor characteristics, the host's immune system also plays a role in the invasion or metastasis of colon cancer.¹³ The host inflammatory response to cancer cells is also associated with tumor progression.¹⁴ Inflammation is closely associated with tumorigenesis. Colorectal cancers are infiltrated by various

immune cells such as neutrophils, T and B lymphocytes, dendritic cells, macrophages, natural killer cells, and mast cells.^{15,16}

The meaning of high NLR remains unclear. NLR can potentially be affected by some conditions, especially chronic diseases.¹⁷ For this reason, these patients were excluded when we were designing our study.

Right colon tumors are considered to be more immunogenic tumors than left colon tumors because of high lymphocyte infiltrations, their association with increased inflammatory response, and high rate of mutation.¹⁸ In the series of Turker et al., it was reported that there was no statistical difference between right and left colon tumors in terms of NLR value.¹⁸ Similarly, Choi et al.¹⁹ reported in their study where the NLR cut off value was 2.6, that there was no correlation between the presence of tumor in the colon or rectum and NLR. In our series, there was no correlation between tumor localization and NLR, in support of the literature.

Kubo T et al.²⁰, in their study where the cutoff for NLR was 2.29, reported that NLR was associated with poorly differentiated tumors. In contrast, Shen J et al. reported that there was no correlation between histological differentiation and NLR when the cutoff value for NLR was taken as 3.²¹ In our series, poorly differentiated tumors were seen more frequently in patients with an NLR above 2.08 (21.5% vs 8.9%, $p=0.031$).

Several studies have been conducted to identify chemical markers predicting increased postoperative complication risk after colorectal surgery. Procalcitonin and complement C3A levels in the first 24 hours after elective colorectal surgery were found to correlate with the presence of systemic inflammatory response syndrome (SIRS).²² In studies investigating the relationship between NLR and postoperative complications, Cook et al.²³ found a similar NLR value in patients with and without complications, while Caputo et al.²⁴ reported in their study including rectum cancer patients who received neoadjuvant treatment, that an NLR over their cutoff value of 3.8 was associated with increased surgical complication rate. In our series, postoperative complications were found to be higher in the high NLR group than in the low NLR group (24.7% vs 10.7%, $p=0.05$).

In response to specific chemokines, different immune cell subsets migrate to the tumor microenvironment and regulate tumor immune responses. Direct and indirect interactions in chemokine pathways can reshape the immune and biological phenotypes of a tumor, render the biological behavior unpredictable and alter its metastatic potential.²⁵ When the relationship between NLR and recurrence or distant metastasis was examined, no difference was found

in the conducted studies.^{24,26,27} In our study, no correlation was found with NLR in terms of local recurrence ($p=0.081$) and distant metastasis ($p=0.075$), similar to the literature.

Chiang SF et al. reported that preoperative high NLR (>3) affects disease-free survival in patients with stage I - III CRC. Elevated NLR (>3) was associated with a worse outcome (5-year disease-free survival 66.3% vs. 78.9% in colon cancer, $p<0.001$; 60.5 % vs. 66.2% in rectal cancer, $p=0.008$).²³ In our series, the mean survival time was lower in the group with NLR higher than 2.08 compared to the group with NLR lower than 2.08 (44.6 months vs. 50.3 months; $p=0.025$). However, the disease-free survival rate was similar in the two groups. Our study was in support of the literature and elevated NLR was associated with poor survival.¹⁷

The most important limitation of our study was its retrospective nature, and being a single-center study. However, our patient population was as large as those reported in the literature.

Conclusion

Various parameters are being investigated to predict the course of CRC disease. We think that NLR, which can be measured easily, is a parameter that can be used to predict the development of postoperative complications and survival. However, further studies are needed.

Ethics

Ethics Committee Approval: After obtaining permission from the Ethics Committee of Çukurova Faculty of Medicine dated 04.09.2019 and numbered 91/29.

Informed Consent:

Peer-review: Internally and externally peer reviewed.

Authorship Contributions

Surgical and Medical Practices: O.Y., U.T., A.G.Ü, İ.C.E., A.R., Concept: O.Y., U.T.,

Design: O.Y., U.T., İ.C.E., Data Collection or Processing: U.T., A.G.Ü, Analysis or Interpretation: O.Y., İ.C.E., A.R., Literature Search: O.Y., U.T., A.G.Ü, İ.C.E., A.R., Writing: O.Y., U.T., İ.C.E.

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

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Melanosis of The Appendix Presenting with the Clinic of Acute Appendicitis

Akut Apandisit ile Bulgu Veren Appendiks Melanozisi

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ABSTRACT

Laxative drugs are frequently used for chronic constipation. The chronic use of laxatives, which contain anthraquinone, mostly causes melanosis coli. A 57-year-old male patient with a history of diabetes mellitus and coronary artery disease, had long-term laxative use due to chronic constipation. The patient was admitted to the emergency service with the complaint of inflammatory abdominal pain that started in the epigastric region one day ago and migrated to the right lower quadrant. During the physical examination, right lower quadrant tenderness and rebound were positive. Imaging examinations and physical examination were consistent with acute appendicitis. The patient underwent an appendectomy via Mc Burney incision under general anesthesia. The postoperative follow-up period was complication-free and the patient was discharged on the second postoperative day. Postoperative specimen pathology was reported as an appendix with melanosis coli findings.

