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The outcomes of partial nephrectomy – considerations that contribute to positive surgical margins

ALEXANDRU IORDACHE[1,2], NICOLETA ALINA MAREŞ[1,3], NICULAE IORDACHE[1,4,5], MIHAELA GABRIELA BERDAN[1,6], MARA MARDARE[7], ALINA IOANA PUŞCAŞU[7], BOGDAN FLORIN GEAVLETE[1,8], DRAGOŞ ADRIAN GEORGESCU[1,8], RĂZVAN-COSMIN PETCA[1,2], VIOREL JINGA[1,2], OCTAV GINGHINĂ[1,7], ALEXANDRU BLIDARU[1,7]

[1] *Carol Davila University of Medicine and Pharmacy, Bucharest, Romania*

[2] *Department of Urology, Prof. Dr. Theodor Burghele Clinical Hospital, Bucharest, Romania*

[3] *Department of Gynecology, Dr. I. Cantacuzino Clinical Hospital, Bucharest, Romania*

[4] *Department of Surgery, Sf. Ioan Emergency Hospital, Bucharest, Romania*

[5] *Academy of Romanian Scientists, Bucharest, Romania*

[6] *Department of Pathology, Prof. Dr. Theodor Burghele Clinical Hospital, Bucharest, Romania*

[7] *Department of Surgery, Prof. Dr. Alexandru Trestioreanu Oncological Institute, Bucharest, Romania*

[8] *Department of Urology, Sf. Ioan Emergency Hospital, Bucharest, Romania*

Abstract

The diagnosis in the early stages of renal tumors, as well as the oncological outcomes equivalent to extensive nephrectomies, have increased interest in partial nephrectomy (PN), which is the preferred method for treating renal cell carcinoma less than 7 cm. The literature confirms that PN offers oncological outcomes equivalent to radical nephrectomy, especially in early stages. This is a prospective study, conducted in a single university center over a period of three years, aimed to evaluate the surgical and oncological outcomes regarding positive safety margins after PN performed using laparoscopic and open approaches. Following the analysis of the causes and consequences of incomplete tumor resection, the obtained results align with data from the literature. We found that specimens from laparoscopic surgery were approximately twice as likely to have positive surgical margins compared to tumors resected using the open approach, meaning that these patients require more intense follow-up both clinically and imaging. According to current published studies, positive safety margins are not predictors for disease recurrence rate, progression-free survival, or overall survival.

Keywords: partial nephrectomy, positive surgical margins, renal cell carcinoma, laparoscopy, histopathology.

Introduction

The incidence of renal cancer is increasing globally, but there is a decrease in mortality in some European countries, likely due to early diagnosis and favorable treatment outcomes. Statistics from 2020 indicate approximately 431 288 new cases of renal cancer worldwide, with about 138 611 new cases in Europe. Global mortality was recorded at 179 368 deaths. Demographically, renal cancer is more common in men (male-to-female ratio 1.5–2.0:1) and older populations [1].

Nephrectomy is one of the most frequently performed procedures by urologists, with multiple approaches such as open surgery, laparoscopy, or robotic surgery. The success of the intervention is directly proportional to a thorough understanding of the chosen technique to provide the best outcomes for each patient. Regardless of the selected technique, the objectives should focus on tumor treatment while preserving as much functional renal parenchyma as possible without compromising oncological limits, requiring a sufficiently wide resection with safe margins.

The diagnosis of renal tumors in their early stages, along with oncological outcomes equivalent to extensive nephrectomies, has increased interest in partial nephrectomy (PN), which is the preferred method for treating renal cell carcinoma less than 7 cm. The literature confirms that PN offers oncological outcomes equivalent to radical nephrectomy (RN), especially in early stages. A 10-year study demonstrated the efficacy of PN, with a reduced rate of intraoperative complications and the preservation of as much functional renal parenchyma as possible without compromising oncological principles. Generally, the cure rate for localized renal cancer is over 90% when diagnosed early and treated surgically [2].

