Trends in the surgical management of Stage 1 Renal Cell Carcinoma: findings from a population-based study

Authors

White V[1,2], Marco DJT[1,2], Bolton D[3], Davis ID[4,5], Jefford M[6,7] Hill D[1,2], Prince HM[6,7] Millar JL[8] Winship IM[9], Coory M[2], Giles GG[1,2]

1. Cancer Council Victoria, Melbourne VIC 3004.
2. University of Melbourne, Parkville VIC 3010.
3. Austin Health, Heidelberg VIC 3084.
4. Monash University Eastern Health Clinical School, Box Hill, Vic 3128
5. Eastern Health, Box Hill VIC 3128.
6. Sir Peter MacCallum Department of Oncology, University of Melbourne, Parkville, VIC 3052
7. Peter MacCallum Cancer Centre, Melbourne VIC 3000.
8. Alfred Health, The Alfred, Melbourne VIC 3004.
9. Royal Melbourne Hospital, Parkville VIC 3052.

Word count

3,813

Funding

Victorian Cancer Agency (VCA Translational Research Grant EOI09_36)

Conflict of interest statements:

Authors White V, Marco DJ, Bolton D, Jefford M, Hill D, Prince HM, Millar JL, Winship IM, Coory M, Giles GG have no conflicts of interest to declare. Prof I Davis sits on or chairs several industry advisory boards for which he receives no remuneration.

DR. VICTORIA WHITE (Orcid ID : 0000-0001-6619-8484)

Article type : Original Article

Corresponding author email id: Vicki.White@cancervic.org.au

Abstract

Objectives

- To determine whether use of nephron sparing surgery (NSS) for treatment of stage 1 renal cell carcinomas changed between 2009 and end 2013 in Australia.

Patients and Methods

- All adult cases of renal cell carcinoma diagnosed in 2009, 2012, and 2013 were identified through the population-based Victorian Cancer Registry.
- For each identified patient, trained data-abstractors attended treating hospitals or clinician rooms to extract tumour and treatment data through medical record review.
- Multivariable logistic regression analyses examined significance of change in use of NSS over time, after adjusting for potential confounders.

Results

- A total of 1836 patients with renal cell carcinoma were identified. Of these, the proportion of cases with stage 1 tumours was 64% in 2009, 66% in 2012, and 69% in 2013.
- For T1a tumours, the proportion of patients residing in metropolitan areas receiving NSS increased from 43% in 2009 to 58% in 2012 (P<.05), and 69% in 2013 (P<.05). For patients residing in non-metropolitan areas, the proportion receiving NSS increased from 27% in 2009 to 49% in 2012, and 61% in 2013 (P<.01).
- Univariable logistic regression showed patients with moderate (OR=0.57, 95%CI 0.35-0.94) or severe comorbidities (OR=0.58, 95%CI 0.33-0.99), residing in non-metropolitan areas (OR=0.65, 95%CI 0.47-0.90), were less likely to be treated by NSS, while those attending high volume hospitals (30+ cases/year: OR=1.79, 95%CI 1.21-2.65) and those with higher socio-economic status (OR=1.45, 95%CI 1.02-2.07) were more likely to be treated by NSS.
- In multivariable analyses, patients with T1a tumours in 2012 (OR=2.00, 95% CI:1.34-2.97) and 2013 (OR=3.15, 95% CI: 2.13-4.68) were more likely to treated by NSS than those in 2009.
- For T1b tumours, use of NSS increased from 8% in 2009 to 20% in 2013 (P<.05).

Conclusion

- This population-based study of the management of T1 renal tumours in Australia found use of NSS increased over the period 2009 to 2013.
- Between 2009 and 2013 clinical practice for the treatment of small renal tumours in Australia has increasingly conformed to international guidelines.

Key words

Renal Cancer, Surgical treatment, Population-based, patterns of care, Radical Nephrectomy, Nephron Sparing Surgery.***Introduction***

Based on evidence showing similar cancer control outcomes are achieved when small tumors of the kidney are treated by nephron sparing surgery (NSS) as when treated by radical nephrectomy (RN)[1], treatment guidelines for the management of patients with renal cell carcinoma published since the late 2000s have recommended NSS as the preferred standard of care for small tumors (<4 cm, cT1a tumors) [2-4]. While European guidelines also recommend NSS as the preferred treatment option for tumors up to 7 cm (cT1b), American (US) guidelines suggest that either NSS or RN can be used for these tumors. Both European and US guidelines state that laparoscopic surgical procedures are preferred for radical nephrectomy [3, 4].

