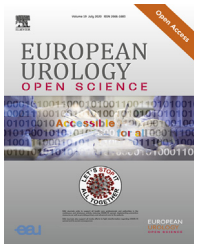
EUROPEAN UROLOGY OPEN SCIENCE 33 (2021) 45–47

available at www.sciencedirect.com
journal homepage: www.eu-openscience.europeanurology.com



European Association of Urology

Open to Debate – Referee

How to Deal with Renal Cell Carcinoma Tumours >7 cm: Referee

Yasmin Abu-Ghanem *, *Ben Challacombe*

Urology Centre, Guy's & St Thomas' NHS Foundation Trust, London, UK

Article info

Article history:
Accepted August 25, 2021

Associate Editor:
Jochen Walz

Renal cell carcinoma (RCC) is the most common primary malignancy of the kidney, representing 2–3% of all adult cancers. To date, surgical resection is the standard treatment for localised tumours, with either radical nephrectomy (RN) or partial nephrectomy (PN) used, depending mainly on the tumour size, stage, and anatomical location [1,2].

While PN is the recommended treatment for patients with T1 (<7 cm) renal tumours, for larger (T2) lesions, RN is still regarded as the reference standard [3]. However, as the technical, oncological, and functional success of PN for T1 tumours has become apparent, there has been judicious extension of this surgical approach to larger tumours, and in recent years PN has become a valid alternative to RN even for T2 and T3 renal masses [4,5]. However, the role of nephron-sparing surgery for large tumours is still controversial, as the question of whether the advantages of PN for T1 renal tumours are maintained for T2 tumours remains to be answered.

Given ongoing technical advances and improvements in surgical skills, the key debate is whether the risks involved in PN outweigh the benefit of a nephron-sparing procedure. When assessing these cases, it is important to consider the impact on kidney function, cardiovascular events, and oncological outcomes, as well as the risk of significant complications. Several systematic reviews suggest that PN confers a survival benefit and a lower risk of chronic kidney disease (CKD) at the "cost" of higher estimated blood loss and the likelihood of complications [6,7]. Hence, the debate regarding whether cT2 renal tumours may be treated with PN is not a question of feasibility, but rather whether PN confers any benefits to the patient. In the debate in this issue of *European Urology Open Science*, each of the author groups has presented compelling evidence to support their point of view, mainly based on a recently published systematic review (SR) and several comparative trials. This arbitration will try to balance these arguments in an attempt to draw a conclusion or recommendations.

To try and provide a balanced view, it is important to review the key reasoning for expanding the current indications for PN for larger tumours. The answer to this lies in the core purpose of any oncological surgery: can we provide the best oncological and functional outcomes with the fewest possible complications?

In the past decade, several retrospective studies have supported the role of PN for such tumours [4,8]. These were further validated by several SRs, with or without meta-analysis. In terms of oncological outcomes, previous studies revealed encouraging results. One example is an SR and meta-analysis from 2017 looking at comparative studies of PN versus RN for cT1b–T2 RCC, in which Mir et al [6] found a better recurrence rate (risk ratio [RR] 0.61; $p = 0.004$) and cancer-specific mortality (RR 0.65; $p = 0.03$) favouring PN over RN. Janssen et al [9] conducted a similar comparison with a long-term follow-up (median 102 mo). Compared to the RN group, the PN cohort had significantly longer median overall survival (OS; $p = 0.014$) and cancer-specific survival ($p = 0.04$). More recently, the ROSULA collaborative group [10] performed a propensity score–matched comparison of

DOIs of original articles: http://dx.doi.org/10.1016/j.euros.2021.07.008, http://dx.doi.org/10.1016/j.euros.2021.09.001.
* Corresponding author. Urology Centre, Guys and Saint Thomas NHS Foundation Trust, London, UK.
E-mail address: yasmin.abughanem@gstt.nhs.uk (Y. Abu-Ghanem).
http://dx.doi.org/10.1016/j.euros.2021.08.006

minimally invasive RN versus PN for cT2a renal masses. Similar to previous studies, the group reported comparable oncological outcomes, including 5-yr OS and disease-free survival. Selection bias is a potential confounder for many of these series, however.

With regard to functional outcomes, it has been demonstrated that PN preserves renal function better than RN, thereby potentially lowering the risk of cardiovascular complications [11,12]. Nevertheless, it has also been shown that patients with normal preoperative renal function and a decrease in estimated glomerular filtration rate (eGFR) after surgical treatment (either RN or PN) generally present with stable long-term renal function [12]. In a large meta-analysis assessing the controversial benefits of PN for renal function and cardiovascular outcomes, Wang et al [13] showed that PN was associated with a 73% reduction in the risk of new-onset CKD for the overall cohort (hazard ratio [HR] 0.27; $p < 0.0001$) and a 65% reduction for patients with tumours >4 cm (HR 0.35; $p < 0.0001$) when compared to RN. These results are supported by other large series, including the ROSULA study, which revealed that the 5-yr rate of onset of stage 3b CKD (eGFR <45 ml/min/1.73 m^2) was significantly higher in the RN compared to the PN group [10]. In the SR by Mir et al [6], PN was associated with better postoperative renal function in terms of higher postoperative eGFR, a lower probability of postoperative CKD onset, and a lower decline in eGFR.

In terms of intraoperative and perioperative complications, PN was associated with higher estimated blood loss [6] and higher complication rates, including more serious Clavien-Dindo grade ≥3 complications [7,14].

Taking the currently available data together, the evidence demonstrates equivalent oncological efficacy of PN to RN in the setting of T2 renal masses, with a renal functional benefit. But does this mean that the benefits outweigh the potential associated morbidity?

