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Contemporary management of renal cell carcinoma (RCC) in Victoria: implications for longer term outcomes and costs

Anthony D. Ta*†, Damien M. Bolton, Margaret K. Dimech‡, Victoria White‡, Ian D. Davis§, Michael Coory¶, Jeremy Millar‡ and Graham Giles‡

*Department of Surgery, Austin and Repatriation Hospitals Medical Centre, Heidelberg; *Departments of Surgery and †Urology, The Austin and Repatriation Medical Centre, Heidelberg; ‡Cancer Epidemiology Centre, Cancer Council Victoria, Melbourne; §Monash University, Eastern Health Clinical School, Melbourne; ¶Murdoch Children's Research Institute, Royal Children's Hospital – Murdoch Children's Research Institute, Parkville, Victoria, Australia*

indicates that both authors contributed equally to this paper.

Objective

- To describe the contemporary patterns of care for renal cell carcinoma (RCC) using a whole of population series from Victoria.

Patients and methods

- Retrospective review of medical records of all patients diagnosed and treated for RCC in Victoria in 2009.
- Patients were identified via the State-wide Victorian Cancer Registry.
- Patient demographic characteristics, symptoms, stage, and first-line treatment were assessed.
- Associations between case residential location (metropolitan or rural) and treatment were examined using multivariate logistic regression after adjusting for age, sex, socioeconomic status, treatment in private or public hospital and comorbidity.

Results

- Data were obtained for 499 of 577 eligible patients.
- In all, 413 patients (83%) underwent surgery.
- Laparoscopic radical nephrectomy (RN) was the most common procedure for Stage I pT1a/pT1b tumours (51.2%); partial nephrectomy (PN) was performed for 27% of Stage I RCC
- In multivariate analysis, regional patients were less likely to receive PN (odds ratio [OR] 0.39, 95% confidence interval [CI] 0.18–0.85) for Stage I RCC, and less likely to receive systemic therapy for Stage IV RCC (OR 0.06, 95% CI 0.01–0.41).
- Multidisciplinary team meetings were recorded for only 25% of patients and 3% were enrolled in a clinical trial.

Conclusion

- Most contemporary patients diagnosed with RCC are still treated with RN, including those with smaller tumours amenable to PN.
- This may impact future outcomes, including increased risk of chronic kidney disease and its potential financial healthcare burden.
- Patterns of treatment also appear to differ between metropolitan and regional populations.

Keywords

renal cell carcinoma (RCC), nephrectomy, cancer registry, Victoria, chronic kidney disease (CKD)

Introduction

RCC represents the most common malignancy affecting the kidney, and accounts for 2–3% of all cancers [1]. Widespread use of abdominal imaging has in large part contributed to a steady increase in incidence of RCC over the last two decades, with the most rapid increase seen for the smallest tumours [2,3]. Consequently, most contemporary patients present with an asymptomatic renal mass [4].

Surgical management of localised RCC has traditionally been radical nephrectomy (RN) for patients with a normal contralateral kidney. However, over the last decade an increasing body of evidence has promoted the management of T1a RCC, and even T1b RCC where possible, with partial nephrectomy (PN) due to equivalent safety and oncological control, but superior preservation of renal function and reduced risk of longer-term chronic kidney disease (CKD) [5–13]. The clinical sequelae and public health costs associated

 | doi:10.1111/bju.12204
Published by John Wiley & Sons Ltd. www.bjui.org

with CKD may be significant [14,15]. Concurrently the development of laparoscopic techniques in renal surgery has seen a shift away from open surgery to less invasive approaches, with laparoscopic RN having equivalent oncological outcomes to open RN, coupled with reduced blood loss, analgesic requirement and length of hospital stay [16,17]. Although technically more challenging, laparoscopic PN has also been shown to have equivalent outcomes to open PN in the appropriate hands [18,19]. Minimally invasive focal ablative techniques, e.g. radiofrequency ablation and cryoablation, have also recently emerged as alternative treatment options for small renal masses and may be suitable for patients with tumours amenable to PN who are otherwise considered poor surgical candidates, either due to age or to pre-existing comorbidities [20,21].

Advances in molecular biology over the last decade have also led to the development of several novel targeted molecular therapies designed to inhibit tumour angiogenesis for patients with metastatic RCC. Commonly used agents include sunitinib and temsirolimus. Traditional immunotherapy agents, e.g. interferon-α and interleukin-2, are now only recommended in guidelines for select patient subgroups [22,23].

Whilst underutilisation of PN has been previously reported in the USA, currently there is a paucity of data about patterns of RCC management in Australia at a population level [24,25]. Furthermore, regional differences in management, including the uptake of newer medical and surgical treatments, are yet to be assessed. To address these concerns, we examined the contemporary clinical management of RCC in Victoria using a whole of population registry of patients diagnosed with RCC.

