

The importance of ischemia vs volume of parenchyma during partial nephrectomy

Volume of parenchyma preserved

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Partial nephrectomy (PN) is currently recommended by the European Association of Urology (EAU) Guidelines as the reference standard treatment for clinically localized T1 renal masses, mostly due to the potential benefit of renal function preservation[1]. Nonetheless, PN is considered unsuitable in some patients with localized renal masses due to the locally advanced tumor growth, the inherent limits of technical feasibility of PN for tumors with unfavorable location or due to the patient's deterioration in general health status. In these cases, radical nephrectomy (RN) is advocated as curative therapy[1]. As such, the new dogma of "PN for all patients for whom the operation is technically feasible" has been challenged and critically discussed in the light of a careful evidence-based analysis of the patient's medical background and perioperative risk [2]. As such, the current Guidelines represent a dynamic "state-of-the-art" rather than definitive evidence and might be prone to substantial changes in the next future. Therefore, a careful assessment of tumor-, surgeon- and patient-related factors is key to evaluate whether nephron-sparing surgery (NSS) does provide a true functional benefit over RN or non-surgical treatments in the single patient with a given life expectancy. The patient's comorbidities and performance status, the surgeon's skill and expertise in PN and the anatomical tumor characteristics do ultimately define the oncological and functional outcomes after surgery.

In this clinical scenario, a careful analysis of the inherent technical characteristics of PN and of the predictors of postoperative functional outcomes after nephron-sparing techniques is key to compare the current surgical series with the aim to define appropriate selection criteria for conservative surgery for localized renal masses in the single patient setting.

The technical pivots of PN are mainly represented by: 1) the strategy of renal pedicle control (clampless vs clamped techniques), that ultimately determines the amount of ischemia experienced by the tumor-bearing kidney and 2) the strategy of tumor excision, which is, together with the technique of renal reconstruction, one of the most relevant determinant of the volume of vascularized renal parenchyma preserved.

Pedicle clamping is performed by most surgeons during PN with the aim to ensure a bloodless surgical field with optimal visualization of tumor contours. However, the increasing interest to maximize the functional outcome after PN pushed the urological community toward the use of off-clamp procedures, as prolonged ischemia time has been associated with a higher risk of developing a chronic kidney disease (CKD)[3].

However, there is still no consensus on the potential definitive functional benefit of the off-clamp techniques, due to the contrasting results of the short- and long-term functional outcomes reported in literature [4]. Moreover, clear evidence regarding the appropriate indications of off-clamp PN according to the tumor- and patient- specific characteristics is lacking.

At the same time, the volume of preserved vascularized parenchyma represents a key determinant of functional recovery after surgery and it might be strongly linked to both the tumor's anatomical complexity and the PN technique [5-8]. Nonetheless, the definition of the

most appropriate margin of healthy renal tissue that should be excised with the tumor and therefore of the safest resection technique (RT) during PN that can guarantee both optimal functional outcomes and oncological efficacy, has been the object of great debate within the urological community in the recent years [9]. Indeed, the EAU Guidelines recommendations changed dramatically during the last years. In 2010, they recommended the removal of a minimal tumor-free surgical margin to avoid local recurrence (yet without any reference to the specific RT), while the subsequent modification in 2013 outlined that if the tumor was completely resected, the thickness of surgical margin (>1mm) did not correlate with the likelihood of local recurrence. Of note, from 2014 they do not provide any kind of recommendation regarding the optimal margin width and/or the most appropriate RT during PN. Moreover, the lack of a standardized nomenclature of different RTs and lack of evidence of the potential role of RT and quality of renal reconstruction undermines the interpretation of such recommendations [10].

Overall, the current evidence supports the hypothesis that preoperative nephron endowment and the percent of functional volume preservation are the primary determinants of the long-term functional outcome after PN in patients with normal preoperative kidney function who have ischemia time within acceptable limits [11-13].

In this complex scenario, the “paradoxical” negative effect of the overwhelming evidence on the role of ischemia vs volume preservation for definitive functional outcomes after PN [6, 7, 14,15] will continue to increase the debate if no standardized descriptors of the critical technical aspects related to PN are used.

PN remains a complex surgical task. Indications and limits of PN for the treatment of localized renal masses are inherently interconnected and linked to the indications/contraindications for RN. Moreover, the degree of complexity in the analysis of the technical and non-technical predictors of PN functional results is extremely high in the single patient scenario as many factors related to the patient comorbidities, the tumor’s anatomical features and the surgeon’s experience, strategy and resection techniques are deeply involved.

To move the field forward and to define evidence-based indications of each surgical technique for the treatment of localized renal tumors, including RN, a change of perspective is needed. As such, the current controversies regarding: 1) the maximal safe WIT to prevent irreversible functional damage after surgery; 2) the open debate over the role of selective clamping vs standard clamping vs clampless procedures for postoperative renal function and the selection of patients who may benefit most from these approaches; 3) the role of RT (enucleation vs enucleoresection vs resection) and renorrhaphy technique for functional volume preservation; 4) the relationship between surgeon-related factors (experience, background, RT) for ultimate functional outcomes need to be solved by a methodologically rigorous assessment. To do so, prospective high-quality randomized controlled trials using standardized classification systems to report all patient-, tumor- and surgery-related features are highly warranted.

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