

Re: Renal Cancer Surgery for Patients Without Preexisting Chronic Kidney Disease: Is There a Survival Benefit for Partial Nephrectomy?

Suk-Ouichai C, Tanaka H, Wang Y, et al

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Experts' summary:

In this retrospective study, Suk-Ouichai and colleagues analysed the 10-yr outcomes for 3133 adult patients without preoperative chronic kidney disease (CKD; estimated glomerular filtration rate [GFR] ≥ 60 ml/min/1.73 m²) treated with partial nephrectomy (PN; $n = 1732$) or radical nephrectomy (RN; $n = 1401$) for presumed renal cancer at a single high-volume institution over a 12-yr period (1997–2008). The median follow-up was 9.3 yr and the primary outcome was non-renal cancer-related mortality (NRCM).

As expected, PN was associated with greater short- and long-term postoperative renal function preservation when compared to RN. Interestingly, NRCM was similar for all patients with new-baseline eGFR ≥ 45 ml/min/1.73 m² but was significantly higher among patients with new-baseline GFR below this cutoff (9.3% of the overall population).

The Kaplan-Meier mortality curves show that patients undergoing RN had significantly greater NRCM compared to patients undergoing PN (17.7% vs 11.3% at 10 yr; $p < 0.001$). Of note, NRCM was also significantly greater after RN when restricting the analysis to patients with new-baseline eGFR ≥ 45 ml/min/1.73 m² ($n = 2843$; 10-yr NRCM 16.3% vs 10.6%; $p < 0.001$). In this patient population, age > 58 yr, male gender, and RN were significantly associated with NRCM on multivariable analysis. Intriguingly, in a multivariable model that included new-baseline eGFR instead of surgical approach, only age and gender significantly predicted NRCM.

Experts' comments:

Decision-making regarding PN versus RN is highly complex in daily surgical practice, especially when the expected risks of PN are high enough to wonder whether it might be better to perform a straightforward RN. The challenge stems from the need to preoperatively balance all potential factors at play [1].

In 2019, current guidelines strongly prioritise PN for all patients with T1 tumours [2]. In light of the evolution of indications for PN, the contemporary key question is whether performing PN in a 58-yr-old binephric patient without pre-existing CKD referred for a 5.4-cm hilar renal mass that is almost completely endophytic is oncologically safe and will have a lower risk of NRCM in comparison to RN, presuming oncological equivalence and accepting a potentially higher risk of perioperative complications. Answering this question requires careful integration of clinical expertise with the best available evidence from systematic research. The current best evidence available for the impact of PN and RN on NRCM is mixed and still controversial [1,3–5]. Recent studies questioned the survival impact of

functional preservation achieved by PN in all patients with T1 renal masses without pre-existing CKD [4,5]. Notably, a marked GFR decrease to < 45 ml/min/1.73 m² following surgery appears to be linked to a higher risk of progressive GFR reduction regardless of preoperative GFR [1]. Moreover, although CKD primarily due to surgical removal of nephrons may have better outcomes than CKD due to medical aetiologies [2], patients with surgically induced CKD appear to be heterogeneous, and those with a lower new-baseline GFR experience significantly poorer survival [3]. Finally, renal function might have an independent relationship with cancer-specific mortality [6].

In this scenario, the study by Suk-Ouichai et al. provides additional evidence to better contextualise the survival advantage of PN relative to RN for patients with localised renal tumours. Intriguingly, the authors argue that selection bias might have substantially influenced their findings and considered the 74% median preservation of global renal function after RN as a relatively favourable result. They conclude that patients with a renal mass and no pre-existing CKD tend to have relatively low NRCM as long as their new-baseline GFR is > 45 ml/min/1.73 m², and that PN should be prioritised to accomplish this goal whenever feasible.