Open PN, with a minimal incision at the level of the 12th rib and no ischemia time for small renal masses, provides satisfactory results in maintaining renal function and leaves an aesthetic scar. This approach, which is quick, safe, and technically easy to perform, remains a significant and feasible option for treating small renal masses. Renal ischemia for preserving renal function during partial resections has been a controversial topic for decades, with

ischemia times below 25 minutes being considered critical for preserving renal function [3]. The relationship between positive margins and oncological prognosis and recurrence risk remains a topic of ongoing debate [4, 5]. On the other hand, some studies indicate that survival rates remain consistent regardless of the postoperative approach [6].

Aim and Objectives

The aim of the study was to assess the surgical and oncological outcomes regarding positive safety margins after PN through laparoscopic and open approaches.

The objectives are: (*i*) to assess the effectiveness of various surgical techniques for PN; (*ii*) to highlight cases with positive safety margins in histopathological (HP) examinations after PN, depending on the approach – open or laparoscopic.

Patients, Materials and Methods

This is a prospective study conducted in a single university center over a period of three years, from 2022 to 2024, including 105 cases of PN performed laparoscopically and through the open approach the groups were distributed approximately equally. The location for the research activities, patient recruitment, and investigation was Prof. Dr. Theodor Burghele Clinical Hospital, Bucharest, Romania. Ethical measures in doctoral research included informed patient consent and approval from the Institutional Ethics Committee.

All patients underwent preoperative examinations following diagnostic and treatment protocols and completed and signed informed consent for the surgical intervention. This included details about the procedure, sample collection for analysis, treatments, as well as potential risks and complications. In addition to discussions about surgery and consent, data on personal and pathological medical history that could influence surgical decisions and subsequent evolution were collected.

Imaging assessments encompassed abdominal ultrasound, magnetic resonance imaging, and computed tomography. Preoperatively, all patients underwent laboratory tests, cardiology consultations and pre-anesthetic evaluations. Laboratory parameters assessed included hemogram, serum creatinine, glomerular filtration rate, hepatic function and coagulation profile and analyses of urine.

Inclusion criteria: benign or malignant renal tumors smaller than 7 cm, requiring surgical intervention.

Exclusion criteria: age over 85 years, widespread infections or decompensated systemic diseases, single kidney or end-stage chronic kidney disease (CKD), and multiple comorbidities requiring prolonged treatment, leading to postponed interventions.

The statistical analysis included descriptive statistics; variables were expressed as proportions to facilitate hypothesis formulation in the conclusions.

Results

Positive resection margins (PRMs) may occur after PN, but its effect on recurrence risk and survival outcomes remains unclear. Investigating the correlation between positive safety margins, recurrence risk after PN, and survival outcomes is essential. PN is widely regarded as the predilect approach for small, localized renal tumors. No surgical approach is without risks, but it is essential for these risks to be known and understood to choose the appropriate technique. All cases were analyzed individually, with attention focused on local, national, or international guidelines and protocols.

The cohort included 105 cases of PN, of which 56 cases were managed using open surgery, and 49 cases were managed using the laparoscopic technique, either transperitoneal or retroperitoneal. HP analysis revealed a count of 25 specimens with positive safety margins, of which nine were obtained through open surgery and 16 through the laparoscopic approach (Figure 1).

The study focused on analyzing PRMs after PN for renal carcinoma, highlighting the importance of achieving negative surgical margins (NSMs), which could potentially improve clinical outcomes. Multiple anatomical aspects, such as tumor size and location, invasion or metastases, as well as HP examination characteristics, including *International Society of Urological Pathology* (ISUP) tumor grade, tumor type, or surgical margins, are prognostic factors for renal cancers. In this study, the surgical approach played a role in determining the probability of residual positive margins.

