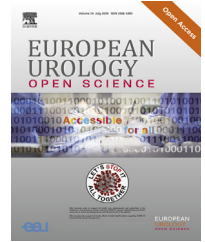




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How to Deal with Renal Cell Carcinoma >7 cm: Radical Surgery

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Introduced in 1969, radical nephrectomy (RN) was the standard treatment for localized renal cell carcinoma (RCC) for a long time [1]. The widespread use of renal ultrasound leading to an increase in the rate of detection of small renal masses and the evolution of surgical techniques led to the dissemination of partial nephrectomy (PN). A nephron-sparing approach reduces the risk of chronic renal insufficiency and thus avoids related sequelae such as cardiovascular events [2]. PN became the new standard surgical treatment for T1a (<4 cm) and selected T1b renal tumors (4–7 cm). It is also applicable for larger tumors (T2, >7 cm), but the question arises whether everything that can be done technically should actually be done.

Overall, data from multicenter cohorts and meta-analyses indicate that equivalent oncologic outcomes may be obtained for PN with a functional benefit over RN. However, in the setting of large tumors, the functional benefit is attenuated by increasing tumor complexity and associated with a higher risk of postoperative complications. The main drawback of these analyses is their retrospective nature. This changed with EORTC 30904, the first randomized clinical trial comparing PN and RN among patients with localized RCC ≤ 5 cm in terms of overall survival (OS). Against the assumption, the intention-

to-treat analysis revealed a significantly higher estimated 10-yr OS rate for RN (81% [$n=273$] vs 76% [$n=268$]; hazard ratio [HR] 1.5, 95% confidence interval [CI] 1.03–2.16; median follow-up 9.3 yr) [3].

Although the target sample size was not reached (slow accrual) and the high rate of conversion from PN to RN (15%, vs 5% crossover from RN to PN), these findings nonetheless suggested that the impact of nephron preservation on OS might not be as profound as was hypothesized. Significantly higher incidence of at least moderate renal dysfunction (estimated glomerular filtration rate [eGFR] <60 ml/min/1.73 m²) was found for RN versus PN in the study population [4]. However, over time, the eGFR of patients with PN and RN converges, as the remaining kidney appears to improve in renal function. Furthermore, the incidence of advanced kidney disease and the rate of kidney failure, defined as eGFR <15 ml/min/1.73 m², was similar between the RN and PN subgroups. In line with the latter observation, an exploratory analysis suggests that preoperative age, performance status of 0 (vs ≥1), and chronic disease (presence vs absence) are the major determinants of mortality, exceeding a possible impact of moderately impaired renal function [4,5].

However, in a retrospective study by Ristau et al [6] that included 212 016 patients from the National Cancer Data Base, PN was not associated with an OS advantage over RN especially for elderly patients with stage 1b–2 renal masses (PN vs RN: HR 0.89, 95% CI 0.76–1.06).

In general, complications (Clavien-Dindo grade ≥3) occur more frequently with PN than with RN for large renal tumors (≥7 cm). In a recent meta-analysis of five studies ($n=248$ PN, $n=653$ RN) the odds ratio (OR) was 2.82 for overall complications and 7.35 for high-grade complications in favor of RN [7]. In the RECORD2 prospective multicenter observational study analyzing periopera-

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tive and mid-term oncologic and functional outcomes after PN for complex renal tumors, severe complication, transfusion, embolization, and reintervention rates were higher for open or laparoscopic PN in comparison to RN. In addition, positive surgical margins (R1 resection) were more frequent in PN. Thus, it is not surprising that trifecta achievement of R0 resection, absence of complications, and warm ischemia time <25 min was significantly higher for RN (47%) than for PN (laparoscopic 38%, open 34%; all $p < 0.02$). This is particularly delicate, as 74% of the surgeries were performed in high-volume centers and only 9.8% of all tumors were >7 cm [8].

Bradshaw et al [9] compared oncologic and functional outcomes and complication rates between robot-assisted PN and minimally invasive RN in a propensity score-matched analysis of the ROSULA (Robotic Surgery for Large Renal Mass) collaborative group. Kaplan-Meier survival analysis revealed no significant difference in 5-yr OS (PN 76.3% vs RN 88.0%; $p = 0.221$) and 5-yr disease-free survival (PN 78.6% vs RN 85.3%; $p = 0.630$) for pT2 RCC, although the RN survival rates were numerically superior to those for PN. However, postoperative complications (22% vs 11%; $p < 0.001$) and serious complications (5.3% vs 2.3%; $p = 0.063$) were twice as frequent in the PN versus the RN group. The rate of R1 resections was more than triple after PN (8.3% vs 2.6%; $p = 0.001$). On the basis of these results, the authors concluded that robot-assisted PN yields similar oncologic outcomes and morbidity profile as minimally invasive RN for cT2a renal masses, while conferring a functional benefit. Consequently, they see robot-assisted PN as a first-line option in this setting, a common perception of many surgeons that is clearly neither supported by the published data nor in line with the arguments presented [9].

Considering the higher R1 resection rate for PN compared to RN, another study is of particular interest. Minervini et al [10] investigated predictors of local (ipsilateral renal) recurrence of RCC, which occurred in 1.4% of 1055 patients, in a retrospective observational study on mid-term oncologic outcomes of PN (RECORD1). Besides an imperative indication (OR 4.14; $p = 0.01$), a positive surgical margin dramatically increased the risk of local recurrence (OR 7.17; $p = 0.005$).

In line with the above-mentioned data, the European Association of Urology guidelines strongly recommend offering laparoscopic RN to patients with T2 tumors [11]. We conclude that for RCC >7 cm, RN does not (negatively) affect all-cause mortality; although PN yields better kidney function preservation, RN results in fewer complications and better oncologic safety (lower R1 rate,

fewer local recurrences) in comparison to PN. These facts must be stressed in shared decision-making between the physician and patient before surgery.

Conflicts of interest: The authors have nothing to disclose.

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