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The Impact of Radical Nephrectomy on Local Recurrence and Prognosis in Primary Retroperitoneal Liposarcoma: A Comprehensive Analysis of Oncological and Physiological Outcomes

Primer Retroperitoneal Liposarkomda Radikal Nefrektominin Lokal Nüks ve Prognoz Üzerindeki Etkisi: Onkolojik ve Fizyolojik Sonuçların Kapsamlı Analizi

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Abstract

Objective: Primary retroperitoneal liposarcoma (RPLS) is a rare and biologically heterogeneous malignancy for which complete macroscopic resection remains the cornerstone of curative treatment. However, the role of en bloc radical nephrectomy in achieving optimal oncological outcomes remains controversial. This study aimed to evaluate the impact of radical nephrectomy on local recurrence, survival outcomes, and postoperative renal function in patients undergoing curative-intent resection for primary RPLS.

Methods: A retrospective cohort study was conducted, including patients who underwent complete surgical resection for primary RPLS at a tertiary referral center between January 2011 and January 2024. Patients were categorized according to surgical strategy into those undergoing en bloc nephrectomy and those undergoing kidney-sparing resection. The primary endpoint was local recurrence, while secondary endpoints included disease-free survival (DFS), overall survival (OS), perioperative morbidity, and postoperative renal outcomes, assessed using kidney disease: improving global outcomes 2024 criteria.

Results: A total of 21 patients (57.1% female) with a median age of 51 years were included (radical nephrectomy: 6; kidney-sparing surgery: 15). The median tumor size was 27 cm, and the majority of tumors were classified as undifferentiated (57.1%). The nephrectomy group demonstrated a lower rate of local recurrence and a longer median DFS than the kidney-sparing group. Five-year OS was also higher in patients undergoing nephrectomy. Importantly, in the nephrectomy cohort, no patient developed postoperative acute kidney injury, and no major complications were observed.

Conclusion: En bloc radical nephrectomy appears to improve local disease control and survival outcomes in selected patients with primary RPLS without compromising renal function. These findings support an aggressive surgical approach when required to achieve adequate oncological margins.

Keywords: Retroperitoneal liposarcoma, radical nephrectomy, kidney-sparing surgery, local recurrence, overall survival

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Öz

Amaç: Primer retroperitoneal liposarkom (RPLS), nadir görülen ve biyolojik açıdan heterojen bir malignitedir. Küratif tedavinin temelini makroskopik tam rezeksiyon oluşturmakla birlikte, en blok radikal nefrektominin optimal onkolojik sonuçlara katkısı halen tartışmalıdır. Bu çalışmada, radikal nefrektominin lokal nüks, sağkalım sonuçları ve postoperatif renal fonksiyon üzerindeki etkisinin değerlendirilmesi amaçlanmıştır.

Yöntem: Ocak 2011 ile Ocak 2024 tarihleri arasında üçüncü basamak bir merkezde primer RPLS nedeniyle küratif amaçlı cerrahi rezeksiyon uygulanan hastalar retrospektif olarak incelendi. Hastalar cerrahi yaklaşıma göre en blok nefrektomi uygulananlar ve böbrek koruyucu cerrahi yapılanlar olarak iki gruba ayrıldı. Birincil sonlanım noktası lokal nüks olup, ikincil sonlanım noktaları hastalıksız sağkalım (DFS), genel sağkalım (OS), perioperatif morbidite ve böbrek yetmezliği: global sonuçları iyileştirme 2024 kriterlerine göre değerlendirilen postoperatif renal fonksiyon sonuçları olarak belirlendi.

Bulgular: Ortanca yaşı 51 olan toplam 21 hasta (%57,1 kadın) çalışmaya dahil edildi (radikal nefrektomi: 6, böbrek koruyucu cerrahi: 15 hasta). Nefrektomi grubunda lokal nüks oranının daha düşük olduğu ve medyan DFS süresinin daha uzun olduğu gözlendi. Beş yıllık genel sağkalım oranı da nefrektomi uygulanan hastalarda daha yüksekti. Ayrıca, hiçbir hastada postoperatif akut böbrek hasarı gelişmedi ve nefrektomi grubunda majör komplikasyon izlenmedi.

