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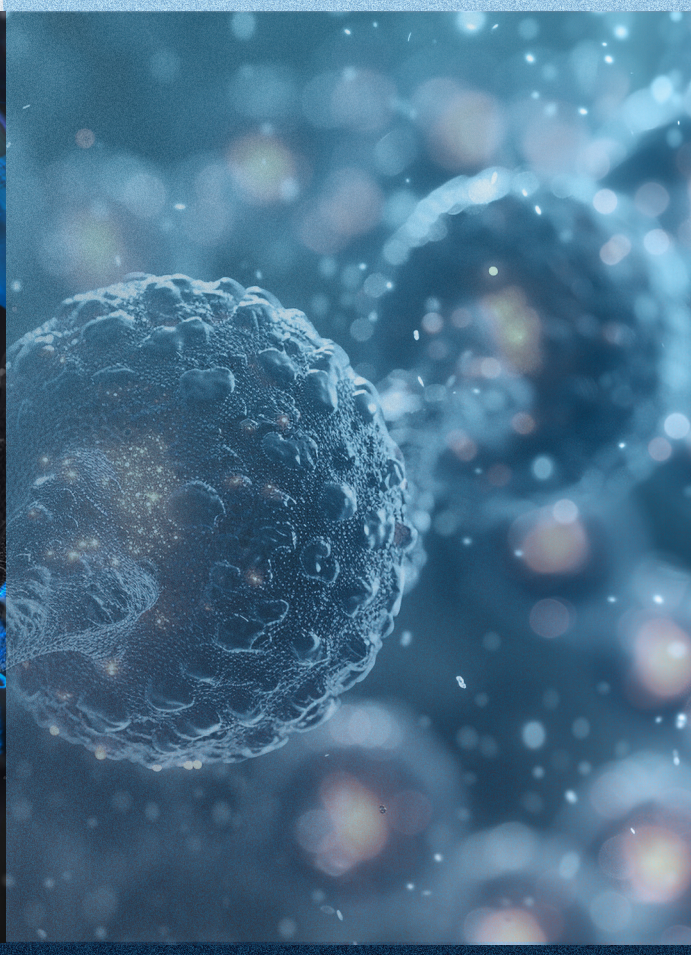

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REVIEW / DERLEME

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Limits of Nephron-sparing Strategies in Small Renal Masses: The Role of Imaging in Surgical Decision-making

Küçük Renal Kitlelerde Nefron Koruyucu Yaklaşımın Sınırları: Cerrahi Karar Sürecinde Görüntülemenin Yeri

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Abstract

Cross-sectional imaging has increased detection of small renal masses (≤4 cm), creating a need for evidence-based management strategies integrating imaging assessment. This review provides a comprehensive, imaging-based clinical framework for managing small renal masses through the R (radius: largest diameter of the mass in centimeters), E (exophytic versus endophytic growth), N (nearness to the collecting system or renal sinus), A (anterior versus posterior location relative to the hilar plane), and L (location relative to the polar lines: upper, middle, or lower pole) (RENAL) nephrometry score, Bosniak classification, and imaging modality comparison. This is a comprehensive narrative review of the contemporary literature on renal mass imaging, risk assessment using RENAL nephrometry and the Bosniak classification, imaging modality selection, and comparative outcomes of nephron-sparing strategies. The RENAL score stratifies masses into complexity categories that predict perioperative outcomes. Bosniak classification (categories I-V) characterizes cystic masses, with categories I-II showing negligible malignancy risk (<1%), categories III and IIF showing 10-50% malignancy risk, and categories IV-V showing high malignancy risk. Multimodal imaging [computed tomography (CT), magnetic resonance imaging (MRI), ultrasound, positron emission tomography-CT (PET-CT)] offers complementary strengths: multiphasic CT provides excellent spatial resolution for initial diagnosis; MRI offers superior soft-tissue contrast without radiation, making it ideal for long-term surveillance; ultrasound serves as a screening tool but has limited diagnostic reliability; PET-CT has limited utility for small, early-stage renal masses. Growth kinetics demonstrate heterogeneity, with 20-30% of masses remaining stable over 10+ years, median growth rates of 0.28 cm/year (range -0.10 to 2.0 cm/year), and 75-80% of masses exhibiting ≤0.5 cm/year growth. Active surveillance outcomes reveal a 25-40% progression to intervention over 3-5 years, with >99% cancer-specific survival. Thermal ablation achieves local recurrence-free survival of 95-98% at 1-2 years for cryoablation and 90-95% for radiofrequency ablation; however, shows recurrence rates of 5-15% and 8-20%, respectively. Partial nephrectomy is associated with a <1-2% local recurrence rate, 95% cancer-specific survival at 5 years, and 85-90% preservation of glomerular filtration rate. An integrated, imaging-based approach utilizing RENAL scoring, Bosniak classification, and quantified management outcomes provides a robust framework for evidence-based surgical decision-making in the management of small renal masses.

Keywords: Small renal mass, active surveillance, partial nephrectomy, thermal ablation, nephrometry score

Öz

Kesitsel görüntüleme yöntemlerinin yaygınlaşması küçük renal kitlelerin (≤4 cm) saptanma sıklığını artırmış olup, görüntüleme temelli, kanıta dayalı yönetim stratejilerine duyulan ihtiyacı gündeme getirmiştir. Bu derleme, küçük renal kitlelerin yönetiminde R (radius: kitlenin

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santimetre cinsinden en büyük çapı), E (ekzofitik veya endofitik büyüme), N (toplayıcı sisteme veya renal sinüse yakınlık), A (hiler düzleme göre anterior veya posterior yerleşim) ve L (polar hatlara göre yerleşim: üst, orta veya alt pol) parametrelerinden oluşan (RENAL) nefrometri skoru, Bosniak sınıflaması ve görüntüleme yöntemlerinin karşılaştırılması temelinde kapsamlı bir klinik çerçeve sunmaktadır. Çalışma; renal kitle görüntülemesi, RENAL nefrometrisi ve Bosniak sınıflaması kullanılarak risk değerlendirmesi, görüntüleme yöntemi seçimi ve nefron koruyucu stratejilerin karşılaştırmalı sonuçlarına ilişkin güncel literatürün kapsamlı bir narratif derlemesidir. RENAL skoru, kitleleri perioperatif sonuçları öngören kompleksite kategorilerine ayırmaktadır. Bosniak sınıflaması (kategori I-V) kistik kitleleri karakterize etmekte olup, kategori I-II ihmal edilebilir malignite riski (<%1), kategori III ve IIF %10-50 malignite riski, kategori IV-V ise yüksek malignite riski göstermektedir. Multimodal görüntüleme [bilgisayarlı tomografi (BT), manyetik rezonans görüntüleme (MRG), ultrasonografi, pozitron emisyon tomografisi-BT (PET-BT)] birbirini tamamlayan üstünlükler sunmaktadır: multifazik BT ilk tanıda mükemmel uzaysal çözünürlük sağlar; MRG radyasyon içermeden üstün yumuşak doku kontrastı sunarak uzun dönem takip için idealdir; ultrasonografi bir tarama aracı olarak kullanılabilir ancak tanısal güvenilirliği sınırlıdır; PET-BT'nin küçük, erken evre renal kitlelerde kullanım alanı sınırlıdır. Büyüme kinetiği belirgin heterojenlik göstermekte olup, kitlelerin %20-30'u 10 yıldan uzun takipte stabil kalmakta, medyan büyüme hızı yılda 0,28 cm (aralık: -0,10 ile 2,0 cm/yıl) olarak bildirilmekte ve kitlelerin %75-80'i yılda ≤0,5 cm büyüme göstermektedir. Aktif izlem sonuçları, 3-5 yıllık süreçte %25-40 oranında girişime geçiş olduğunu, ancak kansere özgü sağkalımın >%99 olduğunu ortaya koymaktadır. Termal ablasyon, 1-2 yıllık takipte kriyoablasyon için %95-98, radyofrekans ablasyon için %90-95 oranında lokal nükssüz sağkalım sağlamakta; ancak sırasıyla %5-15 ve %8-20 oranında nüks görülmektedir. Parsiyel nefrektomi, <%1-2 lokal nüks oranı, 5 yılda %95 kansere özgü sağkalım ve %85-90 glomerüler filtrasyon hızı korunması ile ilişkilidir. RENAL skorlaması, Bosniak sınıflaması ve nicel yönetim sonuçlarının bütünleştirildiği görüntüleme temelli bir yaklaşım, küçük renal kitlelerin yönetiminde kanıta dayalı cerrahi karar sürecinde güçlü bir çerçeve sunmaktadır.

Anahtar Kelimeler: Küçük renal kitle, aktif izlem, parsiyel nefrektomi, termal ablasyon, nefrometri skoru

Introduction

Renal cell carcinoma (RCC) is one of the most common types of cancer worldwide, and its incidence has been increasing in recent years (1). A significant reason for this increase is the rising incidence of incidental detection of small renal masses (≤4 cm) due to the widespread use of diagnostic methods such as ultrasonography, computed tomography (CT), and magnetic resonance imaging (MRI) (1,2). While these lesions were previously treated with radical nephrectomy, today nephron-sparing surgery is the standard approach in clinical T1a tumors (3). However, the possibility of nephron-sparing surgery does not necessarily indicate the need for surgical treatment. The main debate today is which patients should be kept under active surveillance, which patients can undergo thermal ablation, and in which cases partial nephrectomy is the preferred approach (3,4). It has been reported that a significant portion of small renal masses have a slow-progressing biological structure and that the rate of metastasis is low under active surveillance (5,6). The American Urological Association (AUA) guidelines recommend active surveillance, especially for renal masses smaller than 2 cm and selected Bosniak 3/4 lesions (3,4). However, not all small renal masses exhibit similar biological behavior. It has been reported that lesions showing rapid growth, heterogeneous contrast enhancement, or central location are more likely to have more aggressive pathology (7,8). An annual growth rate greater than 0.5 cm has been considered an indicator of progression risk in some studies (6,9). Therefore, in current clinical practice, it is recommended that the dynamic growth pattern and radiological risk indicators be evaluated together with the tumor diameter (7,9).

Literature Review Strategy

This is a comprehensive narrative review of the medical literature regarding the evaluation and management of small renal masses (≤4 cm). The review was conducted by searching PubMed/MEDLINE and by hand-selecting review articles, key studies, and guidelines published between 2005 and 2024. Search terms included combinations of: "small renal masses", "renal mass characterization", "renal mass imaging", "RENAL nephrometry score", "PADUA score", "Bosniak classification", "active surveillance", "renal mass ablation", and "partial nephrectomy".

The selection of articles was based on clinical relevance, methodological quality, and contribution to understanding imaging-based assessment and management of small renal masses. This interpretive synthesis approach allows for a comprehensive review of evidence from diverse sources including prospective series, retrospective cohorts, meta-analyses, systematic reviews, and professional society guidelines (AUA) (3,4), European Association of Urology (10).

The goal of this narrative review is to provide clinicians with an integrated, evidence-informed framework for imaging-guided surgical decision-making in the management of incidentally detected small renal masses by synthesizing the current literature on imaging modalities, complexity scoring systems, growth kinetics, management outcomes, and factors influencing treatment selection.

To standardize the assessment of renal mass complexity and improve treatment planning, two anatomical scoring systems have gained widespread clinical and academic use: the RENAL

nephrometry score and the preoperative aspects and dimensions used for an anatomical (PADUA) classification. Both systems were developed within a similar time frame to formalize what had previously been a largely subjective, size-based assessment of renal tumor complexity, and are now routinely used to inform the choice among partial nephrectomy, thermal ablation, and active surveillance. The R.E.N.A.L. acronym denotes five anatomical parameters that collectively characterize the spatial relationship of a renal mass to critical structures: R (radius: largest diameter of the mass in centimeters), E (exophytic versus endophytic growth), N (nearness to the collecting system or renal sinus), A (anterior versus posterior location relative to the hilar plane), and L (location relative to the polar lines: upper, middle, or lower pole). Each parameter is assigned a numerical score, and the sum yields a total RENAL score ranging from 4 to 14 points (11,12).

The PADUA classification was developed contemporaneously as an alternative anatomical scoring system and was originally validated in a prospective cohort of patients undergoing open nephron-sparing surgery. PADUA scores nine anatomical features-longitudinal (polar) location, exophytic rate, renal rim location, relationship to the renal sinus, relationship to the urinary collecting system, anterior or posterior face, and tumor size-yielding a total score that ranges from 6 to 14 points and stratifies masses into low (6-7), intermediate (8-9), and high (≥10) complexity groups (13). Although RENAL and PADUA were derived independently and weight certain anatomical features somewhat differently (PADUA places additional emphasis on the renal rim and sinus relationship, while RENAL scores exophytic/endophytic growth and polar location as separate discrete parameters), the two systems have shown good correlation with one another and largely overlapping ability to predict perioperative complications and surgical complexity in comparative validation studies (12,13). In practice, the choice between the two scoring systems often reflects institutional or regional preference: RENAL is more widely used in North America, while PADUA has seen broader adoption in Europe, rather than reflecting a clear superiority of one system over the other. Both are considered acceptable by contemporary guidelines for preoperative anatomical risk stratification. The RENAL nephrometry score components and scoring system are detailed in Table 1, which also presents the corresponding PADUA parameters and scoring for comparison.

Clinical Impact of Anatomical Complexity Scoring on Surgical Difficulty and Treatment Selection

Both the RENAL and PADUA scores stratify renal masses into three complexity categories-low, intermediate, and high-and this stratification has direct, well-documented consequences for surgical difficulty, modality selection, and expected oncological outcomes. Low-complexity masses (RENAL 4-6; PADUA 6-7) are generally smaller, more peripheral, and distant from vital structures, making them amenable to multiple treatment modalities, including partial nephrectomy, thermal ablation, or active surveillance. In this group, partial nephrectomy is typically associated with shorter operative times, lower estimated blood loss, and the lowest complication rates, whereas thermal ablation achieves local recurrence rates as low as 2-5%. Intermediate-complexity masses (RENAL 7-9; PADUA 8-9) pose greater anatomical challenges, including closer proximity to the collecting system and partial endophytic growth, and are associated with measurably longer operative and ischemia times during partial nephrectomy as well as higher local recurrence after ablation (approximately 5-10%). Both partial nephrectomy and thermal ablation remain reasonable options in this group, and the choice is often individualized based on patient comorbidity and surgeon experience. High-complexity masses (RENAL 10-14; PADUA ≥10) exhibit features such as large size, central location, intimate association with the renal hilum or collecting system,

Table 1. RENAL nephrometry score and PADUA classification: components and scoring, by anatomical domain

Anatomical domain	RENAL score	PADUA score
Tumor size	R: ≤1 cm=1 | 1.1-2 cm=2 | 2.1-3 cm=3 | >3 cm=4	≤4 cm=1 | 4.1-7 cm=2 | >7 cm=3
Exophytic/endophytic growth	E: ≥50% exophytic=1 | <50% exophytic=2	≥50% exophytic=1 | <50% exophytic=2 | entirely endophytic=3
Relation to renal sinus/ collecting system	N: ≥7 mm from sinus=1 | 4-6 mm=2 | <4 mm (touching)=3	No sinus/collecting-system involvement=1 | involved=2
Anterior vs. posterior face	A: Entirely anterior/posterior=1 | crosses hilar plane=2 (not summed into total)	Recorded as anterior, posterior, or indeterminate (descriptive only, not scored)
Polar (longitudinal) location	L: Entirely above/below polar line=1 | crosses polar line=2 | hilar region=3	Entirely above/below polar line=1 | crosses polar line=2 | entirely between polar lines (mid-pole)=3
Total score range	4-14 points (a recorded but not added to total)	6-14 points
Complexity categories	Low 4-6 | intermediate 7-9 | high 10-14	Low 6-7 | intermediate 8-9 | high ≥10

RENAL: R (radius: largest diameter of the mass in centimeters), E (exophytic versus endophytic growth), N (nearness to the collecting system or renal sinus), A (anterior versus posterior location relative to the hilar plane), and L (location relative to the polar lines: upper, middle, or lower pole), PADUA: Preoperative aspects and dimensions used for an anatomical

or anterior location that may compromise vascular inflow or urinary drainage during nephron-sparing approaches; in this group, partial nephrectomy carries the highest rates of prolonged warm ischemia time, urine leak, and blood transfusion, while thermal ablation carries the highest reported local recurrence rates (10-15%) due to the technical difficulty of achieving a complete ablation margin near the collecting system and adjacent vasculature, which act as a heat sink that limits thermal spread. Consequently, high-complexity masses are generally best managed by partial nephrectomy when surgical intervention is indicated, as this approach maximizes the likelihood of achieving negative surgical margins while preserving renal function and avoiding the disproportionately high ablation failure rate seen in this group (12,13). Risk stratification according to RENAL and PADUA complexity categories, including their respective impact on operative difficulty and local recurrence after ablation, is presented in Table 2.

Extensive literature demonstrates that both the RENAL and PADUA scores predict perioperative outcomes and treatment efficacy across multiple management modalities. In partial nephrectomy cohorts, higher scores on either scoring system correlate with longer operative times, greater estimated blood loss, longer warm ischemia times, and increased perioperative complication rates, thereby helping surgeons anticipate technical difficulty and prepare appropriately-for example, by planning for off-clamp or early-unclamping techniques in lower-complexity cases or by allocating additional operative time and ensuring blood product availability for higher-complexity resections. Similarly, both scores have proven prognostic value in ablation series: intermediate- and high-complexity masses treated with thermal ablation demonstrate consistently higher local recurrence rates than low-complexity masses, with some series reporting 2-5% recurrence in low-complexity masses versus 10-15% in high-complexity masses, which is an association strong enough that many centers use a complexity threshold (for example, a RENAL score above 9-10, or a substantial endophytic and hilar component) as a relative contraindication to ablation in favor of partial nephrectomy. For patients selected for active surveillance, complexity scoring independently predicts progression-free survival and interval growth rates, with higher-complexity masses exhibiting more aggressive growth behavior and shorter time to progression. These associations underscore the importance of incorporating anatomical complexity scoring into pretreatment risk stratification, modality selection, and surveillance planning (12,14).

Given these predictive associations, both the RENAL and PADUA scores have become integral to shared decision-making regarding renal mass management. When counseling patients with newly detected small renal masses, clinicians can provide more accurate information about likely technical challenges, anticipated perioperative risks (including the probability of requiring conversion to radical nephrectomy or experiencing a major complication), and predicted local recurrence risk with ablation based on anatomical complexity scoring. This information facilitates patients' informed choice among treatment modalities, including active surveillance. Additionally, the validation of both scoring systems in multiple international cohorts and their ease of calculation (requiring only standard cross-sectional imaging) make them practical tools for standardizing communication between urologists, radiologists, interventional radiologists, and surgeons regarding mass complexity and treatment recommendations (9,12).

Bosniak Classification System: Characterizing Cystic Renal Masses

For cystic renal masses, the Bosniak classification system has become the standard imaging-based framework for distinguishing benign lesions from those requiring intervention. Developed by Morton Bosniak in the 1980s and subsequently refined, this classification system stratifies cystic masses into five categories based on imaging characteristics observed on contrast-enhanced CT or MRI, including the presence and characteristics of septa and calcifications, cyst wall enhancement, and enhancing solid components. Because benign cysts and malignant cystic neoplasms can have overlapping imaging features, the Bosniak system provides a standardized approach to risk stratification that guides clinical decision-making regarding surveillance versus intervention. Unlike simple renal cysts (Bosniak I), which

Table 2. RENAL and PADUA complexity categories: risk stratification and management implications

RENAL score	PADUA score	Complexity	Management and outcomes
4-6	6-7	Low	Small/peripheral; far from collecting system; all modalities suitable (PN, ablation, AS); lowest morbidity and shortest operative/ischemia time; 2-5% local recurrence with ablation
7-9	8-9	Intermediate	Medium size; mixed location; both PN and ablation appropriate; moderate complexity; longer operative/ischemia time; 5-10% local recurrence with ablation; consider patient factors
10-14	≥10	High	Large/central; intimate hilar association; PN preferred when indicated; highest complexity and morbidity; highest risk of prolonged ischemia, urine leak, and transfusion with PN; 10-15% local recurrence with ablation due to heat-sink effect near hilum

RENAL: R (radius: largest diameter of the mass in centimeters), E (exophytic versus endophytic growth), N (nearness to the collecting system or renal sinus), A (anterior versus posterior location relative to the hilar plane), and L (location relative to the polar lines: upper, middle, or lower pole), PADUA: Preoperative aspects and dimensions used for an anatomical, PN: Partial nephrectomy, AS: Active surveillance

are universally benign and require no follow-up, intermediate-risk cysts (Bosniak IIF and III) present particular diagnostic challenges due to their variable malignancy risk and incomplete natural history data, necessitating individualized management strategies (15). The 2019 revision of the classification further standardized the definitions of septal thickness, wall thickening, and enhancement, and explicitly extended the system's use to MRI in addition to CT, improving reproducibility across imaging platforms and between observers (15). The Bosniak classification system, including imaging features and malignancy risk for each category, is shown in Table 3.

The Bosniak system consists of five categories, each with distinct imaging features and associated risks of malignancy. Bosniak I lesions are simple, thin-walled cysts with no septa, calcifications, or enhancement; they are universally benign with negligible malignancy risk (<1%) and therefore require no imaging follow-up once diagnosed. Bosniak II lesions are minimally complicated cysts containing thin septa (<1 mm), fine calcifications, or homogeneous, hyperdense (non-enhancing) content; these lesions remain benign, with malignancy risk <2%, and generally require no follow-up. Bosniak IIF ("F" designating "follow-up") was introduced to better classify intermediate-risk lesions with features more complex than Bosniak II but not definitively concerning for malignancy. These include cysts with more complex internal architecture, thickened septa (typically <3 mm), or minimal, thin, and smooth enhancement of a septum or wall. Malignancy risk ranges from 5-10%, and these lesions typically warrant short-term imaging surveillance at 3 and 6 months, then annually for 5 years to assess for changes suggesting progression. Bosniak III lesions are cystic masses with imaging characteristics concerning for, but not definitively diagnostic of, malignancy, including thick or irregular septa (>3 mm), thick or irregular calcifications, or measurable enhancement of a thickened wall or septum. These lesions carry a malignancy risk of approximately 20-55% and generally warrant intervention (partial or radical nephrectomy) or close surveillance, depending on clinical circumstances, patient age, comorbidities, and patient preferences. Finally, Bosniak IV lesions represent overtly malignant-appearing masses with gross enhancement and/or large enhancing solid components, whereas Bosniak V lesions are completely solid enhancing lesions arising within a cystic lesion; these categories carry malignancy rates exceeding 85-90% and typically warrant surgical intervention with partial or radical nephrectomy (15).