While the benefits of NSS for the patient includes reduced risk of cardiovascular disease and chronic kidney disease[5][6, 7], other work has suggested it may be associated with a greater complication rate [8] especially in larger tumours[9]. This, coupled with the greater complexity of NSS may suggest that its adoption could be concentrated to more experienced, high volume doctors and centres [10]. However, research from the US has suggested this is not the case, with several population-based studies showing that use of NSS for small tumours increased substantially during the 2000s [11-13] with for instance, one study reporting use of NSS for T1a tumours increased from 5% in 1988 to 40% in 2008 [11], while another reported use increased from 43% in 2004 to 55% in 2009 [14], the year the American Urological Association published their treatment guidelines recommending this NSS for cT1a tumours. Similarly, population-based studies from Europe have suggested that 50% or more of patients with small renal tumours treated by NSS in 2010, with for instance, a population based study from the Netherlands finding that 49% of cT1a tumors were treated by NSS in 2010 [15], while a study of treatment of T1a tumours in 56 centres in France found 77% were treated by NSS in 2010 [16].

In contrast to the patterns found in the US and Europe, in Australia, use of NSS for the treatment of small renal tumours was substantially lower during the 2000s. A population-based study examining the treatment of renal cell cancer in Australia's most populous state, New South Wales, found that the use of NSS for localized renal cancer increased from 11% to 23% between 2001 and 2009 [17]. Unfortunately, this paper did not report data for T1a and T1b tumours separately. However, a population-based study from Australia's second most populated state, Victoria, reported that 27% of all T1 tumours and 39% of T1a tumours were treated by NSS in 2009 [18]. This study also found that NSS for T1a tumours was less likely for patients residing in regional (26%) than metropolitan (43%) areas.

Although Australia does not have its own treatment guidelines for renal cell cancer, the publication of US and European guidelines since 2009 recommending NSS for small kidney tumours may be likely influences on clinical practice in Australia. Contemporary estimates are needed to determine whether use of NSS in the treatment of small renal cell tumours in Australia has increased or whether they still lag behind rates found in Europe and the US. In this paper we use population-based data from the Australian state of Victoria, to examine how the use of NSS for T1 renal cell carcinomas changed between 2009 and 2013.

Patients and Methods

Procedure

The population-based Victorian Cancer Registry (VCR) identified all adult cases (age >18 years) of RCC (ICD-O-3 code C649) diagnosed in the three study periods: i) 1 January 2009 to 31 December 2009, ii) 1 January 2012 to 31 December 2012, and iii) 1 January 2013 to 31 December 2013.The inclusion of data from both 2012 and 2013 allowed an examination of whether any change found between 2009 and 2012, continued into 2013. For each case, the VCR identified the notifying hospital. Public and private hospitals were approached regarding medical record review of each patient attending their service for treatment. If a hospital refused participation, clinicians involved with the care of that

patient, also identified through the VCR were approached regarding medical record review. Trained data managers attended each participating site to extract relevant data by retrospective review of medical records and pathology reports. If a patient attended multiple treatment sites during their cancer care, treatment details were sought from each site. The study had ethical approval from the Cancer Council Victoria and other institutions as needed.

Data extracted included: mode of presentation, diagnostic and staging investigations, clinical and pathological disease stage, and first-line treatment (e.g. type of surgery and surgical procedure). Comorbidity was assessed using information recorded in the medical record on the Adult Comorbidity Evaluation 27 (ACE-27); a validated comorbidity risk assessment tool developed for patients with cancer. Patients were assigned a comorbidity score of 0–3 (0, none; 1, mild; 2, moderate; and 3, severe). Patient's residential postcode was used to determine their socio-economic status (SES) using the area-based Index of Relative Socio-Economic Disadvantage (IRSD) developed by the Australian Bureau of Statistics [19]. The IRSD ranks postcodes from most disadvantaged to least disadvantaged. This ranking was collapsed into three levels to reflect the top 33%, middle 33% and bottom 33%. Patient residency and hospital rurality was also categorised using postcode data into 'major city' and 'non-major city' (referred to hereafter as 'metropolitan' and 'regional/rural', respectively) using the Australian Statistical Geography Standard for Remoteness Structure (ASGS) developed by the Australia Bureau of Statistics [20]. Using sample data, the number of RCC cases treated at each hospital in Victoria was determined. Hospital volume was classified into three groups reflecting the treatment of 1 to 14, 15 to 29, and 30 or more cases per year. The specific cut-points were chosen to allow a similar number of cases in each volume group.

Tumour stage was determined from clinical and pathological T stage, nodal and metastatic disease status. Pathological T stage (pT) was categorised according to the American Joint Committee on Cancer (AJCC) staging system where

nephrectomy specimens were available for pathological review [21]. Information regarding presence of metastatic disease was not available from pathological staging data for 162 patients. Case notes for all 162 patients were reviewed and metastatic disease was indicated for 100 patients who were assigned a M1 classification. For 47 cases, pT stage was supplemented by AJCC clinical stage information from imaging reports and case notes. The remaining 15 cases did not have any staging information available.

For the current paper we focus on patients with stage 1 tumours classified as T1N0M0 according to the AJCC classification [21].