The incidence of melanosis coli increases with the chronic use of laxative drugs. Although melanosis coli is seen as a benign disease, there are no accurate data about whether it increases the risk of colon cancer and the incidence of acute appendicitis.

Keywords: Melanosis coli, laxative, colon cancer, appendix

ÖZ

Laksatif ilaçlar genellikle kronik konstipasyon şikayeti nedeniyle kullanılmaktadır. Antrakinon içeren laksatif ilaçların uzun süre kullanımı sıklıkla melanozis koliye sebep olmaktadır. Fifty-seven yaşında bilinen diyabet, koroner arter hastalığı, kronik konstipasyon nedeniyle uzun süreli laksatif kullanımı olan erkek hasta, bir gündür olan epigastrik bölgeden başlayan ve sağ alt kadrana migrasyon gösteren enflamatuvar tarzda karın ağrısı yakınması, iştahsızlık, bulantı ve kusma şikayeti ile acil servise başvurdu. Yapılan fizik muayenesinde sağ alt kadranda hassasiyet ve rebound pozitifliği. Yapılan laboratuvar tetkiklerinde lökositozu olan, abdomen ultrasonografi ve fizik muayenesi akut apandisiti destekleyen hasta acil operasyona alındı. Hastaya genel anestezi altında Mc Burney insizyonla apendektomi uygulandı. Servis izleminde ek bir komplikasyon gözlenmeyen hasta, postoperatif ikinci gün taburcu edildi. Hastanın postoperatif spesimen patolojisi melanozis koli bulguları gösteren apendiks şeklinde raporlandı. Melanozis koli görülme insidansı kronik laksatif kullanımı ile birlikte artmaktadır. Melanozis koli benign bir hastalık olarak görülmekle birlikte, kolon kanser riskini ve akut apandisit insidansını artırıp artırmadığına yönelik kesin veriler bulunmamaktadır.

Anahtar Kelimeler: Melanozis koli, laksatif, kolon kanseri, apendiks

Introduction

Melanosis coli (MC) is a dark brown pigmentation of the colonic mucosa and also named as psodomelanosis coli.^{1,2} MC often affects the cecum; the rectum is mostly affected secondary to the chronic use of anthraquinone-containing laxatives.^{2,3} MC was first described by Cruveilhier in 1829, and named MC by Virchow in 1857.^{1,2}

Case Report

A 57-year-old male patient with a history of diabetes mellitus and coronary artery disease was admitted to the emergency department with the complaints of abdominal pain, appetite loss, nausea, and vomiting. The abdominal pain started in the epigastric region one day ago and migrated to the right lower quadrant. In the physical examination, right lower quadrant



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tenderness and rebound were positive. The patient had chronic constipation and had a history of long term anthraquinone-containing laxative use. The laboratory tests showed leukocytosis. Abdominal ultrasonography and physical examination supported the diagnosis of acute appendicitis. The patient underwent an emergency operation. Appendectomy was performed via Mc Burney incision under general anesthesia. Postoperative follow-up was uneventful, and the patient was discharged on the second postoperative day without any complication. Postoperative histopathological examination of the specimen was reported as appendix tissue with the findings of MC (Figure 1, 2). In the appendix tissue, histiocytes and some pigmented deposition of histiocytes and histiocytes in the lamina propria were scattered in small groups. Histochemical staining showed no intracytoplasmic pigment staining with iron. The patient was advised to stop taking the laxative, and dietary modifications were adjusted for constipation. Total colonoscopy was performed two months after the surgery, and no additional pathology was observed.

Discussion

The rate of laxative use due to chronic constipation has increased with a sedentary lifestyle. Constipation is a frequently seen gastrointestinal problem, and anthraquinone containing laxatives are frequently used for chronic constipation.^{1,2}

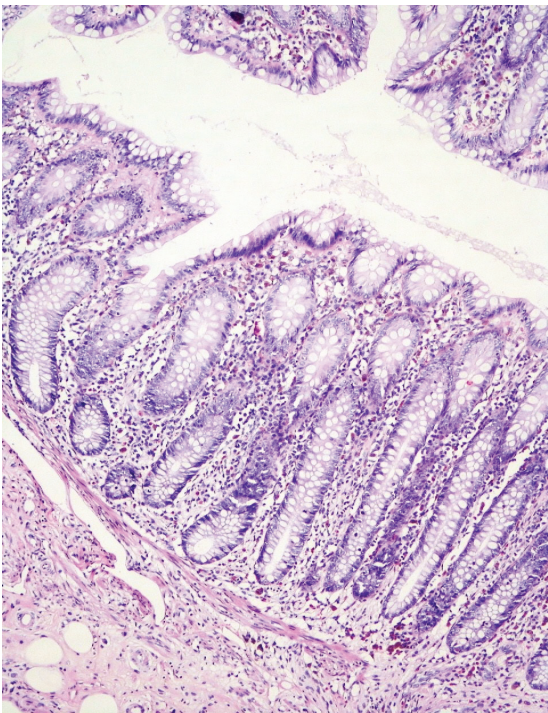


Figure 1. Histiocytes containing brown pigment deposits in the lamina propria of appendiceal mucosa (Hematoxylin and eosin, original magnification x 100)

