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Robotic-assisted partial nephrectomy: the next gold standard for the treatment of intracapsular renal tumors

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“Early feasibility studies have demonstrated that robot-assisted partial nephrectomy provides equivalent oncological results to laparoscopic partial nephrectomy with the further advantage of significantly lower intraoperative blood loss, reduced hospital stay and warm ischemia time.”

Based on the GLOBOCAN 2008 estimates, published in 2011, over 110,000 new kidney cancer cases are expected in 2011, and will account for approximately 43,000 deaths among men from developed countries [1]. Due to increased utilization of diagnostic imaging for evaluation of patients with abdominal symptoms, small renal masses are being diagnosed with greater frequency, and over the last three decades a stage migration has been observed, with an overall decreasing size of stage I renal cell carcinoma (RCC) at diagnosis [2]. Data from the National Cancer Database over the 12-year period between 1993 and 2004 showed an increase in stage I disease and a decrease in stage II, III and IV disease ($p \leq 0.001$). The size of stage I tumors also decreased from a mean of 4.1 cm in 1993 to 3.6 cm in 2003 [3]. In patients who have incidental detection of a renal tumor, there is, on average, a lower pathological stage and grade at diagnosis, which correlates with a significantly increased 5-year cancer-specific survival (CSS) as opposed to patients with symptomatic RCC [4]. Indeed, Jemal *et al.* report that the 5-year survival rate of patients diagnosed with kidney cancer has progressively increased from 51% in the mid-1970s to 69% in the past decade [5], and Kane *et al.* showed a 3.3% increased CSS for patients diagnosed in 1998 compared

with patients diagnosed in 1993 [3]. The increased diagnosis of small renal tumors has led to a concurrent rise in rates of surgical intervention and to an augmented interest in the various techniques of nephron-sparing surgery (NSS) [6]. In this scenario, renal preservation has been progressively prioritized, as approximately 26% of patients have impaired renal function prior to undergoing either NSS or radical nephrectomy (RN) and RN is a recognized independent risk factor in the development of chronic kidney disease postoperatively, cardiovascular events and overall mortality [7]. Weight *et al.* reviewed data of 1004 patients with clinical T1b renal masses undergoing NSS ($n = 524$) or RN ($n = 480$). Those patients undergoing RN lost significantly more renal function than those undergoing NSS. The average excess loss of renal function observed with RN was associated with a 25% (95% CI: 3–73) increased risk of cardiac death and 17% (95% CI: 12–27) increased risk of death from any cause on multivariate analysis [8]. Therefore, NSS is an attractive option and several studies have shown its oncological efficacy compared with RN. A dimensional cutoff is still a matter of discussion, but according to the European guidelines NSS should be performed whenever technically feasible in case of intracapsular RCCs up to 7 cm in diameter (T1a/b stage) [9]. Data

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on 3480 patients from the Surveillance and Treatment Update on Renal Neoplasms (SATURN) project, promoted by the Italian Society of Urology, that collected data from 16 academic centers in Italy, displayed no statistical difference in CSS and recurrence free survival between patients with clinical stage T1 RCC treated with NSS or RN, strongly supporting the use of NSS, consistent with the largest monocentric series published in the literature [10–14].

Due to its wide use and acceptance, open NSS remains the contemporary cornerstone in the management of small renal masses, performed either as partial nephrectomy (PN) or tumor enucleation (TE), which is a tumorectomy performed by a blunt dissection, using the natural cleavage plane between the tumor and normal parenchyma, with no ablation of the tumor bed [15–19]. Nevertheless, because of its major invasiveness, postoperative pain, scarring, longer hospitalization and a slower return to the ordinary activities, in the future fewer NSS procedures will be conducted using an open fashion. First described by Winfield *et al.* in 1993, laparoscopic NSS (LNSS) duplicates the principles of open surgery with several technical variations, as it has been standardized to a great extent [20]. Data from the largest comparative study between open PN (OPN) and laparoscopic PN (LPN) found it to be a technically feasible, safe and effective option in selected patients with RCC who are candidates for a nephron-sparing procedure [21]. Moreover, in the same series comparing LPN to OPN for the treatment of a single renal tumor of 4 cm or less, an equivalent oncologic and functional outcomes is reported [21]. At 7 years, metastasis-free survival was 93 and 95% ($p = 0.7$) after LPN and OPN, respectively. However, when considering the subgroup pT1b/T2 (RCC with a maximum diameter of >4 cm), the 5-year metastasis free-survival was 86 and 97% for patients treated by LPN and OPN, respectively ($p = 0.03$), and this difference was maintained at 7 years of follow-up (82 and 95%, respectively), although it did not reach statistical significance ($p = 0.17$) for the relatively small number of patients in the LPN cohort who completed the 7-year follow-up [21]. The authors concluded that LPN should only be considered if extended knowledge in laparoscopic surgery is available [21,22]. Indeed, LNSS remains a challenging procedure, with a steep learning curve, due to the limited variation of the degree of incidence with the target structures, making both the extirpative and reconstructive step often more demanding and sometimes approximate in respect to the open fashion. Moreover, the laparoscopic approach has been also associated with longer warm ischemia time (WIT) when compared with OPN [22]. Indeed, in a recent single-center series evaluating the short- and long-term renal effect on 362 patients with RCC in a solitary kidney, for each 1 min of increasing of WIT there was a 5% increased in the risk of postoperative acute renal failure. Moreover, evaluating warm ischemia in 5-min increments, a cutoff point of 25 min provided the best stratification of risk of developing acute renal failure or an acute GFR <15 ml/min or a new-onset stage IV chronic kidney disease in the postoperative period [23].