Data analysis

Chi-squared tests were used to examine differences in proportions; ANOVA techniques were used to examine differences in means. Chi-square tests examined associations between patient residential and treatment location, disease characteristics at diagnosis, and patient characteristics (age, sex, comorbidity levels, and SES) and year of study. Chi-square tests also examined the significance of change in the proportion of patients treated by NSS and the proportion treated using laparoscopic surgery between 2009 and 2013, stratifying by patient and treatment centre characteristics. Univariable logistic regression analyses examined the association between patient and treatment centre characteristics and treatment by NSS for T1a and T1b tumours. Multivariable logistic regression examined the association between patient, disease and treatment centre characteristics and treatment by NSS adjusting for other variables in the model.

Results

Responses and caseloads

In 2009, 577 primary RCC tumours were registered with the VCR. Of these, data were collected on 499 patients giving a completion rate of 86%. For the period 1/1/2012 to 31/12/2013 1380 primary RCC tumours were registered and data was

collected on 1337 patients (response rate: 97%). The proportion of stage 1 tumours was 64% in 2009, 66% in 2012, and 69% in 2013 ($\chi^2(2) = 4.33$, P =.12).

Characteristics of patients and tumours

There were no statistically significant differences in the age, gender, urban/rural residence, and comorbidities of patients with stage 1 tumours in the three survey periods (Table 1). Socioeconomic status of patients differed across the three survey years, with more patients in 2009 having a higher SES classification than patients in 2012 or 2013 (P<.05). Around 60% of tumours were diagnosed incidentally in each survey year (Table 1).

In each survey year, around 60% of the T1 tumours were T1a tumours and around 70% were clear cell type. The proportion of cases treated in low volume hospitals reduced over the study period from 30% in 2009 to 17% in 2013 (P<.01). This decrease was associated with an increase in the proportion of cases treated at middle volume hospitals (from 24% to 38%) rather than an increase in the proportion of cases treated at the highest volume hospitals.

Trends in the treatment of T1 tumours

For all T1 tumours and for T1a tumours the proportion of metropolitan and regional/rural patients receiving NSS increased across the survey period (Figure 1). For T1a tumours, the proportion of metropolitan patients receiving NSS increased from 43% in 2009 to 58% in 2012 (P<.05), increasing again to 69% in 2013 (P<.05). For regional patients the proportion receiving NSS increased from 27% in 2009 to 61% in 2013 (P<.01).

Of metropolitan patients with T1a tumours undergoing NSS, the proportion receiving laparoscopic surgery increased significantly from 22% in 2009 to 32% in 2012 (P<.05), but the change between 2012 and 2013 (40%) was not statistically significant (P=.13). The proportion of regional/rural patients with T1a tumours

treated by laparoscopic NSS also increased between 2009 (8%) and 2012 (30%) (P<.01), but did not change significantly between 2012 and 2013 (28%, P=.79).

Univariable and multivariable associations with the use of NSS for T1a tumours are shown in Table 2. In univariable analyses, patients with more comorbidities (P<.05), residing in regional areas (P<.05), those with a lower SES (P<.05) and those attending low volume treatment centres (P<.01) were less likely to be treated by NSS (Table 3). However, in multivariable analyses that included survey year, only year was significantly related to NSS. The odds of a patient with a T1a tumour being treated by NSS were greater in 2012 (OR=2.01 (95% CI: 1.33-3.05)) and in 2013 (OR=3.21, (95% CI: 2.12-4.86)) than in 2009. Further analyses showed that the increase in use of NSS between 2012 and 2013 was significant with odds of those treated in 2013 receiving NSS greater (OR= 1.58, (95% CI: 1.10-2.26)) than the odds of those treated in 2012. There was no significant interaction between year and the demographic factors of age and SES indicating that the increase in use of NSS over time was consistent across the different demographic groups.

Table 3 shows the increase in the use of NSS for T1a tumours within each of the different demographic factors across time. NSS increased in all comorbidity groups, all SES groups and all age groups. In addition, use of NSS increased for patients treated in public and private hospitals. Use of NSS also increased significantly in hospitals with different RCC volumes.

Trends in the surgical care of T1b tumours are shown in Table 4. Of those patients having surgery, use of RN decreased over the study period from 92% in 2009 to 80% in 2013 (P<.05), while use of NSS increased from 8% in 2009 to 20% in 2013 (P<.05). The proportion of patients treated by open or laparoscopic NSS or radical nephrectomy in each study year is shown in Table 4. While there was a significant decrease in the proportion of patients treated by open radical nephrectomy (P<.01), the change in the proportion of cases treated by laparoscopic radical nephrectomy or open or laparoscopic NSS was not statistically significant (Table 4). When any NSS was considered, there was a significant increase in the

proportion of patients under 55 years of age (P=.02), women (P=0.02) and those with no comorbidities (P=.03), having NSS for T1b tumours. While increases in the use of NSS for T1b tumours were found for patients treated in both public and private hospitals and in hospitals with different caseloads, only the increase for patients attending private hospitals was statistically significant (P=.05).