MC is mostly seen as a brownish discoloration of the colonic mucosa during a colonoscopy and occurs due to the chronic use of laxative drugs, especially anthraquinone-containing laxatives.¹ MC is reported to be seen more commonly in the female population. The female-male ratio is two.^{1,2} Although it is frequently located in the colonic mucosa, especially in the the cecum part, MC can be seen in the small intestine as well.³ However, it may be seen in patients with chronic diarrhea, inflammatory bowel disease, and chronic use of non-steroidal anti-inflammatory drugs.^{3,4,5} Improper laxative use due to chronic constipation may cause MC, which is more common in elder patients.^{1,2} Acute appendicitis is one of the most common causes of abdominal pain in patients admitted to the emergency department. The most common etiology is lymphoid hyperplasia and obstruction. In the literature, there are many cases and case series operated for acute appendicitis, and histopathologic examination revealed appendix melanosis. Histological examinations of postoperative appendectomy specimens and MC have been extensively studied, but no specific studies have been conducted to determine whether MC is involved in the etiology of acute appendicitis or not. In a study by Ruttly et al.¹, 7.4% of appendix melanosis was reported in adult patients operated for acute appendicitis. Graf et al.⁶ reported 46% melanosis in 300 appendectomy specimens in the pediatric age group, most of whom were operated for acute appendicitis and abdominal pain. In addition, in this study, the incidence of melanosis was reported to increase with increasing age. Walker et al.⁷ reported that hyperpigmented macrophages due to melanosis migrated to the regional lymph nodes that persisted even after the elimination of the stimulus for submucosa and epithelial apoptosis, and Graf et al.⁶

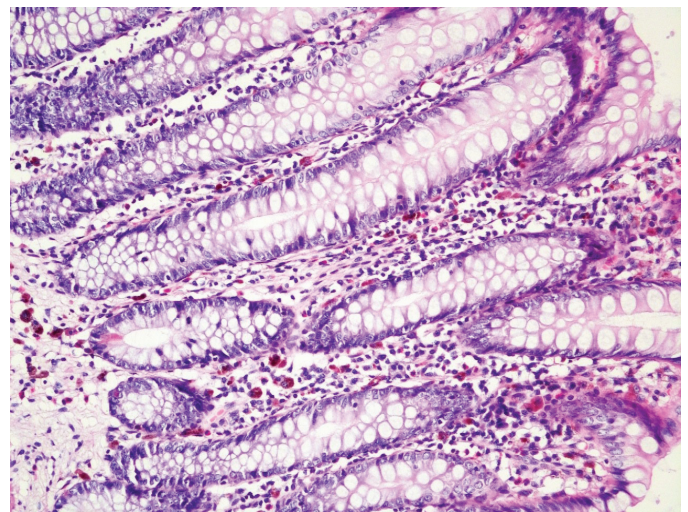


Figure 2. Histiocytes containing brown pigment deposits in the lamina propria of appendiceal mucosa (Hematoxylin and eosin, original magnification x 200)

reported that pigmented macrophages reduced lymphatic clearance. In the literature, Malik et al.⁸ reported a patient operated for colonic pseudoobstruction secondary to melanosis coli. Although there are no studies on this subject, it is known that the etiology of appendicitis is lymphoid hyperplasia and often secondary to fecaloid obstruction. We think that increased epithelial apoptosis and obstruction secondary to decreased lymphoid clearance may play a role in the presentation of patients with appendix melanosis with an acute appendicitis clinic. MC is the dark brown pigmentation of the colonic mucosa caused by the accumulation of pigments in the macrophages of lamina propria.¹ Although the tissue does not contain melanin pigments, the dark pigmentation which has an appearance like melanosis occur due to the increased apoptosis of epithelial cells and lipofuscin. This appearance has consisted of the lipofuscin granules, which occur secondary to the obliteration of apoptotic epithelial cells.⁹ The relationship of MC and neoplasia of the colonic epithelium has long been a subject of interest, but it remains unclarified.^{1,3} Studies have shown that there was an association between MC and the increase in colonic epithelial cell apoptosis.^{2,3} Although MC is usually benign and reversible and resolves within one year after the discontinuation of anthraquinone containing laxatives, there is an increased risk of colorectal carcinoma, which has also been discussed.^{2,3} Lui et al.³ reported that MC was associated with a higher number of colorectal polyps significantly. Moreover, they reported that MC was associated with a higher incidence and number of colonic non-adenoma polyps and low-grade adenomas and higher incidence of distal ileal ulcers due to the chronic injury of colonic and intestinal mucosa.³ In conclusion, although MC is seen as a benign disease, it may be related to an increased risk of acute appendicitis and colorectal carcinoma, which should always be kept in mind, and total colonoscopy is recommended. There are no accurate data as to whether it increases the risk of acute appendicitis and colon cancer. Larger case series are needed to make this relationship clear.