According to current guidelines, the treatment of choice is based mainly on the clinical tumour stage. In fact, size alone is often not the only factor in choosing whether to attempt PN or RN. Selecting the right treatment depends on multiple factors, including tumour-related variables, such as location in the kidney, definition of the border, nephrometry complexity, and suspected venous involvement, as well as patient-related factors such as age, frailty, and significant comorbidities. Finally, surgeon preference and experience play an important role. Consequently, stage based on size alone does not necessarily reflect the ideal approach. As been suggested by the PN advocators, PN is a safe alternative for the management of T2 tumours when technically feasible. Nevertheless, despite technical improvements and increasing experience, potential morbidity and complications should not be disregarded when choosing a surgical approach. Moreover, we agree with the PN objectors that although some of the studies reported improved OS, whether this can be attributed to PN is still unresolved [3]. Therefore, on the basis of current evidence, PN should not be considered as the treatment of choice but merely as an alternative in selected cases. Better patient selection could be enhanced by additional tools such as three-dimensional reconstructions and intraoperative ultrasound guidance.

In conclusion, current studies support the use of PN in T2 RCC, with comparable oncological outcomes, better long-term renal function, and acceptable complication rates in comparison to RN achieved at experienced high-volume centres. Although there is no randomised controlled trial comparing PN to RN in the T2 tumour setting, PN should be deemed as a surgical alternative whenever feasible. Further prospective studies are needed to evaluate the true value of PN for the management of larger kidney tumours.

Conflicts of interest: The authors have nothing to disclose.

References

[1] Chen DYT, Uzzo RG. Optimal management of localized renal cell carcinoma: surgery, ablation, or active surveillance. J Natl Compr Cancer Netw 2009;7:635–42. http://dx.doi.org/10.6004/jnccn.2009.0044.

[2] Klatte T, Ficarra V, Gratzke C, et al. A literature review of renal surgical anatomy and surgical strategies for partial nephrectomy. Eur Urol 2015;68:980–92. http://dx.doi.org/10.1016/j.eururo.2015.04.010.

[3] Ljungberg B, Bensalah K, Canfield S, et al. EAU guidelines on renal cell carcinoma: 2014 update. Eur Urol 2015;67:913–24. http://dx.doi.org/10.1016/j.eururo.2015.01.005.

[4] Long CJ, Canter DJ, Kutikov A, et al. Partial nephrectomy for renal masses ≥7 cm: technical, oncological and functional outcomes. BJU Int 2012;109:1450–6. http://dx.doi.org/10.1111/J.1464-410X.2011.10608.X.

[5] Karellas ME, O'Brien MF, Jang TL, Bernstein M, Russo P. Partial nephrectomy for selected renal cortical tumours of ≥7 cm. BJU Int 2010;106:1484–7. http://dx.doi.org/10.1111/J.1464-410X.2010.09405.X.

[6] Mir MC, Derweesh I, Porpiglia F, Zargar H, Mottrie A, Autorino R. Partial nephrectomy versus radical nephrectomy for clinical T1b and T2 renal tumors: a systematic review and meta-analysis of comparative studies. Eur Urol 2017;71:606–17. http://dx.doi.org/10.1016/j.eururo.2016.08.060.

[7] Deng W, Chen L, Wang Y, Liu X, Wang G, Fu B. Partial nephrectomy versus radical nephrectomy for large (≥7 cm) renal tumors: a systematic review and meta-analysis. Urol Oncol 2019;37:263–72. http://dx.doi.org/10.1016/j.urolonc.2018.12.015.

[8] Bigot P, Hétet JF, Bernhard JC, et al. Nephron-sparing surgery for renal tumours measuring more than 7 cm: morbidity, and functional and oncological outcomes. Clin Genitourin Cancer 2014;12:19–27. http://dx.doi.org/10.1016/j.clgc.2013.09.004.

[9] Janssen MWW, Linxweiler J, Terwey S, et al. Survival outcomes in patients with large (≥7 cm) clear cell renal cell carcinomas treated with nephron-sparing surgery versus radical nephrectomy: results of a multicenter cohort with long-term follow-up. PLoS One 2018;13:e0196427. http://dx.doi.org/10.1371/journal.pone.0196427.

[10] Bertolo R, Autorino R, Simone G, et al. Outcomes of robot-assisted partial nephrectomy for clinical T2 renal tumors: a multicenter analysis (ROSULA Collaborative Group). Eur Urol 2018;74:226–32. http://dx.doi.org/10.1016/j.eururo.2018.05.004.

[11] Capitanio U, Terrone C, Antonelli A, et al. Nephron-sparing techniques independently decrease the risk of cardiovascular events relative to radical nephrectomy in patients with a T1a–T1b renal

mass and normal preoperative renal function. Eur Urol 2015;67:683–9. http://dx.doi.org/10.1016/j.eururo.2014.09.027.

[12] Scosyrev E, Messing EM, Sylvester R, Campbell S, Van Poppel H. Renal function after nephron-sparing surgery versus radical nephrectomy: results from EORTC randomized trial 30904. Eur Urol 2014;65:372–7. http://dx.doi.org/10.1016/j.eururo.2013.06.044.

[13] Wang Z, Wang Master G, Xia Q, et al. Partial nephrectomy vs. radical nephrectomy for renal tumors: a meta-analysis of renal function and cardiovascular outcomes. Urol Oncol 2016;34:. http://dx.doi.org/10.1016/j.urolonc.2016.07.007, 533.e11–9.

[14] Mari A, Tellini R, Porpiglia F, et al. Perioperative and mid-term oncological and functional outcomes after partial nephrectomy for complex (PADUA score $\geq$10) renal tumors: a prospective multicenter observational study (the RECORD2 project). Eur Urol Focus 2020. http://dx.doi.org/10.1016/j.euf.2020.07.004, S2405-4569(20)30210-8. Online ahead of print.