Patients and Methods

All cases of RCC (ICD-O-3 code C649) diagnosed in Victoria between 1 January 2009 and 31 December 2009 and registered with the Victorian Cancer Registry (VCR) were identified. Victorian residents treated in Victoria were eligible for inclusion. For each case the notifying hospital and/or clinician was identified from the VCR records. Public hospitals and private specialist clinics were approached regarding medical record review of the identified patients. Trained data managers extracted relevant data by retrospective review of medical records and pathology reports.

Data extracted included: mode of presentation, diagnostic and staging investigations, clinical and pathological disease stage, first-line treatment, enrolment in clinical trials, and provision of multidisciplinary care. Comorbidity was assessed using the ACE-27, a validated comorbidity risk assessment tool developed for patients with cancer [26]. Patients were assigned a comorbidity score of 0–3 (0, none; 1, mild; 2, moderate; and 3, severe). The area-based Index of Relative Socio-Economic Disadvantage (IRSD) was used as an indicator of socioeconomic status (SES) [27]. This measure was developed by the Australian Bureau of Statistics from 20 direct or indirect indicators of disadvantage obtained from census data. Examples of indicators used for this measure include education and income levels within a postcode, proportion of single parent families, proportion of males and females unemployed and proportion of rental properties within a postcode. The IRSD ranks postcodes from most disadvantaged to least disadvantaged. This ranking was collapsed into three levels to reflect the top 20%, middle 60% and bottom 20%.

Overall tumour stage was determined from pathological T stage, nodal and metastatic disease status. Pathological T stage (pT) was categorised according to the seventh edition (2009) of the American Joint Committee on Cancer (AJCC) staging system where nephrectomy specimens were available for pathological review. Pathological data was not available for 100 patients, including 85 patients where surgery was not performed. For these patients, pT stage was supplemented by AJCC clinical stage group from imaging reports. Patient residency was categorised as metropolitan or regional/rural based on the Department of Human Services Integrated Cancer Services regions.

The study gained ethical approval from the Cancer Council Victoria Human Research Ethics Committee and other ethics committees as required.

Data Analysis

The chi-squared test was used to examine differences in proportions; ANOVA techniques were used to examine differences in means and other linear variables. Bivariate analyses examined associations between patient residential location and disease characteristics at diagnosis, as well as patient characteristics (e.g. age, treatment location, comorbidity levels). Bivariate and multivariate logistic regression models were used to detect associations between patient residence and use of differing types of surgery. Metropolitan residence was the reference category in these models. For multivariate analyses, odds ratios (ORs) were adjusted for age (≤54, 55–64, 65–74, ≥75 years), sex, ACE-27 comorbidity index (none, mild, moderate, severe), SES and treatment in private or public hospital (for analyses of surgical patients). When pT1a and pT1b tumours were combined for analyses, pT stage was included as a covariate in multivariate analyses. A two-sided statistical level of $P < 0.05$ was considered to indicate statistical significance.

Results

In all, 577 patients were eligible for inclusion. Doctors declined consent for review of medical records for 49 (8.5%) patients. For another 29 (5.0%) patients no medical record could be located, including 14 where diagnosis of RCC was identified only by death certificate (2.4%). Data for 499

patients (86.5% of eligible patients) were analysed. Patients not included in record review were similar to those reviewed for age, gender and residential location. However, patients not included were less commonly treated in the public setting.

Baseline Characteristics and Presentation

Baseline patient characteristics and comparisons between metropolitan and regional/rural residency are shown in Table 1. The median (range) age at diagnosis was 63 (14–97) years. Most were male and the most common residential location was metropolitan. Most patients were managed with surgery (about two-thirds) performed in a public hospital setting. A higher proportion of patients from metropolitan regions had no comorbidities at diagnosis (24.7% vs 14.8%; Table 1).

Symptoms at presentation are also shown in Table 1. In all, 302 (60.5%) patients presented with an asymptomatic renal mass diagnosed incidentally during investigation of other disease or non-specific symptoms. Residential location was not associated with incidental diagnosis. One or more of the 'classic' symptoms of RCC were present at diagnosis in 159 (31.9%) patients, but only three displayed the complete triad of flank pain, haematuria and a palpable abdominal mass. Symptoms suggestive of metastatic disease were present in 28 (5.6%) patients at time of diagnosis.

Diagnostic and Staging Investigations

CT of the abdomen (91.4%) was the most common imaging procedure, followed by abdominal ultrasound (47.3%) and CT chest (37.3%). Full blood examination was performed for

Table 1 Patient demographics, presentation and stage.