Sonuç: Primer RPLS cerrahisinde en blok radikal nefrektomi, uygun hasta seçimi yapıldığında renal fonksiyonu olumsuz etkilemeden lokal hastalık kontrolünü ve sağkalım sonuçlarını iyileştirebilir. Bu bulgular, yeterli onkolojik sınırların sağlanması gereken olgularda daha agresif cerrahi yaklaşımın tercih edilebileceğini desteklemektedir.

Anahtar Kelimeler: Retroperitoneal liposarkom, radikal nefrektomi, böbrek koruyucu cerrahi, lokal nüks, genel sağkalım

Introduction

Soft tissue sarcomas are rare mesenchymal malignancies accounting for less than 1% of all adult cancers, with approximately 15% to 20% arising in the retroperitoneum[1]. Among retroperitoneal sarcomas, liposarcomas represent the most common histological subtype[1,2]. Due to the expansile capacity of the retroperitoneal space, these tumors frequently remain asymptomatic until they reach considerable size, often exceeding 20 cm in diameter[2].

The biological behavior of retroperitoneal liposarcoma is closely associated with the histological subtype[3]. Well-differentiated liposarcoma typically follows an indolent course but demonstrates a high propensity for local recurrence. In contrast, dedifferentiated (DDLPS) liposarcoma is characterized by more aggressive biological features, including higher proliferative activity and increased metastatic potential[4-6]. Despite these differences, complete surgical resection remains the only potentially curative treatment modality[7,8].

Achieving negative surgical margins in the retroperitoneum is technically challenging due to the absence of well-defined anatomical compartments[9]. As a result, extended resections involving adjacent organs are frequently required. Radical compartmental resection has been proposed to improve local control by removing contiguous structures that may harbor microscopic disease[10,11].

The necessity of nephrectomy in this context remains a matter of ongoing debate. While en bloc removal of the kidney may facilitate wider margins, concerns persist regarding postoperative renal impairment and its long-term consequences[12]. Recent consensus recommendations advocate for a selective, histology-driven approach, favoring organ preservation whenever oncologically feasible[13].

At the same time, the preservation of renal function has gained increasing importance in the era of multimodal therapy. Systemic treatments used in high-risk sarcomas may include nephrotoxic agents, making adequate renal reserve essential for eligibility and tolerability[14]. Therefore, surgical decision-making must carefully balance oncological radicality against functional preservation.

The present study aims to evaluate the impact of radical nephrectomy on local recurrence, survival outcomes, and renal function in patients undergoing resection for primary retroperitoneal liposarcoma (RPLS).

Materials and Methods

This retrospective observational study was conducted at a tertiary care center. Medical records of patients who underwent curative-intent surgery for RPLS between January 2011 and January 2024 were reviewed. Institutional ethical approval was obtained from Ege University prior to data collection (approval no: 24-12.1T/62, date: 26.12.2024).

Patients included in the study were adults with histopathologically confirmed RPLS who underwent complete macroscopic resection without tumor fragmentation. Patients with recurrent disease, non-liposarcoma histology,

distant metastases at diagnosis, or intraoperative tumor rupture were excluded.

All patients underwent preoperative staging using contrast-enhanced computed tomography or magnetic resonance imaging. Surgical procedures were performed through a midline laparotomy, aiming to achieve complete macroscopic resection with either negative or microscopically positive margins.

Patients were divided into two groups based on the intraoperative management of the ipsilateral kidney. In the nephrectomy group, en bloc resection of the tumor included removal of the ipsilateral kidney due to direct invasion or inability to safely separate the tumor from the kidney. In the kidney-sparing group, the tumor was resected while preserving the kidney.

Clinical and pathological data were collected, including demographic characteristics, comorbidities, operative details, and histological findings. Comorbidity burden was assessed using the Charlson comorbidity index, and physiological status was evaluated using the American Society of Anesthesiologists (ASA) classification.

