Comparison of Non-Hilar Clamping Simple Enucleation and Enucleo-Resection of Exophytic Renal Tumors

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Purpose: To retrospectively evaluate our institutional experience with non-hilar-clamping simple enucleation (SE) and enucleoresection (ER) for the treatment of exophytic renal tumors regarding their oncological outcomes.

Materials and Methods: We retrospectively evaluated patients treated between 2006 and 2013 for clinical exophytic T1-T2a renal tumors using open nephron-sparing surgery.

Results: A total of 33 patients underwent SE and 39 underwent ER. The mean tumor size was 38.7 mm. None of the patients had positive surgical margins. No local recurrences were observed during the postoperative follow-up period (mean 40.7 ± 23.4 months); however, ipsilateral adrenal and contralateral kidney metastasis was detected in one of the patients. There was no statistically significant difference in the R.E.N.A.L Nephrometry Score, operative time, or intraoperative blood loss in the non-hilar-clamping SE and ER groups (P > .05). During the third postoperative month, the estimated glomerular filtration rate (eGFR) levels in the SE group were significantly reduced compared with the preoperative eGFR levels (P = .046).

Conclusion: SE and ER with non-hilar clamping are safe, acceptable approaches for treating exophytic renal tumors.

Keywords: carcinoma, renal cell; surgery; follow-up studies; kidney neoplasms; mortality; nephrectomy; adverse effects; organ sparing treatments; methods; glomerular filtration rate.

INTRODUCTION

During recent decades, modern imaging techniques have facilitated the use of nephron-sparing surgery (NSS) to protect intact tissue when treating small renal tumors, with oncological outcomes similar to those accomplished with radical nephrectomy.1,2 The current gold standard for addressing renal tumors is NSS that includes enucleoresection (ER). With this procedure, the tumor is removed, along with an adequate safety margin of healthy parenchyma.3 As reported in various studies, a minimal tumor-free surgical margin is considered sufficient to avoid the risk of local recurrence and allow the possible use of simple enucleation (SE), a nephron-sparing procedure with oncological effectiveness.4 The aims of NSS are total resection of the tumor with as little intraoperative hemorrhage as possible and leaving as much intact functional parenchyma as possible. Minimal hemorrhage is achieved by clamping the hilar vessels in either a warm or cold ischemia condition. The maximum warm ischemia time during NSS without leading to permanent damage in the kidney is reported to be 30 minutes.5 However, recent studies have decreased this time to 20 minutes. Various studies have claimed that every minute during ischemia, even if it is less than 20 minutes, damages kidney function.6 The aim of the present study was to analyze the patients’ preoperative, intraoperative, and postoperative conditions; positive surgical margins; and the pathological outcome data of 72 patients who underwent non-hilar clamping SE or ER.

MATERIALS AND METHODS

A total of 72 patients who underwent SE and ER from 2006 to 2013 due to exophytic T1-T2a renal tumors were included in this retrospective study. Two surgical teams performed the operations. One team exclusively performed SE, and the other team exclusively performed ER. The preoperative evaluation of all patients included ultrasonography of the kidney, ureter, and bladder, abdominal computed tomography with contrast enhancement, and chest radiography. To determine the location of the tumor in the kidney, we calculated the R.E.N.A.L Nephrometry Score (radius, exophytic or endophytic nearness to the collecting system or sinus, and anterior or posterior location relative to polar lines).

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The E-score of the R.E.N.A.L nephrometry was 1 point for all patients recruited to the study. All patients were considered to be free from distant metastases prior to surgery.

**Technique**

The participants provided written consent before the surgical intervention. An anterior subcostal approach was used in all patients. A direct approach to the kidney was preferred before the kidney was totally separated from the perirenal fat to extricate the exophytic renal tumor that had been detected earlier by imaging. For safety reasons, the renal pedicle was carefully isolated and then suspended with umbilical tape but not clamped. In the patients who underwent SE, the renal capsule at the edges of the mass was denoted using electrocautery. The natural cleavage was opened using clamps. The natural cleavage plane between the tumor and normal parenchyma enabled a 360° turn with the index finger. The mass was totally excised without tumor bed ablation. For hemostasis, the renal parenchyma around the enucleation site was compressed using the thumb and index finger. The renal parenchymal defect was closed with hemostatic material and parenchymal horizontal mattress sutures.

In the ER group, using Gyrus open forceps (Gyrus Medical PK System Seal; Gyrus International, Berkshire, UK), the mass was resected along with 1 to 5 mm of intact parenchyma around the tumor (Figures...
The renal parenchymal defect was closed with hemostatic material and parenchymal horizontal mattress sutures. We observed no parenchymal hemorrhage that necessitated digital compression of the parenchyma due to the thermal effect of the Gyrus open forceps. In both groups, the operation was conducted without clamping the renal artery.