	Metropolitan	Regional/rural	Total	*P*
Patient demographics				
N	**364**	**135**	**499**	
Mean age, years	61.9	65.2	62.8	0.014 ($t_{(497)}$ 2.46)
%:	%	%	%	
Gender, male	63.7	69.6	65.3	0.245 (χ^2 1.5, d.f. 1)
Socio-economic grouping:				
most disadvantaged 20%	13.7	29.3	17.9	
middle 60%	50.8	69.2	55.7	
meast disadvantaged 20%	35.4	1.5	26.4	<0.001 (χ^2 61.66, d.f. 2)
Co-morbidities:				
none	24.7	14.8	22.0	
mild	41.5	50.4	43.9	
moderate	20.9	18.5	20.2	
severe	12.9	16.3	13.8	0.06 (χ^2 7.25, d.f. 3)
Diagnosis:				
incidental finding	62.4	55.6	60.5	0.17 (χ^2 1.91, d.f. 1)
metastatic symptoms	5.2	6.7	5.6	0.533 (χ^2 0.389, d.f. 1)
unknown	0.5	3.0	1.2	0.05 (χ^2 3.77, d.f. 1)
screening	0.3	0.0	0.2	0.542 (χ^2 0.372, d.f. 1)
at least one of the three classic symptom	31.0	34.1	31.9	0.52 (χ^2 0.42, d.f. 1)
Presentation (localised disease)				
N	**345**	**126**	**471**	
%:				
Classic symptoms:				
haematuria	19.8	18.5	19.4	0.74 (χ^2 0.10, d.f. 1)
flank pain	19.8	22.2	20.4	0.55 (χ^2 0.36, d.f. 1)
abdominal mass	2.7	2.2	2.6	0.74 (χ^2 0.11, d.f. 1)
Other presenting symptoms:				
abdominal discomfort	13.6	15.1	14.0	0.69 (χ^2 0.16, d.f. 1)
weight loss	7.0	9.5	7.6	0.353 (χ^2 0.86, d.f. 1)
anaemia	2.9	0.8	2.3	0.18 (χ^2 1.79, d.f. 1)
Tumour stage (all cases):				
%:				
I pT1a	38.7	33.3	37.3	
I pT1b	19.2	21.5	19.8	
II pT2a	3.8	8.9	5.2	
II pT2b	2.5	3.7	2.8	
III pT3a	18.1	10.4	16.8	
III pT3b or pT3c	1.1	4.4	2.0	
IV	16.5	17.8	16.8	0.016 (χ^2 15.66, d.f. 6)
Surgery in Public/Private hospital, %:				
Private Hospital	34.3	28.9	32.9	
Public Hospital	65.7	71.1	67.1	0.25 (χ^2 1.33, d.f. 1)

Table 2 Surgical management of Stage I RCC.

		Metropolitan	Regional/rural	Total	Unadjusted OR (95% CI)	Adjusted# OR (95% CI)
All Stage I RCC	All cases, n	211	74	285		
	%:					
	Laparoscopic PN	15.6	4.1	12.6	0.23 (0.07–0.77)	0.21 (0.06–0.72)
	Open PN	13.3	10.8	12.6	0.79 (0.35–1.83)	0.83 (0.33–2.09)
	Laparoscopic RN	50.2	54.1	51.2	1.17 (0.69–1.98)	1.19 (0.66–2.14)
	Open RN	13.3	23.0	15.8	1.95 (1.00–3.82)	2.31 (1.06–5.02)
	No surgery	7.4	18.1	7.7	1.07 (0.40–2.86)	0.71 (0.18–2.77)
	Operative cases only, n	195	68	263		
	%:					
	Any laparoscopic surgery	71.3	63.2	69.2	0.69 (0.34–1.24)	0.62 (0.32–1.19)
	PN	31.3	16.2	27.4	0.42 (0.21–0.87)	0.39 (0.18–0.85)
Stage pT1a RCC	All cases, n	141	45	186		
	%:					
	Laparoscopic PN	22.7	6.7	18.8	0.24 (0.07–0.814	0.23 (0.06–0.83)
	Open PN	17.0	17.8	17.2	1.05 (0.44–2.55)	1.00 (0.42–2.35)
	Laparoscopic RN	44.7	48.9	45.7	1.18 (0.61–2.32)	1.24 (0.59–2.64)
	Open RN	7.1	20.0	10.2	3.28 (1.24–8.67)	2.56 (0.84–7.80)
	No surgery	8.5	6.7	8.1	0.77 (0.21–2.85)	1.15 (0.17–7.76)
	Operative cases only, n	129	42	171		
	%:					
	Any laparoscopic surgery	73.6	59.5	70.2	0.53 (0.25–1.09)	0.57 (0.25–1.30)
	PN	43.4	26.2	39.2	0.46 (0.21–1.00)	0.43 (0.18–1.02)

NB: of the 499 patients, nine patients' surgery was converted from laparoscopic to open and these are classified as having open surgery. #ORs are adjusted for age, sex, ACE-27 comorbidity index, pT Stage (for analyses of pT1a and pT1b combined), SES level and hospital setting.

nearly all patients (96.4%). Corrected serum calcium (CSC) was obtained for 40.5% of patients; while only 6.4% had a record of serum lactate dehydrogenase levels (LDH).