Clinical Decision-making Implications of Bosniak Categorization

Beyond its descriptive function, Bosniak categorization operates as a direct decision node in clinical practice, and the intermediate-risk categories (Bosniak IIF and III) represent the areas of greatest management complexity. For Bosniak IIF lesions, the 5-10% malignancy risk is generally considered low enough to justify a defined imaging surveillance protocol rather than intervention, provided the patient is able to adhere to follow-up. Because the natural history of individual IIF lesions is heterogeneous, with some remaining stable over many years while others slowly progress to a higher category, any interval increase in septal thickness, new nodular enhancement, or development of a discrete enhancing component during surveillance should prompt re-classification and reconsideration of intervention. Bosniak III lesions pose a more difficult management decision: since the reported malignancy risk (20-55%) means that roughly half of these lesions are ultimately benign or low-grade malignant, yet the diagnostic uncertainty is too substantial to recommend surveillance uniformly. In practice, the decision is individualized: in younger, fit patients with long life expectancy, upfront partial nephrectomy is often favored, because it provides definitive

Table 3. Bosniak classification system: imaging features, malignancy risk, and clinical decision-making

Category	Imaging features	Malignancy risk (%)	Follow-up/ management	Key clinical decision point
I (benign)	Simple, thin-walled; no septa/ calcifications; no enhancement	<1	No follow-up	Diagnosis is final; no further imaging or intervention needed
II (benign)	Thin septa (<1 mm); fine calcifications; homogeneous hyperdense content	<2	No follow-up	Considered definitively benign; reassurance only
IIF (follow-up)	Complex architecture; thickened septa (<3 mm); minimal, smooth septal/wall enhancement	5-10	Surveillance: 3 mo, 6 mo, then annually x 5 yrs	Any interval progression (new nodularity, thicker septa, new enhancement) triggers re-classification and intervention
III (indeterminate)	Thick/irregular septa (>3 mm); thick/ irregular calcifications; measurable wall or septal enhancement	20-55	Intervention (PN preferred) or surveillance	Decision individualized by age, comorbidity, and life expectancy; biopsy has limited yield
IV-V (malignant)	Enhancing solid components/ independent enhancing soft-tissue mass within a cyst	85-100	Intervention: PN or RN	PN vs. RN determined by size, location, and RENAL score rather than Bosniak category

PN: Partial nephrectomy, RN: Radical nephrectomy, RENAL: R (radius: largest diameter of the mass in centimeters), E (exophytic versus endophytic growth), N (nearness to the collecting system or renal sinus), A (anterior versus posterior location relative to the hilar plane), and L (location relative to the polar lines: upper, middle, or lower pole)

histology, preserves renal parenchyma, and is associated with low morbidity when performed for a T1 lesion; in older patients, in those with significant comorbidity, in or those who place a high value on avoiding surgery, active surveillance with short-interval imaging is a reasonable alternative, accepting a small but real risk of delayed diagnosis of malignancy. Renal mass biopsy has a limited role in management decisions because sampling septa or mural nodules has a lower diagnostic yield than sampling solid masses; therefore imaging-based risk stratification, rather than histology, generally remains the primary basis for management of Bosniak III lesions. For Bosniak IV and V lesions, the high malignancy risk makes intervention the default recommendation in nearly all surgical candidates, with the choice between partial and radical nephrectomy governed principally by tumor size, location, and RENAL score complexity rather than by the Bosniak category itself.

The integration of Bosniak classification into the comprehensive management algorithm for small renal masses reflects recognition that many of these lesions are cystic or partially cystic rather than purely solid. The Bosniak system provides risk stratification specifically for cystic masses and complements the RENAL nephrometry score (which applies primarily to solid masses) in guiding clinical decision-making. For patients with solid renal masses, RENAL score assessment determines management recommendations; for those with cystic or partially cystic masses, Bosniak classification is applied. In cases where lesions have both solid and cystic components (Bosniak IV or complex RENAL score patterns), both systems may provide complementary information, and the higher-risk classification of the two should generally guide the management decision. The application of standardized classification systems-RENAL for solid masses and Bosniak for cystic masses-improves communication among physicians, provides prognostic information regarding malignancy risk and the natural history, and facilitates shared decision-making with patients about surveillance versus intervention (16).

Imaging Modalities in Renal Mass Characterization and Surveillance

Accurate characterization and surveillance of small renal masses depend on high-quality cross-sectional imaging. While multiple imaging modalities are available for renal mass assessment, each technique has distinct advantages, limitations, and optimal clinical applications. The choice of imaging modality should consider diagnostic accuracy, radiation exposure, cost, patient factors (age, renal function, contrast allergy), and the clinical context (initial characterization versus surveillance). Beyond simple lesion detection, the imaging protocol should also be adequate to characterize two features with direct clinical consequences: the enhancement pattern of the mass and its anatomical relationship to the collecting system and the renal hilum. Understanding the strengths and weaknesses of each imaging approach for capturing these features is essential for developing personalized, evidence-based surveillance and treatment strategies for patients with small renal masses. Comparative characteristics and optimal applications of imaging modalities are presented in Table 4.

Multidetector CT with contrast enhancement remains the most widely used imaging modality for renal mass detection and characterization (17). Multiphasic CT imaging, including non-enhanced, arterial, corticomedullary, and delayed-phase acquisitions, optimizes characterization of renal masses by demonstrating enhancement patterns suggestive of malignancy. Properly timed arterial phase imaging (approximately 25-35 seconds after intravenous contrast injection) is critical for detecting arterial enhancement, which is the hallmark of RCC, and for characterizing that enhancement as homogeneous or heterogeneous. Heterogeneous enhancement-an irregular, patchy pattern rather than uniform contrast uptake-reflects underlying intratumoral necrosis, hemorrhage, and disorganized

Table 4. Imaging modalities in renal mass evaluation: comparison of characteristics and decision-relevant features

Modality	Spatial resolution and speed	Soft tissue contrast	Radiation	Assesses enhancement heterogeneity?	Assesses central/ hilar location?
CT (multiphasic)	Excellent; fast (30-60 sec)	Good-arterial phase enhancement clear	Yes (~50-100 mSv per scan)	Yes-primary modality	Yes-excellent with MPR
MRI (dynamic+DWI)	Good; moderate (20+ min)	Excellent-superior soft-tissue detail; DWI/ADC useful	No (0 mSv)	Yes-often more conspicuous than CT	Yes-excellent, especially for sinus fat
Ultrasound	Variable, operator-dependent; fast (5-10 min)	Fair-limited for small masses	No (0 mSv)	No-unreliable	No-unreliable
PET-CT (FDG-PET)	Moderate; slower (30-60 min)	Poor for renal masses (low FDG uptake in small RCC)	Yes (~5-10 mSv)	Limited-not routinely used for this purpose	Limited-not routinely used for this purpose

CT: Computed tomography, MPR: Multiplanar reconstruction, MRI: Magnetic resonance imaging, DWI: Diffusion-weighted imaging, ADC: Apparent diffusion coefficient, PET: Positron emission tomography, FDG: Fluorodeoxyglucose, RCC: Renal cell carcinoma

neovascularity and is disproportionately observed in high-grade clear cell RCC and tumors with sarcomatoid dedifferentiation; recognizing this pattern on multiphasic CT should lower the threshold for active treatment rather than surveillance, even in a mass that would otherwise be considered low-risk by size alone. Thin-slice acquisition with coronal and sagittal multiplanar reconstruction also allows precise assessment of the tumor's relationship to the collecting system and renal sinus fat, which is essential for RENAL nephrometry scoring and surgical planning, since centrally located or endophytic tumors carry a higher likelihood of collecting-system invasion and greater technical complexity during partial nephrectomy. The primary advantages of CT include high spatial resolution, rapid acquisition time (allowing imaging during optimal phases), excellent reproducibility of measurements, and widespread availability. CT has proven effective for both initial diagnosis and surveillance of small renal masses, with high sensitivity for detecting size changes. However, CT imaging uses ionizing radiation, which is a significant consideration for younger patients who may require decades of surveillance. Additionally, CT has limitations in characterizing indeterminate cystic masses and in imaging patients with an iodinated contrast allergy or severe renal insufficiency. The cumulative radiation exposure from serial surveillance CT scans is an important consideration when planning long-term follow-up protocols (18).

MRI offers superior soft-tissue contrast resolution compared to CT and avoids ionizing radiation, making it particularly valuable for surveillance of patients requiring long-term imaging follow-up (17). Dynamic contrast-enhanced MRI with appropriate timing of arterial phase acquisition effectively demonstrates renal mass enhancement patterns and improves characterization of both solid and cystic lesions. Its superior contrast resolution can make subtle heterogeneity within a mass, including small areas of necrosis or hemorrhage, more conspicuous than on CT and thus can refine the assessment of aggressiveness in equivocal cases. The addition of diffusion-weighted imaging with apparent diffusion coefficient measurements further enhances diagnostic capability by detecting restricted diffusion, which is more common in malignant than in benign lesions and correlates with higher tumor cellularity. MRI is also well suited to delineating the relationship of a centrally located tumor to the renal sinus fat and collecting system, which can assist preoperative planning when this distinction is equivocal on CT. MRI is particularly useful for patients with iodinated contrast allergy or severe renal insufficiency (avoiding gadolinium-based contrast in patients with very low glomerular filtration rate), and for characterization of complex cystic masses. However, MRI has several disadvantages: longer acquisition times, which increase susceptibility to artifacts from respiratory and patient motion; higher cost compared with CT; contraindications in patients with metallic implants; and concerns regarding nephrogenic systemic fibrosis associated with gadolinium-based contrast agents (though this risk has been substantially mitigated by newer formulations and restrictive usage protocols). Measurement reproducibility with MRI may be slightly inferior to that of CT, although recent advances in imaging sequences have narrowed this gap. For long-term surveillance strategies, MRI offers a compelling alternative to repeated CT scans due to lack of radiation exposure, though the longer acquisition times and higher cost may limit routine use (17).

Renal ultrasound is highly accessible, does not expose patients to ionizing radiation, does not require intravenous contrast, and has no absolute contraindications, making it an attractive option for resource-limited settings and initial screening of incidental renal lesions. However, ultrasound has significant limitations in the evaluation of renal masses: image quality is highly operator- and patient-dependent (obesity and bowel gas substantially impair visualization), inter-observer variability is higher than with CT or MRI, real-time characterization of small masses is unreliable, and measurement accuracy for size assessment is inferior to that of cross-sectional imaging. Ultrasound is also unable to reliably characterize enhancement heterogeneity or delineate the precise relationship of a mass to the collecting system, limiting its usefulness for risk-stratification decisions discussed above. As a result, ultrasound is most appropriate as an initial screening tool for patients at risk of renal masses or for follow-up of clearly benign simple cysts in patients with favorable acoustic windows. Ultrasound is generally not recommended as the primary modality for characterizing solid renal masses nor as a routine surveillance tool for small renal masses, because the accuracy and reproducibility of ultrasound are insufficient to support clinical decision-making about intervention versus observation.

Fluorodeoxyglucose-positron emission tomography (FDG-PET) has limited utility in the initial evaluation of small renal masses. Most small RCCs, particularly low-grade tumors, demonstrate low metabolic activity and minimal FDG uptake, resulting in poor sensitivity for malignancy detection. Consequently, PET-CT is neither recommended as a first-line characterization tool for incidentally detected renal masses nor routinely used in surveillance protocols for small renal masses. PET-CT may have a limited role in the evaluation of advanced RCC with suspected metastatic disease, but this is outside the scope of the management of small renal masses.

Imaging-based Decision-making: Enhancement Pattern and Tumor Location

Two imaging-derived features deserve particular emphasis because they carry direct, actionable implications for

treatment selection, independent of tumor size. The first is the enhancement pattern of the mass. Homogeneous enhancement is more typical of lower-grade, more indolent tumors, whereas heterogeneous enhancement-irregular, patchy, or non-uniform contrast uptake on multiphasic CT or MRI-reflects intratumoral necrosis, hemorrhage, and irregular neovascularity, and is disproportionately observed in high-grade clear cell RCC and in papillary type 2 tumors. Because this pattern has been correlated with higher nuclear grade and adverse pathological features in retrospective series, its presence should lower the threshold for active intervention rather than surveillance, even in a mass that would otherwise be considered low risk on the basis of size alone. The second feature is the tumor location relative to the renal sinus and the collecting system. Masses that are endophytic, abut the renal sinus fat, or cross the hilar plane are more frequently associated with higher-grade histology and a greater likelihood of occult invasion of the collecting system or perinephric fat. From a technical standpoint, central location increases operative complexity for partial nephrectomy, prolonging ischemia time and elevating the risk of urinary leak and bleeding. It also increases the risk of incomplete ablation and residual disease during thermal ablation, since the collecting system and adjacent major vessels act as heat sinks that limit thermal spread. Consequently, centrally located masses generally warrant either upfront partial nephrectomy, when surgically feasible, or closer surveillance intervals if active surveillance is pursued, rather than management according to the same algorithm applied to peripheral, exophytic lesions of comparable size. Because neither enhancement heterogeneity nor central location is reliably assessed by ultrasound, and both are only partially captured by PET-CT, multiphasic CT or dynamic MRI with multiplanar reconstruction should be regarded as the minimum adequate imaging standard whenever these features are likely to influence the treatment decision (17,18).

In clinical practice, CT and MRI are the primary modalities for characterizing small renal masses and performing surveillance. For initial diagnosis and characterization of a newly detected renal mass, multiphasic CT with proper arterial phase timing remains the most practical, cost-effective, and widely available first-line option. CT effectively characterizes most solid masses and provides accurate size measurements for baseline assessment. For patients selected for active surveillance, the choice between CT and MRI should be individualized based on patient factors, including age, renal function, contrast allergy, and anticipated duration of follow-up. Younger patients with long life expectancies may benefit from MRI-based surveillance protocols to minimize cumulative radiation exposure. Conversely, older patients or those with contraindications to MRI may continue with periodic CT imaging. A complementary approach-alternating between CT and MRI at different surveillance intervals-may optimize diagnostic accuracy while minimizing cumulative radiation exposure. Ultrasound may serve a supplementary role in selected patients with optimal acoustic windows for confirming known benign simple cysts, but it should not replace cross-sectional imaging for definitive diagnosis or routine surveillance of solid masses. The development of personalized imaging protocols that account for individual patient characteristics, mass features (size, growth rate, enhancement pattern, and relationship to the collecting system), and clinical context is essential for optimizing outcomes and minimizing unnecessary imaging and patient harm (18). The optimal clinical use of each modality is summarized in Table 5.

Natural Course

The majority of small renal masses consist of low-grade tumors with slow progression (19). In patients followed under active surveillance, the average annual tumor growth rate generally ranges from 0.1-0.3 cm (20). Delayed intervention and surveillance for small renal masses (DISSRM) data have shown that active surveillance is a safe approach in appropriately selected patients and that metastasis rates are low (20). In a natural course analysis conducted by Crispen et al. (5), it was revealed that the vast majority of small renal masses show a slow growth pattern and that the risk of early systemic progression is low. In a multicenter active surveillance series reported by Jewett et al. (6), it was stated that the progression criteria were mostly based on the growth rate and that the metastatic progression rates were below 2%. However, heterogeneous biological behavior should not be ignored; some small renal masses may show aggressive growth characteristics even in the early stages.

Table 5. Optimal clinical use by modality

Modality	Optimal use
CT (multiphasic)	Initial characterization; RENAL scoring and surgical planning; size measurement; rapid surveillance
MRI (dynamic+DWI)	Long-term surveillance; contrast allergy; cystic mass characterization; severe renal impairment; equivocal central/hilar relationship on CT
Ultrasound	Screening tool; confirmation of simple cysts; accessible/low-resource settings
PET-CT (FDG-PET)	Staging of advanced/metastatic RCC only-not for initial characterization or surveillance

RENAL: R (radius: largest diameter of the mass in centimeters), E (exophytic versus endophytic growth), N (nearness to the collecting system or renal sinus), A (anterior versus posterior location relative to the hilar plane), and L (location relative to the polar lines: upper, middle, or lower pole), CT: Computed tomography, MRI: Magnetic resonance imaging, DWI: Diffusion-weighted imaging, PET: Positron emission tomography, FDG: Fluorodeoxyglucose, RCC: Renal cell carcinoma

Therefore, instead of making intervention decisions based solely on the tumor diameter at the time of initial detection, it is recommended to evaluate the growth dynamics over time and radiological features together (5,6).

The growth kinetics of small renal masses under active observation have been extensively studied and demonstrate substantial heterogeneity. Large prospective series indicate that approximately 20-30% of small renal masses do not demonstrate radiographic growth over ≥10 years of follow-up, suggesting truly benign behavior or extremely slow progression. In contrast, other tumors exhibit more rapid growth trajectories, with growth rates ranging from 0.2 to 0.8 cm per year on average, though individual variability is substantial (21). Crispen et al. (5), documented that among 769 patients with untreated renal masses followed prospectively, the median tumor growth rate was approximately 0.28 cm per year (range, -0.10 to 2.0 cm/year). Similarly, the DISSRM registry reported median growth rates of 0.13 cm annually for masses <2 cm at baseline, with approximately 75-80% of masses exhibiting growth rates ≤0.5 cm per year (9). Importantly, growth rate itself does not reliably predict malignancy risk or oncologic outcome; many benign renal masses and low-grade RCCs exhibit slow but persistent growth, while some tumors remain entirely stable. Age at presentation and baseline tumor size represent the strongest predictors of future growth; younger patients and those with larger baseline masses more frequently demonstrate radiographic progression (20,21).

The Role of Renal Mass Biopsy in Treatment Decision-making

Percutaneous renal mass biopsy has an increasingly recognized role in the pretreatment evaluation of small renal masses, particularly when the result would meaningfully change management (22). The strongest indications are found in two clinical scenarios: patients being considered for active surveillance, in whom histological confirmation of a low-grade or indolent tumor [or identification of a benign entity such as oncocytoma or fat-poor angiomyolipoma (AML)] provides reassurance and strengthens adherence to a non-surgical strategy; and patients being considered for thermal ablation, in whom pretreatment biopsy is regarded as standard practice because the ablated tissue is frequently non-diagnostic afterward due to thermal artifact, making pre-procedural histological confirmation the only reliable opportunity to establish tumor type and grade (3,4,22). Additional indications include indeterminate imaging phenotypes, a solitary kidney or borderline renal function where the treatment threshold is higher, suspected metastasis from a non-renal primary, and multifocal or hereditary renal tumor syndromes where histology may alter the surgical or surveillance strategy (22).

Contemporary series report that percutaneous core biopsy achieves diagnostic accuracy of approximately 90-95% for distinguishing malignant from benign renal masses, with a non-diagnostic rate of roughly 10-20% that is highest for small (<1 cm), cystic, or technically difficult-to-access lesions, and that typically prompts repeat biopsy rather than default to intervention (23). Important limitations temper enthusiasm for routine biopsy. Sampling error can lead to grade underestimation in heterogeneous tumors, since a core sample may not capture the highest-grade component of the mass (23). Biopsy also has recognized difficulty in reliably distinguishing oncocytoma from the eosinophilic variant of chromophobe RCC or from hybrid oncocytic tumors in a meaningful minority of cases, which limits its ability to fully substitute for surgical pathology in that specific differential (24). Bosniak cystic lesions are generally poor candidates for biopsy, since sampling of septa or wall components has low diagnostic yield and imaging-based classification remains the primary tool for risk stratification in these masses (15,16). Complication rates are low, with clinically significant bleeding occurring in fewer than 5% of cases and pneumothorax being rare for lower pole lesions (23); needle-tract tumor seeding, though historically a concern, is now recognized to be exceedingly rare (well under 1%) with contemporary coaxial biopsy technique (25).

In practical terms, renal mass biopsy should be integrated into the decision-making algorithm rather than treated as an optional adjunct: it is most valuable when its result will change the recommended management, it has the greatest impact in younger patients steered toward active surveillance and in any patient considered for ablation, and it should be interpreted alongside, rather than in place of, imaging risk features such as RENAL score complexity, enhancement pattern, and Bosniak category when formulating a final treatment recommendation (12,15,22). This practical value has been demonstrated directly. In a multidisciplinary conference on small renal masses, incorporating input from radiology, pathology, and urology, the introduction of routine biopsy discussion was associated with a measurable increase in the selection of active surveillance rather than upfront intervention, confirming that biopsy results meaningfully change real-world management rather than serving as a purely academic exercise (26).

Radiological Differentiation of Benign Mimickers: AML and Oncocytoma

An estimated 20-30% of small renal masses selected for surgical resection ultimately prove to be benign on final pathology, a proportion that increases as tumor size decreases (24). Recognizing the two most common benign mimickers-AML and oncocytoma-on imaging alone is therefore a central and frequently underemphasized component of avoiding

unnecessary surgery, since a confident, non-invasive diagnosis can support surveillance without biopsy or resection, while a genuinely indeterminate appearance should still prompt the biopsy or surveillance pathways discussed above rather than default extirpative surgery.

Classic AML contains macroscopic fat and is one of the few renal masses that can be diagnosed with near-certainty on imaging alone. On unenhanced CT, regions within the mass measuring approximately -10 to -20 Hounsfield units are considered diagnostic of macroscopic fat and, in the absence of calcification or a predominantly solid enhancing component, essentially pathognomonic for AML, obviating the need for biopsy or intervention. On MRI, the same fat content is confirmed by loss of signal on fat-suppressed sequences and on the opposed-phase images of chemical-shift imaging, which is particularly useful when CT findings are equivocal or when radiation exposure should be minimized (8,18). A minority of AMLs (approximately 5%) are fat-poor and lack visible macroscopic fat on either imaging modality, closely mimicking clear cell RCC. features such as marked homogeneity, a relatively higher attenuation on unenhanced CT than typical RCC, and a well-defined angular interface with adjacent renal parenchyma can raise suspicion for fat-poor AML, but none of these features is sufficiently sensitive or specific to reliably exclude malignancy, and such lesions generally still warrant biopsy or continued surveillance with close imaging follow-up rather than a confident benign diagnosis on imaging alone (7,18).