Discussion

This population-based study of the management of T1 renal tumours in Australia found use of NSS for T1a tumours increased substantially between 2009 and 2012 with a further increase found between 2012 and 2013. It also found an increase in the use of NSS in the treatment of T1b tumours over this period. Encouragingly, the increase in use of NSS for T1a tumours was seen in all demographic groups, in both public and private hospital systems and in both low and high volume hospitals, suggesting that all patients were benefiting from these clinical practice changes. Use of laparoscopic surgery for T1a tumours also increased over the study period with this increase found for both metropolitan and regional/rural patients. Taken together, these changes suggest that between 2009 and 2013 clinical practice for the treatment of small renal tumours in Australia has increasingly conformed to international guidelines [2-4] with patients treated by less clinically invasive surgery. The study also suggests that at least in the Australian state of Victoria, specific population groups were not missing out on the benefits of these clinical practice changes.

Sun and colleagues suggested that during the 2000s the treatment of small renal tumours underwent a paradigm shift with NSS becoming the standard of care [11]. Our study shows that, in Australia, this paradigm shift occurred after 2009, with NSS becoming the most commonly used treatment for T1a tumours. We found that the proportion of patients with T1a tumours treated by NSS increased by 77% between 2009 and 2013, and that 62% of T1a tumours were treated by this surgical procedure in 2013. With this change, surgical management of T1a

tumours in the Australian state of Victoria is now similar to practice patterns found The Netherlands [15], Sweden [22] and the UK [23].

The evidence regarding the impact of the publication of clinical guidelines on practice is mixed, with some studies finding a positive [15, 24, 25], some showing only a small impact [26, 27], and others showing no impact [28]. As we do not have data regarding the surgical management of small RCC tumours prior to 2009, we do not know whether use of NSS to treat T1a tumours was increasing during the 2000s, suggesting the increase we found between 2009 and 2013 was simply a continuation of this trend. However, Patel and colleagues [17] showed that use of NSS for all RCC tumours was relatively stable between 2005 and 2008 at 20% in the Australian state of New South Wales. While not conclusive, this could suggest the increase in NSS found in this study is in response to the publication of the international guidelines recommending use of NSS for small renal tumours.

Similar to other studies [10, 12] we found that receiving NSS for the treatment of T1a tumours was associated with some demographic and treatment centre characteristics. In univariate analyses, older patients, those with more comorbidities, those with a lower SES regional patients and those treated at low volume treatment centres were less likely to be treated by NSS. However, in multivariate analyses that included study year, only patients' SES remained significantly associated with NSS, with high SES patients more likely to receive NSS than patients from the lowest SES group. As there was no significant interaction between year and SES, our study suggests that although use of NSS for low SES patients with T1a tumours increased between 2009 and 2013, this increase was not sufficient to ameliorate differences in the surgical approach used for high and low SES patients with T1b tumours.

Over the period of our study, the proportion of patients treated in low volume hospitals decreased, while the proportion treated in middle volume hospitals increased. As several studies, including ours in univariable analyses, have shown a positive association between higher hospital renal cancer volumes and likelihood

of NSS [10, 17, 22], this change is encouraging. However, unlike findings from a recent European study that found no change in the use of NSS for T1 tumours in low volume hospitals[29], our study found an increasing trend towards NSS for small renal tumors even in low volume hospitals. As our study used slightly different definitions for low volume hospitals, we repeated our analyses using the same volume definitions as the European study[29], and found the same pattern of results as presented here. The increase in the use of NSS in low, middle and high volume hospitals over the study period demonstrates that change in surgical management of T1a renal tumours need not be restricted to only high volume treatment centres. As simulation training has been found to promote skills and technique in different urological surgical techniques[30], encouraging clinicians to undertake simulation training in relation to NSS techniques may help to further increase the use of NSS for small renal tumours.

Our multivariable analyses that adjusted for study year and patient characteristics, did not find a significant association between hospital volume and NSS for T1a tumours. Indeed in these analyses, study year was the only variable significantly associated with NSS. Other studies have also failed to find a significant association between hospital volume and NSS for small renal tumours in multivariable analyses that adjust for patient factors, diagnosis year, surgeon volume and/or hospital type (e.g. community, university etc)[31]. It was not possible to identify individual surgeon volume in this study. As this factor has been found to be an important determinant of surgical procedures for small renal tumours[31], its omission may have influenced the results from our multivariable analyses. Future research needs to investigate the relative role of surgeon and hospital characteristics in the use of NSS for small renal tumours.

A study from The Netherlands reported that rates of NSS were slightly less at university hospitals than at other hospitals due to university hospitals more likely to use ablation procedures for the treatment of small tumours [15]. As we did not examine the use of these minimally invasive procedures, we cannot determine

whether the lower rates of NSS in high volume hospitals in 2013 was due to greater use of other treatment procedures at these centres. However we did not find a change change in the proportion of cases not treated by surgery at high volume hospitals over the study period (data not shown). Future studies need to include the use of ablation in the treatment of small renal tumours and determine whether use of this procedure differs by characteristics of the treatment centre and/or patient.