Our key conclusion is instead to never limit PN for technical reasons unless it would be oncologically unsafe. To move beyond the “selection bias” explanation for the survival advantage of PN, key issues of the study design should be further appraised. First, the follow-up duration might have been too limited to show an impact of new-baseline renal function on NRCM. Thus, younger patients without pre-existing CKD and life expectancy of > 15 – 20 yr are likely to substantially benefit from PN. Second, the analyses by Suk-Ouichai et al. did not consider key potential predictors of renal function preservation after PN, which may impact decision-making and potentially NRCM. Third, all PNs were considered “equal” in terms of renal function preservation. Considering the evolution of PN over time towards the concepts of minimally invasive, minimal-margin tumour excision and nephron-sparing renal reconstruction [7], it is likely that, all other factors being equal, the functional preservation of PN increased over time as well. Finally, the multivariable model presented by the authors assumed independence of gender and new-baseline eGFR; interestingly, gender-related differences in kidney function and mechanisms to cope with the stress of renal cancer surgery might have influenced new-baseline GFR [8].

As previously proposed [1], the authors argue that a randomised trial of PN versus RN will be required to address the ongoing controversies and move this field forward. Such a trial would perhaps provide clinicians with the answers they need, but patients are likely to refuse randomisation. In addition, given the extreme variability of clinical scenarios and the nuanced decision-making [1], a randomised trial in this setting might potentially violate the principle of clinical equipoise. For this reason, we believe in a “nephron-sparing” philosophy when counselling patients with local-

ised renal masses for whom PN is not oncologically unsafe and appears to be technically feasible in experienced hands.

More research is needed to improve the prediction of cancer-specific mortality and define the true oncological limits of PN, as well as of patients' life expectancy and NCRM, to evaluate whether they might benefit from PN. In the meantime, under elective conditions, we should pursue the concept of precision surgery and never limit PN for technical reasons unless it would be oncologically unsafe.

Conflicts of interest: The authors have nothing to disclose.

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Re: Extended Versus Limited Lymph Node Dissection in Bladder Cancer Patients Undergoing Radical Cystectomy: Survival Results from a Prospective, Randomized Trial

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Experts' summary:

This prospective, randomized, multicenter phase 3 trial investigated the oncological impact of the extent of lymph node dissection (LND) in patients undergoing radical cystectomy (RC) for bladder cancer (BC) [1]. A total of 401 patients were randomized to receive either limited LND (bilateral obturator and internal and external iliac nodes) or extended LND (also including deep obturator fossa, common iliac, presacral, paracaval, interaortocaval, and para-aortal nodes up to the inferior mesenteric artery). Limited LND was performed in 203 patients (group A) and extended LND in 198 patients (group B). The 5-yr recurrence-free (RFS), cancer-specific (CSS), and overall survival (OS) rates were 59.2%, 64.5%, and 49.7% in group A, and 64.6%, 75.9%, and 58.9% in group B. However, these differences did not reach statistical significance (all $p > 0.05$). Overall, 30-d and 90-d complications did not

differ between the groups. In summary, extended LND did not convey a clinical benefit over limited dissection.

Experts' comments:

RC with bilateral pelvic LND, eventually accompanied by perioperative platinum-based systemic chemotherapy, is the standard of care for the treatment of muscle-invasive and very high-risk non-muscle-invasive BC. LND in BC is generally performed with two aims: diagnostic and therapeutic. The ability of nodal status to predict oncological outcomes is well established, with CSS rates varying from 44% in N1 patients to 27% and 0% in N2 and N3 patients, respectively [2]. Likewise, it has been shown that lymph node density can predict CSS among patients with node-positive disease after surgery and, in some trials, has superior accuracy to TNM classification [3]. Moreover, understanding the pathological nodal status of patients undergoing RC plays a fundamental role in decision-making regarding the indication for adjuvant systemic therapy and follow-up intensity. Finally, retrospective evidence suggests that LND may improve oncological outcomes in selected patients, such as those with metastases or micrometastases to a few nodes. On the basis of this evidence, LND is mandatory in all patients undergoing RC for BC.