Oncocytoma differentiation is comparatively difficult, since no imaging feature reliably distinguishes it from RCC, particularly from the eosinophilic variant of chromophobe RCC, with which it shares histogenetic features. The classically described central stellate scar and segmental enhancement inversion pattern (early peripheral enhancement with subsequent central fill-in) are more common in oncocytoma than in RCC, but both signs have limited sensitivity, may be absent in a substantial proportion of oncocytomas, and can occasionally be seen in malignant tumors; therefore, neither should be used in isolation to defer treatment. A more quantitative approach-the peak early-phase enhancement ratio measured on multiphasic CT or MRI-has shown considerably better discriminative performance, reliably separating oncocytoma and indolent hybrid oncocytic tumors from chromophobe RCC, particularly when combined with clinical risk factors and CD117 immunohistochemistry on biopsy material (24). Even so, imaging alone cannot yet definitively exclude malignancy in an oncocytic-appearing mass, which is why oncocytoma remains, in practice, principally a biopsy-supported rather than a purely radiological diagnosis (24).

The clinical implications of these two entities differ. When imaging demonstrates unequivocal macroscopic fat consistent with classic AML, active surveillance without biopsy or intervention is appropriate, and surgery should be reserved for lesions that cause symptomatic hemorrhage or that exceed a size threshold (typically around 4 cm) associated with the risk of spontaneous bleeding. When a mass is fat-poor or shows radiological features suggestive of, but not diagnostic for, oncocytoma, the appropriate next step is the biopsy-integrated decision pathway described above rather than proceeding directly to partial or radical nephrectomy, since a meaningful minority of these lesions will prove benign and a substantial proportion of the remainder will be low-grade, favorably behaving tumors for which surveillance or a nephron-sparing approach remains appropriate (8,24).

Active Surveillance

Active surveillance is considered a safe option in the management of small renal masses, especially in patients with comorbidities, advanced age, or those at surgical risk (27). A study reported from Türkiye also emphasized that active surveillance is a safe and rational approach in a significant portion of small renal masses in the advanced age group (≥75 years), and that the treatment decision should be made not only based on tumor size but also on comorbidities and renal function reserve (28). Contemporary guideline statements and systematic reviews of published surveillance protocols support active surveillance as an appropriate initial strategy for solid renal masses smaller than 2 cm and for selected cystic lesions, particularly in patients whose competing comorbidities make the risks of intervention outweigh the risks posed by the tumor itself (27). DISSRM data have shown that when careful patient selection is made, metastasis rates are low under active surveillance and delayed intervention does not negatively affect oncological outcomes (29).

Recommended Surveillance Imaging Protocol

Despite broad endorsement of active surveillance as a management option, published protocols have historically varied in the imaging modality used and in the frequency of follow-up, and this heterogeneity has itself been identified as a barrier to standardized care (27). Drawing on the surveillance schedules most consistently reported across systematic reviews of active surveillance protocols, a practical, guideline-concordant follow-up strategy can be summarized as follows. When a small renal mass is selected for surveillance, baseline cross-sectional imaging (multiphasic CT or dynamic contrast-enhanced MRI, chosen according to the criteria discussed in the imaging modalities section) should be obtained to document the mass's size, enhancement pattern, and relationship to the collecting system, thereby establishing the reference point against which future growth is measured. Repeat imaging is then recommended at approximately 3 to 6 months after the baseline study to establish the tumor's early growth kinetics, since this initial interval is the

most informative for identifying unexpectedly rapid growers who may warrant earlier intervention. If the mass remains stable at this first reassessment, imaging is generally continued every 6 months through the first 1-2 years of surveillance (27). Once a lesion has demonstrated a consistent pattern of slow or absent growth over this initial period, the surveillance interval can reasonably be extended to annual imaging, continued indefinitely for as long as the patient remains a surveillance candidate and is fit enough that a change in management would still be pursued (27,29). Ultrasound may be used to supplement CT or MRI in selected patients with favorable acoustic windows, once a benign-appearing growth pattern has been established, but it should not replace cross-sectional imaging as the primary surveillance tool, given its limitations in reproducibly measuring size and in characterizing enhancement, as discussed above. The specific imaging modality selected for serial follow-up should be individualized to the patient's renal function, contrast allergy status, and anticipated duration of surveillance: MRI-based protocols are favored in younger patients expected to undergo many years of follow-up to limit cumulative radiation exposure, whereas CT-based protocols are preferred where availability, cost, or claustrophobia make MRI impractical.

The most frequently used criteria for triggering a transition from surveillance to intervention include an absolute tumor diameter exceeding 3 cm, an annual growth rate greater than 0.5 cm, or a definite radiological stage progression (27). However, growth rate does not follow a linear course in all patients, and some lesions may transition to a plateau phase after an initial period of more rapid growth; the decision to intervene should therefore not be based on a single measurement or a single rapid interval, but on the dynamically evaluated growth pattern of the mass across serial imaging studies. In addition, the decision to continue or discontinue active surveillance should be shaped not only by tumor characteristics and growth kinetics but also by individual factors such as the patient's life expectancy, renal function status, and personal preferences (29).

Large prospective series examining outcomes of active surveillance protocols report favorable safety profiles, with low rates of progression to unresectable disease. Approximately 25-40% of patients selected for active surveillance ultimately require delayed intervention, with the timing of intervention typically triggered by imaging evidence of rapid growth (>0.4-0.5 cm/year), imaging characteristics evolving toward features concerning for malignancy, or patient preference (27). The progression to intervention typically occurs over 3-5 years for most patients, permitting extended periods of observation while minimizing the risk of missing optimal surgical windows. When delayed intervention is performed after active surveillance, partial nephrectomy remains technically feasible in approximately 80-85% of cases, with complication rates similar to those following upfront partial nephrectomy. Cancer-specific and overall survival in patients managed with active surveillance are excellent; mortality attributable to renal cancer is extremely rare, even in extended follow-up studies spanning 10+ years. This outstanding long-term oncologic control reflects the indolent behavior of most small renal masses, the effectiveness of a structured, dynamically-monitored delayed intervention strategy when necessary, and the careful selection of patients for surveillance based on favorable prognostic factors (27,29).

The Role of Thermal Ablation

Thermal ablation is a minimally invasive alternative treatment, especially for patients at high surgical risk and for small renal masses in anatomically suitable locations. High local control rates are achieved in peripherally located and exophytic lesions ≤3 cm in diameter with radiofrequency ablation and cryoablation techniques (14,17). Meta-analyses have shown that the short-term oncological results of ablation are comparable to partial nephrectomy; however, local recurrence rates may be slightly higher compared to surgery (29). On the other hand, thermal ablation has been shown to be advantageous with respect to perioperative morbidity, bleeding, and length of hospital stay. The most suitable candidates for ablation are lesions that are peripherally located, distant from the renal hilum, unrelated to the collecting system, and ≤3 cm in size (29). In centrally located and endophytic tumors, the risk of residual disease after ablation increases, and evaluating treatment response with imaging becomes more difficult. Therefore, it seems appropriate to make the decision for thermal ablation not only based on the tumor size but also considering the anatomical location and neighboring relationships of the tumor (30).

Thermal ablation (cryoablation and radiofrequency ablation) has gained widespread adoption as a minimally invasive alternative to surgical intervention in select patients with small renal masses. Systematic reviews and meta-analytic studies comparing partial nephrectomy to percutaneous ablative techniques demonstrate equivalent short-term cancer control, with local recurrence-free survival rates of 95-98% for cryoablation and 90-95% for radiofrequency ablation at 1-2 years (30). However, longer-term follow-up studies reveal some divergence: local recurrence rates increase to approximately 5-15% for cryoablation and 8-20% for radiofrequency ablation when follow-up extends beyond 5 years, although distant metastatic disease remains uncommon in early-stage renal cancer managed with ablation. The rate of local recurrence appears to correlate with tumor size, complexity (RENAL score), and ablation technique, with superior outcomes achieved for smaller (<3 cm), low-complexity masses and complete ablation at initial procedure (29). Perioperative morbidity following percutaneous ablation is generally lower than that following partial nephrectomy, with major complication rates of 5-10% for ablation versus 15-25%

for surgical approaches, though specific complications, such as ureteral injury with ablation in hilar masses, require thoughtful case selection and technique modification (29,30).

Partial Nephrectomy: Indications, Outcomes, and Technical Considerations

Partial nephrectomy is currently accepted as the standard treatment approach in clinical T1a renal tumors due to its ability to provide long-term oncological control (31). With the widespread use of minimally invasive techniques, especially robotic surgery, partial nephrectomy has become feasible with lower morbidity and better perioperative outcomes (32). However, technical feasibility does not mean that surgery is necessary in every patient. Because some small renal masses exhibit indolent biology, surgical treatment may lead to unnecessary nephron loss in some patients. Renal function loss after partial nephrectomy is related to the complex structure of the tumor, ischemia time, and resection volume (32). Especially for lesions with high nephrometry scores or with completely endophytic or hilar localization, surgical difficulty and the risk of complications increase. A Turkish study evaluating the results of early robotic retroperitoneal partial nephrectomy emphasized that surgical success should be considered holistically, based on parameters such as ischemia time, surgical margins, and complications (32,33). Therefore, instead of directly applying surgical treatment to all small renal masses, it is more rational to evaluate the tumor's biological risk and anatomical structure together. In the current approach, partial nephrectomy remains a strong option, especially in young patients, lesions with a high risk of progression, and complex masses that are anatomically suitable for surgery (34).

Partial nephrectomy has evolved into the gold-standard surgical approach for small renal masses in patients with preserved baseline renal function and a favorable operative-risk profile. Contemporary series demonstrate negative surgical margin achievement in >99% of cases, with local recurrence rates <1-2% at 5-year follow-up when complete tumor excision with a margin of normal parenchyma is achieved (34). Cancer-specific survival following partial nephrectomy for T1a tumors exceeds 95% at 5 years and 85-90% at 10 years; most patients die of competing causes rather than from renal cancer progression. The functional outcomes of partial and radical nephrectomy differ substantially: parenchymal preservation with partial nephrectomy preserves mean glomerular filtration rate (GFR) at 85-90% of baseline values, compared with a 25-35% loss of GFR after radical nephrectomy (34). This preservation of renal function is clinically significant because chronic kidney disease, stage 3b or worse (GFR <45 mL/min/1.73 m^2), is associated with increased cardiovascular morbidity and mortality. Perioperative complications of partial nephrectomy include bleeding (3-8%), infection (1-3%), urine leak (1-2%), and acute kidney injury (2-5%), with major complication rates increasing modestly for high-complexity masses (RENAL score ≥10) managed via open or robot-assisted approaches (12,33). Contemporary robot-assisted partial nephrectomy demonstrates comparable oncologic outcomes to open surgery with potentially lower morbidity in appropriately selected patients (32,34).

Clinical Decision Framework

The fundamental challenge in managing small renal masses is correctly distinguishing the availability of a technically feasible surgical option from an oncological necessity. While the widespread use of minimally invasive surgery has made partial nephrectomy safer and more accessible, this does not mean that every small renal mass requires surgical intervention. Data on the natural course show that active surveillance is a safe option, especially for lesions with low growth rates and diameters ≤2 cm. In this patient group, early surgical intervention leads to both unnecessary nephron loss and exposure to the potential risks of surgery without providing long-term oncological benefits.

In contrast, the likelihood of biological aggressiveness increases in rapidly growing lesions with heterogeneous contrast enhancement that are located centrally or at the hilum. In such masses, surgical intervention is considered a more rational approach. In the decision-making process regarding the treatment method, not only tumor diameter but also tumor growth kinetics, radiological indicators of aggressiveness, and tumor structural complexity should be evaluated together.

This comprehensive decision-making framework integrates imaging-based assessment of anatomical complexity using nephrometry scoring systems (RENAL score, range 4-12 with low-risk 4-6, intermediate-risk 7-9, and high-risk ≥10; PADUA score, range 6-14 with low-risk 6-7, intermediate-risk 8-9, and high-risk ≥10), tumor size, cystic characteristics (Bosniak classification), and patient-specific factors (age, comorbidities, baseline renal function, and surgical fitness) to guide individualized management of incidentally discovered small renal masses, as summarized in Table 6.

Treatment Modality Insights

Partial Nephrectomy: Remaining a strong option in young patients with long life expectancy, lesions with a high risk of progression, and complex tumors anatomically suitable for surgery.

Thermal Ablation: Offers an effective alternative in patients with suitable anatomical features, peripherally located lesions ≤3 cm in size, and high comorbidities. However, since the risk of residual disease and local recurrence may increase after ablation in masses with complex anatomical features, appropriate patient selection is vital.

Table 6. Clinical decision-making framework for small renal mass management

Clinical presentation	RENAL score	PADUA score	Tumor size	Patient factors	Recommended management	Expected oncologic outcomes
Benign lesion	N/A	N/A	Any	Any	Imaging surveillance every 3 years	No intervention needed; excellent prognosis
Low-complexity, indeterminate/RCC	4-6	6-7	<2 cm	Age <70 years, preserved renal function, no significant comorbidity	Partial nephrectomy (preferred)	<1-2% local recurrence; 95% cancer-specific survival at 5 years; GFR preservation 85-90%
Low-complexity, indeterminate/RCC	4-6	6-7	<2 cm	Age >75 years OR significant comorbidity OR borderline renal function	Active surveillance OR thermal ablation	AS: 25-40% progression at 5 years, >99% cancer-specific survival; ablation: 90-95% recurrence-free survival at 1-2 years, 5-10% major complications
Intermediate complexity	7-9	8-9	2-3 cm	Any patient	Partial nephrectomy (preferred) OR thermal ablation (alternative)	PN: 95% cancer-specific survival at 5 years, 15-20% major complications; ablation: 80-92% recurrence-free survival at 5 years
High complexity, suspicious for RCC	≥10	≥10	3-4 cm	Fit for major surgery, preserved baseline renal function	Partial nephrectomy (preferred) OR radical nephrectomy	PN: 85-95% cancer-specific survival at 5 years (size/grade dependent); radical PN: >95% cancer-specific survival but GFR loss 25-35%
High complexity, suspicious for RCC	≥10	≥10	3-4 cm	Poor surgical candidate OR significant comorbidity OR advanced age	Thermal ablation OR active surveillance	Ablation: 85-95% recurrence-free survival at 5 years, 5-10% major complications; AS: >99% cancer-specific survival but 40-50% may require future intervention

RENAL: R (radius: largest diameter of the mass in centimeters), E (exophytic versus endophytic growth), N (nearness to the collecting system or renal sinus), A (anterior versus posterior location relative to the hilar plane), and L (location relative to the polar lines: upper, middle, or lower pole), PADUA: Preoperative aspects and dimensions used for an anatomical, RCC: Renal cell carcinoma, OR: Odds ratio, N/A: Not applicable, GFR: Glomerular filtration rate, AS: Active surveillance, PN: Partial nephrectomy

Active Surveillance and Delayed Intervention: Growth kinetics during active surveillance (monitoring every 3-6 months with imaging) should inform the timing of delayed intervention. Crucially, partial nephrectomy remains technically feasible in 80-85% of cases initially managed conservatively.

Conclusion: This framework emphasizes the importance of individualized decision-making that balances oncologic control, functional outcomes (renal preservation), and patient-specific factors to optimize both short- and long-term outcomes.

Conclusion

The current approach in the management of small renal masses is evolving from uniform surgical strategies based on tumor diameter to individualized decision models in which treatment type is determined by biological behavior and radiological risk indicators. Natural course data reveal that active surveillance is a safe option, especially in lesions with low growth rates and diameters of ≤2 cm, while rapid growth patterns and aggressive radiological features may indicate the need for surgical intervention. Thermal ablation offers an effective, minimally invasive alternative in selected patients with suitable anatomical features, while partial nephrectomy remains a strong option for oncological control in young patients with a high risk of progression. The main goal in the management of small renal masses is not to remove every tumor that is technically possible, but to ensure both oncological safety and the prevention of unnecessary nephron loss by correctly distinguishing lesions that require biological intervention and by deciding on the appropriate treatment method.

Footnotes

Authorship Contributions

Concept/Design: M.Ç., O.B.K., Data Collection or Processing: T.Ç., H.M.D., A.A., Analysis or Interpretation: M.Ç., H.M.D., Literature Review: M.Ç., O.B.K., Writing, Reviewing and Editing: M.Ç., T.Ç.

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Pancreatic Neuroendocrine Tumors: Our Clinical Experience and Oncological Outcomes

Pankreas Nöroendokrin Tümörler: Klinik Deneyimimiz ve Onkolojik Sonuçlarımız

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Abstract

Objectives: Pancreatic neuroendocrine tumors (pNETs) are rare neoplasms with heterogeneous clinical presentation and variable biological behavior, posing diagnostic and therapeutic challenges. The aim of this study was to evaluate the clinical characteristics, diagnostic approaches, surgical management, and oncological outcomes of patients with pNETs who were treated in our clinic and compare the results with the current literature.

Material and Methods: In this study, data from 10 patients who underwent surgery for pNET between 2018 and 2023 at the Department of General Surgery, Çukurova University Faculty of Medicine were retrospectively reviewed. Demographic characteristics, clinical presentation and symptoms, biochemical parameters, imaging findings, surgical procedures, pathological results, and 3-year postoperative follow-up data were evaluated.

Results: The mean age of the patients was 55.5 years, with equal numbers of women and men. 60% of cases were diagnosed with insulinoma, 20% with gastrinoma, and 20% with somatostatinoma. 60% of the patients presented with hypoglycemic attacks and 40% with abdominal pain. The mean tumor size was 11 mm, and the majority of tumors were located in the pancreatic head. 70% of the patients underwent a Whipple procedure, 20% underwent enucleation, and 10% underwent central pancreatectomy. Lymph node metastasis was detected in 30% of cases during the 3-year follow-up period, and one patient experienced recurrence. Analysis of the data from these patients revealed that they continued their treatment at another center. No major morbidity or mortality was observed in the postoperative period.

Conclusion: Although pNETs are rare tumors, favorable oncological outcomes can be achieved with appropriate diagnostic evaluation and timely surgical intervention. pNETs should be considered in the differential diagnosis of patients presenting with recurrent hypoglycemia or unexplained abdominal pain. Surgical management, performed in experienced centers using a multidisciplinary approach, offers effective treatment with acceptable morbidity and low recurrence rates.

Keywords: Insulinoma, gastrinoma, neuroendocrine tumor, pancreas, somatostatinoma, Whipple procedure

Öz

Giriş / Amaç: Pankreas nöroendokrin tümörleri (pNET), nadir görülmelerine rağmen heterojen klinik prezentasyonları ve değişken biyolojik davranışları nedeniyle tanı ve tedavi sürecinde zorluklar içeren neoplazmlardır. Bu çalışmada, kliniğimize hipoglisemi ve karın ağrısı ile

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başvuran pNET tanılı hastaların klinik özelliklerinin, tanısal yaklaşımlarının, cerrahi tedavi yöntemlerinin ve onkolojik sonuçlarının değerlendirilmesi ve bulguların güncel literatür ile karşılaştırılması amaçlanmıştır.

Gereç ve Yöntem: Bu çalışmada, 2018-2023 yılları arasında Çukurova Üniversitesi Tıp Fakültesi, Genel Cerrahi Anabilim Dalı'nda pNET tanısı ile opere edilen 10 hastanın verileri retrospektif olarak incelendi. Hastaların demografik özellikleri, klinik başvuru semptomları, biyokimyasal parametreleri, görüntüleme bulguları, uygulanan cerrahi prosedürler, patolojik sonuçlar ve postoperatif takip verileri değerlendirildi.

Bulgular: Hastaların ortalama yaşı 55,5 olup kadın ve erkek oranı eşitti. Olguların %60'ı insülinoma, %20'si gastrinoma ve %20'si somatostatinoma tanısı aldı. Hastaların %60'ı hipoglisemi atakları, %40'ı karın ağrısı ile prezente oldu. Ortalama tümör boyutu 11 mm idi ve tümörlerin büyük çoğunluğu pankreas baş lokalizasyonundaydı. Hastaların %70'ine Whipple prosedürü, %20'sine enükleasyon ve %10'una santral pankreatektomi uygulandı. Lenf nodu metastazı %30 oranında saptandı ve bir hastada takip sürecinde nüks gelişti. Postoperatif dönemde majör morbidite veya mortalite izlenmedi.

Tartışma / Sonuç: pNET'ler nadir tümörler olmakla birlikte, uygun tanısal yaklaşım ve zamanında cerrahi tedavi ile başarılı onkolojik sonuçlar elde edilebilmektedir. Özellikle sık hipoglisemi atakları ve açıklanamayan karın ağrısı ile başvuran hastalarda pNET olasılığı mutlaka akılda tutulmalıdır. Deneyimli merkezlerde multidisipliner yaklaşım ile uygulanan cerrahi tedavi, düşük morbidite ve kabul edilebilir nüks oranları ile etkin bir tedavi seçeneği sunmaktadır.

Anahtar Kelimeler: İnsülinoma, gastrinoma, nöroendokrin tümörü, pankreas, somatostatinoma, Whipple prosedürü

Introduction

Pancreatic neuroendocrine tumors (pNETs) are a heterogeneous group of neoplasms originating from pancreatic islet cells and account for approximately 1-2% of all pancreatic tumors; however, they represent the second most common type of rare solid pancreatic neoplasms (1). According to the World Health Organization (WHO), the annual incidence of pNETs is reported to be 0.48 per 100.000 individuals (2).

These tumors arise from hormone-producing cells and are clinically classified as functional or non-functional. Functional pNETs include insulinoma, gastrinoma, glucagonoma, VIPoma, and somatostatinoma. The clinical manifestations of functional tumors result from excessive hormone secretion; therefore, hormonal assays play a critical role in both diagnosis and follow-up. Non-functional pNETs are not associated with hormonal syndromes and usually present at advanced stages with non-specific symptoms such as abdominal pain, weight loss, or mass effect (2,3).

pNETs may occur sporadically or in association with hereditary syndromes such as multiple endocrine neoplasia type 1. However, the molecular pathogenesis of these tumors has not yet been fully elucidated. Various imaging modalities are used for tumor localization, including ultrasonography, computed tomography, magnetic resonance imaging, endoscopic ultrasonography, selective arterial catheterization with hepatic venous sampling, octreotide scintigraphy, and DOTA-TATE peptide positron emission tomography (3,4).