Despite guidelines suggesting that NSS should be considered when treating T1b tumours, our study found that of the patients having surgery, the vast majority were treated by radical nephrectomy (80%) in 2013. While there was some increase in the use of NSS in this group, our data suggest that only a small minority of T1b tumours having surgery for their renal cancer were treated by NSS in Australia. While we did find that NSS for T1b tumours increased in the different demographic and hospital groups, few differences were statistically significant, possibly due to small number of cases with T1b tumours in our dataset. Larger studies are needed to determine the significance of changes in the surgical management of T1b tumours for different sociodemographic groups. While use of open radical nephrectomy decreased over the study period, there was little change in the proportion of T1b patients treated by laparoscopic radical nephrectomy. This suggests that the decrease in use of open radical nephrectomy was due to an increase in use of NSS rather than clinicians shifting to a laparoscopic procedure for radical nephrectomy. While others have suggested that greater use of laparoscopic surgical procedures may be hindering the uptake of NSS for T1b tumours [14], our results suggest that this may not be the case in Australia. Our rates of NSS for T1b tumours in 2013 were similar to levels found in the US in 2009 (18%), but lower to levels seen in The Netherlands (28%) in 2013 [15]. Our study suggests that in Australia T1b tumours are still largely treated by radical nephrectomy.

There is some suggestion that the diagnosis of asymptomatic renal tumours has increased due to greater proportion of cases detected incidentally [32]. Although we found a decrease in the proportion of symptomatic cases between 2009 and 2013, this change may have been an artefact of the data collection process as there were a greater proportion of cases with missing data on this variable in 2012-13 than in 2009. As the proportion of T1a tumours did not change over the study period, our data suggest that there has not been a substantial increase in the diagnosis of small asymptomatic tumours over the study period.

A strength of our study is its population based approach that enabled us to gather treatment data on all patients diagnosed with renal cancer in Victoria. This approach meant that our study was able to assess community wide practice patterns rather than assessing the treatment delivered at a specific treatment centre. Rather than asking clinicians to report on the care they delivered to specific patients, our study assessed treatment through review of medical records. While this meant we could gather unbiased information on the treatment patients actually received, it relies on good documentation of all procedures received in the medical records. Procedures that are not documented in the medical record could not be gathered in this study. As our study did not involve clinicians or patients, we do not know what role clinician experience or patient preferences have played in determining the treatment received. We did not collect data on the management of renal cancers diagnosed in 2010 and 2011 and are unable to determine whether the increase in the use of NSS for T1a tumours commenced from 2009 or slightly later. Administrative data sets, that can stratify cases by their cT stage, would enable long-term year-on-year change in use of NSS for small renal tumors to be examined. As oncocytomas may be indistinguishable from renal cancers radiologically[33], it is possible that some cT1a tumours among those that did not have surgery were oncocytomas. Finally, while we attempted to examine factors associated with use of NSS for T1b tumours the small number of cases with tumours this size meant our analyses were limited in scope and statistical power.

Despite these limitations, we believe our study has provided important new information regarding the treatment of T1 renal tumours in Australia. Our study has shown that the treatment of small renal tumours in Australia has undergone a substantial change in a relatively short period, with NSS now the standard of care for T1a tumours. Our data suggests that while the treatment of small renal tumours is increasingly in line with international standards, this is not the case for the treatment of larger T1 tumours. The slow adoption of NSS in the treatment of T1b tumours warrants further investigation to identify barriers to its use.

Acknowledgements

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

ID Davis is supported by an NHMRC Practitioner Fellowship (APP1102604)

We would like to acknowledge the work of Ms Margaret Dimech for managing and co-ordinating 2009 data collection and Ms Leah Laurenson for managing and co-ordinating the 2012/2013 data collection. We would also like to acknowledge of the work of the data collectors for each study and the assistance of treatment centres and clinicians in gathering the data.

References

1. 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(1):41-6.

2. Escudier B, Porta C, Schmidinger M, et al. Renal cell carcinoma: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2014;25:49-56.

3. Motzer RJ, Agarwal N, Beard C, et al. NCCN Clinical Practice Guidelines in Oncology for Kidney Cancer. J Natl Comp Cancer Network. 2011;9(9):960-77.

4. Ljungberg B, Cowan NC, Hanbury DC, et al. EAU guidelines on renal cell carcinoma: the 2010 update. Eur Urol. 2010;58(3):398-406.

5. Forbes CM, Rendon RA, Finelli A, et al. Disease progression and kidney function after partial vs. radical nephrectomy for T1 renal cancer. Urol Oncol. 2016;34(11):486.

6. Huang WC, Levey AS, Serio AM, et al. Chronic kidney disease after nephrectorny in patients with renal cortical turnours: a retrospective cohort study. Lancet Oncology. 2006;7(9):735-40.

7. Touijer K, Jacqmin D, Kavoussi LR, et al. The expanding role of partial nephrectomy: a critical analysis of indications, results, and complications. Eur Urol. 2010;57(2):214-22.

