



Partial nephrectomy versus thermal ablation for clinical T1 renal tumours

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The incidence of renal tumours has been increasing over the last decades because of more frequent abdominal imaging, leading to higher numbers of renal tumours identified at an early stage (1). Guidelines emphasise surgery as a preferred treatment modality for patients with clinical T1N0M0 tumours, but consider thermal ablation and active surveillance as an alternative approach for T1a lesions (2,3). High-quality studies comparing partial nephrectomy (PN) and thermal ablation are sparse, and the majority of studies are limited by small numbers, short follow-up and their retrospective design.

A study by Andrews *et al.* (4) published in *European Urology* aimed to provide more evidence on management strategies for the clinical T1N0M0 renal tumour. The authors reported on oncological outcomes of 1798 patients, who underwent PN or percutaneous thermal ablation [radiofrequency ablation (RFA) or cryoablation (CA)] at the Mayo Clinic in Rochester, United States, between 2000 and 2011. Outcomes were stratified according to clinical T1a (confined to the kidney, ≤ 4 cm) and clinical T1b (confined to the kidney, 4.1–7 cm). All patients were first evaluated in the Department of Urology, and those interested in thermal ablation or deemed to be unfit for surgery were referred to interventional radiology for discussion of thermal ablation. After a median follow-up of 6.0 to 9.4 years, there were no statistically significant differences in local recurrence-free survival, metastasis-free survival and cancer-specific

survival between PN and thermal ablation for both T1a and T1b tumours. Patients treated with thermal ablation had greater all-cause mortality, because older and comorbid patients with limited life expectancy had thermal ablation rather than PN. This study provides evidence that, with appropriate patient selection and treatment at a high-volume tertiary care centre, excellent long-term outcomes can be achieved by both PN and thermal ablation. The study did not comment on renal functional outcomes or complications.

Despite the large number of patients studied, conclusions might only be drawn for clinical T1a tumours. As per local policy at the Mayo Clinic, patients with T1b tumours underwent CA rather than RFA if thermal ablation was contemplated. The numbers of patients undergoing CA for T1b tumours was fairly small ($n=52$), which limits conclusions in this subgroup. There was no difference in local recurrence-free survival after CA and PN, but metastasis-free survival and cancer-specific survival appeared to be worse after CA despite absence of statistical significance. In contrast, data from the Cleveland Clinic showed that CA conveyed worse local recurrence-free survival than PN in clinical T1b tumours [estimated 5-year probability: 70% *vs.* 100%, (5)]. These data appear to be in line with RFA outcomes reported by Psutka *et al.* (6), although definitions of recurrence varied across studies. In view of the limited evidence on thermal ablation, it must be

concluded that surgery remains the mainstay of therapy for T1b tumours, but thermal ablation may be considered as an option for highly selected patients.

Among the “small” (i.e., clinical T1a) tumours analysed, there was significant selection bias. The authors were not able to account for anatomical scoring systems such as the PADUA or the RENAL nephrometry score (7), but it is fairly evident that there were significant differences between groups. RFA was generally performed in patients with peripheral, posterior tumours ≤ 3 cm which showed no proximity to the ureter. It is therefore highly likely that the majority of RFA patients had low complexity T1a lesions, in contrast to those undergoing PN or CA. The relatively low 5-year metastasis-free survival probability of 93.9% for RFA (compared with 98.0% for PN and 100% for CA) should therefore be seen with a cautious eye. As increasing tumour complexity correlates with adverse pathological features such as higher grades (8), the relative difference in metastasis-free survival between RFA and PN/CA may actually increase if one would adjust for a nephrometry score.

A significant proportion of patients did not have a renal tumour biopsy prior to thermal ablation, especially prior to RFA. Among those with available histology, between 21% (PN) and 35% (CA) had treatment for a benign T1a renal tumour. At many centres, the histology is only obtained at the time of PN or thermal ablation, and has virtually zero impact on management decisions. In contrast, uncoupling a renal tumour biopsy from actual treatment benefits patient counselling and might avoid overtreatment of benign tumours. Indeed, Tanabalan *et al.* (9) reported the outcomes of a prospective study from a high volume kidney cancer specialist centre, in which all patients with cT1a renal tumours were offered a biopsy over a 2-year period. Among the 266 patients who underwent a biopsy, 78 (29%) were found to have benign pathology. Seventy-five of the 78 patients (96%) chose no intervention, which corresponds to 28% of all patients with cT1a tumours. However, treatment and thus potentially overtreatment of benign renal tumours is still common, and morbidity from these interventions is not negligible. In a nationwide study of 1,202 patients with surgically treated oncocytoma, 20% had in-hospital complications and 5 patients died within 60 days after surgery (10).

Another important limitation of this study is that it does not include patients managed by active surveillance, which is an accepted management strategy for small renal tumours. A meta-analysis of 8 uncontrolled studies showed

excellent short- to intermediate-term metastasis-free and cancer-specific survival outcomes (11), comparable to the outcomes reported by Andrews *et al.* after intervention (4). Further, data from the prospective Delayed Intervention and Surveillance for Small Renal Masses (DISSRM) registry suggest that active surveillance is not inferior to immediate intervention (12), and that there is little difference in patient reported quality of life (13). Active surveillance can be recommended to patients of advanced age and multiple comorbidities, or to those in which other conditions take priority at a given time. It is worth mentioning that observation of small renal tumours often represents watchful waiting rather than active surveillance.

The optimal management strategy for clinical T1 renal tumours can only be determined by prospective clinical trials. Unfortunately, the study by Andrews *et al.* (4) represents another retrospective case series. Case series are cheap and easy to accomplish, but provide the weakest evidence for assessing the efficacy of treatment (14). There are only a limited number of completed and reported prospective surgical trials, and retrospective case series and expert opinions provide most evidence for clinical practice guidelines. More than 20% of surgical trials are discontinued early, most commonly owing to poor recruitment (15), and trials on surgical management of renal tumours are no exception. Indeed, both SURAB (ISRCTN31161700) and CONSERVE (ISRCTN23852951) did not complete recruitment in the feasibility phase. Recently, a feasibility trial of a cohort embedded randomised controlled trial comparing Nephron Sparing Treatment (NEST) has started to recruit in the United Kingdom (ISRCTN18156881). Although NEST will mainly compare percutaneous CA with robotic PN in patients with biopsy-proven renal cell carcinoma, those patients screened but not invited for treatment will remain part of the trial cohort. As such, oncological outcomes, patient reported outcome measures and biomarkers will also be assessed in those not assigned to the treatment or control arm. The feasibility phase will be conducted at a single high-volume centre and is expected to progress to a full multicentre trial if recruitment is successful (16). The randomised Robot-assisted Surgical Resection *vs.* Cryoablation of Localised Renal Cancer (ROAST) trial will be launched in Denmark in September 2019 (NCT03390413). The primary outcome of this trial is change in renal function at 6 months, and secondary outcomes include incomplete treatment, complications and costs. Finally, the European Active Surveillance of Renal Cell Carcinoma (EASE) study is currently recruiting

patients with biopsy proven renal cell carcinoma ≤ 4 cm. The primary objective of this prospective registry is to evaluate overall survival. These trials will shed light on the optimal management of patients with early stage renal tumours.

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Footnote

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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