Tumour enucleation vs partial nephrectomy: Long term results

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Introduction

The treatment of small renal masses (SRMs) represents an area of increasing interest. Since the initial description of NSS, a number of technical strategies for tumor excision have been described. These strategies can be grouped into three main categories: simple enucleation (SE), enucleoresection (ER), also referred to as standard partial nephrectomy (SPN)), and wedge resection (WR). SPN is defined as the excision of the tumor and of an additional margin of healthy peritumoral renal parenchyma, while SE as the excision of the tumor by blunt dissection following the natural cleavage plane between the peritumoral pseudocapsule and the renal parenchyma without removing a visible rim of healthy renal tissue.

Enucleative partial nephrectomy: long-term results

Surgical approach: Enucleative PN has been first described as an open technique but it can be feasible also during the laparoscopic or the robotic procedure. A matched-pair analysis of 392 patients treated with SE for T1a-T1b renal tumors, including 160 patients in the open group and 80 in the robotic group (Endoscopic Robotic Assisted Simple Enucleation, ERASE), showed that ERASE is a feasible technique with a positive surgical margin rate comparable to the open technique; it showed WIT and complication rates similar to the open approach, along with the advantages of mini-invasivity [3].

Indications

SE can be used for the elective treatment of sporadic renal masses regardless tumor dimension [4], but also for relative and absolute indications to NSS [4, 5]. It is has been reported a possible advantage using SE especially when facing tumors with most unfavourable nephrometry (PADUA $\geq$ 10; RENAL $\geq$ 10, totally endorenal tumors, cT1b with endophytic growth into the medulla and close to main intrarenal vessels and collecting system). However, the majority of the studies on the perioperative results of TE does not analyse subgroups of challenging tumors [6-8]. In a recent study, that assessed the perioperative results of SE in 244 patients, a substantial 21% had a PADUA score $\geq$10 thus confirming that SE might wide the technical indications of NSS including the most challenging cases [9]. With the advent of nephrometric scores, it would be important in the future to further test the efficacy of SE for the treatment of tumors with adverse nephrometric scores and to compare the results with those of standard PN [10,11].

Exclusion criteria to enucleative partial nephrectomy: High Fuhrman grade (Fuhrman grade 4) might be a contraindication for SE. Indeed, a recent paper from the SATURN project showed that patients who underwent SE for Fuhrman grade 4 disease had significantly worse cancer specific survival compared to those undergoing standard PN but patients were too few (20 Standard PN versus 4 SE) to make this observation nothing more than a suggestion for future studies [6].

Warm ischemia time (WIT), functional outcomes and perioperative complications: Some Authors have hypothesized that SE might be associated with shorter WIT and could be protective against complications being possibly associated with a lower rate of major bleeding and urinary fistula compared to standard PN [10]. Indeed, SE showed in single center prospective series a low incidence of postoperative complications requiring reintervention, a low rate of urinary fistulas and of ureteral stenting [7, 9]. However, in a large multicenter prospectively derived dataset (RECORd project), a matched-pair comparison of 396 patients showed that SE and standard PN are associated with similar WIT and similar incidence of overall, surgical and medical complications [8]. In the same study, SE was associated with shorter operative time and lower blood loss if compared to standard PN [8]. No comparative data on mid- and long-term functional outcomes between SE and standard PN have been reported to date.

Surgical margin status

The achievement of negative surgical margins is one of the major challenges of NSS. PSM after NSS occurs in 0-8% of patients. The presence of PSM as risk factor for disease recurrence after NSS is still a matter of debate, however, it should prompt more frequent and intensive surveillance. The incidence of positive surgical margins has been consistently very low in SE series [13, 14]. The protective effect of a blunt enucleation towards the risk of positive margins has been demonstrated in a prospective pathological study on 90 RCCs that showed the presence of an inflammatory tissue with a median thickness of 1mm which allowed the presence of negative surgical margins also for tumors microscopically extending beyond the tumor capsule [15]. This thin layer of normal tissue was present as "leopard spots" on the intact tumor capsule, and always present in case of neoplastic penetration of the capsule into the kidney tissue [15]. A recent prospective study on 304 patients evaluated the prognostic effect of capsule penetration on local recurrence after SE [16]. At a median (range) follow-up of 52 months (12–96), there was no statistically significant difference in progression-free survival (PFS) between patients with an intact tumor capsule and those who had neoplastic penetration of the capsule into the kidney tissue (5-year PFS 97.5% and 96.7%, respectively) [16]. In the latter the crude local recurrence rate was 3.2% [16]. Two recent multicentre papers have showed a significantly lower incidence of PSM after SE when compared to standard PN [4, 8]. Longo et al. in the first multicentre matched-pair analysis aiming to compare the perioperative outcomes of SE versus standard PN in clinical T1 renal tumors showed that the incidence of positive margins was significantly lower in patients treated with SE and 4.7 higher in pts undergoing standard PN [8]. In this regard we can conclude that SE is at least non inferior to standard PN for what concern the risk of positive margins; however, further studies using a standardized classification of different NSS techniques are warranted to render definitive conclusions regarding the risk of positive margins with different types of NSS.