The operation time, intraoperative blood loss, preoperative and postoperative hemoglobin (Hb) levels, serum creatinine levels, estimated glomerular filtration rate (eGFR), and R.E.N.A.L Nephrometry Score were evaluated in all patients undergoing the NSS techniques (SE and ER). Glomerular filtration speed was calculated using the Chronic Kidney Disease Epidemiology Collaboration formula. Pathological tumor size, 2010 TNM (tumor, node, metastasis) stage, the surgical margin in the specimens, and histological subtypes according to the World Health Organization (WHO) classifications were recorded. During the postoperative follow-up, all patients underwent radiological reevaluations for local recurrence and metastasis. The study was presented to the local ethics committee. This study followed the Declaration of Helsinki statement on medical protocol and ethics.

**Statistical Analysis**

The Statistical Package for the Social Science (SPSS Inc, Chicago, Illinois, USA) version 18.0 was used for statistical analysis. The data are recorded as the mean ± standard deviation (SD) and percentage values. For the parameters with a normal distribution, Student’s t-test was used to compare the two groups. Comparisons of categorical data were made using a χ² test. Variant analyses were used to test the difference in the GFR and creatinine levels in repetitive measurements. Bonferroni’s correction was used to determine differences between the groups. P = .05 was considered to indicate statistical significance.

**RESULTS**

**Patient Characteristics**

The data obtained from 72 patients were evaluated. When the two groups (SE and ER) were compared, the mean ages of the patients were 55.5 ± 11.0 and 54.6 ± 12.9 years, respectively (P = .76). The male/female ratios were 21 (63.6%) and 24 (61.5%) for males and 12 (36.4%) and 15 (38.5%) for females in the SE and ER groups, respectively (P = .85; Table 1).

**Event Characteristics**

The mean tumor size was 36.8 ± 13.3 mm in the SE group and 40.4 ± 15.2 mm in the ER group (P = .17). The mean R.E.N.A.L Nephrometry Score was 4.55 ± 0.87 (range 4-6 points) in the SE group and 4.64 ± 0.78 (range 4-6 points) in the ER group (P = .39). In terms of localization of the mass in the kidneys, 17 (51.5%) and 18 (46.1%) lesions were on the right side in the SE and ER groups, respectively, whereas 16 (48.5%) and 21 (53.9%) lesions were on the left side in the SE and ER groups, respectively (P = .83).

The numbers of histological types of tumors (clear cell renal cell carcinoma [RCC], papillary RCC, chromophobe RCC, other RCC, non-RCC) were 16 (48.5%), 8 (24.3%), 2 (6%), 3 (9.1%), and 4 (12.1%), respectively, in the SE group and 25 (64.1%), 7 (18%), 5 (12.8%), 2 (5.1%), and 0, respectively, in the RE group. In the SE group, four non-RCC tumors were noted, two of which were angiolipomas and two were oncocytomas. The histopathological analysis of the surgical specimens revealed negative surgical margins in all specimens.

The TNM 2010 classifications (pT1a, pT1b, and pT2a)

![Figure 1. Exophytic tumor located at the lower pole of the kidney.](image-url)
were assigned to the lesions as follows: 21 (63.6%), 11 (33.4%), and 1 (3%), respectively, in the SE group and 23 (58.9%), 15 (38.5%), and 1 (2.6%), respectively, in the RE group.

The average operation durations for the SE and ER groups were 100.0 ± 13.2 and 106.7 ± 14.1 minutes (P = .61), respectively. The average blood loss volumes were 286.7 ± 143.1 and 313.8 ± 169.7 mL (P = .47), respectively, and the average Hb drop measurements were 1.55 ± 1.20 and 1.07 ± 1.58 mg/dL (P = 1.19), respectively. The intraoperative blood loss ranged between 50 and 750 mL. Blood transfusion was performed in three patients in whom the preoperative Hb level of 10 mg/dL decreased postoperatively to 8 mg/dL (two in the SE group and one in the ER group).

The drains were removed on the third postoperative day. Prolonged urinary drainage (6 days) was observed in one patient in the ER group. One patient in the SE group had gross hematuria for 7 days that resolved spontaneously during the follow-up. The mean follow-up was 40.5 ± 21.5 months after SE and 41.5 ± 24.3 months after ER (P = .5). The median follow-up was 19 months (2-80 months) for the SE group and 41 months (1-96 months) for the ER group.