Tumour Characteristics

The predominant histological subtype was clear cell RCC (59.1%), followed by papillary (10.8%) and chromophobe (6.4%) RCC. Sarcomatoid RCC (1.2%) was uncommon. Histological subtyping was not available for 61 (12.2%) patients and 33 (6.6%) had no histological confirmation of the tumour. Absence of histological confirmation was associated with older age ($P < 0.001$) and higher comorbidity scores ($P = 0.05$), suggesting increased usage of surveillance or watchful waiting amongst this patient subgroup.

The distribution of RCC stage groups is shown in Table 1. Pathological T stage was not available for 100 patients, including 85 who did not have surgery. Most tumours were Stage I pT1a/pT1b (57.1%). At diagnosis, 16.8% of patients had evidence of Stage IV disease.

Treatment of RCC

In all, 82.9% of patients underwent surgical treatment. While treatment with surgery was not related to residential location, it was inversely associated with age and comorbidities (both $P < 0.001$). Of the 413 patients where surgery was performed, RN was performed in 336 (81.2%), and the preferred operative approach for RN was laparoscopic, representing 61.3% of all cases of surgery. For pT1 and pT2 tumours, laparoscopic surgery was more common for smaller tumours, with 70.2% of pT1a tumours having laparoscopic surgery compared with 44.0% of pT2a and 28.6% of pT2b tumours. Overall, nine patients were converted from laparoscopic to open, and were classified as open. Only four cases of focal ablation were performed.

The surgical management of Stage I pT1a tumours is shown in Table 2. PN for stage I RCC (regardless of operative approach) was less common for cases from regional/rural areas (16.2%) than those from metropolitan regions (31.3%), and this difference was statistically significant in multivariate analyses (OR 0.39, 95% CI 0.18–0.85). Patients from regional/rural areas were more likely to receive open RN for stage I RCC (OR 2.31, 95% CI 1.06–5.02). For the subgroup of Stage I pT1a tumours, the odds of patients residing in regional/rural areas receiving PN were ≈50% less than the corresponding odds for metropolitan cases (OR 0.43, 95% CI 0.18–1.02), while there was a trend towards increasing likelihood of open RN (OR 2.56 95% CI 0.84–7.80). However, residential location was not associated with treatment for Stage I pT1b tumours (data not shown).

The surgical treatment of Stage II and III tumours (excluding pT3b/T3c tumours) is shown in Table 3, comparing usage of laparoscopic to open surgery. There were no PNs performed for these tumours. Although cases residing in regional/rural areas were more likely to be treated by open RN than those from metropolitan areas on unadjusted analysis, this

Table 3 Surgical treatment of Stage II and III RCC (pT2 and pT3a).

	Metropolitan	Regional/rural	Total	Unadjusted OR (95% CI)	Adjusted# OR (95% CI)
All cases, n	88	31	119		
%:					
Laparoscopic RN	47.7	32.3	43.7	0.52 (0.22–1.23)	0.43 (0.15–1.19)
Open RN	46.6	67.7	52.1	2.41 (1.02–5.70)	2.25 (0.83–6.11)
Of those who have had surgery, n:	87	31	98		
%:					
Laparoscopic surgery	50.6	32.3	45.8	0.47 (0.20–1.10)	0.43 (0.16–1.16)
RN	95.4	100	96.6	0.52 (0.20–1.32)	

#ORs are adjusted for age, sex, ACE-27 comorbidity index, SES level and hospital setting.

Table 4 Treatment of Stage IV RCC.

	Metropolitan	Regional/rural	Total	Unadjusted OR (95% CI)	Adjusted# OR (95% CI)
All cases, n	59	24	83		
%:					
No surgery	66.0	79.2	69.9	1.95 (0.63–5.99)	1.62 (0.37–6.98)
Laparoscopic RN	11.9	0	8.4	0.24 (0–1.68)	0.25 (0–2.29)
Open RN	22.0	20.8	21.7	0.95 (0.30–3.04)	1.56 (0.34–7.20)
Any systemic therapy	56.7	37.5	51.2	0.45 (0.17–1.21)	0.06 (0.01–0.41)

#ORs are adjusted for age, sex, ACE-27 comorbidity index, SES level and hospital setting.

difference did not remain statistically significant on multivariate analysis.

The treatment of Stage IV cases is shown in Table 4. Patients from regional/rural areas were less likely to receive systemic therapy (OR 0.06, 95% CI 0.01–0.41) compared with those in metropolitan areas. In all, 32 patients with Stage IV disease received sunitinib, representing 74.4% of all patients receiving systemic therapy. Radiotherapy was used for 26 patients (31.0%) with Stage IV disease, and this was not associated with residential location.