Following the local surgical resection of the tumor, there is a risk of histological remanent disorder, defined by positive safety margins, but their impact on oncological outcomes remains uncertain. Even when positive surgical margins (PSMs) are present histologically, the residual cells might not survive after electrocoagulation.

Based on HP examinations, PRMs were found in 32.6% of the laparoscopic cases compared to 16.3% for the open approach, indicating that the minimally invasive technique has certain limitations that can influence long-term prognosis (Figure 2).

Of all cases, renal cancer was confirmed in 89 patients, approximately 85% of all operated cases. This emphasizes the importance of surgical intervention that ensures complete tumor resection. The renal cancer subtypes with PRMs were predominantly clear cell renal carcinomas, two cases of papillary renal carcinoma, and two other cases of chromophobe cell carcinoma, with one specimen for each surgical approach (Figure 3, A–C). The other histopathologically examined specimens were benign tumors (15%), such as renal angiomyolipoma, lipoma and oncocytoma.

Regarding the proportion of cases with PRMs based on the category of renal masses, there was no significant difference between the types of tumors identified through imaging, the preoperative scoring system used, and postoperative outcomes. The RENAL preoperative score (Radius, Exophytic/Endophytic, Nearness to collecting sinus, Anterior/Posterior, Location relative to polar lines) was used to quantify the complexity of the surgery and predict postoperative outcomes. Based on this scoring system, positive margins were detected in an approximately equal number of cases classified as low or intermediate risk, with no cases in the high-risk category.

In the laparoscopic group of PNs, out of the 16 cases with PSMs: six (37.5%) cases were classified as low-risk (RENAL 4–6), seven (43.75%) cases were classified as intermediate-risk (RENAL 7–9), including: three (18.75%) cases with a RENAL score of 7 and four (25%) cases with a RENAL score of 8. The remaining three cases were represented by Bosniak cysts (one type III and two type IV) (Figure 4).

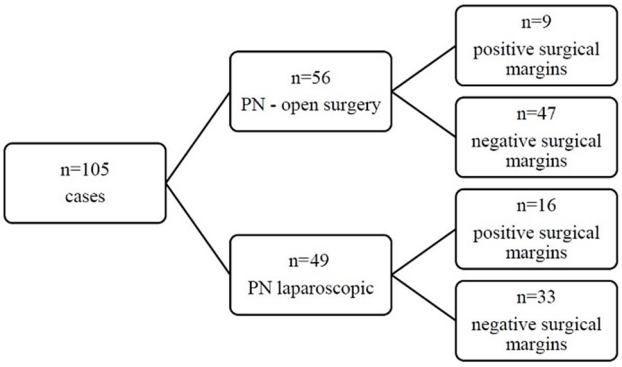

Figure 1 – ***Sample size included in the descriptive analysis (n=105). PN: Partial nephrectomy.***

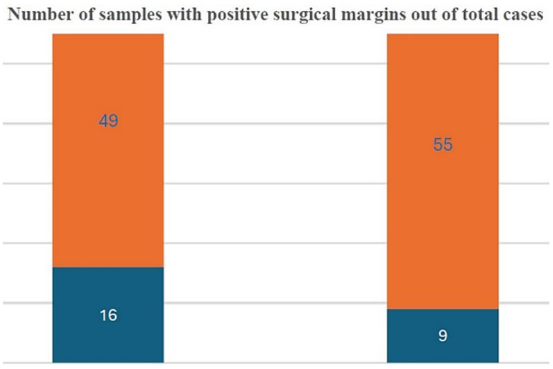

Figure 2 – ***Number of specimens with positive surgical margins following histopathological examination, from a total of 105 PN cases: (Column I) 16 of 49 cases of laparoscopic PN had residual margins, compared to (Column II) nine of 56 cases of open PN. PN: Partial nephrectomy.***