Ethics

Informed Consent: Written informed consent was obtained from the patient for publication and any accompanying images.

Peer-review: Internally peer reviewed.

Authorship Contributions

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

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

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Is Tocilizumab A Risk Factor for Lower Gastrointestinal Perforations? Isolated Cecal Necrosis: A Rare Case Report

Tocilizumab; Alt Gastrointestinal Sistem Perforasyonları için Bir Risk Faktörü Mü? İzole Çekum Nekrozu: Nadir Bir Olgu Sunumu

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ABSTRACT

Isolated cecal necrosis is a rare seen clinical condition. A 53-year-old woman with a history of rheumatoid arthritis and hypertension presented to the emergency room with complaints of abdominal pain and vomiting that persists for two days. She had been using tocilizumab (TCZ) for the last 5 months. Physical examination was compatible with acute abdomen. Abdomen computerized tomography showed a wall thickness approximately 3 cm on ascending colon that surrounded with significant inflammation. She was operated with a presumptive diagnosis of acute abdomen. During laparotomy, isolated necrosis with 10x9 cm diameter was observed in the cecum. A right hemicolectomy and ileocolostomy was performed. She was discharged on the 8th postoperative day. Postoperative specimen pathology was showed mucosal necrosis sharply separated from normal mucosal walls. Although the side effect profile of newly used drugs such as TCZ is not clear yet; with larger case reports and series can be contributed.

Keywords: Ischemic colitis, necrosis, tocilizumab

ÖZ

Elli üç yaşında kadın hasta, bilinen romatoid artrit ile hipertansiyon tanıları olup karın ağrısı ve kusma şikayetiyle acil servise başvurdu. Son 5 aydır tocilizumab (TCZ) kullanımı mevcuttu. Fizik muayene akut batın ile uyumlu idi. Yapılan abdomen bilgisayar tomografisinde çıkan kolonda 3 cm'lik alanda duvar kalınlık artışı ve çevresinde belirgin enflamasyon mevcuttu. Hasta acil operasyona alındı. Çekumda 6x8 cm'lik alanda nekroz izlendi. Hastaya sağ hemikolektomi ve ileokolostomi uygulandı. Postoperatif 8. günde sorunsuz taburcu edildi. Postoperatif spesimen patolojisinde normal mukozal duvarlardan keskin şekilde ayrılan mukozal nekroz izlendi. TCZ gibi yeni kullanılmaya başlanan ilaçların yan etki profilleri henüz netleşmemekle birlikte olgu takdimleri ile buna katkı sağlanmaktadır.

Anahtar Kelimeler: İskemik kolit, nekroz, tocilizumab

Introduction

Isolated cecal necrosis (ICN) is a rare and life-threatening condition. Colonic ischemia may be related to hypoperfusion in mesenteric vessels, which is generally encountered in the elderly population. Its incidence is estimated to be 16 cases

per 100,000 person-year.¹ Its diagnosis is difficult due to the lack of specific history, physical examination and imaging findings. It is seen more often in patients with aortoiliac reconstruction, cardiopulmonary bypass, congestive heart failure, atherosclerotic vascular disease, chronic renal failure requiring hemodialysis.



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In this study, we aimed to present the ICN case that resulted in a right hemicolectomy in a patient having the diagnosis of rheumatoid arthritis (RA) and using tocilizumab (TCZ).

Case Report

A 53-year-old female patient presented to the emergency room with the complaints of abdominal pain, nausea, vomiting and loss of appetite ongoing for 2 days. She stated that her abdominal pain had increased intensely for the last 12 hours. She had no history of surgical operation except radiotherapy, trauma and laparoscopic cholecystectomy. The body mass index of the patient was 39.9. She had a history of different doses of methylprednisolone, oral/subcutaneous methotrexate (MTX), and antihypertensive drug use for 16 years due to RA and hypertension. Five months ago, TCZ was started to be 8 mg/kg/month, along with the use of methylprednisolone 4 mg/day, hydroxychloroquine 200 mg/day, leflunamide 20 mg/day, candesartan cilexetil + hydrochlorothiazide 16 mg-12.5 mg/day, calcium carbonate + cholecalciferol 600 mg-400 IU/day. On physical examination, there was widespread tenderness and rebound in the abdomen, which was evident in the right lower quadrant. In the laboratory parameters, there was no feature other than WBC $10700 \times 10^3/uL$. In IV contrast abdominal computed tomography (CT), the lateral wall of the cecum was very thin, the ascending colon had an increase in wall thickness in the 3 cm segment and there were changes secondary to inflammation around the cecum. In addition, no signs were found in favor of arterial thrombus or embolism (Figure 1). Free air was not observed in the pneumatosis intestinalis or abdomen. The patient was evaluated as acute abdomen and a laparotomy decision was taken.