There was a documented multidisciplinary team meeting review in 124 (24.8%) patients and this was not associated with residential location or tumour stage. During the study period, 14 (2.8%) patients were enrolled in a clinical trial.

Discussion

The present population-based study of the treatment patterns for RCC found that most patients diagnosed with RCC are asymptomatic at presentation and present with early-stage, localised disease. Although most RCC tumours were small at diagnosis, RN was the most common treatment with 60% of Stage I pT1a tumours managed with RN. Residential location was a significant predictor of treatment. We found that patients residing in regional/rural areas were less likely to be treated with PN, while those with Stage IV disease were less likely to receive systemic therapy.

Only three patients (0.6%) presented with the 'classic triad' of haematuria, flank pain and a palpable abdominal mass, which appears lower than the expected rate of 6–10% as reported in the literature [22]. While the reasons for this difference are not clear, it might reflect the increasing incidental diagnosis of RCC through the investigation of other medical conditions. Abdominal imaging and staging investigations were commonly performed and recorded. Conversely, CSC and LDH levels were not regularly undertaken, despite elevated CSC and LDH levels being independent predictors of poor prognosis from RCC [28,29].

Historically RN has been considered the standard treatment for localised RCC. More recent studies instead have offered support to nephron-preserving surgery through PN, and the demonstrated equivalence of oncological control and superior preservation of renal function has led to recommendations by various international guidelines for PN to be standard of care for T1a RCC, and for some T1b RCC where technically feasible [5–12,22,23]. A notable finding in the present study was the limited use of PN in the surgical management of pT1a RCC, where it represented ≈40% of patients of pT1a RCC managed operatively. Furthermore, there was a significant trend towards regional/rural patients with pT1a tumours being less likely to receive PN (Table 2). Patient suitability for PN could not be analysed in the present study, but this trend remains clear despite controlling for important variables that may influence treatment choice, e.g. patient age, comorbid

status, SES, and private or public hospital treatment. However, surgeons may prefer to avoid complex renal surgery in regional centres where there may be a lack of ancillary services, e.g. intensive care or interventional radiography.

An ideal rate of PN for pT1a tumours remains unclear. Comparisons between population-based data and high-volume institutional series, where rates of PN for pT1a tumours approaches 90%, is inappropriate [30]. However, patterns of utilisation of PN for pT1a tumours similar to those reported here have been seen in USA population-based data, although some of these studies have used less contemporary population samples [24,25]. Whilst more recent USA data from the Surveillance Epidemiology and End Results Program (SEER) and the National Cancer Database have shown increasing use of nephron-preserving surgery with PN and ablative techniques, significant underutilisation still exists according to the investigators [31,32]. Interestingly, SEER data from 2006 showed PN to represent 45% of kidney surgery for renal tumours of ≤4cm, a figure slightly higher than seen in the present population [32]. Whether or not true underutilisation of PN for pT1a RCC has taken place in the present study remains unclear, as population-based data does not allow for control of important parameters that influence suitability for PN, e.g. tumour location within the kidney, patient preference, pre-existing renal function and surgeon experience.

The widespread adoption of PN as definitive surgical management of small renal masses has arguably been impeded by the incorporation of laparoscopic RN into the technical skill-set of urologists. This approach offers reduced blood loss and analgesic requirement, rapid convalescence, improved cosmesis and, importantly, equivalent cancer control to open RN [16,17]. Furthermore, there is a lack of randomised prospective data comparing long-term outcomes of RN and PN. To date, only one such trial has been performed, and reported outcomes with a median 9-year follow-up showed no advantage of PN over RN in improving overall mortality [11]. This may provide some explanation for the common usage of laparoscopic RN in the present study, which represented half (49.7%) of all surgeries performed for pT1a tumours. Whilst this may arguably be regarded as potential over-treatment for these smaller tumours, longer-term follow-up of patients in the present study is required to evaluate any associations between surgical treatment and mortality.

Although prospective data addressing mortality (both overall and cancer-specific) is limited, there is increasing evidence that the use of RN where PN may be appropriate increases the risk of long-term patient morbidity resulting from CKD [6,8,9,12,33,34]. This risk is potentially increased in patients with diabetes and hypertension, who have been shown to receive similar rates of PN to patients without these comorbidities [35]. CKD is associated with increased risk of cardiovascular morbidity, progression requiring dialysis, further hospitalisation and all-cause mortality [9,14]. Furthermore, CKD is a significant contributor to healthcare-related costs. Recent data from the USA Renal Data System showed that overall Medicare expenditure for CKD (excluding end-stage kidney disease) reached $33.8 billion in 2009 [15]. The costs associated with CKD are also likely to continue to increase, as evidenced by the proportion of Medicare expenditure towards CKD increasing from 5.8% in 2000 to 15.9% in 2009.