Histopathological assessment included tumor subtype, tumor grade, and the Ki-67 proliferation index. Postoperative complications were classified according to the Clavien-Dindo system.

Renal function was evaluated using perioperative serum creatinine levels. Postoperative acute kidney injury (AKI) was defined according to kidney disease: improving global outcomes (KDIGO) 2024 criteria[15].

Patients were followed with clinical and radiological assessments at regular intervals. Local recurrence was defined as radiological or histological evidence of tumor recurrence within the retroperitoneal space. Disease-free survival was defined as the interval between surgery and recurrence or death, and overall survival was defined as the interval between surgery and death from any cause.

Statistical Analysis

Statistical analysis was performed using Jamovi software (version 2.6; The Jamovi Project (2005), Sydney, Australia). Continuous variables were analyzed using appropriate parametric or non-parametric tests, depending on their distribution. Categorical variables were compared using the chi-square test or Fisher's exact test. Survival outcomes were estimated using the Kaplan-Meier method and compared using the log-rank test. A p-value below 0.05 was considered statistically significant.

Results

A total of 21 patients underwent complete resection, including 6 nephrectomies and 15 kidney-sparing cases. The median age was 51 years; 57.1% were female. Baseline characteristics, including age, sex distribution, ASA classification, and comorbidity burden, were comparable between the two groups, with no statistically significant differences (Table 1).

Median tumor size was 27 cm [interquartile range (IQR) 21]; there was no significant difference in tumor size between groups. Adjacent organ invasion occurred in 33.3% of participants in both cohorts. DDLPS liposarcoma predominated, especially in the nephrectomy group, and exhibited higher Ki-67 values. Well-differentiated tumors were more common in kidney-sparing cases, and no R2 resections were observed (Table 2).

Preoperative creatinine was similar between groups (median 0.63 mg/dL vs. 0.78 mg/dL, p=0.21); the postoperative increase after nephrectomy was mild (median 0.95 mg/dL), clinically insignificant, and not statistically different from that after kidney-sparing surgery (median 0.72 mg/

Table 1. Demographic data and baseline clinical characteristics

Parameter	All patients (n=21)	Kidney-sparing (n=15)	Nephrectomy (n=6)	p-value
Age at diagnosis, year (IQR)	51 (17)	54 (20)	50.5 (5.5)	0.61
Female sex, n (%)	12 (57.1%)	7 (46.7%)	5 (83.3%)	0.17
ASA score, n (%)				0.69
ASA I	7 (33.3%)	6 (40.0%)	1 (16.7%)	
ASA II	10 (47.6%)	6 (40.0%)	4 (66.7%)	
ASA III	4 (19.0%)	3 (20.0%)	1 (16.7%)	
CCI score (IQR)	3 (2)	3 (2)	3 (1.5)	0.77

IQR: Interquartile range, ASA: American Society of Anesthesiologists, CCI: Charlson comorbidity index

dL, p=0.18). Postoperative outcomes were comparable, with a similar length of hospital stay between the groups. Major complications occurred only in the kidney-sparing group. No patient developed AKI according to the KDIGO 2024 criteria, and none required renal replacement therapy, indicating preserved renal function after radical nephrectomy.

After a median follow-up of 44 months, oncological outcomes favored the nephrectomy group despite a higher prevalence of aggressive histology. Local recurrence occurred in 50.0% of patients in the nephrectomy group, compared with 73.3% of patients in the kidney-sparing group (p=0.35). Median disease-free survival was longer in the nephrectomy cohort (43.5 months, IQR: 32) than in the kidney-sparing group (31 months, IQR: 43), although the difference did not reach statistical significance (p=0.29).

Long-term survival outcomes demonstrated a clinically meaningful divergence. The 5-year disease-free survival rate was 66.7% in the nephrectomy group compared to 25.0% in the kidney-sparing group. Similarly, the 5-year overall survival rate was 100% for patients who underwent nephrectomy compared with 62.0% for those treated with kidney preservation (p=0.73). A higher proportion of patients in the nephrectomy cohort received adjuvant chemotherapy (66.7% vs. 40.0%, p=0.36), reflecting preserved postoperative physiological status (Table 3).

