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 Referring to the article published on pp. 435–443 of this issue

Is Laparoscopic Cryoablation a Less Invasive and Effective Procedure to Treat Small Renal Masses?

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About 88 000 cases of kidney cancer were diagnosed in Europe in 2008 [1], with a consistent number being represented by incidentally detected small renal masses (SRMs). Those tumors present favorable histopathologic features and better prognosis in comparison with bigger tumors. Moreover, SRMs are more frequently detected in elderly patients with a higher risk of comorbidities [2]. The clinical consequence is that most elderly patients with SRMs die of causes other than kidney cancer [3], and such a discrepancy can be amplified by the high risk of cardiovascular events observed in patients who develop renal insufficiency after radical nephrectomy [4].

Similar to prostate cancer, these last considerations highlight the potential role of active surveillance and ablative therapies (cryoablation and radiofrequency) [5] as alternatives to partial nephrectomy [PN] in the treatment of SRMs. Specifically, both European Association of Urology and American Urological Association guidelines consider patients with significant comorbidity who are unfit for PN as potential candidates for an ablative approach or for active surveillance in those who wish to avoid treatment [6,7].

Ablative therapies can be performed using either a laparoscopic or percutaneous approach. The first requires general anesthesia and is the technique used most frequently for cryoablation, whereas a less invasive percutaneous approach is preferred for radiofrequency ablation (RFA) [5]. Regardless of the invasiveness of the procedure, a meta-analysis of the studies published between 1980 to 2008 reported better oncologic outcomes in patients who underwent laparoscopic cryoablation [LCA] in comparison with those who received RFA [8].

In the present issue of *European Urology*, Klatté et al. presented a new systematic review and cumulative analysis

of the literature concerning complications and oncologic outcomes of LCA and both open and laparoscopic PN [9]. In this excellent paper, the authors identified 98 studies reporting data on cancer control and perioperative complications in >6000 and 10 000 patients treated with LCA or PN, respectively. Taking into account the different patients' characteristics by both multivariable analysis and propensity score adjustment, the authors found that LCA was followed by a significantly higher risk of local recurrence (three- to five-fold increase according to the different statistical analyses), whereas the risk of distant progression was similar in both study groups. Conversely, a significantly higher risk of perioperative major complications was observed following PN (a 10-fold higher risk was identified in regression analysis and a 7-fold higher risk was identified in the propensity score adjustment analyses) [9].

Lacking randomized controlled trials, those conclusions were based on a few comparative studies and on indirect comparisons of surgical series (level 3 evidence). Moreover, although the authors should be commended for their enormous effort in putting together a methodologically correct systematic review, the conclusions remain influenced by numerous potential biases. Consequently, some issues must be highlighted.

First, if LCA requires general anesthesia, is the procedure less invasive than PN in elderly patients with relevant comorbidities? Looking at data reported by Klatté et al. in their systematic review [9], patients who received LCA experienced a significantly lower percentage of major complications in comparison to those who received PN (10% vs 19%). However, the increased risk of major complications in PN did not reflect the different anatomic and topographic characteristics of the treated SRMs.

DOI of original article: 10.1016/j.eururo.2011.05.002

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Recently, some nephrometry scores (ie, RENAL nephrometry, PADUA classification, and concordance index) have been proposed to estimate the risk of complications after PN. However, such measures were not adopted in any of the reported studies evaluating LCA. Conversely, we reported 14- and 30-fold increases in the probabilities of complications following open PN in intermediate- or high-risk groups, respectively, according to PADUA score [10]. Considering that tumors treated with LCA are more frequently exophytic, are located at the level of the lateral rim of the kidney, and are distant from the upper collecting system and renal sinus in comparison to those receiving open or laparoscopic PN, it is possible that the highest percentages of complications observed in PN series were the effect of selection bias more than the consequence of a less invasive procedure. Studies comparing LCA and PN adjusted for nephrometry scores are needed to solve this relevant issue. In our opinion, the conclusion that the risk of perioperative complications is lower following LCA is strongly affected by such selection biases.

Second, with regard to oncologic outcomes, local recurrence data are more reliable than those analyzing the risk of distant progression, as correctly reported by Klatte et al. [9]. Although it is likely that tumors treated with partial nephrectomy had more unfavorable histopathologic characteristics, the cumulative analysis performed by Klatte et al. demonstrated that LCA is associated with a significantly higher risk of local progression in comparison to PN. Moreover, such a risk increases by 85% for each 1-cm rise in tumor size in the range of 0.5–3 cm. These data must be strongly considered during preoperative patient counseling, must be adequately discussed with the patient, and must strongly limit the potential widening of the indications for LCA in patients with larger tumors.

Third, although the results of the meta-analysis showed overlapping results between LCA and PN in terms of risk of distant progression, these data cannot be considered definitive. Looking at the reported weighted mean follow-ups, patients treated with LCA had significantly shorter follow-up durations (29 mo vs 57 mo). Consequently, the true risk of distant metastases following LCA series is underestimated due to the short period of follow-up and is biased by the most favorable histopathologic features of the lesions treated by LCA.

In conclusion, the data of the systematic review by Klatte et al. [9] highlighted that the potential advantages of LCA in terms of major complication rates could be the effect of some selection biases more than the real effect of a less invasive procedure; that the reported oncologic outcomes are in favor of PN, mainly in terms of risk of local progression; and that well-done, prospective, comparative studies considering

nephrometry scores are urgently needed. In our opinion, the currently available data seem to counsel caution in the selection of patients to be treated with LCA rather than support a widening of the indication for such ablative therapy in SRMs. Tumors with aggressive behavior should be surgically removed whenever the patients is willing and fit to undergo PN. Currently and, hopefully more commonly in the future, the indications for treatment of SRMs should be based in part on histologic features (histologic subtype and grade) from renal tumor biopsies. We hope that the definition of the histologic and cytogenetic profile on SRM biopsy (eg, by the identifications of chromosome deletions or gains) could improve the current knowledge of tumor biology to tailor patient treatment more appropriately.

Conflicts of interest: The authors have nothing to disclose.

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doi:10.1016/j.eururo.2011.05.059