8. Stephenson AJ, Hakimi AA, Snyder ME, et al. Complications of radical and partial nephrectomy in a large contemporary cohort. J Urol. 2004;171(1):130-4.

9. Mir MC, Derweesh I, Porpiglia F, et al. Partial Nephrectomy Versus Radical Nephrectomy for Clinical T1b and T2 Renal Tumors: A Systematic Review and Meta-analysis of Comparative Studies. Eur Urol 2016:S0302-2838(16)30533-4.

10. Kim SP, Shah ND, Weight CJ, et al. Contemporary Trends in Nephrectomy for Renal Cell Carcinoma in the United States: Results From a Population Based Cohort. J Urol. 2011;186(5):1779-85.

11. Sun M, Abdollah F, Bianchi M, et al. Treatment Management of Small Renal Masses in the 21st Century: A Paradigm Shift. Ann Surg Oncol. 2012;19(7):2380-7.

12. Woldrich JM, Palazzi K, Stroup SP, et al. Trends in the surgical management of localized renal masses: thermal ablation, partial and radical nephrectomy in the USA, 1998-2008. BJU Int. 2013;111(8):1261-8.

13. Laydner H, Autorino R, Spana G, et al. Robot-assisted partial nephrectomy for sporadic ipsilateral multifocal renal tumours. BJU Int. 2012;109(2):274-80.

14. Banegas MP, Harlan LC, Mann B, et al. Toward greater adoption of minimally invasive and nephron-sparing surgical techniques for renal cell cancer in the United States. Urol Oncol. 2016.

15. Aben KKH, Osanto S, Hulsbergen-van de Kaa CA, et al. Adherence to guideline recommendations for management of clinical T1 renal cancers in the Netherlands: a population-based study. World J Urol. 2016;34(8):1053-60.

16. Pignot G, Mejean A, Bernhard JC, et al. The use of partial nephrectomy: results from a contemporary national prospective multicenter study. World J Urol. 2015;33(1):33-40.

17. Patel MI, Strahan S, Bang A, et al. Predictors of surgical approach for the management of renal cell carcinoma: a population-based study from New South Wales. ANZ J Surg. 2016.

18. Ta AD, Bolton DM, Dimech MK, et al. Contemporary management of renal cell carcinoma (RCC) in Victoria: implications for longer term outcomes and costs. BJU Int. 2013;112 Suppl 2:36-43.

19. Australian Bureau of Statistics. 2033.0.55.001 Socio-Economic Indexes for Areas (SEIFA). Canberra, Australia: Australian Bureau of Statistics, 2011.

20. Australian Bureau of Statistics. 1270.0.55.001 Australian Statistical Geography Standard (ASGS). Canberra, Australia: Australian Bureau of Statistics, 2011.

21. Edge SB, Compton CC. The American Joint Committee on Cancer: the 7th Edition of the AJCC Cancer Staging Manual and the Future of TNM. Ann Surg Oncol. 2010;17(6):1471-4.

22. Thorstenson A, Harmenberg U, Lindblad P, et al. Impact of quality indicators on adherence to National and European guidelines for renal cell carcinoma. Scandinavian Journal of Urology. 2016;50(1):2-8.

23. Hadjipavlou M, Khan F, Fowler S, et al. Partial vs radical nephrectomy for T1 renal tumours: an analysis from the British Association of Urological Surgeons Nephrectomy Audit. BJU Int. 2016;117(1):62-71.

24. Ray-Coquard I, Philip T, de Laroche G, et al. Persistence of medical change at implementation of clinical guidelines on medical practice: a controlled study in a cancer network. J Clin Oncol. 2005;23(19):4414-23.

25. White V, Pruden M, Giles G, et al. The management of early breast carcinoma before and after the introduction of clinical practice guidelines. Cancer. 2004;101(3):476-85.

26. Lainez N, Garcia-Donas J, Esteban E, et al. Impact on clinical practice of the implementation of guidelines for the toxicity management of targeted therapies in kidney cancer. The protect-2 study. Ann Oncol. 2016;16.

27. Taggar A, Alghamdi M, Tilly D, et al. Assessing guideline impact on referral patterns of post-prostatectomy patients to radiation oncologists. Can Urol Assoc J. 2016;10(9-10):314-8.

28. White V, Pruden M, Kitchen P, et al. The impact of publication of Australian treatment recommendations for DCIS on clinical practice: A population-based, "before-after" study. Eur J Surg Oncol. 2010;36(10):949-56.

29. Simone G, De Nunzio C, Ferriero M, et al. Trends in the use of partial nephrectomy for cT1 renal tumors: Analysis of a 10-yr European multicenter dataset. Eur J Surg Oncol. 2016;42(11):1729-35.

30. Rashid P, Gianduzzo TR. Urology technical and non-technical skills development: the emerging role of simulation. BJU Int. 2016;117(Suppl 4):9-16.

31. Tan HJ, Daskivich TJ, Shirk JD, et al. Health status and use of partial nephrectomy in older adults with early-stage kidney cancer. Urol Oncol 2016:S1078-439(16)30373-8.