Oncologic outcomes, from pathology reports to mid- and long-term follow up studies: The oncologic safety of blunt SE has been demonstrated by retrospective studies which demonstrated that the width of the surgical margin was not associated with the oncological prognosis and by prospective pathological studies [15-17]. Several retrospective studies have confirmed good oncologic results of SE and some of these studies have demonstrated also a similar local recurrence-free survival and cancer specific survival rates between SE and standard PN, for renal tumors with clinical diameter up to 7 cm; one study have also confirmed similar cancer specific survival between SE and radical nephrectomy [18-25].

Future perspectives

Unfortunately, standardized definitions for each resection technique during NSS are lacking. Indeed, the descriptors SE, ER, and WR are used largely interchangeably. The precise resection methodology is rarely reported in the published series, despite a relationship between technique and complication rates, preserved parenchymal volume, surgical margins (SMs), local recurrence, and oncologic outcomes. The main limitation of such definitions is that they are based on the surgeon's preoperative resection strategy rather than the actual postoperative surgical result (resection technique). In this context, a more thoughtful vision of tumor excision during partial nephrectomy would be to clearly divide the concepts of the surgeon's resection strategy from that of the actual resection technique. The surgeon's resection strategy can be conceptually divided into two clearly defined options according to the resection plane developed for tumor excision. Indeed, the preoperative intent of the surgeon (resection strategy) can be described as anatomic or nonanatomic according to the dissection plane chosen by the surgeon, being anatomic when the natural cleavage plane between the tumor with its pseudocapsule and the normal healthy parenchima, is developed. While, the actual postoperative surgical result (resection technique) could be classified according to a careful analysis of the specimen after surgery. In this regard, the Surface-Intermediate-Base (SIB) Margin score was recently proposed to provide the literature with a standardized reporting system of resection techniques during NSS and we recently validated the model from the histopathological perspective [1,2]. We have shown that the visual definitions of resection techniques used to calculate the score do significantly mirror histopathological analysis to quantify and report the thickness of healthy renal margin resected by the surgeon. In the final

analysis, the SIB score represents a simple tool to classify the true, post-operative resection technique. In conclusion, in order to describe accurately the complexity of tumor excision, each PN should include a definition of both resection strategy (anatomic vs nonanatomic) and resection technique (pure or hybrid enucleation, pure or hybrid enucleoresection and resection) according to the SIB classification system. Dividing the concepts of resection strategy and resection technique will allow the surgeon to describe the complexity of each tumor excision during NSS in the very best way.

Conclusions

In summary, the long-terms results of enucleative PN are at least comparable to SPN with regard to both oncological efficacy and surgical safety. However, 1) the lack of standardized terminology to describe NSS techniques; 2) the current inability to communicate the complexity that may be inherent in a given tumor's resection, and (3) the nearly complete absence of routine reporting of resection type potentially may undermine the interpretation of NSS outcomes and may prohibit meaningful comparisons of results among surgeons and institutions.

As such, we believe standardized definitions of both the surgeon's preoperative intent and the actual postoperative surgical result (resection technique, according to the SIB score) should be mandatory in future series to significantly raise the quality of the reported NSS data making outcome assessments and comparisons more meaningful.

Further research is needed to define the best surgical strategy and technique for PN in each individual patient. As such, prospective high-quality studies are needed. However, whether a randomized controlled trial is really needed is still controversial, as many methodological and conceptual limitations associated with the randomization process may undermine the overall interpretation of the final results. In particular, since the preoperative intent of the surgeon does not necessarily translate into the expected resection technique, it would be complex to assign each tumor resection to enucleation or enucleoresection a priori. Accordingly, a well-designed, prospective cohort study including a detailed reporting of both resection strategy and technique might be the most thoughtful answer to this controversial topic.

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