Our use of pathological T stage may have over-estimated the number of small malignant tumours due to post-surgery tumour size reduction. However, as a similar proportion of cases were found to have RN when clinical T stage (based on imaging alone) was analysed, the use of pathological T stage does not appear to have overestimated usage of RN for small renal tumours (analyses not shown). Furthermore, the VCR does not contain information on benign tumours, which can represent up to 25% of small kidney tumours presumed to be RCC on imaging before surgery [36,37].

Whilst laparoscopic surgery was commonly used in the treatment of Stage I RCC, we found that the uptake of this minimally invasive approach was not even across Victoria. For such tumours, cases from regional areas were twice as likely to receive open RN compared with metropolitan cases. This disparity might be partly explained by selective referral to metropolitan hospitals for laparoscopic surgery, individual surgeon experience or preference, or accessibility to the disposable equipment required for laparoscopic surgery in more regional hospitals. Unfortunately, these variables were not captured in the present study. USA population-based data has similarly shown that PN or laparoscopic procedures are more likely to be performed in teaching, high nephrectomy volume hospitals in an urban setting [24,32,38]. Whilst laparoscopic PN has similar efficacy to open PN, it is a technically challenging procedure most often performed in tertiary hospitals by experienced high-volume laparoscopic surgeons [18,19]. In the present study, we found that all laparoscopic PNs for pT1a tumours were performed in metropolitan hospitals (data not shown). This disparity may become less significant with time, with increased training and provision of resources to allow more complex surgery to be performed in more regional settings.

Half of the cases diagnosed with metastatic disease in the present study received systemic therapy, with regional cases less likely to receive this therapy than those from metropolitan areas. Whilst these findings may raise some concern and potentially reflect a degree of inequality of access to newer and recommended therapies, the use of systemic therapies for RCC is complex and we cannot comment on individual clinician treatment decisions and case suitability for these systemic treatments. Furthermore, while sunitinib was the

most commonly used agent in the present study, it was only listed for subsidy on the Australian Pharmaceutical Benefits Scheme in May 2009, thus potentially limiting its use for cases diagnosed before this date [39].

We found <3% of patients with RCC diagnosed in 2009 were involved in a clinical study of any type, including sponsored trials. A similarly low rate of 2% was also reported by Yabroff et al. [38] from SEER data. Several barriers to referral to clinical trials may have been present, e.g. accessibility for regional cases and likely pharmaceutical industry driven promotional activity in larger metropolitan centres during the study period. Whilst efforts should be made wherever possible to promote participation in clinical trials, the significance of this finding is limited as we cannot comment on individual case eligibility.

The present study has several strengths. Our observations from this State-wide whole-of-population dataset reflect contemporary patterns of care across Victoria, accounting for differing practice patterns by clinicians and treatment centres, limiting potential biases seen in institutional or sampled population studies locally or internationally. Whilst the dataset does not represent the entire Australian population, it reflects contemporary treatment patterns in a significant proportion of the Australian population. The present study has significant importance as few previous studies have addressed patterns of modern RCC management in Australia. However, the present study was potentially underpowered to detect anything but large differences due to case residential location. Furthermore, we did not have information on surgeon or patient preferences for care, or surgeon experience, which may have significantly influenced treatment decision-making. Further work is required to examine the role of patients and clinicians in selecting surgical and medical therapies for the management of RCC.

In conclusion, contemporary population-based data shows that the most common treatment for localised RCC is RN, including for small tumours that may have been amenable to nephron-preserving surgery. This may have consequences in terms of the potential morbidity and treatment costs associated with CKD, but the role of PN in reducing overall mortality still remains controversial. Patterns of treatment appear to differ between metropolitan and regional populations after diagnosis, with a suggestion that patients from regional/rural locations in Victoria may be less likely to receive recognised contemporary best evidence-based management. Further work is needed to better understand the reasons for these differences, which are likely to be multifactorial and influenced by patient preferences for care. These findings should help develop and implement strategies for the diffusion and dissemination of newer surgical and medical treatment options throughout Victoria.

Acknowledgements and funding

This work was funded by a Translational Cancer Research Funding grant from the Victorian Cancer Agency (#EOI09_36) for the IMPROVE (Improving Management by Participatory Research in Oncology; the Victorian Experiment) Study.

The IMPROVE Investigators are: Graham Giles, Victoria White, Michael Coory, Jeremy Millar, Damien Bolton, Ian Davis, Ingrid Winship, Ian Roos, Melissa Southey, Gianlucca Severi, Miles Prince, Simon Harrison, John Seymour, Michael Jefford, David Hill, Anne Kay

Ian D. Davis was supported by an National Health and Medical Research Council (NHMRC) Practitioner Fellowship (487907)

Conflict of Interests

No conflict of interests requiring disclosure.