Most pNETs present as solitary, well-circumscribed, contrast-enhancing solid masses arising in a specific region of the pancreas. Although most tumors exhibit slow growth, they possess malignant potential. Tumor stage, lymph node involvement, distant metastasis, and tumor size are significant prognostic factors affecting survival. An aggressive treatment strategy, consisting of surgery, local treatment, systemic therapy, and management of complications, is recommended (4,5).

The aim of this study was to evaluate the clinical characteristics, diagnostic approaches, surgical treatments, and oncological outcomes in patients with pNETs and compare the findings with the current literature.

Materials and Methods

This retrospective study was conducted in accordance with the principles of the Declaration of Helsinki. The study was approved by the Ethics Committee of Çukurova University Faculty of Medicine (approval no: 22, date: 09.01.2026).

Patients who underwent surgery for a pNET at the Department of General Surgery, Çukurova University Faculty of Medicine, between 2018 and 2023 were included in the study. Patient data were obtained from the hospital's electronic medical record system.

Inclusion criteria were age ≥18 years and availability of complete clinical, laboratory, radiological, and pathological data. Patients under 18 years of age, those with incomplete hospital records, and those whose examinations, performed at external centers, could not be accessed were excluded from the study.

Patients were classified into three groups according to diagnosis: insulinoma (n=6), gastrinoma (n=2), and somatostatinoma (n=2).

In our study, in which median values were used due to the small sample size, laboratory findings and radiological examinations, such as ultrasonography, endoscopic ultrasonography, computed tomography, magnetic resonance imaging, and positron emission tomography, were evaluated preoperatively

in symptomatic or incidentally detected pNET cases. Data on the treatment received by patients in the preoperative period were also included in the study.

Postoperative follow-up data included: hormone levels, pathological examination results, early and late complications, surgical methods, length of hospital stay, recurrence status, and need for additional medical treatment.

Demographic characteristics and preoperative laboratory parameters, including white blood cell count, hemoglobin, hematocrit, platelet count, C-reactive protein, insulin, C-peptide, glucose, and HbA1c levels, were recorded.

Statistical Analysis

All collected data were recorded, median values were calculated, and the results were compared with extensive studies in the literature.

Results

The mean age of the 10 patients included in the study was 55.5 years. Five patients (50%) were male and five (50%) were female. According to the distribution of diagnoses, 60% (n=6) of the patients were diagnosed with insulinoma, 20% (n=2) with gastrinoma, and 20% (n=2) with somatostatinoma.

Four patients (40%) presented with abdominal pain, while six patients (60%) presented with hypoglycemic attacks. All patients who presented with hypoglycemia were diagnosed with insulinoma. Among patients presenting with abdominal pain, two were diagnosed with gastrinoma and two with somatostatinoma.

In patients diagnosed with insulinoma, the mean insulin level at presentation was 10.17 µU/mL (0.91-21.21), the mean C-peptide level was 3.53 ng/mL (2.37-5.72), and the mean glucose level was 107.6 mg/dL (49-146).

Pancreaticoduodenectomy (Whipple procedure) was performed in seven patients (70%), enucleation in two (20%), and central pancreatectomy in one (10%).

The mean tumor size was 11 mm (10-15 mm). Tumors were localized in the pancreatic head in eight patients (80%), in the periampullary region in one patient (10%), and in the pancreatic uncinate process in one patient (10%).

Lymph node metastasis was detected in three patients (30%), but not in seven patients (70%). During follow-up, recurrence occurred in one patient who had lymph node metastasis. No major postoperative morbidity or mortality was observed.

Discussion

Despite their rarity, pNETs are clinically important because of their diverse presentation, biological behavior, and treatment strategies. In large series reported in the literature, the median age of patients diagnosed with pNETs has been reported to range between 50 and 60 years (1,3). The mean age in our study was 55.5 years, which is consistent with these reports. Gender has not been shown to influence the incidence of pNETs (4), and a similar distribution was observed in our cohort.

Among functional pNETs, insulinoma is the most frequently reported subtype in the literature (5). Recent studies have emphasized insulinoma as the predominant functional pNET subtype (6). In our study, insulinomas accounted for 60% of cases, consistent with published data.

Placzkowski et al. (7) reported that patients with insulinoma commonly present with neuroglycopenic hypoglycemic symptoms and that hypoglycemia is a highly specific clinical finding for insulinoma. All patients presenting with hypoglycemia in our study were diagnosed with insulinoma, which supports this observation.

Other functional pNET subtypes, such as gastrinoma and somatostatinoma, often present with non-specific symptoms (8). Garbrecht et al. (9) reported that somatostatinomas frequently present with abdominal pain, weight loss, and diarrhea. In our study, all patients diagnosed with gastrinoma or somatostatinoma presented with abdominal pain.

Although pNETs may arise in any region of the pancreas, several studies have reported a predominance in the pancreatic head (10). In our cohort, 80% of tumors were located in the pancreatic head, which explains the high rate of pancreaticoduodenectomy.

Surgical resection remains the cornerstone of curative treatment in localized pNETs. Enucleation is recommended for small, well-demarcated, low-grade tumors, whereas formal pancreatic resection is preferred for larger tumors or those with malignant potential (11). The surgical approaches applied in our study are consistent with these recommendations.

Lymph node metastasis is considered one of the most important prognostic factors in pNETs and is emphasized in the WHO 2022 classification (2). In our study, lymph node metastasis was detected in 30% of patients, and recurrence occurred only in patients with nodal involvement.

The absence of major postoperative morbidity and mortality in our study demonstrates that surgical treatment of pNETs can be performed safely in experienced centers.

Study Limitations

This study has several limitations. First, its retrospective design, based on data obtained from existing medical records, carries a risk of missing data and selection bias. In addition, the limited number of patients reduces the statistical power of subgroup comparisons and restricts the generalizability of the findings. Furthermore, since the study reflects the experience of a single center, the results may not be directly applicable to other institutions or broader populations.

Moreover, the relatively short follow-up period in some patients may have limited the evaluation of long-term recurrence and survival outcomes. Another limitation is the lack of routine molecular and genetic analyses, which restricts a more detailed assessment of prognostic factors. Future multicenter, prospective studies with larger patient populations may provide stronger evidence and more generalizable results.

Conclusion

pNETs, though rare, require careful consideration during diagnosis and treatment because of their heterogeneous clinical presentations and variable biological behavior. Our retrospective clinical experience in this study, covering patients who were operated on between 2018 and 2023 and followed for three years, supports the conclusion that the diagnostic and surgical treatment approaches for pNETs are consistent with the literature and are effective.

Insulinomas presenting with hypoglycemic attacks facilitate an early and specific diagnosis; however, in other functional subtypes, such as gastrinoma and somatostatinoma, non-specific symptoms can lead to delayed diagnosis. In localized pNETs, surgical treatment is the cornerstone of curative management. Surgery planned according to tumor size, location, and lymph node involvement provides successful oncological outcomes with low recurrence rates and acceptable morbidity. These findings demonstrate that evaluation of pNETs at experienced centers with a multidisciplinary approach, appropriate patient selection, and timely surgical intervention are crucial to achieving curative results.

Ethics

Ethics Committee Approval: The study was approved by the Ethics Committee of Çukurova University Faculty of Medicine (approval no: 22, date: 09.01.2026).

Informed Consent: Retrospective study.

Footnotes

Authorship Contributions

Concept/Design: E.U., İ.A., A.T.A., Data Collection or Processing: E.U., İ.C.Y., İ.A., A.Ü., A.T.A., Analysis or Interpretation: E.U., Y.K., A.G.S., A.T.A., Literature Review: İ.C.Y., Writing, Reviewing and Editing: E.U., İ.C.Y., Y.K., A.T.A.

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Concordance Between AI-generated Recommendations and Multidisciplinary Tumor Board Decisions in Postoperative Breast Cancer Management: A Retrospective Validation Study

Postoperatif Meme Kanseri Yönetiminde Yapay Zeka Tarafından Oluşturulan Öneriler ile Multidisipliner Tümör Konseyi Kararları Arasındaki Uyumluluk: Retrospektif Bir Validasyon Çalışması

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Abstract

Objectives: This study aimed to evaluate the concordance between artificial intelligence (AI)-generated treatment recommendations and real-world multidisciplinary tumor board (MDT) decisions in postoperative breast cancer management.

Material and Methods: This retrospective validation study included 30 female patients with breast cancer who were previously discussed in a MDT. Demographic, clinical, pathological, and molecular data were retrospectively collected from institutional records and anonymized before analysis. Structured clinical scenarios were created for each patient and entered into an AI-based decision-support system, developed using ChatGPT version 5.2, in accordance with current ESMO, NCCN, and ASCO guidelines. AI-generated recommendations for systemic therapy, radiotherapy, and genomic testing were compared with corresponding MDT decisions. Concordance was assessed for each treatment domain.

Results: The mean age was 52±13.1 years, and the median interval from pathology reporting to MDT discussion was 7 days (interquartile range, 4-11). Neoadjuvant therapy was administered to 11 patients (36.7%), and 4 (36.6%) achieved a pathological complete response. Breast-conserving surgery was performed in 22 patients (73.3%). Concordance between AI and MDT varied by treatment modality. Agreement was highest for radiotherapy (90.0%), followed by anti-human epidermal growth factor receptor 2 (HER2) therapy (73.3%) and endocrine therapy (70.0%). Lower concordance rates were observed for genomic testing (53.3%) and chemotherapy (33.3%). Chemotherapy showed the highest discordance rate (66.7%).

Conclusion: AI demonstrated high concordance with MDT decisions in treatment domains guided by standardized criteria, particularly radiotherapy, endocrine therapy, and anti-HER2 therapy. Lower agreement was observed for chemotherapy and genomic testing, suggesting that these decisions require more individualized clinical judgment. AI may serve as a useful decision-support tool within multidisciplinary breast cancer care.

Keywords: Artificial intelligence, breast cancer, multidisciplinary tumor board

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Öz

Giriş / Amaç: Bu çalışmanın amacı, postoperatif meme kanseri yönetiminde yapay zeka (YZ) tarafından oluşturulan tedavi önerileri ile gerçek yaşam multidisipliner tümör konseyi (MTK) kararları arasındaki uyumu değerlendirmektir.

Gereç ve Yöntem: Bu retrospektif validasyon çalışmasına, daha önce MTK'da değerlendirilmiş 30 kadın meme kanseri hastası dahil edildi. Demografik, klinik, patolojik ve moleküler veriler kurumsal kayıtlardan retrospektif olarak toplandı ve analiz öncesinde anonimleştirildi. Her hasta için yapılandırılmış klinik senaryolar oluşturuldu ve bu senaryolar, güncel ESMO, NCCN ve ASCO kılavuzlarına uygun şekilde yapılandırılmış, ChatGPT sürüm 5.2 tabanlı YZ destekli karar destek sistemine girildi. Sistemik tedavi, radyoterapi ve genomik testlere ilişkin YZ önerileri, ilgili MTK kararları ile karşılaştırıldı. Her tedavi alanı için uyum değerlendirildi.

Bulgular: Ortalama yaş 52±13,1 yıl olup, patoloji raporundan MTK değerlendirmesine kadar geçen medyan süre 7 gün (IQR, 4–11) idi. On bir hastaya (%36,7) neoadjuvan tedavi uygulanmıştı ve bunların 4'ünde (%36,6) patolojik tam yanıt elde edildi. Meme koruyucu cerrahi 22 hastada (%73,3) uygulanmıştı. YZ ile MTK arasındaki uyum tedavi alanına göre değişkenlik gösterdi. En yüksek uyum radyoterapi için saptandı (%90). Bunu anti-insan epidermal büyüme faktörü reseptörü (HER2) tedavi (%73,3) ve endokrin tedavi (%70) izledi. Daha düşük uyum genomik test (%53,3) ve kemoterapi (%33,3) alanlarında görüldü. En yüksek uyumsuzluk oranı kemoterapi kararlarında saptandı (%66,7).

Tartışma / Sonuç: YZ, özellikle radyoterapi, endokrin tedavi ve anti-HER2 tedavi gibi standart ölçütlerle yönlendirilen tedavi alanlarında MTK kararları ile yüksek düzeyde uyum göstermiştir. Kemoterapi ve genomik test alanlarında ise daha düşük uyum saptanmış olup, bu durum söz konusu kararların daha fazla bireyselleştirilmiş klinik değerlendirme gerektirdiğini düşündürmektedir. YZ, multidisipliner meme kanseri yönetiminde yararlı bir karar destek aracı olarak kullanılabilir.

Anahtar Kelimeler: Yapay zeka, meme kanseri, multidisipliner tümör konseyi

Introduction

Breast cancer is the most common cancer among women (1). Over the past decades, advances in screening, surgical techniques, and oncological therapies have significantly improved survival outcomes. However, these advances have also made treatment strategies more complex, requiring a more individualized and multidisciplinary approach to patient care. This multidisciplinary approach requires a team built on the collaboration of breast surgeons, medical oncologists, radiation oncologists, pathologists, and radiologists (2).

Decision-making in cancer care relies on both structured frameworks from international guidelines and individualized patient evaluation. Multidisciplinary tumor boards (MDTs) are central to combining these elements for clinicians and patients (3,4). While MDTs are necessary, their meetings also have practical limitations. Because coordinating multiple specialists means meetings are typically held at set intervals, this can limit flexibility and possibly cause delays. Furthermore, the increasing patient load and the complexity of treatment algorithms add to the burden on multidisciplinary teams (4).

The use of artificial intelligence (AI) and, more recently large language models (LLMs), has rapidly expanded in healthcare (5). These systems can interpret clinical data and guideline-based recommendations. They can also generate structured treatment suggestions when given appropriate inputs (6). In oncology, decision-making often relies on integrating multiple variables. AI-based tools can support clinicians with consistent, guideline-informed recommendations (7).

Given these developments, new AI and LLM technologies can be integrated into daily practice to support clinicians' decision-making. In this study, we aim to evaluate the concordance between an AI-based decision-support system and real-world MDTs in postoperative breast cancer treatment recommendations.

Materials and Methods

This retrospective validation study evaluated the concordance between an AI-based decision support system and real-world MDT decisions in postoperative breast cancer management.

The AI-based decision support system was developed using ChatGPT, version 5.2. It followed current international clinical guidelines, including those of ESMO, NCCN, and ASCO. The tool is guideline-informed, not an autonomous decision-making system. For each patient, it generated structured recommendations for systemic therapy, radiotherapy, and genomic testing. The system operated in a locked configuration, with no changes to the model version, architecture, or prompt strategy during the study.

Patients evaluated by a multidisciplinary breast cancer tumor board were identified retrospectively. Demographic, clinical, pathological, and molecular data were extracted from institutional records. All data were anonymized before analysis. For each patient, structured clinical scenarios were created. These included age, tumor stage, family history, BRCA mutation, histopathological characteristics, hormone receptor status, human epidermal growth factor receptor 2 (HER2) status, Ki-67 index, molecular subtype, breast-conserving surgery status, axillary management, and postoperative tumor-node-metastasis

staging. No personally identifiable information was provided to the AI system.

Anonymized patient scenarios were entered into the AI-based decision support system. The generated recommendations were recorded under predefined categories: systemic therapy strategy, radiotherapy indication, and genomic testing recommendation. Outputs were then compared with the corresponding real-world MDT decisions for the same patients. The level of agreement was classified as concordant or discordant for each parameter.

The AI system was not used in real-time clinical decision-making and did not influence patient management. All AI-generated outputs were evaluated solely for validation purposes in a shadow mode setting.

Statistical Analysis

All statistical analyses were performed using Jamovi software, version 2.6. Categorical variables were presented as frequencies and percentages. Continuous variables were summarized as mean ± standard deviation or median with interquartile range (IQR), depending on data distribution.

The primary endpoint of the study was the concordance between AI-generated recommendations and MDT decisions. Concordance rates were calculated as the proportion of cases in which AI recommendations and MDT decisions agreed.

All data were anonymized and handled in accordance with data protection regulations. The study followed ethical standards for retrospective observational research. The Acıbadem Mehmet Ali Aydınlar University Institutional Review Board approved the study (approval number: 2026/02, date: 22.02.2026).

Results

A total of 30 female patients with breast cancer were included in the study. The mean age of the cohort was 52±13.1 years, and the median interval from pathology reporting to MDT discussion was 7 days (IQR, 4-11). Nineteen patients (63.3%) were postmenopausal, while 11 (36.7%) were premenopausal (Table 1).

Most tumors were invasive carcinomas (n=27, 90.0%). Three patients (10.0%) had *in situ* disease. Among invasive tumors, cT2 was the largest subgroup (59.3%). Seventeen patients (63%) had node-negative disease, and 10 (37%) patients had nodal involvement. All tumors were ductal carcinomas. Thirteen patients (44.8%) had grade 2 tumors; 16 (55.2%) had grade 3 tumors. Estrogen receptor positivity was observed in 20 patients (66.7%), and progesterone receptor positivity was observed in 14 patients (46.7%). HER2 status was negative in 16 patients (57.1%), positive in 6 (21.4%), and inconclusive in 6 (21.4%). The median Ki-67 index was 17%.

Table 1. Patient characteristics

	Variable	n (%)
Age		52±13.1
Pathology-MDT day		7 (4-11)
Menopause	Postmenopausal	19 (63.3)
	Premenopausal	11 (36.7)
Tumor type	Invasive carcinoma	27 (90.0)
	In situ	3 (10.0)
T stage	T0	2 (7.4)
	T1	1 (3.7)
	T1a	2 (7.4)
	T1b	2 (7.4)
	T1c	4 (14.8)
	T2	16 (59.3)
N stage	N0	17 (63.0)
	N+	10 (37)
Histology	Ductal carcinoma	30 (100)
Tumor grade	Grade 2	13 (44.8)
	Grade 3	16 (55.2)
ER	Positive	20 (66.7)
	Negative	10 (33.3)
PR	Positive	14 (46.7)
	Negative	16 (53.3)
HER2	Negative	16 (57.1)
	Positive	6 (21.4)
	Inconclusive	6 (21.4)
Ki-67 (%)		17 (12-35)
ECOG	0	9 (39.1)
	1	12 (52.2)
	2	2 (8.7)
Fertility preservation	Yes	6 (20.0)
	No	24 (80.0)
Surgery	Breast-conserving surgery	22 (73.3)
	Mastectomy	8 (26.7)
Axillary management	Sentinel biopsy	28 (93.3)
	Axillary dissection	2 (6.7)
Neoadjuvant therapy	Yes	11 (36.7)
	No	19 (63.3)
pCR	Yes	4 (13.3)
	No	26 (86.7)

MDT: Multidisciplinary tumor board, ER: Estrogen receptor, PR: Progesterone receptor, HER2: Human epidermal growth factor receptor 2, ECOG: Eastern Cooperative Oncology Group, pCR: Pathological complete response

Neoadjuvant therapy had been administered to 11 patients (36.7%), whereas the remaining 19 patients (63.3%) underwent upfront surgery. Among those who received neoadjuvant treatment, 4 patients (36.6%) achieved a pathological complete

response. Breast-conserving surgery was performed on 22 patients (73.3%), while 8 patients (26.7%) underwent mastectomy. Axillary staging was performed by sentinel lymph node biopsy in 28 patients (93.3%), whereas axillary dissection was required in 2 patients (6.7%).

Concordance between AI-generated recommendations and MDT decisions varied according to treatment modality. The highest concordance was observed for radiotherapy, with 27 cases (90%) in agreement. Concordance was also relatively high for anti-HER2 therapy and endocrine therapy, with agreement rates of 73.3% and 70.0%, respectively. In contrast, concordance was lower for genomic testing and chemotherapy (53.3% and 33.3%, respectively) (Table 2).

Chemotherapy had the highest discordance rate: 20 cases (66.7%) showed disagreement. Among these discordant cases, the AI recommended chemotherapy in 6 cases (30%) while the MDT did not; conversely, the MDT recommended chemotherapy in 4 cases (20.0%) while the AI suggested genomic testing. In 5 additional cases (25%), the AI recommended genomic testing when the MDT did not, and in 5 cases (25%), the MDT recommended genomic testing when the AI did not.

Table 2. Concordance

Chemotherapy	Concordance	10 (33.3)
	Discordance	20 (66.7)
	MDT genomic, AI chemotherapy	5 (25)
	MDT chemotherapy, AI genomic	4 (20)
	MDT no chemotherapy, AI genomic	5 (25)
	MDT no chemotherapy, AI chemotherapy	6 (30)
Endocrine therapy	Concordance	21 (70)
	Discordance	9 (30)
	MDT recommended endocrine, AI did not	5 (55.6)
	AI recommended endocrine, MDT did not	4 (44.4)
Anti-HER2 therapy	Concordance	22 (73.3)
	Discordance	8 (26.7)
	MDT recommended anti-HER2, AI did not	3 (37.5)
	AI recommended anti-HER2, MDT did not	5 (62.5)
Radiotherapy	Concordance	27 (90)
	Discordance	3 (10)
	Clinical risk-based MDT decision	3 (100)
Genomic testing	Concordance	16 (53.3)
	Discordance	14 (46.7)
	MDT recommended genomic test, AI did not	5 (35.7)
	AI recommended genomic test, MDT did not	9 (64.3)

AI: Artificial intelligence, MDT: Multidisciplinary tumor board, HER2: Human epidermal growth factor receptor 2

For endocrine therapy, discordance was observed in 9 cases (30%). In 5 of these cases (55.6%), the MDT recommended endocrine therapy, whereas the AI did not; conversely, in 4 cases (44.4%), the AI recommended endocrine therapy, whereas the MDT did not. Discordance in anti-HER2 therapy was observed in 8 cases (26.7%), including 3 cases (37.5%) in which the MDT recommended anti-HER2 therapy but the AI did not, and 5 cases (62.5%) in which the AI recommended anti-HER2 therapy, but the MDT did not.