The patients were re-evaluated during the postoperative follow-up period for local recurrence and metastasis. Two years after the operation, ipsilateral adrenal and probable contralateral kidney metastases were detected in one patient in the ER group who had a history of histologically diagnosed papillary RCC. No local recurrence or metastasis was observed in any other patients.

**DISCUSSION**

Czerny first described NSS for treating renal tumors in 1890. In 1950, Vermooten proposed that peripheral encapsulated renal neoplasms could be excised locally by leaving a margin of normal parenchyma around the tumor. Although radical nephrectomy (RN) has been a proven effective treatment modality since the 1950s, NSS has only limited applications. Many researchers have published their results after kidney-preserving surgical interventions and have demonstrated the validity of this approach in cases in which RN could not be conducted. Moreover, various retrospective studies have demonstrated that survival is enhanced with NSS due to preserved renal function. The European Organization for Research and Treatment of Cancer randomized trial 30904 demonstrated that NSS has a reduced overall survival rate compared with RN. The study also demonstrated that NSS reduced the incidence of moderate renal failure. In line with the recent increase in incidental tumor diagnosis, the focus on NSS has also increased. Today, according to European Association of Urology guidelines, NSS has become the standard treatment modality for tumors < 4 cm. The aim of NSS is total resection of the renal tumor while retaining as much functional parenchyma as possible. Several tumor-related factors, i.e., renal tumor...
size, location, and depth, are visible on preoperative imaging and can affect the tumor resection technique. Hence, various NSS techniques are available. The most common NSS technique is clamping the renal artery with or without the renal vein and sharply excising the renal mass. The time frame during which a vessel is clamped is called the “warm ischemia time.” A safe warm ischemia time is still under discussion; however, it is generally accepted to be 20 to 30 minutes.\(^{6,16}\) Removing a 1-cm margin of normal parenchyma may lead to complications, such as increased hemorrhage risk, potential renal hilum injury, collecting system injury, the need for renal vessel clamping, and prolonged ischemia time.\(^{17}\)

When the concept of an NSS surgical technique was initiated, it involved excising a 1-cm margin of peritumor normal renal parenchyma to ensure a negative surgical margin. In recent decades, however, various authors have demonstrated that intact parenchyma surrounding the tumor can be limited to a few millimeters while preserving the oncological safety of NSS.\(^{18}\) Despite the fact that the mean thickness of the safety margin surrounding the tumor ranges from 2.5 to 5.0 mm, various studies have demonstrated that the minimum thickness of the safety margin is 0 to 1 mm, which is most important at the bottom of the tumor. Various recent studies have assumed no association between margin size during NSS of small renal masses and the recurrence of RCC.\(^2\)

With NSS, especially in single, small (< 4 cm) tumors limited to the kidney, oncological outcomes are similar to those of RN outcomes, whereas renal function is better preserved. This finding is especially important for patients with a solitary functioning kidney. Most of these patients had pre-existing renal insufficiency. Thus, their quality of life, i.e., having dialysis-free and tumor-free renal function, is positively affected.\(^{19}\) The 5-year disease-specific survival rates can increase up to 97%, differentiating NSS from RN.\(^{20}\) Although the upper tumor size limit for elective NSS is defined as 4 cm, tumors up to 7 cm might be appropriate for treatment using NSS in cautiously selected patients.\(^{14,21,22}\)

Following these developments, SE and ER techniques have been used.\(^{14,21}\) Small RCCs may frequently be well bordered and have a pseudocapsule. These are not true capsules, however, and might be invaded by the tumor. Therefore, if a small portion of the healthy parenchyma surrounding the renal tumor is not excised, it may lead to incomplete resection because of microscopically sized residual tumors. Therefore, in the case of simple tumor enucleation, frozen section analysis from the resection borders and the coagulation of the tumor bed is suggested.\(^{23}\) Alternatively, as with the ER technique, the mass is debulked with a cautery dissection 1 to 5 mm away from the peritumoral capsule.

With SE, the tumor is excised with blunt dissection following the natural cleavage plane between the peritumoral capsule and the renal parenchyma, leaving behind a visible border of healthy renal tissue. Evaluations of progression-free and cancer-specific survival (CSS) data revealed that renal tumor enucleation is a more oncologically sound procedure than NSS.\(^{24}\) Lapini and colleagues reported on the results of enucleation of small RCCs (median 2.5 cm) combined with tumor bed coagulation with diathermy spray coagulation or an argon beam. The 107 patients were followed for a mean of 88.3 months. The authors reported 99% 5-year and 97.8% 10-year CSS rates for this patient series. The 5- and 10-year progression-free survival rates were 98.1% and 94.7%, respectively.\(^{25}\) However, recent data suggested that enucleation of RCCs without tumor bed ablation may produce similar oncological outcomes.