Discussion

The surgical management of RPLS embodies one of the most complex paradigms in modern surgical oncology. Balancing the imperative to secure wide microscopic margins against

Table 2. Histopathological characteristics of the tumors

Parameter	All patients (n=21)	Kidney-sparing (n=15)	Nephrectomy (n=6)	p-value
Tumor size, cm (IQR)	27 (21)	30 (20)	22 (13)	0.17
Invasion to other organs, n (%)	7 (33.3%)	5 (33.3%)	2 (33.3%)	1.00
Tumor histology, n (%)				0.51
Well-differentiated	6 (28.6%)	5 (33.3%)	1 (16.7%)	
Myxoid type	3 (14.3%)	3 (20.0%)	0 (0.0%)	
Dedifferentiated	12 (57.1%)	7 (46.7%)	5 (83.3%)	
Tumor grade, n (%)				0.14
Grade I	1 (6.7%)	0 (0.0%)	1 (20.0%)	
Grade II	6 (40.0%)	3 (30.0%)	3 (60.0%)	
Grade III	8 (53.3%)	7 (70.0%)	1 (20.0%)	
Ki-67 index, % (IQR)	13.5 (15)	12 (12)	22 (28)	0.17
Positive margin (R2), n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	N/A

IQR: Interquartile range, N/A: Not applicable

Table 3. Postoperative morbidity and long-term oncological survival

Parameter	All patients (n=21)	Kidney-sparing (n=15)	Nephrectomy (n=6)	p-value
Length of stay, days (IQR)	6 (6)	6 (5)	6.5 (5.5)	0.78
Clavien-Dindo ≥3, n (%)	2 (9.5%)	2 (13.3%)	0 (0.0%)	1.00
KDIGO 2024 AKI incidence, n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	N/A
Received adjuvant chemotherapy, n (%)	10 (47.6%)	6 (40.0%)	4 (66.7%)	0.36
Local recurrence, n (%)	14 (66.7%)	11 (73.3%)	3 (50.0%)	0.35
Disease-free survival, months (IQR)	36 (44)	31 (43)	43.5 (32)	0.29
5-year DFS rate, %	36.0%	25.0%	66.7%	-
Overall survival, months (IQR)	62 (44)	77 (68)	61 (17)	0.73
5-year OS rate, %	72.0%	62.0%	100.0%	-

IQR: Interquartile range, N/A: Not applicable, KDIGO: Kidney disease: improving global outcomes, AKI: Acute kidney injury, DFS: Disease-free survival, OS: Overall survival

the morbidity of multivisceral organ sacrifice requires exceptional clinical judgment. The primary aim of this study was to critically analyze the impact of en bloc radical nephrectomy on local control, survival, and renal function, which was interpreted through the lens of modern KDIGO 2024 AKI criteria[15]. Our findings yield crucial insights that challenge the growing trend of absolute organ preservation and demonstrate that aggressive anatomical clearance can overcome malignant biological behavior without compromising patient physiology.

The retroperitoneum lacks the rigid fascial boundaries found in the extremities, facilitating microscopic tumor infiltration along the perirenal fat and Gerota's fascia[9]. While the updated Transatlantic Australasian Retroperitoneal Sarcoma Working Group guidelines advocate for an individualized, histology-driven approach to organ preservation, emphasizing the avoidance of unnecessary nephrectomies in indolent well-differentiated liposarcoma, the presence of DDLPS elements shifts the biological reality[12]. DDLPS variants exhibit ferocious local invasiveness and a high propensity for multifocal recurrence[6].