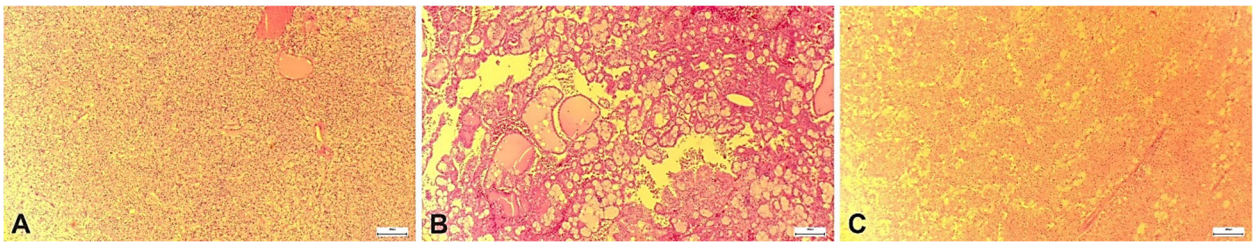

Figure 3 – ***Histopathological examination, microscopic features of samples after partial nephrectomy: (A) Clear cell renal carcinoma – cells with clear cytoplasm arranged in a compact, alveolar pattern; (B) Papillary renal carcinoma – cuboidal cells with eosinophilic cytoplasm, the papillae containing macrophages in their central cores; (C) Chromophobe renal cell carcinoma – cells with varying sizes with well-defined cytoplasmic boundaries and a perinuclear halo. HE staining: (A–C) ×100. (Collection of Dr M.G. Berdan). HE: Hematoxylin–Eosin.***

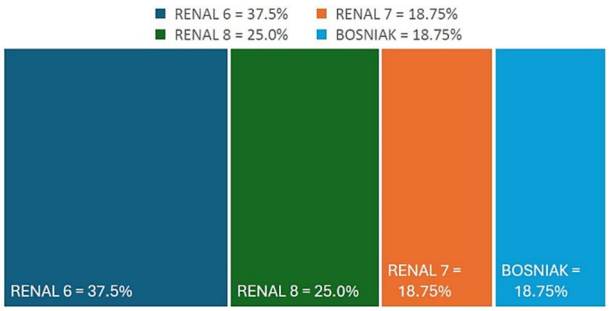

Figure 4 – ***Proportion of cases with positive resection margins based on the category of renal masses.***

In the open PN group, seven of nine cases with PRMs were classified as intermediate-risk, suggesting that for low-risk cases, the classical surgical approach may lead to better oncological outcomes.

Additionally, a detailed analysis of the tumor location revealed that most specimens with PRMs originated from tumors located on the posterior renal valve in laparoscopic PN cases – nine of 16 cases. The rest were located medio-renally or on the anterior valve. These observations were not evident in the open PN cases, leading to the conclusion that minimally invasive surgery might have limitations in addressing tumors localized in the posterior valve. Also, this approach is influenced by the operator's experience.

As mentioned, in addition to tumor characteristics, postoperative outcomes are influenced by the surgical approach, with a twofold higher number of cases showing histologically positive margins in laparoscopic PN. These results align with findings from literature.

Discussions

PN is the most commonly recommended technique due to its lower risks relative to RN while ensuring favorable oncological results.

The oncological safety of the laparoscopic approach compared to the open technique has been examined exclusively in studies with short follow-ups. In centers with laparoscopic expertise, no difference was found in progression-free survival (PFS) or overall survival (OS) between the two mentioned surgical techniques [7, 8].

A large retrospective study involving 42 114 patients who underwent PN, of whom 2823 (6.7%) patients had PSMs, showed an increased presence of PSMs in pT3a tumors (14.1%), higher all-cause mortality in patients with PSMs, and a lower 5-year OS rate in pT3a tumors (PSMs: 69% *vs.* 90.9% for negative safety margins). Though, only a fraction of patients with histologically unsafe margins develops residual malignancy. Local recurrences occurred in 16% of patients with PSMs compared to 3% in those with negative margins [9, 10].