References

1 **Giles G, Thursfield V, Farrugia H, Robertson** P. *Cancer in Victoria 2009*. 2011. Available at: http://www.cancervic.org.au/downloads/cec/CanStats/50-Cancer-in-Victoria-2009.pdf. Accessed February 2012

2 **Chow WH, Devesa SS.** Contemporary epidemiology of renal cell cancer. *Cancer J* 2008; 14: 288–301

3 **Hock LM, Lynch J, Balaji KC.** Increasing incidence of all stages of kidney cancer in the last 2 decades in the United States: an analysis of surveillance, epidemiology and end results program data. *J Urol* 2002; 167: 57–60

4 **Jayson M, Sanders H.** Increased incidence of serendipitously discovered renal cell carcinoma. *Urology* 1998; 51: 203–5

5 **Fergany AF, Hafez KS, Novick AC.** Long-term results of nephron sparing surgery for localized renal cell carcinoma: 10-year followup. *J Urol* 2000; 163: 442–5

6 **Huang WC, Levey AS, Serio AM et al.** Chronic kidney disease after nephrectomy in patients with renal cortical tumours: a retrospective cohort study. *Lancet Oncol* 2006; 7: 735–40

7 **Lee CT, Katz J, Shi W, Thaler HT, Reuter VE, Russo P.** Surgical management of renal tumors 4 cm. or less in a contemporary cohort. *J Urol* 2000; 163: 730–6

8 **Malcolm JB, Bagrodia A, Derweesh IH et al.** Comparison of rates and risk factors for developing chronic renal insufficiency, proteinuria and metabolic acidosis after radical or partial nephrectomy. *BJU Int* 2009; 104: 476–81

9 **Weight CJ, Larson BT, Fergany AF et al.** Nephrectomy induced chronic renal insufficiency is associated with increased risk of cardiovascular death and death from any cause in patients with localized cT1b renal masses. *J Urol* 2010; 183: 1317–23

10 **Tan HJ, Norton EC, Ye Z, Hafez KS, Gore JL, Miller DC.** Long-term survival following partial vs radical nephrectomy among older patients with early-stage kidney cancer. *JAMA* 2012; 307: 1629–35

11 **Van Poppel H, Da Pozzo L, Albrecht W et al.** A prospective, randomised EORTC intergroup phase 3 study comparing the oncologic outcome of elective nephron-sparing surgery and radical nephrectomy for low-stage renal cell carcinoma. *Eur Urol* 2011; 59: 543–52

12 **McKiernan J, Simmons R, Katz J, Russo P.** Natural history of chronic renal insufficiency after partial and radical nephrectomy. *Urology* 2002; 59: 816–20

13 **Antonelli A, Ficarra V, Bertini R, et al.** Elective partial nephrectomy is equivalent to radical nephrectomy in patients with clinical T1 renal cell carcinoma: results of a retrospective, comparative, multi-institutional study. *BJU Int* 2012; 109: 1013–8

14 **Go AS, Chertow GM, Fan D, McCulloch CE, Hsu CY.** Chronic kidney disease and the risks of death, cardiovascular events, and hospitalization.[Erratum appears in N Engl J Med. 2008;18(4):4]. *N Engl J Med* 2004; 351: 1296–305

15 US Renal Data System: Costs of Chronic Kidney Disease. 2011. Available at: http://www.usrds.org/2011/pdf/v1_ch06_11.pdf. Accessed February 2012

16 **Chan DY, Cadeddu JA, Jarrett TW, Marshall FF, Kavoussi LR.** Laparoscopic radical nephrectomy: cancer control for renal cell carcinoma. *J Urol* 2001; 166: 2095–100

17 **Hemal AK, Kumar A, Kumar R, Wadhwa P, Seth A, Gupta NP.** Laparoscopic versus open radical nephrectomy for large renal tumors: a long-term prospective comparison. *J Urol* 2007; 177: 862–6

18 **Gill IS, Kavoussi LR, Lane BR et al.** Comparison of 1,800 laparoscopic and open partial nephrectomies for single renal tumors. *J Urol* 2007; 178: 41–6

19 **Lane BR, Gill IS.** 7-year oncological outcomes after laparoscopic and open partial nephrectomy. *J Urol* 2010; 183: 473–9

20 **Stern JM, Gupta A, Raman JD et al.** Radiofrequency ablation of small renal cortical tumours in healthy adults: renal function preservation and intermediate oncological outcome. *BJU Int* 2009; 104: 786–9

21 **Zagoria RJ, Pettus JA, Rogers M, Werle DM, Childs D, Leyendecker JR.** Long-term outcomes after percutaneous radiofrequency ablation for renal cell carcinoma. *Urology* 2011; 77: 1393–7