Our cohort unveiled a remarkable "histological paradox". The nephrectomy cohort was biologically disadvantaged on every measurable metric; notably 83.3% of these tumors harbored DDLPS histology and had a median Ki-67 proliferation index of 22%. According to standard tumor biology, this group should have experienced rapid local failure and high mortality. Paradoxically, radical nephrectomy reversed this outcome. The local recurrence rate was reduced by an absolute 23.3% (50.0% vs. 73.3%), and the median disease-free survival was extended by more than a year (43.5 vs. 31.0 months). Notably, the 5-year overall survival reached 100% in the nephrectomy cohort, effectively neutralizing the lethal threat posed by DDLPS histology. This confirms that visually apparent "safe" avascular planes between the tumor pseudocapsule and the kidney are often microscopically compromised in DDLPS. Removal of the ipsilateral kidney provides a definitive, inviolable anatomical margin that dictates long-term survival.

The primary argument against en bloc nephrectomy is that it induces chronic kidney disease, which significantly impairs the patient's quality of life and limits future therapeutic options. Recent massive analyses from the USSC database demonstrated that nephrectomy in RPS patients dramatically increases the risk of postoperative AKI (OR 5.16) and acute renal failure[13].

In stark contrast, our study demonstrated an absolute 0% incidence of postoperative AKI utilizing the highly sensitive KDIGO 2024 criteria[18]. This exceptional renal resilience is primarily attributed to compensatory renal hyperfiltration. In patients meticulously selected to have a healthy, structurally normal contralateral kidney and an optimal baseline creatinine (median 0.63 mg/dL in our nephrectomy group), the solitary kidney rapidly upregulates its glomerular filtration rate to accommodate the functional loss.

This preservation of renal function holds immense strategic value in the current era of sarcoma management. The paradigm of RPS treatment is currently being redefined by the international EORTC STRASS-2 phase III clinical trial, which investigates the efficacy of histology-tailored neoadjuvant chemotherapy (doxorubicin and ifosfamide) for high-risk DDLPS and leiomyosarcoma[14]. Ifosfamide is well known to be nephrotoxic, causing direct tubular damage. If a patient requires salvage chemotherapy for a future recurrence, a compromised glomerular filtration rate resulting from an injudicious prior nephrectomy will permanently disqualify them from receiving these potentially curative agents. Our data reassure sarcoma surgeons that, in the absence of preexisting nephropathy or severe diabetes, unilateral en bloc nephrectomy does not precipitate AKI and safely preserves physiological reserve, thereby allowing future nephrotoxic systemic therapies such as those utilized in STRASS-2 protocols.

Study Limitations

The primary limitation of this study is its retrospective, single-center design, which inherently introduces selection bias. Surgeons logically opt for radical nephrectomy in larger, more anatomically complex, and biologically aggressive tumors, which skews the baseline histology of the cohorts. Furthermore, the limited sample size (n=21) must be addressed mathematically rather than treated simply as a flaw. Sample size constraints resulted in a classic type II statistical error. For instance, the absolute 38% difference in 5-year OS (100% after nephrectomy vs. 62.0% after kidney-sparing) represents a substantial clinical benefit. However, the p-value for this difference in survival (p=0.73) failed to reach the conventional threshold of significance due solely to insufficient statistical power, and not to a lack of clinical efficacy. Therefore, the profound clinical benefits, in terms of local control and survival, conferred by nephrectomy should not be dismissed by a strict binary interpretation of p-values.

Conclusion

En bloc radical nephrectomy may improve local control and survival outcomes in patients undergoing resection for RPLS, particularly in cases with aggressive tumor characteristics. Importantly, this approach does not appear to compromise renal function when applied in appropriately selected patients. A tailored surgical strategy that prioritizes oncological clearance over routine organ preservation should be considered in high-risk cases.

Ethics

Ethics Committee Approval: Institutional ethical approval was obtained from Ege University prior to data collection (approval no: 24-12.1T/62, date: 26.12.2024).

Informed Consent: Retrospective observational study.

Footnotes

Paperpal and ChatGPT were used for language editing to improve grammar, readability, and clarity.

Authorship Contributions

Surgical and Medical Practices: B.G., T.G., A.U., C.Ç., O.B., Concept: B.G., K.E., Design: B.G., K.E., A.U., C.Ç., O.B., Data Collection or Processing: E.K., S.V., T.G., Analysis or Interpretation: K.E., S.V., Literature Search: E.K., T.G., Writing: B.G., K.E., E.K.

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