First reported in 2004 by Gettman *et al.*, robot-assisted partial nephrectomy (RAPN) using the da Vinci Surgical System (Intuitive Surgical, CA, USA) represents an alternative procedure

to LNSS and open NSS for the treatment of intracapsular RCCs and has steadily gained acceptance between surgeons [24]. Early feasibility studies have demonstrated that RAPN provides equivalent oncological results to LPN with the further advantage of significantly lower intraoperative blood loss, reduced hospital stay and WIT [25]. Recent studies have also shown that RAPN can be effectively utilized for the treatment of larger renal tumors that are over 4 cm in diameter and in cases of parahilar lesions [26,27]. Indeed, the 3D vision associated with the 'endowrist' technology allows for excellent vision of the operative field and the possibility of dissecting the tissue optimally by varying the degree of incidence with the target structures. This is translated into a precise and fine renal hilum definition, with the possibility of secondary and tertiary arterial branch dissection, in order to perform selective or even superselective vascular clamping, providing a zero-ischemia partial nephrectomy [28]. After the initial dissection directed towards defining the renal hilum and once the tumor margins are clearly identified, before clamping, the excision template is marked with cautery, a few millimeters away from the lesion. More refined instruments and probes are becoming available to help surgeons in identifying the correct margins, such as near-infrared fluorescence of intravenously injected indocyanine green and Tile-Pro [29,30]. At this step of the procedure the 3D vision and the endowrist also help to decrease the positive surgical margins as they typically provide optimal dissection angles [26,31]. Therefore, a faster and precise extirpative step, without the need of repositioning the kidney to achieve an incidental angle, that is mandatory during LNSS, allows the surgeon to perform a more ergonomic and 'intuitive' tumorectomy and to approach even more difficult cases, such as large, intraparenchymal or parahilar tumors [26,27]. In these latter cases, when the depth of the lesion or the proximity to important vascular structures makes the procedure more challenging, the adoption of the TE technique can be decisive, as the blunt dissection provides a clear dissection plane identification, helping the surgeon to discriminate the natural cleavage plane existing between the tumor and the renal parenchyma. Moreover, TE provides maximal parenchymal preservation and minimizes incidental calyceal tearing or vascular injuries [32–34].

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The reconstructive phase of the da Vinci system has the clear advantage of being rapid and effective, since the sutures can be placed very precisely and with a considerable reduction of time, as there is no need to place both the resection bed and the needle holder in the most convenient position. The result of this higher precision and velocity reflects on WIT and on intra- and

post-operative complication rates. Indeed, a recent multicenter analysis that examined surgical outcomes from three experienced robotic surgeons reported significantly shorter WIT for RAPN when compared with LPN (19.7 vs 28.4 min; $p = 0.0001$) and reported a postoperative complication rate for RAPN of 9.8%, comparing favorably with the postoperative complication rate in both LPN (18.6%) and OPN (13.7%) [25]. Furthermore, a prospective report on 86 consecutive patients who underwent LPN ($n = 59$) or RAPN ($n = 27$) showed that an early unclamping technique was used for 22 patients (82%) in the RAPN cohort and six patients (10%) in the LPN cohort ($p < 0.001$), with a lower WIT in the RAPN cohort (mean: 18.5 vs 28.0 min; $p < 0.001$) [35]. Additionally, RAPN has been shown to have a relatively shorter learning curve when compared with LPN [25]. The widespread use of single-port RAPN will require substantial changes in existing robotic instrumentation, since at present it has no proven efficacy

and is of interest only for anecdotal reports [36]. In conclusion, the favorable early-intermediate outcomes of RAPN will extend the benefits of the minimally invasive NSS to a wider audience of patients and surgeons, making RAPN both the present and imminent future of the conservative treatment of kidney cancer. Moreover, the da Vinci Surgical System provides the possibility of a precise TE, allowing maximal parenchymal preservation and minimizing incidental vascular and calyceal tearing.

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