Minervini and colleagues reported the results of a series of consecutive patients undergoing enucleation without ablation of the renal tumor surgical bed. According to their report, all of the patients had positive surgical margins, but only 3 of the 164 patients (1.8%) developed a local recurrence, of which only one (0.6%) was a true local recurrence in the enucleation bed. To date, this study is the largest consecutive series of RCCs treated with enucleation with no ablation of the surgical bed.\(^{24}\) In the present study, only 1 of the 72 patients who underwent either SE or ER had a positive surgical margin and developed metastasis and/or local recurrence during the mean 40.7-month follow-up. Two years after the operation, ipsilateral adrenal and contralateral kidney metastases were detected in this patient, who was in the ER group and was formerly diagnosed with histologically diagnosed papillary RCC. Despite the fact that our mean postoperative follow-up period was short (40.7 months), neither of the surgical techniques was superior to the other in terms of survival rates.

Three anatomical classification and scoring systems are used to identify the predictive characteristics of renal tumors and can be used to identify the risk of a prolonged warm ischemia time or surgical complications: the R.E.N.A.L Nephrometry Score, Padua score, and C (centrality) index.\(^{16}\) R.E.N.A.L nephrometry scores impact the preoperative approaches to kidney tumors. According to one retrospective study, this scoring system is a useful tool when using NSS to remove a cT1
renal cancer.\(^{(28)}\) In another study on the predictive value of the R.E.N.A.L Nephrometry Score in regard to performing robotic partial nephrectomy, a strong positive relation was observed between the R.E.N.A.L Nephrometry Score and the warm ischemia time.\(^{(27)}\)

To decrease hemorrhage during NSS, the renal pedicle is frequently clamped. However, recent studies have claimed that warm ischemia of > 20 minutes might lead to serious kidney damage. The increased popularity of laparoscopic NSS with a prolonged operation time among NSS procedures exposes the kidney to more ischemia, leading to long-lasting harm. Thompson and colleagues demonstrated that a prolonged ischemia time in patients with solitary kidneys has undesirable long-term effects on renal function.\(^{(29)}\)

Despite the fact that the use of NSS has been described with open, laparoscopic, and robotic methods, the most important point for the patient is to preserve renal function.\(^{(29)}\) Marszalek and colleagues reported that when open NSS (ONSS) is compared to laparoscopic surgery the warm ischemia time is shorter with ONSS, although the hemorrhage levels are the same.\(^{(30)}\) Lucas and colleagues, in a study of 96 patients with kidney tumors with a mean size of 2.3 cm and a Nephrometry Score of 6, reported that renal function preservation, complication rates, and surgical margin positivity were comparable for all three methods.\(^{(31)}\) The mean operation time was 147 minutes in the ONSS group, which included a significantly shorter (12 minutes) warm ischemia time. However, the hemorrhage amount was > 250 mL. In the same study, a decrease of > 10% in the eGFR levels of 44 patients was significant.

In the 72 NSS cases in this study, the mean tumor size was 36.8 mm in the SE group and 40.4 mm in the ER group, respectively. The R.E.N.A.L Nephrometry Scores were 4.55 ± 0.87 and 4.64 ± 0.78, respectively. The mean hemorrhage amount during the intervention was 301.4 ± 157.5 mL, which is consistent with the findings in the literature. The pedicle was not clamped in any of the patients during the operation, and the kidney was not exposed to warm ischemia. During the SE procedure, while the tumor was enucleated and the parenchyma sutured, the enucleation site and surrounding parenchyma were compressed between the thumb and index finger for homeostasis. During the ER procedure, Gyrus open forceps were used, and some intact tissue was excised together with the tumor. There was some concern that the Gyrus open forceps might affect the eGFR by its thermal energy. We did not observe any eGFR change at the 3-month follow-up evaluation in the ER group (\(P = .636\)). However, we identified a significant change in the SE group from the preoperative eGFR level (\(P = .046\)). Although the compression time and compression force applied to the parenchyma were not clear, we thought that the decrease in the eGFR scores at the 3-month follow-up might be attributed to the renal parenchymal compression that was achieved using the thumb and index finger, perhaps causing mechanical or ischemic stress.

The small sample size, short follow-up period, and retrospective nature of the study design are the limitations of this study. Hence, there is need for well-designed prospective studies.

**CONCLUSIONS**

Non-hilar clamping SE and ER are safe, acceptable approaches for treating exophytic renal tumors. No statistically significant differences were noted in the R.E.N.A.L Nephrometry Scores, operative times, or intraoperative blood loss in the non-hilar clamping SE and ER groups.

**CONFLICT OF INTEREST**

None declared.

**REFERENCES**