Radiotherapy had the lowest discordance rate, with 3 cases (10%) showing disagreement. Genomic testing showed discordance in 14 cases (46.7%). Overall, agreement was higher for radiotherapy, endocrine therapy, and anti-HER2 therapy, whereas it was lower for chemotherapy and genomic testing.

Discussion

In this study, we evaluated the concordance between AI-generated treatment recommendations and decisions made by an experienced MDT in patients with breast cancer. Our findings indicate that agreement between the AI system and the MDT varied across treatment modalities, highlighting several key factors.

Radiotherapy demonstrated the highest concordance rate (90%). This finding is not unexpected, as radiotherapy decisions in breast cancer are largely based on standardized treatment algorithms incorporating surgical procedure, tumor stage, and nodal status (8). In such relatively structured and guideline-driven settings, AI systems may be able to reproduce clinical decision pathways with a high degree of consistency.

Similarly, concordance was relatively high for endocrine therapy (70.0%) and anti-HER2 therapy (73.3%). These treatment decisions are primarily determined by receptor status and well-established therapeutic algorithms, which may explain the higher level of agreement between AI-generated recommendations and MDT decisions (9).

In contrast, chemotherapy demonstrated the lowest concordance rate (33.3%). Most discordant cases arose when the AI recommended chemotherapy, whereas the MDT favored genomic testing or clinical observation. This finding suggests that AI systems may rely more heavily on guideline-based risk stratification, while clinicians often incorporate additional contextual and patient-specific factors when determining the indication for chemotherapy (10). Variables such as patient

age, tumor grade, proliferative activity, comorbidities, and clinical judgment may affect treatment selection beyond what algorithm-based systems can fully capture.

A similar pattern was observed for genomic testing, with moderate concordance between AI and MDT (53.3%). The AI system recommended genomic testing more frequently than the MDT. This may reflect the tendency of AI models to favor molecular testing in borderline cases where guidelines support the use of genomic assays as adjunctive decision-making tools, whereas clinicians may choose to omit such testing when the result is unlikely to alter the treatment plan (10).

Taken together, these findings stress an important distinction between treatment decisions that are predominantly guideline-driven and those that require more individualized clinical interpretation. AI-based systems appear to perform well in structured decision-making contexts, although they show lower agreement in more detailed scenarios that depend on physician experience and broader clinical judgment.

Study Limitations

This study has several limitations. First, the sample size was relatively small, which may limit the generalizability of the findings. Second, the analysis was conducted within a single-institution MDT setting, and treatment decisions may vary across institutions according to local practice patterns, clinical expertise, and patient characteristics. In addition, the AI system was evaluated retrospectively in shadow mode and, therefore, was not assessed within a real-time clinical workflow.

Regardless of these limitations, the present study provides preliminary insight into the interaction between AI-based decision support tools and multidisciplinary clinical decision-making in breast cancer care. Rather than replacing clinicians, such systems may serve as complementary tools that support clinical reasoning and facilitate guideline-informed treatment planning.

Conclusion

AI demonstrated high concordance with MDT decisions across treatment modalities that were largely guided by standardized criteria, including radiotherapy, endocrine therapy, and anti-HER2 therapy. By contrast, lower agreement was observed in modalities requiring more individualized judgment, particularly in chemotherapy and genomic testing. These findings suggest that AI may be most useful as a decision-support tool integrated into multidisciplinary clinical practice rather than as a substitute for expert clinical evaluation.

Ethics

Ethics Committee Approval: The Acıbadem Mehmet Ali Aydınlar University Institutional Review Board approved the study (approval number: 2026/02, date: 22.01.2026).

Informed Consent: Retrospective study.

Footnotes

Authorship Contributions

Concept/Design: A.U.M., E.Ç., C.U., Data Collection or Processing: A.U.M., E.Ç., N.B., Analysis or Interpretation: A.U.M., N.B., Literature Review: A.U.M., E.Ç., H.K., O.D., N.B., C.U., Writing, Reviewing and Editing: A.U.M., E.Ç., H.K., O.D., N.B., C.U.

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Oncological Significance of Proximal Resection Margin Length in Proximal Gastric and Gastroesophageal Junction Adenocarcinoma: A Single-center Retrospective Analysis

Proksimal Mide ve Gastroözofageal Bileşke Adenokarsinomunda Proksimal Rezeksiyon Sınırı Uzunluğunun Onkolojik Önemi: Tek Merkezli Retrospektif Bir Analiz

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Abstract

Objectives: The proximal margin required for oncologically sound resection of proximal gastric and gastroesophageal junction (GEJ) adenocarcinoma has not been established. We examined whether the pathological distance from the tumor to the proximal transection line was associated with postoperative oncological outcomes after curative-intent surgery.

Material and Methods: We retrospectively evaluated 186 patients who underwent total gastrectomy, distal esophagectomy, and lymphadenectomy for proximal gastric or GEJ adenocarcinoma at a single center. Clinicopathological data, relapse patterns, and survival were reviewed. Multivariable Cox proportional hazards models were used to determine factors independently associated with recurrence and overall survival.

Results: The pathological proximal margin averaged 2.5±1.0 cm. Over a mean follow-up of 26.3±22.8 months, 51 patients (27.4%) experienced recurrence and 88 (47.3%) died. Margin distance was comparable between the recurrence and non-recurrence groups (p=0.081) and did not independently predict relapse. Recurrence was independently associated with limited lymphadenectomy [recorded as "palliative lymphadenectomy" in the operative records; hazard ratio (HR): 2.99, p=0.014], pathological N3 stage (HR: 5.60, p<0.001), and splenectomy (HR: 2.74, p=0.007). Overall survival was independently associated with neural invasion, metastatic lymph node burden, recurrence, and the length of esophagus resected.

Conclusion: Among patients undergoing curative-intent resection of proximal gastric or GEJ adenocarcinoma, pathological proximal-margin distance was not independently associated with recurrence after microscopic clearance (R0) was achieved. Because no margin cut-off analysis was performed, the observed mean distance of 2.5 cm should not be interpreted as a definitive adequacy threshold.

Keywords: Gastric adenocarcinoma, gastroesophageal junction neoplasms, surgical margins, lymph node dissection, tumor recurrence, survival analysis

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Öz

Giriş / Amaç: Proksimal mide ve gastroözofageal bileşke (GEJ) adenokarsinomlarının onkolojik açıdan uygun rezeksiyonu için gerekli proksimal cerrahi sınır mesafesi henüz belirlenmemiştir. Bu çalışmada, tümörden proksimal transeksiyon hattına kadar olan patolojik mesafenin, küratif amaçla gerçekleştirilen cerrahi sonrasındaki onkolojik sonuçlarla ilişkili olup olmadığını değerlendirdik.

Gereç ve Yöntem: Tek bir merkezde proksimal mide veya GEJ adenokarsinomu nedeniyle total gastrektomi, distal özofajektomi ve lenfadenektomi uygulanan 186 hasta retrospektif olarak değerlendirildi. Klinikopatolojik veriler, nüks paternleri ve sağkalım sonuçları incelendi. Nüks ve genel sağkalımla bağımsız olarak ilişkili faktörleri belirlemek için çok değişkenli Cox orantısal risk modelleri kullanıldı.

Bulgular: Patolojik proksimal cerrahi sınır mesafesi ortalama 2,5±1,0 cm idi. Ortalama 26,3±22,8 aylık takip süresince 51 hastada (%27,4) nüks gelişti ve 88 hasta (%47,3) yaşamını yitirdi. Cerrahi sınır mesafesi nüks gelişen ve gelişmeyen gruplar arasında benzerdi (p=0,081) ve nüksü bağımsız olarak öngörmedi. Nüks; sınırlı lenfadenektomi [ameliyat kayıtlarında "palyatif lenfadenektomi" olarak belirtilen; tehlike oranı (HR): 2,99, p=0,014], patolojik N3 evresi (HR: 5,60, p<0,001) ve splenektomi (HR: 2,74, p=0,007) ile bağımsız olarak ilişkiliydi. Genel sağkalım ise perinöral invazyon, metastatik lenf nodu yükü, nüks ve rezeke edilen özofagus uzunluğu ile bağımsız olarak ilişkiliydi.

Tartışma / Sonuç: Proksimal mide veya GEJ adenokarsinomu nedeniyle küratif amaçlı rezeksiyon uygulanan hastalarda, mikroskobik cerrahi sınır negatifliği (R0) sağlandıktan sonra patolojik proksimal cerrahi sınır mesafesi nüks ile bağımsız olarak ilişkili bulunmadı. Herhangi bir cerrahi sınır eşik değeri analizi yapılmadığından, gözlenen ortalama 2,5 cm'lik mesafe kesin bir yeterlilik eşiği olarak yorumlanmamalıdır.

Anahtar Kelimeler: Mide adenokarsinomu, gastroözofageal bileşke neoplazileri, cerrahi sınırlar, lenf nodu diseksiyonu, tümör nüksü, sağkalım analizi

Introduction

Although the overall incidence of gastric cancer has declined over recent decades, it continues to account for a substantial proportion of cancer deaths worldwide. Its anatomical distribution has also changed: lesions of the proximal stomach and gastroesophageal junction (GEJ) now constitute a relatively greater share of cases, especially in Western populations (1,2). This shift has intensified interest in how best to resect these technically demanding tumors.

For localized gastric and GEJ adenocarcinoma, the principal curative option is complete surgical excision with tumor-free margins (3,4). Proximal clearance warrants particular attention because malignant cells can extend through submucosal or lymphatic channels beyond the macroscopically apparent margin. Microscopic involvement of the proximal margin has been linked to more local failures and poorer long-term outcomes (5).

The amount of gross proximal clearance needed to secure a negative microscopic margin remains uncertain. Traditional recommendations called for at least 5 cm in intestinal-type cancers and an even greater distance in diffuse tumors because occult intramural extension may be longer in the latter group (6,7). Such recommendations encouraged surgeons to resect a substantial segment of the esophagus to achieve adequate clearance.

More recent evidence has prompted reconsideration of these broad distance thresholds. Improvements in staging, intraoperative evaluation, specimen assessment, and perioperative systemic therapy allow surgeons to target an R0 resection without automatically maximizing the length of esophagus removed (8,9). Contemporary cohorts have accordingly described acceptable cancer control with shorter margins when the transection line is microscopically negative (10).

This question is especially consequential in Siewert II and III disease, where the tumor spans the anatomical transition between the distal esophagus and the proximal stomach. In this setting, both the operative route and the length of proximal esophageal resection remain debated (2,4). Guidelines consistently require microscopic margin negativity, yet they offer limited high-level evidence for a single distance that reliably prevents recurrence (3,8).

We therefore assessed whether the measured pathological proximal margin was associated with recurrence or overall survival after total gastrectomy and distal esophagectomy for proximal gastric or GEJ adenocarcinoma. The specific objective was to determine whether shorter, but histologically negative, proximal margins compromised oncological outcomes.

Materials and Methods

Study Design and Ethical Approval

This single-center retrospective cohort study was conducted in the Department of General Surgery at Van Yüzüncü Yıl University Faculty of Medicine. Approval was granted by the Van Yüzüncü Yıl University Non-Interventional Clinical Research Ethics Committee (approval no: 2020/10-03, date: 11.12.2020). All study procedures conformed to the Declaration of Helsinki. Because

existing records were analyzed retrospectively, the committee waived individual informed consent.

Patient Population

Institutional operative reports, pathology reports, oncology follow-up records, and electronic medical records were searched to identify consecutive patients who had undergone surgery with curative-intent for adenocarcinoma of the proximal stomach or GEJ.

Inclusion required histological confirmation of proximal gastric or GEJ adenocarcinoma, treatment consisting of total gastrectomy with distal esophagectomy and regional lymphadenectomy, a documented pathological measurement of the proximal margin, and sufficient postoperative follow-up information.

We excluded patients with any of the following: metastases at presentation; who underwent palliative operations; macroscopic residual tumor (R2); recurrent disease; a histological diagnosis other than adenocarcinoma; a synchronous malignant tumor; a complete pathological response after neoadjuvant therapy that precluded margin measurement; or missing clinicopathological data.

Surgical Treatment

Operations were performed by surgeons experienced in upper gastrointestinal oncology. Selection of the operative approach took into account tumor position and local extension, patient-related factors, and the operating surgeon's judgment.

Every patient underwent total gastrectomy and distal esophagectomy. The regional lymph node dissection followed the gastric cancer standards applicable during the treatment period, and continuity was restored with a Roux-en-Y esophagojejunostomy. For this study, the term "palliative lymphadenectomy", as retained from the operative records, denoted a lymph node dissection less extensive than a standard D1 or D2 dissection because of intraoperative technical or patient-related constraints. Nevertheless, these procedures were performed with curative-intent and without macroscopic residual tumor. The term did not refer to a palliative resection. In the manuscript, this category is described as limited lymphadenectomy (recorded as "palliative lymphadenectomy").

The gross cranial extent of the lesion was assessed intraoperatively by visual inspection and palpation. Surgeons selected a proximal transection point intended to balance technical practicality with achieving a tumor-free, oncologically acceptable margin.

Pathological Evaluation

Dedicated gastrointestinal pathologists evaluated all surgical specimens. After opening and fixation in accordance with local laboratory procedures, the specimens were assessed for tumor dimensions, histological type and grade, lymphovascular and perineural invasion, nodal metastases, pathological stage, and involvement of resection margins.

For this analysis, the pathological proximal margin was defined as the minimum microscopic distance between the most proximal tumor focus and the cut end of the specimen. Distances documented in millimeters were converted to centimeters before statistical analysis.

Resections were categorized by the presence or absence of microscopic residual disease. R0 denoted the absence of tumor at every examined margin, whereas R1 denoted the presence of microscopic cancer at one or more margins.

Pathological T and N categories were assigned using the edition of the American Joint Committee on Cancer (AJCC) tumor-node-metastasis system that was current when each specimen was reported.

Data Collection

The dataset included age, sex, tumor site, histological category, differentiation, pathological T and N categories, lymphovascular and perineural invasion, numbers of examined and of metastatic lymph nodes, proximal margin distance, receipt of adjuvant treatment, recurrence, and survival status.

Follow-up Protocol

Postoperative surveillance was performed through the institutional gastric cancer follow-up program. Assessments consisted of clinical examination and laboratory tests; upper gastrointestinal endoscopy, thoracoabdominal computed tomography, or other imaging were obtained when clinically indicated.

Relapse was recorded when supported by radiological, endoscopic, histological, or clinical evidence following curative resection. Disease at the anastomosis or operative bed was considered local recurrence; hematogenous and peritoneal spread were categorized as distant recurrence.

Overall survival was measured from surgery until death from any cause, with living patients censored at their most recent follow-up. Disease-free survival was measured from surgery to the first recurrence or death.

Statistical Analysis

Analyses were conducted with IBM SPSS Statistics for Windows, version 27.0 (IBM Corp., Armonk, NY, USA).

Continuous-variable distributions were examined graphically with histograms and probability plots, and were also tested using the Kolmogorov-Smirnov procedure. Normally distributed data are reported as mean $\pm$ standard deviation; skewed data are given as median with minimum and maximum values. Counts and percentages describe categorical data.

For two-group comparisons, normally distributed continuous measures were analyzed with the independent-samples Student's t-test and non-normally distributed measures were analyzed with the Mann-Whitney U test. Pearson's chi-square test was used for categorical comparisons unless sparse cell counts required Fisher's exact test.

Kaplan-Meier estimates were used to construct overall and disease-free survival curves, and differences between curves were assessed by the log-rank test.

Candidate variables that were associated with recurrence or survival at $p<0.10$ in univariable testing were entered into multivariable Cox proportional hazards models. Effect estimates are presented as hazard ratios (HRs) with 95% confidence intervals (CIs).

All hypothesis tests were two-tailed, with $p<0.05$ defining statistical significance.

Results

The analysis included 186 patients who were treated with curative-intent for proximal gastric or GEJ adenocarcinoma. Mean age was 61.0±10.5 years, and 114 participants (61.3%) were men. The proximal pathological margin averaged 2.5±1.0 cm and the distal margin 9.5±3.0 cm. Patients had a median of 3 metastatic lymph nodes and a mean of 28.2±13.4 nodes examined. Mean observation time after surgery was 26.3±22.8 months. Baseline demographic, pathological, and follow-up data are detailed in Table 1.

Table 1. Baseline clinicopathological characteristics of the study population (n=186)

Variable	Value
Age (years), mean ± SD	61.0±10.5
Male sex, n (%)	114 (61.3)
Female sex, n (%)	72 (38.7)
Tumor diameter (cm), mean ± SD	4.8±2.7
Tumor volume (cm^3), mean ± SD	37.5±60.6
Positive lymph nodes, median (range)	3 (0-48)
Retrieved lymph nodes, mean ± SD	28.2±13.4
Resected esophageal segment (cm), mean ± SD	8.4±1.5
PCS (cm), mean ± SD	2.5±1.0
DCS (cm), mean ± SD	9.5±3.0
Follow-up duration (months), mean ± SD	26.3±22.8
Recurrence, n (%)	51 (27.4)
Mortality, n (%)	88 (47.3)

PCS: Proximal resection margin, DCS: Distal resection margin, SD: Standard deviation

Extended total gastrectomy accounted for 81.2% of procedures. Lymphadenectomy was classified as D2 in 59.1% of cases, D1 in 30.6%, and limited (recorded as "palliative lymphadenectomy") in 10.2%. 31.7% of patients received neoadjuvant treatment, and 95.7% received postoperative adjuvant therapy. Table 2 provides the complete distribution of operative and treatment variables.

Recurrence was documented in 51 patients (27.4%); no recurrence was recorded in 135 patients (72.6%). Locoregional disease alone occurred in 21 patients (11.3%), distant metastasis alone in 21 patients (11.3%), and both components in 5 patients (2.7%). By the end of follow-up, 88 patients (47.3%) had died.

The recurrence group had features indicative of more advanced disease. Its median metastatic node count was 7 (2-12), compared with 2 (0-5) in patients without recurrence ($p<0.001$). Splenectomy was more frequent in the recurrence group (23.5% vs. 8.9%, $p=0.016$), as was mortality (78.4% vs. 35.6%, $p<0.001$). Recurrence was unrelated to distal margin distance or to the length of esophagus resected. The pathological proximal margin was also similar between groups: 2.2 cm (2.0-3.0) in patients with recurrence and 2.5 cm (2.0-3.0) in patients without recurrence ($p=0.081$). Group comparisons are summarized in Table 3.

Factors associated with recurrence in preliminary analyses were jointly evaluated in a Cox model. Relative to D2 dissection, limited lymphadenectomy (recorded as "palliative lymphadenectomy") was associated with a higher recurrence hazard (HR: 2.99, 95% CI: 1.24-7.20, $p=0.014$). The hazard was also greater for pathological N3 disease than for N0 disease (HR: 5.60, 95% CI: 2.22-14.15, $p<0.001$) and for patients undergoing splenectomy (HR: 2.74, 95% CI: 1.32-5.69, $p=0.007$). Proximal margin distance did not remain in the model as an independent predictor. Full model estimates appear in Table 4.

Table 2. Surgical and treatment characteristics

Variable	n (%)
Extended total gastrectomy	151 (81.2)
ETG+splenectomy	22 (11.8)
ETG+phrenolaparotomy	8 (4.3)
Total gastrectomy	3 (1.6)
ETG+splenectomy+pancreatectomy	2 (1.1)
D2 lymphadenectomy	110 (59.1)
D1 lymphadenectomy	57 (30.6)
Palliative lymphadenectomy	19 (10.2)
Neoadjuvant therapy	59 (31.7)
No neoadjuvant therapy	124 (66.7)
Adjuvant therapy	178 (95.7)
No adjuvant therapy	4 (2.2)

ETG: Extended total gastrectomy

Table 3. Clinicopathological characteristics according to recurrence status

Variable	No recurrence (n=135)	Recurrence (n=51)	p-value
Positive lymph nodes	2 (0-5)	7 (2-12)	<0.001
Retrieved lymph nodes	28 (19-36)	21 (15-34)	0.063
Resected esophageal segment (cm)	8 (8-9.5)	8 (7-10)	0.249
PCS (cm)	2.5 (2-3)	2.2 (2-3)	0.081
DCS (cm)	9 (8-12)	10 (7-12)	0.581
Splenectomy, n (%)	12 (8.9)	12 (23.5)	0.016
Mortality, n (%)	48 (35.6)	40 (78.4)	<0.001

PCS: Proximal resection margin, DCS: Distal resection margin

Table 4. Independent predictors of recurrence

Variable	HR	95% CI	p-value
D1 vs D2 lymphadenectomy	1.55	0.825-2.917	0.173
Palliative vs. D2 lymphadenectomy	2.99	1.244-7.202	0.014
N1 vs. N0	1.19	0.414-3.397	0.751
N2 vs. N0	2.18	0.754-6.323	0.150
N3 vs. N0	5.60	2.217-14.145	<0.001
Splenectomy	2.74	1.324-5.688	0.007

HR: Hazard ratio, CI: Confidence interval

Table 5. Multivariable Cox regression analysis for overall survival

Variable	HR	95% CI	p-value
Neural invasion	2.00	1.169–3.412	0.011
Positive lymph node count	2.36	1.521–3.670	<0.001
Resected esophageal segment length	0.62	0.397–0.959	0.032
Recurrence	2.43	1.577–3.754	<0.001

Cox proportional hazards regression model (Omnibus test p<0.001)
HR: Hazard ratio, CI: Confidence interval

A separate multivariable model evaluated overall survival. Neural invasion was associated with a twofold increase in mortality hazard (HR: 2.00, 95% CI: 1.17-3.41, p=0.011), and greater metastatic node burden predicted poorer survival (HR: 2.36, 95% CI: 1.52-3.67, p<0.001). Recurrence conferred an approximately 2.4-fold increase in mortality hazard (HR: 2.43, 95% CI: 1.58-3.75, p<0.001). In contrast, a longer resected esophageal segment was associated with a lower hazard of death (HR: 0.62, 95% CI: 0.40-0.96, p=0.032). Table 5 lists the complete results.

Taken together, recurrence and survival were driven mainly by nodal burden, lymphadenectomy category, splenectomy, neural invasion, and relapse. After an R0 resection had been obtained, the measured proximal margin distance showed no independent association with recurrence.