During the operation, there was fluid in the abdomen in the form of broth. A necrotic wall lesion of approximately 6x8 cm was observed at the lateral of the cecum (Figure 2). Right hemicolectomy and side-to-side ileocolostomy were performed to the patient. She was discharged on the 8th postoperative day without any problem.

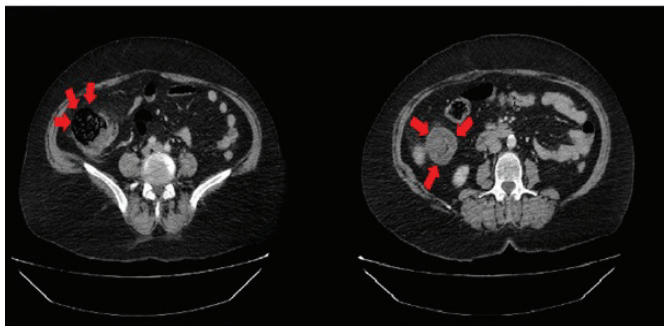


Figure 1. Thinned cecum wall and pericecal contamination

In the pathological examination of the specimen, an intestinal segment, which was sharply separated by normal mucosal tissues, was observed in an area of 10x9 cm in the macroscopically excised colon segment. Mucosal necrosis, edema, congestion (Figure 3) and active chronic inflammatory granulation tissue extending to the serosa, which microscopically showed a sharp transition with normal mucosa (Figure 4), were observed. No signs of malignancy were seen. Among the specific histopathological findings that would support mesenteric ischemia, which was included in the differential diagnosis of these findings,



Figure 2. View during operation



Figure 3. Sharp passage of normal colon mucosa and ischemic bowel segment (H&E, x40)

there were no findings such as phlebitis and thrombus in the vascular structures in the mesenteric adipose tissue.

After the operation, the treatment of the patient was replaced by adalimumab, which is the tumor necrosis factor -a monoclonal antibody. Along with other treatments available, she uses adalimumab 760 mg instead of TCZ.

Discussion

ICN is a rare surgical pathology. In general, it occurs secondary to intestinal ischemia, which develops as a result of the inability to meet the oxygen and nutrients required for cellular metabolism due to a decrease in blood flow.² Due to the richness of colon vascularity, it can be fed from many areas. Its having extensive collateral circulation prevents the development of colonic ischemia. However, splenic flexura and rectosigmoid junction contain the areas of the colon that we call “watershed” areas.³ Since collateral blood flow is weaker here, they are especially more prone to ischemia. It is thought that ICN can develop secondary to the pathology in the end branches of the arteries feeding the cecum. The exact cause of isolated ischemia in this area is unknown. Risk factors associated with colonic ischemia are previous abdominal or cardiovascular surgery, atherosclerosis, arrhythmias, chronic obstructive pulmonary disease, hypotension conditions, shock, irritable bowel syndromes, drugs, diabetes mellitus, RA and other rheumatological diseases.^{2,4} Prevalence increases with increasing age and comorbidities. This leads to an increase in the incidence of ischemic colitis as the population ages.⁴ In a retrospective study conducted on 209 patients, an increase in the incidence of ischemic colitis has been shown in people aged 65 years and over.⁵

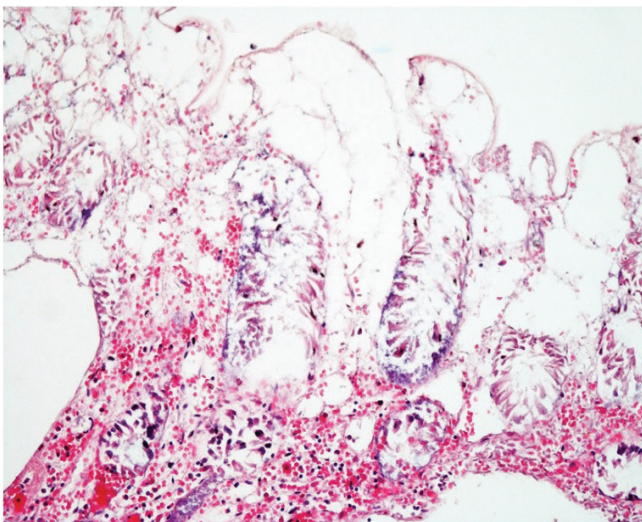


Figure 4. Mucosal necrosis, congestion and edema in the colon (H&E, x200)

Colonic ischemia should be suspected in patients presenting with nonspecific findings such as pain in the lower quadrants of the abdomen, bloody diarrhea, and hematochezia. Having advanced age and additional diseases makes diagnosis difficult. Although there is only localized necrosis at the beginning, if it is complicated (perforation, intra-abdominal abscess, fecal peritonitis), it causes an increase in mortality and morbidity.