Thus, RN or reintervention could potentially result in overtreatment in many cases. Nevertheless, NSMs do not guarantee protection against recurrence, which has been observed in up to 1.5% of cases within one study [11].

Additionally, data from the literature comparing surgical margins with different surgical approaches (open, laparoscopic, robotic) remain indefinite despite large cohort sizes [12–16]. For example, a large study that included over 11 500 patients from a national database highlighted that PN performed laparoscopically or robotically had higher rates

of PSMs compared to open nephrectomy. Thus, laparoscopic and robotic PN show higher PSM rates compared to open PN for cT1a renal carcinoma, but the impact of margin status on long-term oncological effects is still under evaluation [12].

There are also numerous studies on small, single-center or multi-center cohorts analyzing the differences between surgical approaches, detection rates of positive margins, and risks of recurrence or OS. The published results are similar, and no precise variables were identified to have a significant influence.

Positive safety margins are more common in cases where surgery is imperious (single kidney or bilateral tumors), such as in patients with unfavorable characteristics of the tumors (pT2a, pT3a, grade III–IV). A study published in *European Urology* examined the impact of clinical and pathological variables on survival for cases with both positive and negative resection margins. Multivariate Cox analysis showed that two factors predicted recurrence: indication (p=0.017) and tumor location (p=0.02). While PSMs are more common in cases requiring surgical intervention, they do not appear to affect cancer-specific survival (CSS), underscoring the need for continued follow-up [14, 17, 18].

López-Costea *et al.*, in a 2016 retrospective study that included 198 PNs for malignant renal tumors with an average follow-up of 56 months, conducted a comprehensive statistical analysis to evaluate predictors for OS and disease recurrence. The study concluded that no statistically significant differences were found between patients with PSMs and those with negative margins regarding oncological outcomes, and recurrence could be due to tumor bilaterality [19].

Most prospective or retrospective studies have suggested that PSMs do not necessarily imply a higher risk of recurrence or a decrease in CSS [17, 20, 21]. Instead, a separate single-center retrospective study identified PSMs as an independent predictor of survival without progression of cancer linked to a higher incidence of both local and distant recurrences [8, 22, 23]. However, randomized controlled trials are still needed to evaluate the oncological outcomes of laparoscopic *vs.* open nephrectomy.

Patients with HP results showing the presence of PSMs in the resected specimen were informed that they would require more intensive follow-up, both clinically and through imaging, given their elevated risks for secondary local treatments.

Conclusions

Regarding the identification of cases with positive safety margins in HP examinations and the analysis of the causes and consequences of incomplete tumor resection, the results align with data from literature. We found that specimens from laparoscopic surgery had approximately twice as many PSMs compared to specimens resected through the open approach. These patients require more intensive follow-up, both clinically and through imaging. According to current published studies, positive safety margins are not predictors for recurrence rates, PFS, or OS. We believe these objectives could have a significant impact on research if given practical value. Regardless of the chosen surgical approach, the success of the intervention depends on a thorough understanding of the technique used and the pathology's impact. These considerations are part of the development process for every practitioner. Laparoscopic PN is promising as it offers multiple benefits, and we are considering additional studies on long-term oncological outcomes.

Conflict of interests

The authors have declared no conflict of interests.

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Corresponding authors

Niculae Iordache, Professor, MD, PhD, Faculty of Medicine, Carol Davila University of Medicine and Pharmacy, 37 Dionisie Lupu Street, Sector 2, 020021 Bucharest, Romania; Academy of Romanian Scientists, Bucharest, Romania; Phone +40744–329 431, e-mail: niculae.iordache@umfcd.ro

Octav Ginghină, Associate Professor, MD, PhD, Faculty of Medicine, Carol Davila University of Medicine and Pharmacy, 37 Dionisie Lupu Street, Sector 2, 020021 Bucharest, Romania; Phone +40744–319 404, e-mail: octavginghina@gmail.com

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