Discussion

The increasing proportion of cancers arising in the proximal stomach and GEJ has sustained debate over the operation and resection extent most likely to provide durable cancer control (1,2). Complete excision remains essential, but the minimum acceptable proximal margin has not been determined. International recommendations prioritize R0 status while acknowledging uncertainty about the distance required for long-term safety (3,4).

Our central observation was the lack of an independent association between pathological proximal margin distance and recurrence after achieving microscopically negative margins. The margin was numerically shorter in patients who relapsed; however, the between-group difference was not statistically significant and was no longer evident in adjusted analyses. The cohort therefore provides no evidence that routinely removing a wider proximal segment improves oncological outcome after R0 resection. However, because proximal margin distance was analyzed as an observed continuous measure and no cut-off analysis was performed, the mean value of approximately 2.5 cm cannot be considered a definitive minimum adequate margin.

Concern about occult intramural extension historically favored generous proximal resections. Data published more recently do not uniformly support that practice. In the multi-institutional analysis by Postlewait et al. (11), proximal margin distance did not independently determine survival after resection of proximal gastric adenocarcinoma. Mine et al. (12) likewise reported acceptable outcomes in Siewert II and III cancers managed with limited proximal margins when histological clearance was confirmed. Our results align with those studies and suggest that the presence or absence of a tumor at the margin is more informative than distance alone.

Anatomical and biological heterogeneity across the esophagogastric junction partly explains why operative strategies remain variable. Changes incorporated into the AJCC system have affected how GEJ tumors are staged (13), whereas surgeons continue to use the Siewert categories when selecting an operative approach (14). Histological diversity within the junction further complicates uniform decision-making (15). Accordingly, institutions differ in their choice of access, the extent of esophageal resection, and nodal dissection.

Nodal status had a much stronger association with recurrence than did proximal margin distance. Pathological N3 disease was associated with a marked excess of relapse compared with N0 disease, consistent with the established prognostic importance of nodal burden in proximal gastric and GEJ cancer (16,17). Hasegawa et al. (16) used lymphatic dissemination patterns to define priorities for dissection in Siewert II/III tumors, and Barbour et al. (17) emphasized that an adequate nodal harvest

improves both staging and prognostic assessment in GEJ adenocarcinoma.

The category of nodal dissection was also relevant: patients in the limited lymphadenectomy category (recorded as "palliative lymphadenectomy" in the operative records) had a higher adjusted recurrence hazard. This label described a dissection less extensive than standard D1 or D2 lymphadenectomy and did not indicate that the gastric resection itself was palliative. The association should therefore be interpreted as reflecting both reduced nodal clearance and the adverse clinical or technical circumstances that led to a limited dissection. Previous work has similarly linked patterns of lymphatic spread and the extent of dissection to outcomes in junctional malignancies (18,19). Yamashita et al. (18) evaluated the optimal nodal field for Siewert II tumors, while Song et al. (19) showed that depth and site influence nodal distribution. These observations favor tailoring lymphadenectomy to disease anatomy rather than applying an identical field to every patient.

Splenectomy was independently associated with a greater risk of recurrence. The procedure was historically added to permit clearance of splenic hilar nodes, but routine splenectomy has been questioned because it increases morbidity without a consistent survival advantage (20,21). In our cohort, the association probably reflects selection of patients for splenectomy who have more locally advanced, biologically aggressive tumors, rather than a direct causal effect of organ removal.

The survival model identified neural invasion, metastatic node burden, and recurrence as adverse factors. This pattern is consistent with evidence that biological aggressiveness and the extent of nodal disease dominate prognosis after curative-intent resection (22,23). The magnitude of the effect of recurrence on mortality further underscores the need for effective local and systemic control.

A longer esophageal segment in the specimen was associated with better overall survival. Comparative studies of gastrectomy and esophagectomy for junctional cancer have also raised the possibility that a broader mediastinal component may benefit selected patients (24). However, this finding should be interpreted with caution because a retrospective cohort study cannot establish whether the length of the esophagus removed directly improves survival.

Study Limitations

Interpretation of these findings requires consideration of several limitations. The retrospective design permits selection bias and unmeasured confounding, and does not support causal inference. Results from one institution may not be extrapolated to centers with different case mixes or treatment pathways. The study covered a period during which staging, operative practice, perioperative care, and systemic therapy changed. Margin distance may have been influenced by tissue contraction and non-uniform specimen processing. No receiver operating characteristic, spline, or other cut-off analysis was performed; consequently, the observed mean proximal margin cannot establish a minimum adequate threshold. The limited lymphadenectomy category was based on terminology used in the operative records and may also reflect residual confounding from clinical or technical factors that prompted a less extensive dissection. Information on the precise pattern of recurrence and on adherence to adjuvant treatment was incomplete for some patients, and the number of relapse events limited the power of subgroup analyses.

The study nevertheless provides a comparatively large and clinically consistent series of patients who underwent total gastrectomy and distal esophagectomy. Detailed pathological margin measurements and parallel analyses of recurrence and mortality permitted a focused assessment of whether proximal margin distance contributes prognostic information beyond that provided by established disease-related factors.

Conclusion

Pathological proximal margin distance did not independently predict recurrence after curative-intent R0 resection of proximal gastric or GEJ adenocarcinoma. The observed mean proximal margin of approximately 2.5 cm describes this cohort and should not be interpreted as a definitive adequacy threshold.

Prognosis was more closely related to the biological and nodal extent of disease. Pathological N3 category, limited lymphadenectomy (recorded as "palliative lymphadenectomy"), and splenectomy were independently associated with recurrence; neural invasion, metastatic node burden, recurrence, and esophageal specimen length were independently associated with overall survival.

These results support an operative objective of microscopic tumor clearance combined with an appropriate lymphadenectomy, rather than the routine pursuit of an arbitrarily long proximal margin. Prospective multicenter studies incorporating prespecified margin cut-off analyses are warranted to define patient-specific resection requirements for proximal gastric and GEJ adenocarcinoma.

Ethics

Ethics Committee Approval: Approval was granted by the Van Yüzüncü Yıl University Non-Interventional Clinical Research Ethics Committee (approval no: 2020/10-03, date: 11.12.2020).

Informed Consent: Because existing records were analyzed retrospectively, the committee waived individual informed consent.

Footnotes

A generative artificial intelligence tool was used solely to assist with language revision and rephrasing. It was not used to design the study, generate or analyze data, or interpret the results. The authors reviewed and approved the final text and accepted full responsibility for its content.

Authorship Contributions

Concept/Design: O.O., M.B.Y., S.B., A.Ö., İ.Ö., İ.Ç., M.Ç.K., Data Collection or Processing: O.O., A.R.K., A.Ö., F.A., İ.Ç., M.Ç.K., Analysis or Interpretation: O.O., M.B.Y., S.B., A.Ö., İ.Ö., İ.Ç., R.K., M.Ç.K., Literature Review: O.O., M.B.Y., S.B., F.A., R.K., M.Ç.K., Writing, Reviewing and Editing: O.O., M.B.Y., S.B., A.R.K., İ.Ö., İ.Ç., M.Ç.K.

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CASE REPORT / OLGU SUNUMU

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Revision of a Prolapsed Ileostomy Using a Stapling Technique

Prolabe Olmuş İleostominin Stapler Yardımıyla Revizyonu

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Abstract

Stoma prolapse is one of the late complications of ileostomy and colostomy, with a reported incidence ranging from 2% to 22%. The rate of prolapse is particularly high in loop stomas. Several factors contribute to the development of prolapse, including obesity, conditions associated with increased intra-abdominal pressure, and creation of an excessively wide abdominal wall opening during stoma formation. Stoma complications are generally managed conservatively; however, because these approaches are often not definitive, surgical interventions are frequently required. In this case report, we present a 56-year-old male patient with a loop ileostomy who was admitted for stoma prolapse accompanied by impaired stomal circulation. The prolapsed stoma was successfully revised locally with a linear stapler, obviating the need for laparotomy.

Keywords: Ileostomy, stapler, stoma prolapse, stoma revision

Öz

Stoma prolapsusu, ileostomi ve kolostominin geç dönem komplikasyonlarından biridir. Görülme sıklığı %2-22 oranında bildirilmektedir. Özellikle loop stomalarda prolapsus oranı daha yüksektir. Prolapsus gelişiminde obezite, karın içi basıncı artıran durumlar ve stoma oluşturulurken karın duvarında geniş açıklık bırakılması gibi birçok faktör rol oynamaktadır. Stoma komplikasyonları genelde konservatif olarak yönetilir; fakat bu yöntem kalıcı olmadığı için cerrahi yöntemlere yönelinir. Bu olgu sunumunda da loop ileostomisi olan 56 yaşındaki erkek hastada gelişen stoma prolapsusu ve stomada meydana gelen dolaşım bozukluğuyla başvuran hastada laparotomi uygulanmaksızın lineer stapler yardımıyla lokal olarak revizyonu sunulmuştur.

Anahtar Kelimeler: İleostomi, stapler, stoma prolapsusu, stoma revizyonu

Introduction

Several risk factors have been identified for stomal prolapse. The most widely accepted theory suggests that an excessively long and mobile mesentery of the small intestine may lead to intussusception and, consequently, prolapse. In addition, an excessively wide fascial opening at the stoma site and increased intra-abdominal pressure are considered risk factors for stomal prolapse.

Stomal prolapse is a late complication of ileostomy or colostomy and has been reported to occur in 2-22% of loop stomas (1). Moreover, the overall morbidity rate associated with stomas ranges from 20% to 70%, representing a substantial clinical

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burden (2). Prolapse adversely affects patients' quality of life and may result in peristomal dermatitis, difficulty in fitting stoma appliances, bleeding, stomal discharge, obstruction and, in some cases, strangulation (3-5).

Most stoma-related complications are initially managed conservatively; however, since this approach is often not definitive, surgical intervention is frequently required. Although several surgical techniques and approaches have been described, there is still insufficient evidence to support the superiority of one technique over another.

In this case report, we present the local stapler-assisted treatment of a loop ileostomy prolapse that developed in a patient who had previously undergone low anterior resection for rectal cancer, without the need for laparotomy.

Case Presentation

Written informed consent was obtained from the patient for publication of this case report and the accompanying images. A 56-year-old male patient with no known comorbidities underwent low anterior resection with creation of a protective loop ileostomy for rectal cancer one month prior. Approximately one month after surgery, the patient presented to our clinic with complaints of prolapse of the ileostomy and discoloration of the stoma.

On physical examination, the abdomen was soft, with no guarding or rebound tenderness. Marked prolapse of the intestinal mucosa was observed at the distal limb of the loop ileostomy, and was accompanied by significant edema and impaired circulation in the prolapsed bowel segment (Figure 1). The proximal limb of the ileostomy was normal, with adequate discharge of enteric contents.

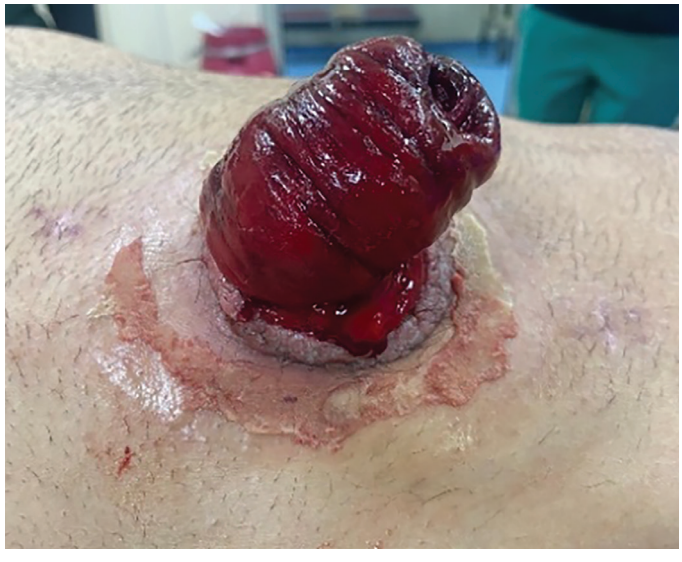

Figure 1. Prolapsed loop ileostomy

The patient was taken emergently to the operating room. The procedure was initiated with the patient sedated in the supine position. A gastrointestinal linear stapler was applied to the prolapsed distal limb of the ileostomy (Figure 2). The superior aspect of the prolapsed ileostomy was transected in the sagittal plane at the 12 o'clock position, maintaining a distance of 0.5 cm from the skin (Figure 3).

In the second stage, the stapler was positioned on the inferior aspect of the prolapsed ileostomy at the 6 o'clock position and fired in the sagittal plane, maintaining a distance of 0.5 cm from the skin (Figures 4 and 5). These two staple lines divided the prolapsed ileostomy segment into two parts along the sagittal plane.

In the third step, each segment was resected at its base using a stapler, parallel to and 0.5 cm from the skin (Figures 6 and 7).

Thus, a total of four stapler cartridges were used throughout all steps of the procedure. In the final stage, the entire prolapsed segment was excised, and the circumferential edge of the ileostomy was rematured at a distance of 0.5 cm from the skin (Figure 8).

Figure 2. Placement of the stapler into the ileostomy lumen

The total operative time was 20 minutes, and the patient was discharged uneventfully at 24 hours postoperatively. Follow-up evaluation of the ileostomy was performed 10 days after surgery. The patient's symptoms had resolved, and there was no evidence of stoma prolapse. Adequate passage of gas and stool was observed, and complete wound healing was noted (Figure 9).

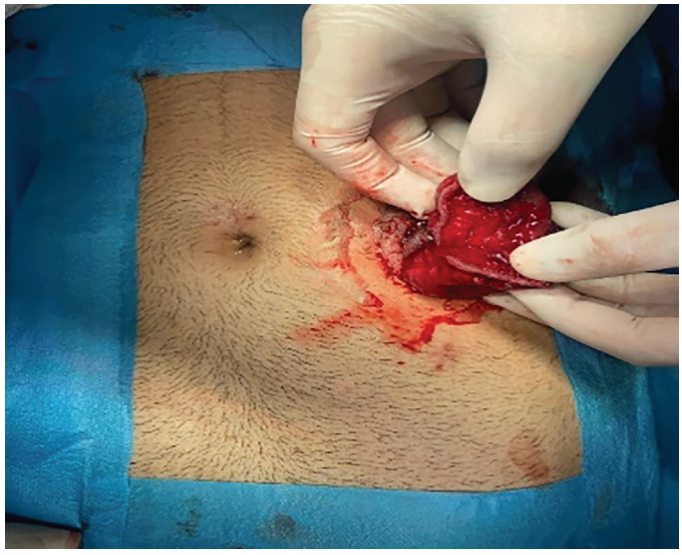

Figure 3. Sagittal transection at the 12 o'clock position

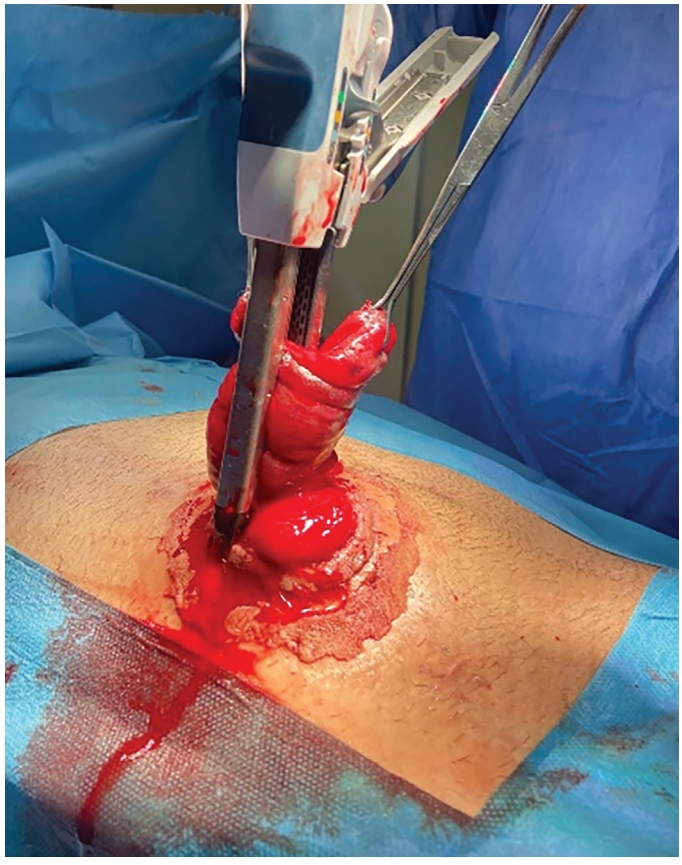

Figure 4. Placement of the linear stapler at the 6 o'clock position

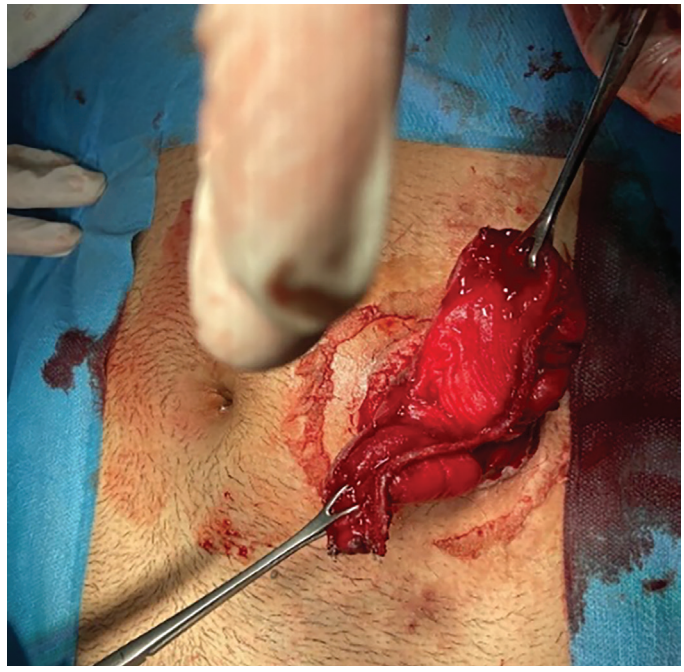

Figure 5. Sagittal transection at the 6 o'clock position

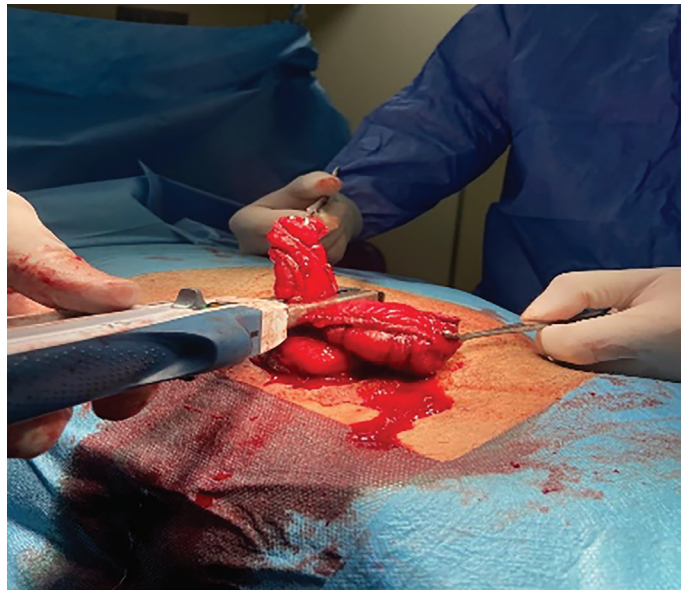

Figure 6. Resection of the superior segment

Discussion

Stoma creation is commonly performed in colorectal surgery, particularly for malignant diseases and inflammatory bowel disorders. Stomas may be temporary or permanent and can be fashioned as ileostomies or colostomies. Stomas are classified according to their configuration as end, Hartmann-type, or loop. Stomal prolapse has been reported to occur more frequently in loop stomas than in end stomas, and it typically involves the distal limb (6,7). In our case, the patient had a loop ileostomy; consistent with the literature, a prolapse developed in the distal segment.

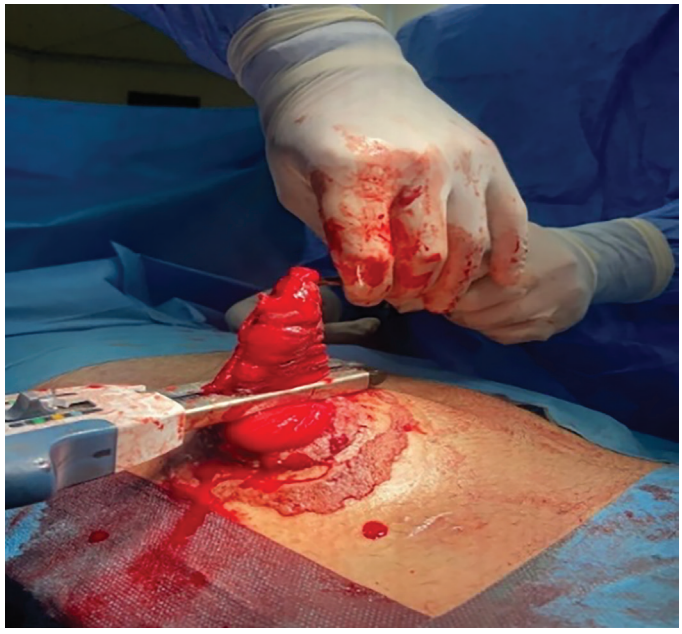

Figure 7. Resection of the inferior segment

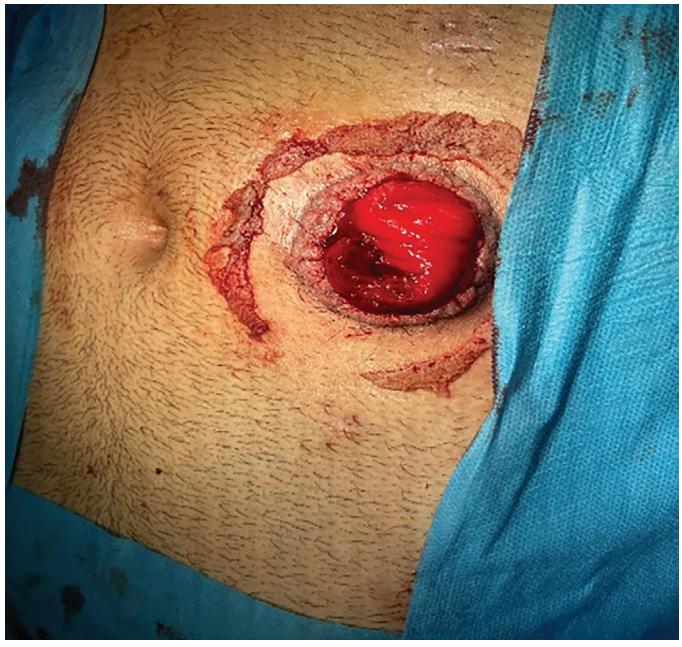

Figure 8. Appearance of the ileostomy after revision

Multiple factors have been implicated in the development of stomal prolapse, including obesity, creation of an excessively wide fascial opening during stoma formation, conditions associated with increased intra-abdominal pressure, and the presence of an excessive length of bowel proximal to the stoma (8). It has been reported that failure to suture the mesentery to the peritoneum during stoma creation does not have a significant effect on the development of prolapse, as prolapse is most commonly of the sliding type (9). In our case, no identifiable predisposing factors for stomal prolapse were detected.