Drug research is still ongoing for the treatment of autoimmune diseases and many new drugs are used in treatment. One of them, which is used in the treatment of RA, TCZ, is a monoclonal antibody producing IL-6 receptor blocker. TCZ can be used alone or together with disease-modifying antirheumatic drugs (DMARDs) in the treatment of RA. There are limited number of studies showing that TCZ increases the risk of perforation of the lower gastrointestinal (GI) system. It has been reported that GI perforations are observed more frequently in patients receiving TCZ therapy as monotherapy or in combination for RA treatment.^{6,7,8} It is known that treatments such as MTX, nonsteroidal anti-inflammatory drugs (NSAIDs) or glucocorticoids, which patients have used or are still using, contribute to the development of GI perforations and increase the risk of perforation.^{9,10} As the effect of TCZ, although the exact mechanism of GI perforations due to IL-6 receptor blockade is not yet understood, it is thought they may be associated with the effects of IL-6 inhibition on vascular endothelial growth factor (VEGF).¹¹ VEGF plays an important role in maintaining the integrity of the intestinal mucosa in intestinal damage caused by acute or chronic processes, and it is a targeted cytokines in many cancer treatments as it is highly effective during angiogenesis.¹² Similar to TCZ, clinical studies have shown that drugs with active substance of bevacizumab, another VEGF inhibitor, are also associated with GI perforations.¹³

Therefore, a decrease in VEGF levels may increase the risk of GI perforation.¹¹ Especially in the treatment of elderly RA patients with a history of diverticulitis, the use of these drugs should be paid attention; likewise, the use of TCZ alone in patients with a history of diverticulitis increases the risk of lower GI perforation.^{10,14} In ancient times, GI complications were among the most common causes of death in patients diagnosed with RA.¹⁵ In colon diseases requiring surgical intervention, increased survival rate was provided with early diagnosis and an appropriate definitive surgery.

Besides medical treatments used, GI perforations in patients with RA suggest that the disease may be secondary to the occurrence of vasculitis or other autoimmune causes. In the presented case, the absence of systemic disease other than HT and the history of TCZ started in the last 6 months due to RA suggested that TCZ might be associated with ICN,

in other words ischemic colitis. In the literature, a patient diagnosed with pneumatosis due to the use of TCZ and followed non-operatively has also been presented.¹⁶ The side effect profile of newly used drugs such as TCZ has not been clarified yet, but case reports and series contribute to it.

In conclusion, it should be kept in mind that one of the above mentioned risk factors and one of the complications related to the drugs used in the treatment of these risk factors may be ischemic colitis. Although the relationship between TCZ and intestinal perforation is not yet clear, pathophysiology can be elucidated by studies in this direction. Shortly after the patient's symptoms started, her applying to the emergency room and a quick decision-making for operation enabled the completion of the treatment without any complications associated with the disease.

Ethics

Informed Consent: Written informed consent was obtained from the patient who participated in this study.

Peer-review: Internally and externally peer reviewed.

Authorship Contributions

Concept: E.K.A., S.D.A., S.E., C.A., T.K., C.T., Design: E.K.A., S.D.A., S.E., C.A., T.K., C.T., Data Collection or Processing: E.K.A., S.D.A., S.E., C.A., T.K., C.T., Analysis or Interpretation: E.K.A., S.D.A., S.E., C.A., T.K., C.T., Literature Search: E.K.A., S.D.A., S.E., C.A., T.K., C.T., Writing: E.K.A., S.D.A., S.E., C.A., T.K., C.T.

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A Rare Case of Colonic Schwannoma

Nadir Bir Kolonik Schwannoma Olgusu

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ABSTRACT

Schwannomas are tumors originating from schwann cells in the nervous system. Colonic location is rarely seen and there are a few case reports published in the literature. We report a 53 year-old female who presented with abdominal pain, nausea, diarrhea ongoing for 2 years. Computer Tomography scan revealed a solid mass in size of 12.5x8 cm originating from the ascending colon and multiple lymphadenopathies in surrounding area. The patient underwent extended right hemicolectomy. The histopathological examination demonstrated a benign colonic schwannoma. Preoperative diagnosis of Colonic schwannoma seems to be difficult and usually schwannoma is diagnosed in the postoperative pathological examinations.

Keywords: Colonic schwannoma, gastrointestinal stromal tumor, schwannoma

ÖZ

Schwannomlar, sinir sistemindeki schwann hücrelerinden kaynaklanan tümörlerdir. Kolonik yerleşim nadir görülür ve literatürde yayınlanmış az sayıda olgu sunumu vardır. İki yıldır devam eden karın ağrısı, bulantı ve ishal şikayeti ile başvuran 53 yaşında bir kadın hastayı sunuyoruz. Bilgisayar Tomografi taramasında, çıkan kolonda 12.5x8 cm boyutlarında solid bir kitle ve çevresindeki alanda birden fazla şüpheli lenfadenopati saptandı. Hastaya genişletilmiş sağ hemikolektomi yapıldı. Histopatolojik inceleme sonucunda benign kolonik schwannoma tanısı kondu. Kolonik schwannomanın preoperatif tanısı zordur. Schwannoma tanısı genellikle postoperatif patolojik inceleme sonucu konulmaktadır.