22 **Ljungberg B, Cowan NC, Hanbury DC et al.** EAU guidelines on renal cell carcinoma: the 2010 update. *Eur Urol* 2010; 58: 398–406

23 **Motzer RJ, Agarwal N, Beard C et al.** NCCN clinical practice guidelines in oncology: kidney cancer. *J Natl Compr Canc Netw* 2009: 7: 618–30

24 **Hollenbeck BK, Taub DA, Miller DC, Dunn RL, Wei JT.** National utilization trends of partial nephrectomy for renal cell carcinoma: a case of underutilization? *Urology* 2006; 67: 254–9

25 **Miller DC, Hollingsworth JM, Hafez KS, Daignault S, Hollenbeck BK.** Partial nephrectomy for small renal masses: an emerging quality of care concern? *J Urol* 2006; 175: 853–8

26 **Piccirillo JF, Tierney RM, Costas I, Grove L, Spitznagel EL Jr.** Prognostic importance of comorbidity in a hospital-based cancer registry. *JAMA* 2004; 291: 2441–7

27 **Australian Bureau of Statistics.** *Information Paper: Census of Population and Housing: Socio-Economic Indexes for Areas, Australia 2001*. Canberra: Australian Bureau of Statistics, 2003: Catalogue No. 2039.0.

28 **Bensalah K, Pantuck AJ, Crepel M et al.** Prognostic variables to predict cancer-related death in incidental renal tumours. *BJU Int* 2008; 102: 1376–80

29 **Motzer RJ, Mazumdar M, Bacik J, Berg W, Amsterdam A, Ferrara J.** Survival and prognostic stratification of 670 patients with advanced renal cell carcinoma. *J Clin Oncol* 1999; 17: 2530–40

30 **Thompson RH, Kaag M, Vickers A et al.** Contemporary use of partial nephrectomy at a tertiary care center in the United States. *J Urol* 2009; 181: 993–7

31 **Cooperberg MR, Mallin K, Kane CJ, Carroll PR.** Treatment trends for stage I renal cell carcinoma. *J Urol* 2011; 186: 394–9

32 **Dulabon LM, Lowrance WT, Russo P, Huang WC.** Trends in renal tumor surgery delivery within the United States. *Cancer* 2010; 116: 2316–21

33 **Lau WK, Blute ML, Weaver AL, Torres VE, Zincke H.** Matched comparison of radical nephrectomy vs nephron-sparing surgery in patients with unilateral renal cell carcinoma and a normal contralateral kidney. *Mayo Clin Proc* 2000; 75: 1236–42

34 **Miller DC, Schonlau M, Litwin MS, Lai J, Saigal CS.** Renal and cardiovascular morbidity after partial or radical nephrectomy. *Cancer* 2008; 112: 511–20

35 **Abouassaly R, Finelli A, Tomlinson GA, Urbach DR, Alibhai SMH.** How often are patients with diabetes or hypertension being treated with partial nephrectomy for renal cell carcinoma? A population-based analysis. *BJU Int* 2011; 108: 1806–12

36 **Frank I, Blute ML, Cheville JC, Lohse CM, Weaver AL, Zincke H.** Solid renal tumors: an analysis of pathological features related to tumor size. *J Urol* 2003; 170: 2217–20

37 **Pahernik S, Roos F, Hampel C, Gillitzer R, Melchior SW, Thuroff JW.** Nephron sparing surgery for renal cell carcinoma with normal contralateral kidney: 25 years of experience. *J Urol* 2006; 175: 2027–31

38 **Yabroff KR, Harlan L, Stevens J, Martin A.** Patterns of care in adults with renal cell carcinoma: findings in a population based sample. *J Urol* 2009; 181: 2462–9

39 **Pfizer.** News and Media. Media Releases. 2009. Available at: http://www.pfizer.com.au/sites/au/news_and_media/media_releases/Pages/SUTENTrlistedonPBSfrom1stMay2009.aspx. Accessed February 2012

Correspondence: Damian M. Bolton, Department of Surgery, University of Melbourne, Austin and Repatriation Hospitals Medical Centre 5/210 Burgundy Street, Heidelberg 3084, Australia.

e-mail: damienmb@unimelb.edu.au

Abbreviations: ACE-27, Adult Comorbidity Evaluation-27; AJCC, American Joint Committee on Cancer; CKD, chronic kidney disease; CSC, corrected serum calcium; IRSD, Index of Relative Socio-Economic Disadvantage; LDH, lactate dehydrogenase levels; OR, odds ratio; PN, partial nephrectomy; RN, radical nephrectomy; SEER, Surveillance Epidemiology and End Results Program; SES, socioeconomic status; VCR, Victorian Cancer Registry.