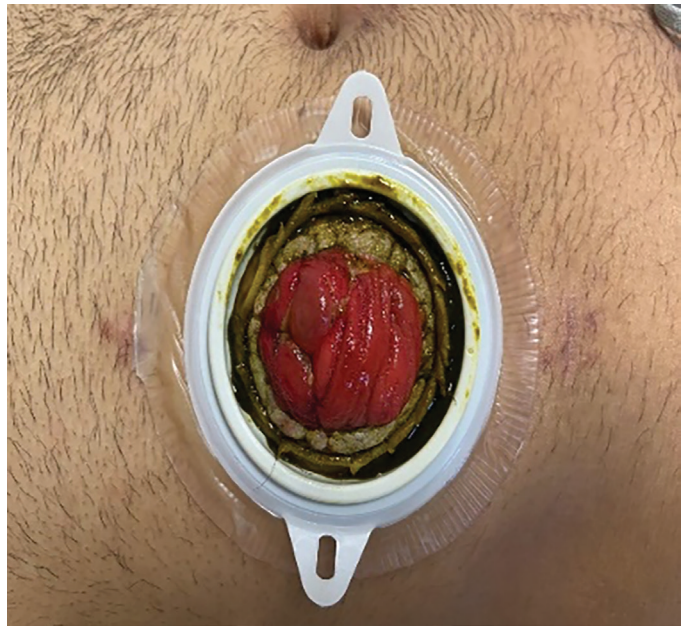

Figure 9. Appearance of the ileostomy 10 days after surgery

Various surgical techniques have been described for the revision of stomal prolapse. Resection of the prolapsed segment through the stoma and conversion of a loop colostomy to an end-loop colostomy have long been used as surgical treatment options. However, these techniques are associated with disadvantages such as the need for laparotomy, prolonged hospital stay, wound infections, and in some cases, reoperation. Another commonly used method, button-pexy fixation, is associated with high recurrence rates, particularly in patients with large prolapses (10). Repair of stomal prolapse using a linear stapler was first described by Maeda et al. (11). With the increasing surgical use of stapling devices, case series have reported successful stapler-assisted revisions of loop colostomies, loop ileostomies, and rectal prolapse (1,11,12). In our case, stapler-assisted stoma prolapse revision was performed to avoid complications associated with conventional surgical methods described in the literature. This approach eliminated the need for laparotomy and reduced the risk of prolonged hospitalization and postoperative wound infection, both commonly associated with traditional surgical techniques.

Conclusion

Stapler-assisted stoma revision for patients with stomal prolapse is a technique that allows stoma correction without laparotomy. Compared with conventional surgical approaches for stomal prolapse, this method offers several advantages, including shorter operative time, shorter postoperative hospital stay, and lower risk of postoperative complications.

Ethics

Informed Consent: Written informed consent was obtained from the patient for publication of this case report and the accompanying images.

Footnotes

Authorship Contributions

Concept/Design: İ.A., Data Collection or Processing: İ.Ç., Analysis or Interpretation: S.G., Literature Review: Z.Z., Writing, Reviewing and Editing: Y.K., İ.C.E.

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

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CASE REPORT / OLGU SUNUMU

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Ovarian Brenner Tumor Colliding with Mucinous Cystadenoma: A Case Series

Over Kaynaklı Brenner Tümörü ile Müsinöz Kistadenom Birlikteliği: Bir Olgu Serisi

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Abstract

Ovarian Brenner tumors are rare epithelial neoplasms often found in association with mucinous tumors, particularly mucinous cystadenomas. However, their combined presentation may pose diagnostic challenges due to overlapping clinical and radiological features with those of malignant ovarian neoplasms. We report three cases of ovarian Brenner tumors coexisting with mucinous cystadenomas in postmenopausal women, aged 67-77 years. Clinical manifestations ranged from abdominal distension and pain to incidental findings. Imaging studies consistently demonstrated cystic-solid adnexal masses, sometimes with calcifications or ascites, raising suspicion for malignancy. Histopathological examination confirmed the coexistence of a Brenner tumor and a mucinous cystadenoma in all cases, including one borderline Brenner tumor. Immunohistochemistry supported the diagnosis, with Brenner components expressing urothelial markers such as CK7, p63/p40, and GATA3, while mucinous components displayed distinct immunohistochemical profiles. These cases highlight the importance of recognizing this entity to avoid misdiagnosis and suggest a possible histogenetic relationship between Brenner and mucinous tumors.

Keywords: Brenner tumor, case report, collision tumor, ovarian mucinous cystadenoma

Öz

Over Brenner tümörleri, nadir görülen epitelyal neoplazmlardır ve sıklıkla müsinöz tümörlerle, özellikle müsinöz kistadenomlarla birlikte bulunurlar. Bununla birlikte, bu tümörlerin birlikte görülmesi, malign over neoplazmları ile örtüşen klinik ve radyolojik özellikler nedeniyle tanısal zorluklara yol açabilir. Bu çalışmada, 67-77 yaş aralığında postmenopozal üç kadında Brenner tümörü ile müsinöz kistadenom birlikteliği sunulmaktadır. Klinik bulgular, abdominal distansiyon ve ağrıdan tesadüfi saptamalara kadar değişkenlik göstermiştir. Görüntüleme incelemelerinde, bazen kalsifikasyon veya asit eşlik eden kistik-solid adneksiyal kitleler izlenmiş ve malignite şüphesi doğurmuştur. Histopatolojik inceleme, tüm olgularda Brenner tümörü ile müsinöz kistadenomun birlikte bulunduğunu doğrulamış, bunlardan birinde borderline Brenner tümörü saptanmıştır. İmmünohistokimyasal bulgular tanıyı desteklemiş; Brenner komponentlerinin CK7, p63/p40 ve GATA3 gibi ürotelyal belirteçleri eksprese ettiği, müsinöz komponentlerin ise farklı profiller gösterdiği izlenmiştir. Bu olgular, yanlış tanıyı önlemek açısından bu varlığın tanınmasının önemini vurgulamakta ve Brenner ile müsinöz tümörler arasında olası bir histogenez ilişkisini düşündürmektedir.

Anahtar Kelimeler: Brenner tümörü, olgu sunumu, çarpışma tümörü, over müsinöz kistadenomu

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Introduction

Brenner tumors are uncommon ovarian epithelial neoplasms, usually benign and characterized by transitional-type epithelial nests within dense fibrous stroma, although borderline and malignant variants exist (1,2). They frequently coexist with mucinous ovarian tumors, particularly mucinous cystadenomas, suggesting a possible shared histogenesis. Clinically and radiologically, these lesions often present as cystic-solid adnexal masses, sometimes with calcification, making preoperative diagnosis challenging. We report three cases of ovarian Brenner tumor associated with mucinous cystadenoma and summarize their clinicopathological and imaging features to improve recognition of this diagnostically important entity.

Case Presentation

Case 1

A 77-year-old woman presented with a 4-month history of lower abdominal distension and urinary frequency, without an obvious precipitating cause. She denied any other relevant medical history. Physical examination revealed a palpable mass in the lower abdomen with limited mobility, without tenderness or rebound tenderness. Laboratory tests revealed elevated tumor markers, including carbohydrate antigen (CA) 125 at 53.10 U/mL and CA19-9 at 205.48 U/mL. Abdominal computed tomography (CT) and magnetic resonance imaging (MRI) demonstrated a giant cystic-solid pelvic mass measuring approximately 17.1×13.2×20.8 cm. The lesion showed heterogeneous density and signal intensity, with multiple calcifications visible within it. No obvious pelvic effusion or abnormally enlarged lymph nodes were identified. Imaging revealed that the pelvic mass was predominantly cystic, with a few internal septa and soft tissue components. On MRI, the lesion showed low signal intensity on T1-weighted imaging and high signal intensity on T2-weighted imaging (T2WI). Contrast-enhanced imaging demonstrated marked enhancement of the solid components, whereas the cystic components showed no obvious enhancement. Cystadenocarcinoma was initially suspected (Figure 1).

The patient underwent a total abdominal hysterectomy with bilateral salpingo-oophorectomy. Postoperative pathological examination confirmed a borderline Brenner tumor of the left ovary coexisting with a mucinous cystadenoma, with multifocal stromal calcification. Immunohistochemical staining showed that the tumor cells were positive for CK-P, CK7, p63, p53, ER, CA125, and GATA3 and were negative for PR, CK20, CgA, NSE, and S-100. The Ki-67 labeling index was approximately 20%. No recurrence was observed at the 1-year postoperative follow-up.

Case 2

A 71-year-old woman was admitted with a 2-day history of lower abdominal pain. Physical examination revealed lower abdominal distension with mild tenderness, without rebound tenderness. Laboratory tests showed markedly elevated tumor markers, including CA125 at 934 U/mL and CA19-9 at 43.05 U/mL.

Abdominal CT demonstrated a mixed cystic-solid soft-tissue-density mass in the pelvis, with the larger lesion located on the right side and measuring approximately 17.9×12.3×17.0 cm. Contrast-enhanced imaging showed moderately heterogeneous enhancement. The surrounding bowel loops were compressed, and the lesion contained non-enhancing cystic areas and calcifications. In addition, a solid, soft-tissue-density mass measuring approximately 4.6 cm in diameter was identified in the left pelvis; it contained multiple punctate calcifications. Pelvic effusion was also present (Figure 2). The patient underwent a laparoscopic bilateral salpingo-oophorectomy.

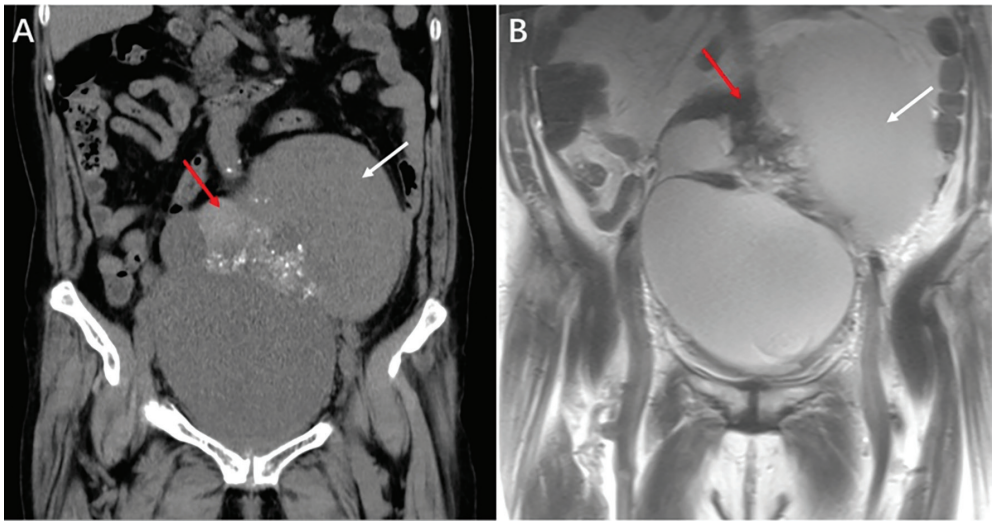

Figure 1. Coronal computed tomography and coronal magnetic resonance imaging demonstrate a large cystic-solid pelvic mass

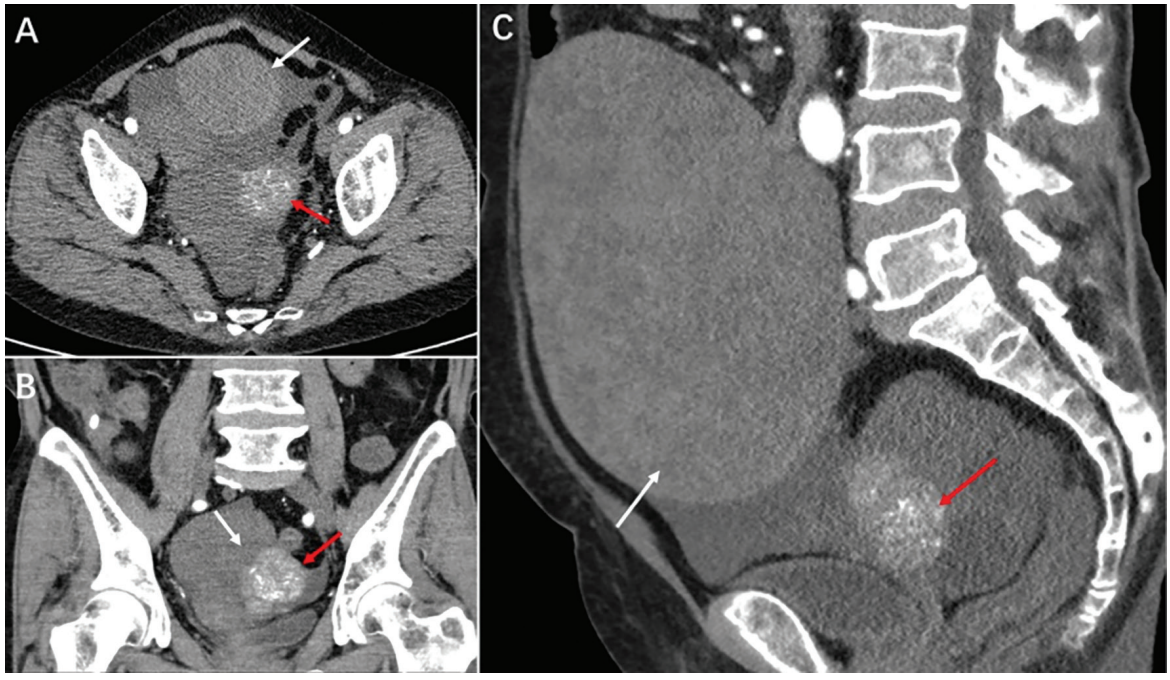

Figure 2. An abdominal computed tomography scan shows a cystic-solid pelvic mass accompanied by pelvic effusion

Postoperative pathological examination revealed a mucinous cystadenoma coexisting with a Brenner tumor in the left ovary. Immunohistochemical and special staining findings were as follows: nests of epithelial-like cells were positive for CK-P, EMA, CK7, WT-1, GATA3, and CA19-9, and negative for CK20, calretinin, and inhibin-α. P53 showed weak-to-moderate positivity in approximately 80% of cells, and the Ki-67 labeling index was 2%. PAS staining was positive. The mucinous epithelium was positive for CKpan, EMA, CK7, and CA19-9, and negative for CK20, calretinin, inhibin-α, WT-1, and GATA3. P53 was partially positive, and the Ki-67 labeling index was 10%. PAS staining was also positive. The patient was lost to follow-up after surgery.

Case 3

A 67-year-old woman was incidentally found to have a pelvic cystic mass on routine ultrasonography 2 months earlier and subsequently presented with dull pain in the left lower abdomen. Her medical history was significant for hypertension for 6 years and for surgery for lung cancer 3 years previously. Laboratory tests showed CA125 of 9.90 U/mL, CA19-9 of 4.52 U/mL, and squamous cell carcinoma antigen of 1.8 ng/mL (elevated). Cervical human papillomavirus testing and cervical cytology showed no obvious abnormalities.

Pelvic MRI demonstrated a round cystic-solid mass in the left adnexal region with well-defined margins, measuring approximately 53×38×46 mm. The lesion showed heterogeneous signal intensity, and part of the cystic fluid exhibited markedly low signal intensity on T2WI. The solid component showed mildly increased signal intensity on diffusion-weighted imaging and mildly decreased signal intensity on the apparent diffusion coefficient map. Contrast-enhanced imaging demonstrated marked enhancement. A small pelvic effusion was present, and no enlarged lymph nodes were identified. Struma ovarii was initially considered, but an epithelial mucinous tumor could not be excluded (Figure 3).

The patient underwent laparoscopic bilateral salpingo-oophorectomy. Postoperative pathological examination supported the diagnosis of an ovarian Brenner tumor with mucinous metaplasia and calcific deposition, coexisting with an ovarian mucinous cystadenoma with focal epithelial hyperplasia. Immunohistochemical analysis showed that the tumor cells were positive for CK5/6, p40, CK7, CAM5.2, Ki-67 (approximately 25%), p53 (wild-type expression), and GATA3 (partially positive), and were negative for uroplakin 2. No recurrence was observed at the 3-month postoperative follow-up.

Informed consent was obtained from the patient for the anonymous use and publication of clinical and imaging data.

Discussion

Among ovarian tumors, epithelial neoplasms are the most common tumor type and include mucinous and Brenner tumors. Ovarian mucinous tumors account for approximately 10%-15% of all ovarian neoplasms, of which about 80% are benign (1). In contrast, Brenner tumor is a relatively rare epithelial ovarian neoplasm, representing only 1%-2% of all ovarian tumors (2,3).

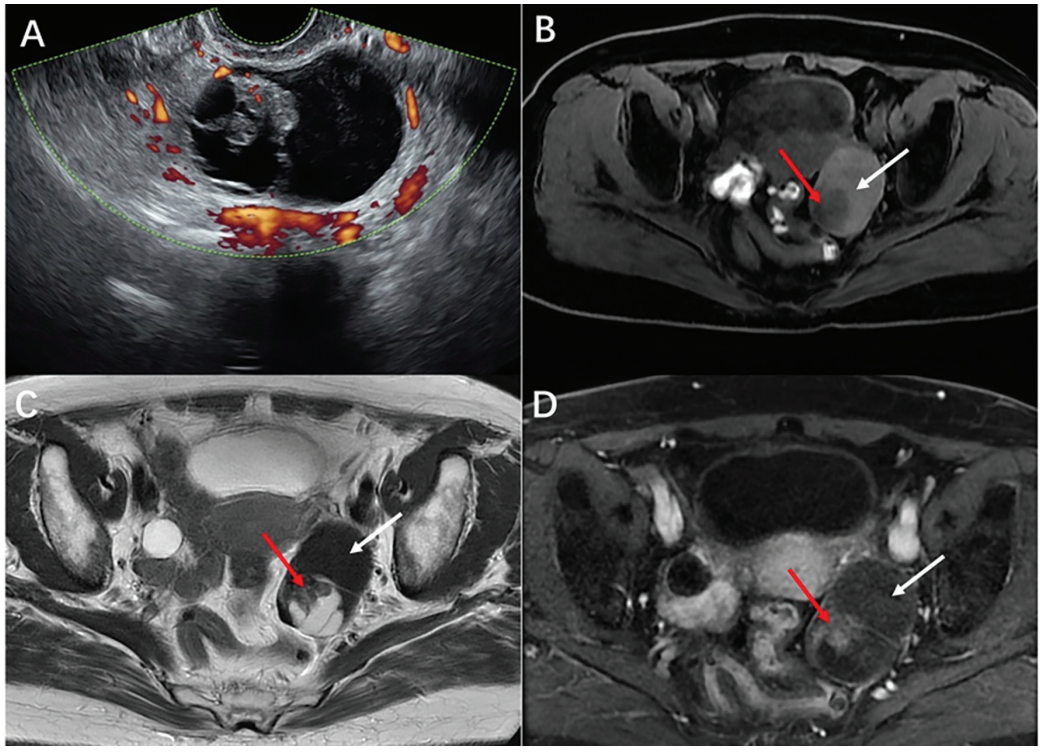

Figure 3. Pelvic ultrasound reveals a cystic-solid mass in the left adnexal region; pelvic magnetic resonance imaging demonstrates a heterogeneous mass in the same region with enhancement of the solid components

It occurs predominantly in postmenopausal women, and the vast majority (approximately 99%) are benign (1).

Brenner tumors are usually small, lack specific clinical manifestations, and are therefore often discovered incidentally during imaging examinations or surgery. In some cases, Brenner tumors may coexist with other types of epithelial ovarian tumors, among which mucinous cystadenoma is the most common. It has been reported that approximately 10% of Brenner tumors are associated with a mucinous tumor component, suggesting a possible biological relationship between these two entities (2). It is currently widely accepted that the coexistence of Brenner tumor and mucinous cystic tumor may arise from a shared origin in the ovarian surface epithelial-stromal complex, whose cells possess multidirectional differentiation potential and are capable of differentiating into different epithelial components (4-6). Some investigators have proposed that the mucinous component may originate from mucinous metaplasia of the Brenner tumor epithelium or that both components may arise from the same precursor lesion. Although the exact pathogenesis has not yet been fully elucidated, molecular pathological studies have identified KRAS mutations in both tumor components in some cases, thereby supporting the hypothesis of a possible clonal origin (7).

From a diagnostic perspective, the mucinous cystic component is often dominant and may obscure the smaller Brenner tumor component, which typically presents as solid nodules embedded within the cyst wall and can therefore be overlooked. Consequently, careful gross intraoperative examination, systematic postoperative sampling, and meticulous histopathological evaluation are essential for establishing an accurate diagnosis. Although imaging modalities such as ultrasonography and CT are highly sensitive in detecting cystic lesions, their ability to identify small solid nodules is limited, which is a major reason for preoperative or intraoperative misdiagnosis.

From a clinical management perspective, the vast majority of Brenner tumors and mucinous cystadenomas are benign lesions, and complete surgical excision usually results in favorable outcomes. For postmenopausal women, especially when malignancy cannot be completely excluded preoperatively, total hysterectomy with bilateral salpingo-oophorectomy is generally recommended (2). In the present case, the patient was perimenopausal, and the nature of the tumor remained uncertain; therefore, this surgical approach was selected.