Anahtar Kelimeler: Kolonik schwannom, kolon tümörü, schwannom

Introduction

Schwannomas are tumors originating from schwann cells in the nervous system.¹ Schwannoma of the gastrointestinal tract is extremely rare.² It is most commonly seen in the stomach and small intestines.^{3,4} Colonic localization is seen rare and there are a few case reports in the literature. High mitotic index, the size of tumor and Ki-67 index are used as malignancy features of schwannoma on pathological examination. Preoperative diagnosis is extremely difficult and patients are usually diagnosed after pathological examinations.

Case Report

A 53 year-old female applied to outpatient clinic with the complaints of abdominal pain, diarrhea and nausea

ongoing for 2 years. The patient was previously diagnosed with diabetes mellitus and chronic hypertension and did not have any history of previous abdominal surgery. On physical examination, the patient had abdominal defense and suspicious intra-abdominal mass with palpation in the right lower quadrant. Laboratory results were found to be normal. Computer tomography (CT) scan revealed a solid mass in size of 12.5x8 cm originating from the ascending colon and multiple lymphadenopathies in surrounding area (Figure 1). There were no signs of solid organ metastasis or vascular invasion. The patient underwent total colonoscopy which demonstrated a narrowing in the lumen of the ascending colon resulting from the compression of a mass originating from colonic wall but not invading mucosa of the colon.

The patient was operated with the laparoscopic extended



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right hemicolectomy. The patient's postoperative course was uneventful and was discharged on postoperative day 6. The histopathological examination demonstrated a benign colonic schwannoma in size of 12x8x7. Extracted lymph nodes from the specimen were found to be reactive. Immunohistochemical analysis showed that the tumor was diffuse positive with S-100, and negative with desmin, caldesmon, CD117, CD34 and SMA. The proliferation index for Ki-67 was lower than 1% and the number of mitosis was 1-2/50 (Figure 2, 3, 4). Upon these results no additional treatments were recommended to the patient.

Discussion

Schwannoma is a tumor derived from Schwann cells in neural crest and commonly localized in the myenteric plexus of the

peripheric nervous system.¹ Rarely, schwannomas can be originated from the myenteric plexus of the gastrointestinal system which are also classified as mesenchymal tumors. The incidence of schwannoma is 2-6% in gastrointestinal mesenchymal tumors and are most commonly located in the stomach (83%) and small intestines (12%).^{2,3,4}

Colonic schwannoma is a rare tumor commonly reported as benign with a very low mitotic index and is frequently diagnosed as a submucosal mass or polyp.⁵ It is reported that colonic schwannomas are usually located in the right colon (30.2%) followed by sigmoid colon, rectum, left colon and transverse colon (Table 1). Although mucosal biopsies are often inconclusive because of its submucosal location, with deep submucosal biopsies or resections, schwannoma can be differentiated from other common submucosal gastrointestinal tumors such as gastrointestinal stromal tumors (GIST), leiomyomas and neuroendocrine tumors.^{3,6}

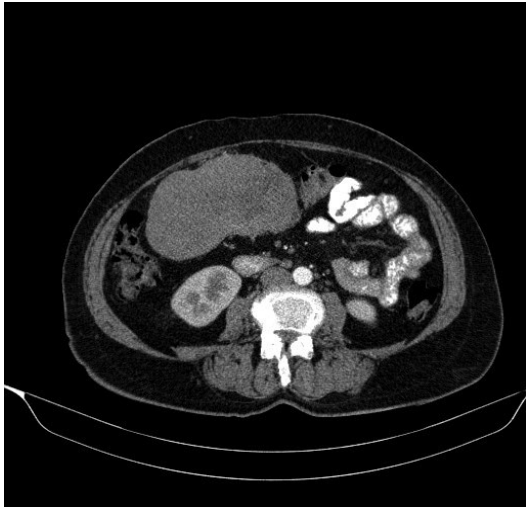


Figure 1. A solid mass in size of 12.5x8 cm originating from the ascending colon and multiple lymphadenopathies in surrounding area