32. Chow WH, Devesa SS, Warren JL, et al. Rising incidence of renal cell cancer in the United States. JAMA. 1999;281(17):1628-31.

33. Liu S, Lee S, Rashid P, et al. Active surveillance is suitable for intermediate term follow-up of renal oncocytoma diagnosed by percutaneous core biopsy. BJU Int. 2016;118 (Suppl 3):30-4.

Table 1: Demographic and clinical characteristics of T1N0M0 tumours in the three survey periods

T1N0M0	**2009**	**2012**	**2013**	***P***
N	318	415	490	
Mean age, years	61.5	62.1	61.7	.77 (*F* 0.26, d.f. 2)
	%	%	%	
Gender, male	61.0	64.3	61.2	.55 (χ^2 1.20, d.f. 2)
Residential location				
Major city	73.0	69.6	72.0	
Regional/Rural	27.0	30.4	28.0	.58 (χ^2 1.11, d.f. 2)
Socio-economic disadvantage				
Highest disadvantage (33%)	34.3	35.2	37.1	
Middle (33%)	24.8	30.8	32.2	
Lowest disadvantage (33%)	40.9	34.0	30.6	.04 (χ^2 10.19, d.f. 4)
Comorbidities				
None	23.6	30.6	31.8	
Mild	46.2	44.8	43.1	
Moderate	17.6	13.7	14.9	
Severe	12.6	10.8	10.2	.23 (χ^2 8.15, d.f. 6)
Diagnosis				
Incidental finding	60.7	60.0	63.5	
Symptoms	37.1	24.1	24.1	
Unknown (inc. missing)	2.2	15.9	12.4	<.01 (χ^2 47.52, d.f. 4)
T stage				
T1a	59.7	61.0	59.6	
T1b	40.3	39.0	40.4	.91 (χ^2 0.20, d.f. 2)
Tumour type				
Clear cell	64.8	67.5	72.2	
Non clear cell	35.2	32.5	27.8	.07 (χ^2 5.43, d.f. 2)
Hospital setting				
Public	62.9	56.6	57.6	
Private	37.1	43.4	42.4	.19 (χ^2 3.31, d.f. 2)

Hospital volume				
1-14 cases/yr	29.9	23.6	17.3	
15-29 cases/yr	23.9	35.9	37.6	
30+ cases/yr	46.2	40.5	45.1	<.01 (χ^2 27.07, d.f. 4)

Table 2: Univariable and multivariable associations between treatment by NSS and demographic, clinical and treatment centre characteristics and study year for T1a tumours.

T1a	NSS (%)	Univariable OR (95% CI)	Multivariable OR (95% CI)
Age			
<55 years	61.6	Ref	Ref
55-64 years	56.5	0.81 (0.55-1.20)	0.89 (0.58-1.33)
65+	49.6	0.62 (0.43-0.89)	0.67 (0.45-1.01)
Sex			
Male	55.4	Ref	Ref
Female	55.1	0.99 (0.72-1.34)	1.00 (0.72-1.38)
Comorbidities			
None	62.2	Ref	Ref
Mild	54.6	0.73 (0.51-1.05)	0.86 (0.57-1.28)
Moderate	48.4	0.57 (0.35-0.94)	0.64 (0.37-1.09)
Severe	48.6	0.58 (0.33-0.99)	0.66 (0.37-1.20)
Socio-economic disadvantage			
Highest disadvantage (33%)	50.4	Ref	Ref
Middle (33%)	56.4	1.27 (0.87-1.86)	1.22 (0.81-1.90)
Lowest disadvantage (33%)	59.6	1.45 (1.02-2.07)	1.47 (0.97-2.22)
Tumour type			
Clear cell	54.8	Ref	Ref
Non clear cell	56.5	1.07 (0.77-1.50)	1.17 (0.83-1.67)
Residential location			
Metro	58.5	Ref	Ref
Regional	47.8	0.65 (0.47-0.90)	0.76 (0.52-1.11)
Hospital setting			
Public	55.6	Ref	Ref
Private	54.8	0.97 (0.72-1.31)	0.93 (0.65-1.33)
Hospital volume			
1-14 cases/yr	44.3	Ref	Ref

15-29 cases/yr	58.1	1.73 (1.15-2.59)	1.36 (0.86-2.13)
30+ cases/yr	58.8	1.77 (1.20-2.62)	1.42 (0.92-2.19)
Study year			
2009	38.3	Ref	Ref
2012	55.3	2.00 (1.34-2.97)	2.01 (1.33-3.05)
2013	66.2	3.15 (2.13-4.68)	3.21 (2.12-4.86)

Table 3: Proportion of T1a tumours treated by NSS in each study year by patient demographic characteristics (age, sex, comorbidities and socioeconomic status) and treatment centre characteristics.