Overall, the postoperative prognosis of this type of tumor is favorable. However, it should be noted that both Brenner and mucinous tumors may rarely present as borderline or malignant subtypes, further underscoring the importance of comprehensive histopathological evaluation. In the present case, no obvious malignant features, such as significant cytologic atypia, increased

mitotic activity, or stromal invasion, were identified, thereby confirming that both tumor components were benign.

Conclusion

This case highlights the importance of recognizing composite ovarian tumors, particularly the relatively uncommon but diagnostically significant coexistence of a Brenner tumor and a mucinous cystadenoma. Greater awareness of this entity may help pathologists avoid missed or incorrect diagnoses, while also providing an important basis for appropriate surgical planning and prognostic assessment in clinical practice.

Ethics

Informed Consent: Informed consent was obtained from the patient for the anonymous use and publication of clinical and imaging data.

Footnotes

Authorship Contributions

Concept/Design: W.Y., C.H., Data Collection or Processing: W.Y., Analysis or Interpretation: W.Y., C.H., Literature Review: W.Y., C.H., Writing, Reviewing and Editing: W.Y., C.H.

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

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CASE REPORT / OLGU SUNUMU

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Gastrointestinal Stromal Tumor of the Jejunum with Recurrent Bleeding: A Case Report and a Brief Literature Review

Tekrarlayan Kanamalı Jejunum Gastrointestinal Stromal Tümörü: Bir Olgu Sunumu ve Kısa Literatür Taraması

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Abstract

Bleeding from gastrointestinal (GI) stromal tumour (GIST) of the jejunum is rare and is reported in the literature as isolated clinical observations or small series. In the present study, we report a case of a 64-year-old woman who presented with recurrent GI bleeding. Upper endoscopy revealed no signs of bleeding. A contrast-enhanced computed tomography (CT) scan was performed, and a predominantly intraluminal, heterogeneous, tumour-like mass in the proximal jejunum was visualised, with dimensions 4.6x4.4x6.1 cm. A midline laparotomy was performed, and exploration of the abdominal cavity revealed a tumour in the lumen of the jejunum located 30 cm from the ligament of Treitz. Segmental resection of the jejunum with tumour, followed by anastomosis, was performed. On pathologic examination and immunohistochemistry, a spindle cell variant of GIST (c-KIT/CD117 +++) with negative resection margins (R0) was recognised. GIST of the jejunum is a relatively rare cause of gastrointestinal bleeding. The main diagnostic method is contrast-enhanced CT. The treatment of choice for bleeding jejunal GIST is segmental resection with a negative surgical margin (R0 resection), without compromising tumor integrity.

Keywords: Small bowel, gastrointestinal stromal tumor, intermittent GI bleeding

Öz

Jejunum gastrointestinal (GI) stromal tümör (GIST) kaynaklanan kanama, nadir görülen bir kanama nedenidir ve literatürde münferit klinik gözlemler veya küçük olgu serileri şeklinde yer almaktadır. Bu çalışmada, tekrarlayan GI kanama semptomları ile başvuran 64 yaşındaki bir kadın hastanın olgusunu sunuyoruz. Üst endoskopi incelemesinde: kanama bulgusu yoktu. Kontrastlı bilgisayarlı tomgrafi (BT) taraması yapıldı ve proksimal jejunumda boyutları 4,6x4,4x6,1 cm olan, ağırlıklı olarak lümen içi, heterojen, tümör benzeri bir kitle saptandı. Orta hat laparotomi yapıldı ve karın boşluğunun incelenmesi sonucunda Treitz bağından 30 cm uzaklıkta jejunum lümeninde bir tümör saptandı. Tümörlü jejunumun segmental rezeksiyonu ve ardından anastomoz uygulandı. Patolojik inceleme ve immünohistokimyada: rezeksiyon sınırları negatif (R0) olan GIST'nin iğ hücreli varyantı (c-KIT/CD117 +++) tanındı. Jejunum GIST'ı, GI kanamanın oldukça nadir bir nedenidir. Ana tanı yöntemi kontrastlı BT'dir. Kanamalı jejunal GIST için tercih edilen tedavi, tümörün bütünlüğünü bozmadan negatif cerrahi marjlı (R0 rezeksiyon) segmental rezeksiyondur.

Anahtar Kelimeler: İnce bağırsak, gastrointestinal stromal tümör, aralıklı GI kanama

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Introduction

Gastrointestinal (GI) stromal tumours (GISTs) are the most frequent sarcomas of the GI tract (1-3). GISTs are most commonly localised in the stomach (50-70%), in the small intestine 32%, in the colon and rectum 6% and in the oesophagus <1% (2). GISTs of the jejunum are quite rare and account for 0.04% of all GI neoplasms (4).

Bleeding from the small intestine is quite rare and accounts for 5-10% from the whole spectrum of GI haemorrhages (5). Moreover, bleeding from GIST of the jejunum is rare and is reported in the literature as isolated clinical observations (2-4,6-18) or as small series (19). Given the low incidence of jejunal GIST as a cause of lower GI bleeding, we present our documented clinical case.

Case Presentation

A 64-year-old female was transferred from a district hospital after three days of treatment for GI bleeding of unclear aetiology. On admission, the patient complained of persistent rectal bleeding (hematochezia) for three days, weakness, and dizziness. For the last two years, the patient has experienced a similar episode of GI bleeding from an unidentified source, which was managed conservatively. Over the last six years, type II diabetes mellitus has been diagnosed and managed with drug therapy.

The patient's general condition was assessed as moderately severe. On physical examination, cutaneous pallor was noted. Respiratory rate -18/min. Heart rate -100/min. Blood pressure 110/70 mmHg. The abdomen participates in the act of breathing; no tenderness was noted. No masses are detected; the liver and spleen are not palpated. On examination per rectum, signs of blood were noted on the glove. On upper GI endoscopy examination: gastritis, no signs of bleeding.

On admission, general blood analysis: red blood cell count $2.2x10^{12}$/L (reference range, 3.3-5.5 $x10^{12}$/L), haemoglobin 72 g/L (reference range, 120-160 g/L), haematocrit 21.1% (reference range, 35-52%), platelets $108x10^{9}$/L (reference range, 172-380$x10^{9}$/L), leukocytes $14.5x10^{9}$/L (reference range, 3.5-10.0$x10^{9}$/L), neutrophils 89.2% (reference range, 45-73%), lymphocytes 4.5% (reference range, 19-37%), monocytes 4.4% (reference range, 3-11%), eosinophils 4.9% (reference range, 0.5-5%), basophils 0.4% (reference range, 0-1%).

Biochemical tests: urea 8.5 mmol/L (reference range, 2.8-9.2 mmol/L), creatinine 61.2 µmol/L (reference range, 44-106 µmol/L), glucose 7 mmol/L (reference range, 4.1-5.9 mmol/L), alanine aminotransferase 12.4 U/L (reference range, 0-45 U/L), aspartate aminotransferase 18 U/L (reference range, 0-35 U/L), total bilirubin 7.3 µmol/L (reference range, 2-21 µmol/L, total protein 30.8 g/L (reference range, 66-87 g/L), albumin 19.9 g/L (reference range, 35-52 g/L), potassium 3.75 mmol/L (reference range, 3.5-5.5 mmol/L), sodium 141 mmol/L (reference range, 135-145 mmol/L), chlorine 106.8 mmol/L (reference range, 98-108 mmol/L), prothrombin 72% (reference range, 70-120%), fibrinogen 1.88 g/L (reference range, 2-4 g/L), thrombin time 16.63 sec. (<30 sec.), international normalized ratio 1.03.

The patient was admitted to the intensive care unit, haemostatic therapy was started, and a transfusion of erythrocyte mass and fresh-frozen plasma was performed. The patient's condition was stabilized, with no signs of persistent bleeding.

A contrast-enhanced computed tomography (CT) scan was performed (Figure 1A, B). In the proximal jejunum, a predominantly intraluminal, heterogeneous, tumour-like mass was visualised, with dimensions 4.6x4.4x6.1 cm and native density from +17 to +26 Hounsfield units (HU). Single punctiform calcifications are observed within the tumour. On contrast-enhanced CT scans, an increase in tumour density from

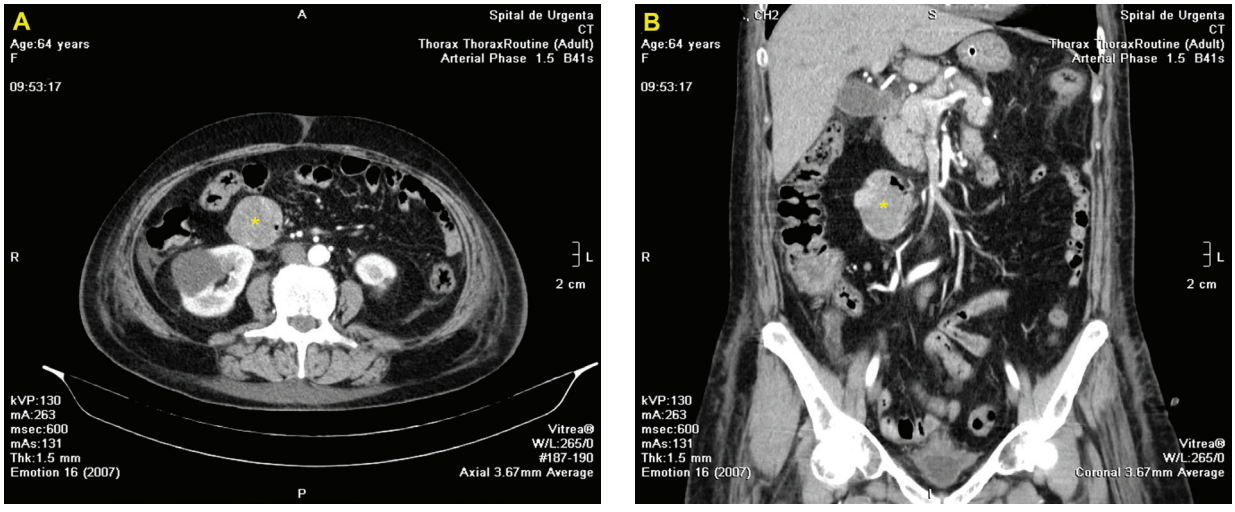

Figure 1. Computed tomography (CT) with angiography (A) axial and (B) coronal projections: a 4.6x4.4x6.1 cm solid mass in the proximal jejunum (*)

+31 to 60 HU was noted. Conclusion: jejunal tumour, most likely a GIST.

A midline laparotomy was performed. Exploration of the abdominal cavity revealed a tumour in the lumen of the jejunum at a distance of 30 cm from the Treitz's ligament (Figure 2). Segmental resection of the jejunum with tumour, followed by anastomosis was performed.

On pathologic examination, a spindle cell variant of GIST was found with low mitotic activity (<5/50HPF). Immunohistochemical examination revealed diffuse cytoplasmic expression of c-KIT/CD117 in tumour cells (Figure 3), as well as diffuse expression of CD34. According to the morphological study, the resection margins were classified as R0.

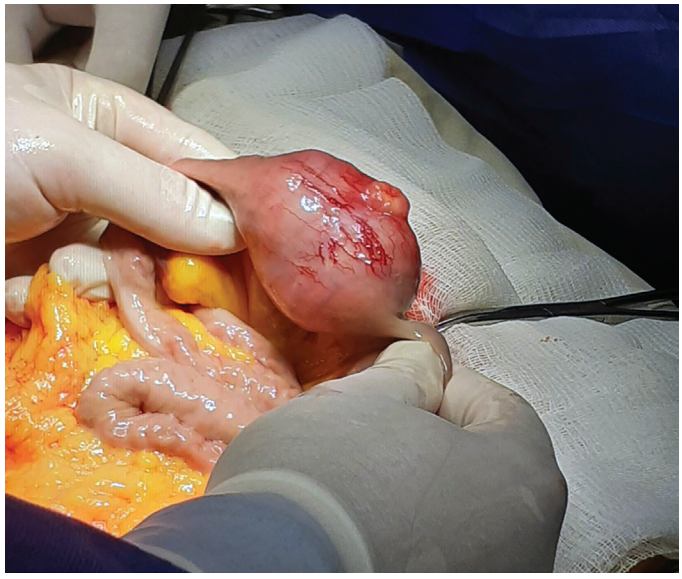

Figure 2. Intraluminal tumour of the jejunum (intraoperative photo)

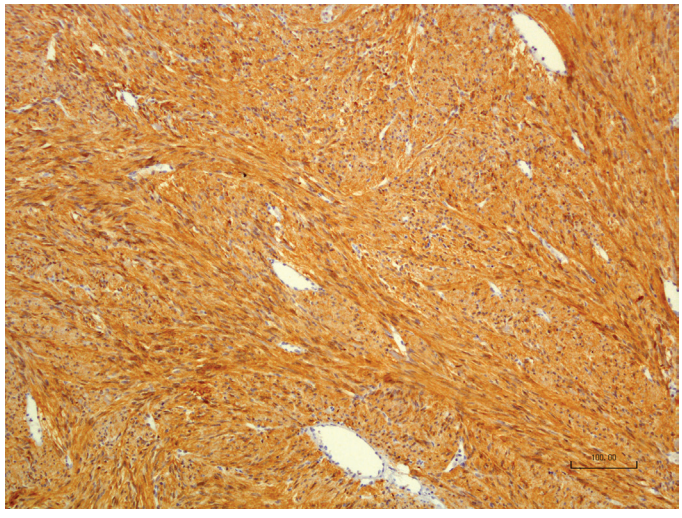

Figure 3. Immunohistochemistry: diffuse cytoplasmic expression of CD 117 (c-kit) (3,3'-diaminobenzidine x100) in tumour cells

The postoperative period was uneventful. The patient was discharged in good condition on postoperative day 14 and was referred to the Research Institute of Oncology for further treatment. The multidisciplinary team reviewed the patient and decided to initiate targeted therapy with imatinib mesylate 400 mg daily. Examined 14 months later, the patient was asymptomatic.

Oral and written informed consent was obtained from the patient to publish the patient-related data in anonymized form.

Discussion

It is generally accepted that GIST originate from interstitial cells of Cajal or their precursors located in the muscle layer and are the pacemaker of the GI tract (1-3,15,20). GISTs are characterized by overexpression of the tyrosine-kinase receptor c-KIT and are primarily associated with activating mutations in KIT (exons 9, 11, 13, 17) and PDGFRA (exons 12, 14, 18) (3). The majority of GIST cases (70-80%) harbor a mutation in *KIT* gene and in less than 10% -in *PDGFRA* gene, otherwise 10-15% are wild-type GIST (1).

The incidence of GISTs in most studies is 1-2 cases per 100.000 populations per year (1,20). The mean age of patients with GIST is typically 60-65 years and the male to female ratio approaches 1:1 (3,12,20). In the vast majority of cases GISTs are sporadic, but in some cases these neoplasms are associated with neurofibromatosis type 1-NF1 (von Recklinghausen disease), Carney triad, Carney-Stratakis syndrome (3,9,20). An analysis of the surveillance, epidemiology, and end results database that included 702 patients with small intestinal GISTs found differences between tumors in the jejunum and ileum. Thus, compared with ileal localization, GISTs were localized significantly more often in the jejunum (67.2%), were smaller, and were observed more frequently in male patients. Traditionally, GISTs in the ileum are considered more frequent than in the jejunum, with a ratio of 60% vs. 40% (1).

The clinical manifestations of GISTs are non-specific and depend on tumor size, localization, predominant pattern of neoplasm growth (intraluminal or extraluminal), and in 20% of cases these neoplasms are asymptomatic (1,11). Clinical symptoms of GISTs include: GI bleeding (30-40%), abdominal pain (20-50%), and obstructive syndrome (10-30%) (1,13).

Factors contributing to the development of bleeding in GIST are: tumors localized in the small intestine, tumor size ≥5 cm, mitotic count ≥5/HPF and tumor rupture (1,11,20). Nevertheless, in the literature there are descriptions of massive bleeding from smaller size intestinal GIST and low mitotic activity of the tumor (13).

The age of patients with bleeding from GISTs of jejunum ranged from 32 to 80 years (2-4,6-19) and this pathology was observed more frequently in men (2,4,6,8,10-13,15,17-19) than in women (3,7,9,14,16).

The main clinical manifestations of bleeding from a jejunal GIST are signs of acute or chronic intraluminal bleeding, including discharge of unchanged blood through the rectum (hematochezia) (7,8,11,15,18) and repeated episodes of melena and anemia (2,6,9,12-14,17). In exceptional cases, vomiting of blood was noted (4,10). Multiple episodes of bleeding from GIST of the jejunum are typical and in quite rare cases massive bleeding with hemodynamic instability of patients can be noted (10,11,13,14,16,17,19).

The issues of diagnosis and therapeutic management of bleeding from small intestinal GIST remain rather no-standardized (11). Early diagnosis of jejunal GIST is quite difficult due to inaccessibility to standard endoscopy, and often leads to delayed surgical treatment (2,4,7,11,14,15,17-19). Double-balloon enteroscopy and capsule endoscopy are the preferred methods for diagnosing the source of bleeding from the small intestine, and in case of GIST they reveal a submucosal tumor with ulceration of the mucosa above it (9,15). However, due to the exophytic component of GIST, these diagnostic methods may sometimes be non-informative (6,17).

When double-balloon enteroscopy and capsule endoscopy are not available, contrast-enhanced CT is recommended (4,7,8,11-14,16,17,19). This method allows visualization of a jejunal tumor accumulating contrast and in some cases with extravasation (8,9,13). Neirouz et al. (2) described an observation of accurate preoperative diagnosis using CT with contrast of a small bowel intussusception caused by a 2 cm jejunal tumor with recurrent bleeding. In our case, contrast-enhanced abdominal CT played the main role in establishing the preoperative diagnosis and the therapeutic management strategy.

Today, surgical resection with negative margins (R0) is the gold standard in the treatment of localized and non-metastatic GIST (3,6,13,19,20). In case of bleeding from GIST of the jejunum, it was intraoperatively found that neoplasms were localized at a distance from 15 to 170 cm from the ligament of Treitz (2,6-8,10,11,13,14,16,17). Traditionally, the surgical operation was performed through laparotomic access and the extent of surgery consisted of segmental resection of the intestine en bloc with tumor and restoration of GI passage by end-to-end or side-to-side anastomosis using both manual sutures and stapling devices (2,4,6,7,10,11,13,14,16,18). In the described case, the preferred method was open access with careful exploration of the abdominal cavity. At the same time, Saeidi et al. (17) described an observation of the use of damage control principle in massive, life-threatening bleeding from GIST of the jejunum. Due to the failure of hemodynamically stabilize the patient with high doses of inotrop and vasopressor support, only the resection stage was performed at the first, and 48 hours later, after complete stabilization of the patient, the final stage was performed-restoration of GI passage (17). A mandatory condition during surgeries for GIST is to preserve the integrity of the tumor pseudocapsule to prevent its recurrence (1,6,20). At the same time, lymph node dissection was not performed due to the extremely rare metastasis of GIST to lymph nodes (1,3,6). In a number of reports on jejunal GIST, surgical interventions were performed using laparoscopic techniques (8,9,15,19). Huynh and Rust (12) described an observation of successful resection of proximal jejunal GIST using robotic technique, in which bowel resection and subsequent intracorporeal anastomosis were performed using staplers, and the adequacy of intestinal perfusion was assessed using indocyanine green.

Macroscopically, jejunal GIST represents a lobular tumor of gray color spreading from the submucosal layer to the serosa of the intestine with significant extraluminal growth (4,6-8,10,11,13,14,16,18) and with sizes ranging from 2 cm to 9 cm (2,4,6,9-11,14,16,17). The main cause of bleeding in GIST of the jejunum is necrosis and ulceration of the mucosa as a result of the compression effect of the tumor on the intestinal wall (6,8,9,11,13,14).

Histopathologic examination revealed a spindle cell variant of GIST in the majority of cases (8,10,13,14,16,18) and extremely rare epithelioid (9) and mixed variants (7,17). This pattern is observed for GIST of all localizations, where the spindle cell tumor variant is the most frequent (77%) and in smaller proportions-the epithelioid (8%) and mixed types (15%) (1,3).

According to immunohistochemical study, positive expression in tumor cells for CD117/c-KIT (4,6-13,16-18), DOG-1 (4,6,9-12,14,16-18), CD34 (9,11,13,14,18) and negative reaction for desmin (4,10), smooth muscle actin (10), CD34 (16) was established. When proliferative activity was evaluated, <5 mitoses/5 mm^2 was noted (2,6,8,9,12,13,15-18).

As adjuvant therapy imatinib (a tirozin kinase receptor inhibitor) in the regimen of 200-400 mg/day was used (7,9,10). It was found that imatinib was effective in cases harboring a mutation in exon 11 of the *c-KIT* gene, whereas a mutation in exon 9 may produce a response to targeted therapy only at higher drug doses. In the absence of mutations in the *c-KIT* gene, resistance to imatinib is observed (3,20).

The absence of tumor recurrence and metastases was noted within the follow-up period from 3 months to 6 months after surgical treatment (6,9). Prognostic factors in GIST are: tumor localization and size, the number of mitoses, as well as the presence of neoplasm rupture (17,20). According to international guidelines the risk of recurrence in our case was 3a (moderate

risk) and the patient started targeted treatment with imatinib mesilat (20).

Conclusion

GIST of the jejunum is a rather rare cause of GI bleeding. The main diagnostic method is contrast-enhanced CT. The treatment of choice for bleeding jejunal GIST is segmental resection with a negative surgical margin (R0 resection), performed without compromising tumor integrity, to prevent local recurrence and possible metastasis.

Ethics

Informed Consent: Oral and written informed consent was obtained from the patient to publish the patient-related data in anonymized form.

Footnotes

Authorship Contributions

Concept/Design: M.C., I.M., Data Collection or Processing: A.S., I.V., V.G., Analysis or Interpretation: M.C., I.M., Literature Review: M.C., A.S., I.V., V.G., I.M., Writing, Reviewing and Editing: M.C., A.S., I.V., V.G., I.M.

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