Simple Enucleation is Equivalent to Traditional Partial Nephrectomy for Renal Cell Carcinoma: Results of a Nonrandomized, Retrospective, Comparative Study

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Abbreviations and Acronyms

CSS = cancer specific survival
CT = computerized tomography
EAU = European Association of Urology
ECOG = Eastern Cooperative Oncology Group
NSM = negative surgical margin
NSS = nephron sparing surgery
PFS = progression-free survival
PN = partial nephrectomy
PS = performance status
RCC = renal cell carcinoma
RN = radical nephrectomy
SATURN = Surveillance and Treatment Update Renal Neoplasms
SE = simple enucleation

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Purpose: The excision of the renal tumor with a substantial margin of healthy parenchyma is considered the gold standard technique for partial nephrectomy. However, simple enucleation showed excellent results in some retrospective series. We compared the oncologic outcomes after standard partial nephrectomy and simple enucleation.

Materials and Methods: We retrospectively analyzed 982 patients who underwent standard partial nephrectomy and 537 who had simple enucleation for localized renal cell carcinoma at 16 academic centers between 1997 and 2007. Local recurrence, cancer specific survival and progression-free survival were the main outcomes of this study. The Kaplan-Meier method was used to calculate survival functions and differences were assessed with the log rank statistic. Univariable and multivariable Cox regression models addressed progression-free survival and cancer specific survival.

Results: Median followup of the patients undergoing traditional partial nephrectomy and simple enucleation was 51 ± 37.8 and 54.4 ± 36 months, respectively ($p = 0.08$). The 5 and 10-year progression-free survival estimates were 88.9 and 82% after standard partial nephrectomy, and 91.4% and 90.8% after simple enucleation ($p = 0.09$). The 5 and 10-year cancer specific survival estimates were 93.9% and 91.6% after standard partial nephrectomy, and 94.3% and 93.2% after simple enucleation ($p = 0.94$). On multivariable analysis the adopted nephron sparing surgery technique was not an independent predictor of progression-free survival (HR 0.8, $p = 0.55$) and cancer specific survival (HR 0.7, $p = 0.53$) when adjusted for the effect of the other covariates.

Conclusions: To our knowledge this is the first multicenter, comparative study showing oncologic equivalence of standard partial nephrectomy and simple enucleation.

Key Words: nephrectomy; carcinoma, renal cell

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In the last 2 decades several authors have demonstrated the oncologic equivalence between PN and RN in the treatment of T1 renal cell carcinoma.[1–3] Currently NSS is the standard treatment for solitary RCC up to a diameter of 7 cm, whenever technically feasible.[4,5] The excision of the tumor with a substantial margin of normal renal parenchyma is considered the standard technique for PN to minimize the risk of local recurrence.[1] However, in the last few years the width of healthy tissue that should be excised with the lesion to ensure negative margins has been the object of great debate, and some authors have demonstrated that NSMs can be achieved while reducing the safety margin to 5 mm.[6,7] Consequently the EAU guidelines recommended the presence of a minimal tumor-free surgical margin of healthy renal parenchyma surrounding the resected tumor to reduce the risk of local relapse or progression without specifying the exact minimum thickness of the healthy parenchyma to be taken.[4] In this scenario some authors have supported the oncologic efficacy of SE instead of traditional PN.[8–10] SE consists of incision of the renal parenchyma within a few millimeters of the tumor, and blunt dissection of a plane between the capsule of the tumor and the healthy renal tissue without the inclusion in the removed tissue of any visible normal renal parenchyma. Although published studies showed excellent long-term oncologic results,[8–10] many urologists still consider SE an unsafe technique with a high risk of incomplete tumor excision especially for larger lesions.[11] To date no study has compared oncologic outcome after SE and standard PN. Thus, in this retrospective, multicenter study we compared the risk of local recurrence, PFS and CSS probability after SE and standard PN removing an adequate margin of healthy parenchyma around the tumor.

PATIENTS AND METHODS

The SATURN project was promoted by the Leading Urological No-Profit Foundation of Advanced Research (LUNA) of the Società Italiana di Urologia. A total of 16 academic centers in Italy provided data. The initial database comprised 5,463 patients who underwent RN or PN for renal cell carcinoma between 1995 and 2007. For the objectives of this study patients with synchronous metastases (508, 9.2%) and those who underwent RN for nonmetastatic disease (3,436 or 62.8%) were excluded from analysis. The remaining 1,519 patients treated with a conservative approach were analyzed.

PS was assigned according to ECOG criteria.[12] The mode of presentation was distinguished according to the Patard classification.[13] Clinical staging included at least abdominal CT and chest x-rays. Bone scans and brain CT were obtained only when indicated by signs and symptoms.

Surgical procedures were performed by several surgeons. In patients with a contralateral normal kidney an elective conservative approach had been routinely indicated in the presence of single tumors 4 cm or smaller. Some referral centers extended the indications to larger tumors according to the EAU and American Urological Association guidelines.[4,5] Imperative NSS had been performed in patients with bilateral tumors or with neoplasia involving anatomically or functionally solitary kidneys.

Traditional PN has been defined as the excision of the tumor and of an additional margin of healthy peritumor renal parenchyma. This definition includes enucleoresection, polar resection and wedge resection techniques. Simple enucleation has been defined as tumor excision without a visible rim of parenchymal tissue around the capsule. The choice among the different nephron sparing techniques was based on the academic center and surgeon preference, and the type of surgical technique adopted was reviewed from each institutional database originated from copies of original operative reports.

Pathological Evaluation

Tumors were staged according to the American Joint Committee on Cancer–Union Internationale Contre le Cancer TNM classification.[14] The Heidelberg and Fuhrman classifications were used to assign histological type and nuclear grade, respectively.[15,16] Moreover the presence of microscopic tumor necrosis, sarcomatoid differentiation and margin status were evaluated. There was no central pathological slide review.

Followup Regimen

Patients were generally observed every 3 to 4 months for the first year after surgery, every 6 months from postoperative years 2 to 5 and annually thereafter. Followup consisted of physical examination, routine blood analysis, chest radiography and radiographic evaluation of the kidneys. Elective bone scan, chest CT and magnetic resonance imaging were used when clinically indicated. Cause of death was determined by the treating physicians, by chart review corroborated by death certificates or by death certificates alone. Most patients who were identified as having died of kidney cancer had progressive, widely disseminated metastases at the time of death.

Statistical Analysis

Continuous variables were reported as mean (SD) and range or as median and IQR, as appropriate. The Student t test and the Mann-Whitney U test were used to compare continuous variables, as appropriate. The Pearson chi-square test was used to compare categoric variables. The Kaplan-Meier method was used to calculate survival functions and differences were assessed with the log rank statistic. Univariable and multivariable Cox regression models addressed time to PFS and CSS after surgery. Patients alive and disease-free or who had died of other causes were censored. Statistical significance in this study was set as $p = 0.05$. All reported p values were 2-sided and analyses were performed with SPSS® version 17.0 software.