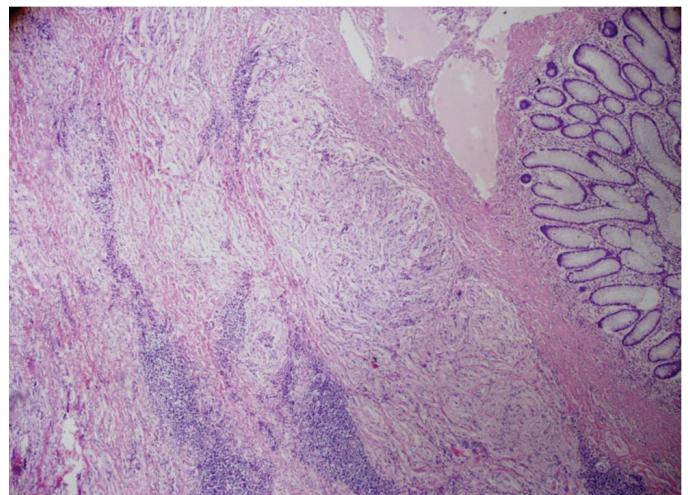


Figure 3. Schwannoma areas with degenerative changes of spindle cells in the colon wall

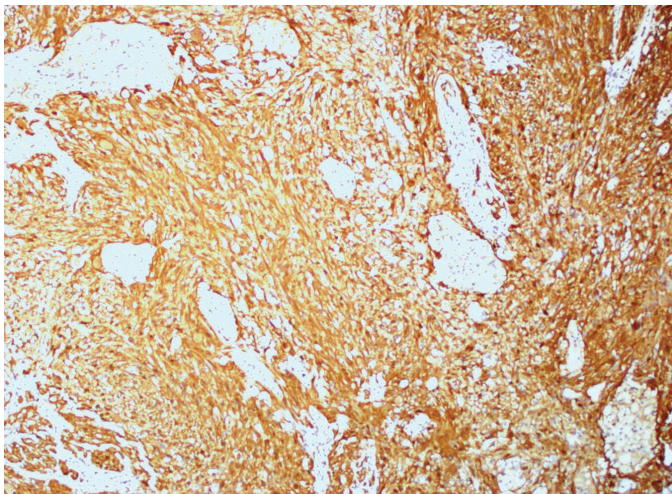


Figure 2. Spindle cells diffuse positive with S-100

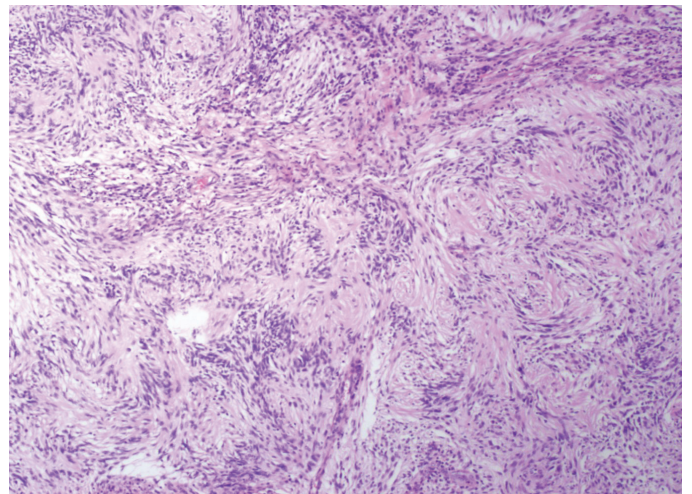


Figure 4. Palisading spindle cells and Verocay Bodies

Table 1. Frequencies of the schwannomas according to their localizations in the colon³

Localization	Frequency (%)
Right colon and cecum	30.2
Sigmoid colon	28.1
Rectum	21.9
Left colon	8.3
Transverse colon	5.2
Appendix	1

Table 2. Comparison of the schwannoma and GIST in immunohistochemical analyses¹

Immuno- histochemical markers	Schwannoma	GIST
CD-117 and CD-34	Negative	Positive
S-100	Positive	Negative
SMA	Negative	Negative
GFAP	Positive	Negative
Desmin	Negative	Negative

However, GIST has a much more heterogeneous appearance on CT compared to schwannomas because of the presence of haemorrhage, necrosis, and cystic change, most of the schwannoma cases are diagnosed as GIST on CT scan.^{7,8}

The definitive diagnosis is usually made with pathological result and immunohistochemical analysis of resected specimen.⁴ The differential diagnosis with GIST should carefully be made by using immunohistochemical analysis including S-100, CD117 and CD34. S-100 and GFAP are characteristically found to be positive in schwannoma, whereas CD117 and SMA are negative (Table 2).

Malignant gastrointestinal schwannomas are very uncommon and associated with poor prognosis.⁹ Malignancy features of schwannoma on pathological examination are high mitotic index, the size of tumor, high values of Ki-67 index than 10%, and the presence of hemorrhage, necrosis and ulceration on macroscopic examination.¹⁰

The prognosis of benign schwannomas was reported as excellent with complete resection of tumor and additional treatments are not recommended.¹¹

Because of the schwannoma's rare incidence, appropriate treatment following surgery has not been well-established and long-term results are unknown.

Ethics

Informed Consent: Informed consent was taken from the patient.

Peer-review: Internally and externally peer reviewed.

Authorship Contributions

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

Conflict of Interest: There is no conflict of interest related to any person and/or institution.

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