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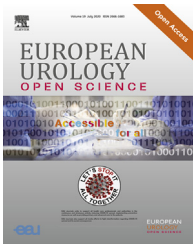

European Association of Urology

Open to Debate For

How To Deal with Renal Cell Carcinoma Tumors >7 cm: The Role of Nephron-sparing Surgery

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Partial nephrectomy (PN) is universally acknowledged as the gold standard for surgical management of clinical T1 renal cell carcinoma (RCC). Undoubtedly PN should be preferred to radical nephrectomy (RN) whenever technically feasible, since it has shown comparable oncologic outcomes with the additional benefit of renal function preservation [1]. In the past few years, enthusiasm for nephron-sparing surgery (NSS) has progressively increased for highly complex and cT2 renal tumors as well.

The debate on whether cT2 renal tumors may be amenable to PN is still open and no definitive conclusions can be drawn, since PN inevitably involves a non-negligible risk of perioperative morbidity. Currently, the upper limit for PN indication remains undefined and is mainly set by individual surgeons according to their individual expertise and preference. For elective indications, we truly believe that NSS for cT2 renal masses may represent a safe treatment option as long as the oncologic radicality is not undermined and the related benefits clearly exceed the potential harms, as in imperative conditions for which anything possible needs to be done to preserve residual kidney function.

One systematic review and meta-analysis in 2017 showed that PN is a viable treatment option for larger renal tumors. PN yielded acceptable surgical outcomes and equivalent cancer control in comparison to RN, with the potential benefit of renal function preservation and lower all-cause mortality [2]. More recently, the ROSULA collaborative group conducted a propensity score–matched analysis of 648 patients with cT2 renal tumors treated with either PN or RN [3]. The results revealed that the rate of onset of 5-yr stage 3b chronic kidney disease (estimated glomerular filtration rate [eGFR] <45 ml/min/1.73 m2) was significantly higher in the RN cohort, with oncologic outcomes comparable between the PN and RN groups [3]. Although tumor dimension is not a limit per se for NSS, recognizing the conditions that require radical treatment is of paramount importance to avoid exposing patients to potentially unnecessary risks or compromising oncologic radicality. Undeniably, evidence of intraparenchymal or perirenal infiltrative tumor growth represents an absolute contraindication for PN. Conversely, the presence of peritumoral angiogenesis and suspected urinary collecting system involvement or intrarenal venous thrombus may represent relative contraindications to NSS for cT2 renal masses. Moreover, proper candidate selection should take into account baseline patient-related features and the preoperative comorbidity burden. In this regard, Larcher et al [4] demonstrated that NSS decreases other-cause mortality only in specific subgroups of patients when compared to RN. In particular, sicker

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patients with relevant comorbidities are those who benefit the most from NSS [4].

In such a scenario, several cornerstones and technical nuances should be kept in mind for safe and effective NSS. Careful preoperative evaluation of the tumor and its anatomical complexity plays a pivotal role. In this regard, computed tomography images may be not entirely appropriate in tailoring the surgical strategy for complex renal masses since they rely on a static evaluation of tumor characteristics. The use of three-dimensional (3D) reconstructions for cT2 renal tumors can improve the assessment of tumor anatomy, permitting better-informed surgical planning and better functional preservation owing to more precise perception of the vascular anatomy and potentially facilitating a selective or "hybrid" (selective plus total) clamping strategy [5]. In addition, intraoperative ultrasound guidance, especially for mainly endophytic renal masses, may significantly improve the surgeon's perception of the tumor burden.

Furthermore, recent evidence points to the resection technique as being a key driver of local oncologic control and volume of vascularized parenchyma preserved, and thus postoperative renal function [6]. In particular, following an enucleative resection plane might allow surgeons to extend the indications for PN to challenging, highly complex renal masses, especially for masses not perfectly round in shape or in close contact with the urinary collecting system [7]. Experienced surgeons do acknowledge the fact that for some complex hilar renal masses, tumor enucleation is the only possible technique to avoid RN and simultaneously achieves two goals: (1) it limits injuries to the intrarenal vasculature in the case of large renal masses abutting the renal sinus; and (b) it facilitates "nephron-sparing renorrhaphy", which in turn will positively influence postoperative renal function recovery. In experienced hands, tumor enucleation yielded negative surgical margins in the vast majority of PN procedures assessed, ultimately providing excellent mid-term local control and oncologic outcomes [8].

Finally, the emergence of robotic assistance has undoubtedly modified the surgical treatment for RCC. Use of a robotic platform allows very precise tumor excision, minimizing the risk of violating the tumor boundaries. In several multicenter series, the robotic approach was found to be protective in terms of the onset of acute kidney injury, postoperative complications, and failure to achieve the trifecta when compared to open and laparoscopic PN [9,10]. Of note, Derweesh and coworkers [11] recently published the largest comparative analysis between open and robotic PN for cT2 renal masses, reporting a significantly higher rate of trifecta achievement in the robotic group. Taken together, these findings strongly suggest that robotic PN may be considered as a first-line treatment option for selected patients with cT2a renal masses when feasible and safe.

Finally, it is of paramount importance to refer such patients to high-volume centers. NSS for cT2 renal tumors should only be performed by surgeons with solid experience in kidney cancer surgery since nuanced differences attributable to the operator experience may explain the intersurgeon variability for PN outcomes [12].

Accreditation of only tertiary referral centers might pave the way to progressive widening of PN indications, maximizing the surgical outcomes and cost-effectiveness of PN.

In conclusion, if NSS is planned for a cT2 renal tumor, the following cornerstones should be borne in mind:

(1) Prompt recognition and exclusion of conditions requiring radical treatment;
(2) Careful evaluation of tumor anatomy and vascularization via 3D reconstructions and intraoperative ultrasound guidance;
(3) Adoption of an enucleative strategy;
(4) Robotic assistance may further maximize postoperative outcomes; and
(5) Surgery should be performed by experienced surgeons in high-volume centers.

Conflicts of interest: The authors have nothing to disclose.

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