T1a	2009 (%)	2012 (%)	2013 (%)	Change 2009-2013 (%)	*P*[†]
Age					
<55 years	43.1	62.9	72.0	28.9	<.01 (χ^2 11.11)
55-64 years	45.6	54.2	66.2	20.6	.05 (χ^2 6.05)
65+	28.4	50.5	61.8	33.4	<.01 (χ^2 18.70)
Sex					
Male	33.6	56.8	68.0	34.4	<.01 (χ^2 31.56)
Female	45.6	53.1	63.1	17.5	.07 (χ^2 5.31)
Comorbidities					
None	40.5	63.0	71.1	30.6	<.01 (χ^2 10.19)
Mild	39.6	54.5	65.9	26.3	<.01 (χ^2 14.59)
Moderate + Severe	34.0	46.2	60.6	26.6	.02 (χ^2 7.92)
SES					
Highest disadvantage (33%)	34.9	47.6	61.3	26.4	<.01 (χ^2 11.54)
Middle (33%)	32.4	57.5	67.6	35.2	<.01 (χ^2 12.30)
Lowest disadvantage (33%)	44.0	61.2	71.1	27.1	<.01 (χ^2 12.62)
Residential location					
Metro	19.0	34.1	47.0	28.0	<.01 (χ^2 20.04)
Regional	14.3	35.7	50.0	35.7	<.01 (χ^2 14.33)
Hospital setting					
Public	43.6	52.4	65.8	22.2	<.01 (χ^2 13.12)
Private	31.1	58.6	66.7	35.6	<.01 (χ^2 23.93)
Hospital volume					
1-14 cases/yr	32.1	47.5	54.5	22.4	.07 (χ^2 5.34)
15-29 cases/yr	31.6	56.0	69.4	37.8	<.01 (χ^2 16.95)
30+ cases/yr	45.2	60.0	67.5	22.3	<.01 (χ^2 10.10)

[†]Degrees of freedom = 2 for all comparisons reported.

Table 4: Surgical procedures for T1b tumours for in each survey year and proportion having NSS by patient and treatment centre characteristics.

T1b		2009 (%)	2012 (%)	2013 (%)	Change 2009-2013 (%)	$P^{\dagger}$
	N	128	162	198		
Surgical treatment						
RN (open)		22.7	12.1	8.8	-13.9	<.01 (χ^2 13.12)
RN (lap)		64.1	69.4	66.0	1.9	.66 (χ^2 0.97)
NSS (open)		3.9	7.0	7.9	4.0	.35 (χ^2 2.08)
NSS (lap)		3.9	8.2	8.4	4.5	.25 (χ^2 2.77)
No surgery		5.5	1.9	5.9	0.4	.17 (χ^2 3.51)
% of Cases having NSS						
Age						
<55 years		12.5	17.9	36.7	24.2	.02 (χ^2 8.15)
55-64 years		8.6	19.5	16.7	8.1	.40 (χ^2 1.85)
65+		4.3	14.3	13.3	9.0	.21 (χ^2 3.11)
Sex						
Male		9.9	20.9	20.2	10.3	.12 (χ^2 4.19)
Female		6.0	6.4	20.8	14.8	.02 (χ^2 8.15)
Comorbidities						
None		5.4	14.6	25.4	20.0	.03 (χ^2 6.91)
Mild		12.5	14.5	19.5	7.0	.54 (χ^2 1.25)
Moderate + Severe		5.6	22.5	15.2	9.6	.11 (χ^2 4.34)
SES						
Highest disadvantage (33%)		10.0	14.0	19.3	9.3	.44 (χ^2 1.66)
Middle (33%)		2.9	15.2	21.2	18.3	<.05 (χ^2 6.08)
Lowest disadvantage (33%)		10.6	20.4	20.4	9.8	.34 (χ^2 2.14)
Hospital setting						
Public		9.8	14.9	17.5	7.7	.33 (χ^2 2.23)
Private		5.1	19.0	23.6	18.5	.05 (χ^2 6.21)
Hospital volume						
1-14 cases/yr		3.1	3.6	16.7	13.6	.07 (χ^2 5.24)
15-29 cases/yr		11.4	15.3	25.0	13.6	.18 (χ^2 3.39)
30+ cases/yr		9.3	22.9	18.6	9.3	.14 (χ^2 3.98)

[†]Degrees of freedom = 2 for all comparisons reported.

Author/s:
White, V; Marco, DJT; Bolton, D; Davis, ID; Jefford, M; Hill, D; Prince, HM; Millar, JL; Winship, IM; Coory, M; Giles, GG

Title:
Trends in the surgical management of stage 1 renal cell carcinoma: findings from a population-based study

Date:
2017-11-01

Citation:
White, V., Marco, D. J. T., Bolton, D., Davis, I. D., Jefford, M., Hill, D., Prince, H. M., Millar, J. L., Winship, I. M., Coory, M. & Giles, G. G. (2017). Trends in the surgical management of stage 1 renal cell carcinoma: findings from a population-based study. BJU INTERNATIONAL, 120 (S3), pp.6-14. https://doi.org/10.1111/bju.13889.