

Cardiovascular outcomes in kidney cancer patients

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Abstract

Introduction: In the surgical management of small renal tumours, current guidelines recommend that partial nephrectomy should be the preferred option wherever possible. This is based on evidence suggesting improved quality of life outcomes, morbidity and mortality and equivalent oncological outcomes when compared with radical nephrectomy. Chronic kidney disease is a significant risk factor for cardiovascular disease and subsequent mortality. This study explored differences in cardiac-related events and co-morbidity, using linked registry data for patients undergoing radical or partial nephrectomy for T1 renal tumours.

Methods: Data from the National Cancer Registration Service was searched to identify T1 renal cancer diagnoses between 1999 and 2012. This data was matched against hospital episode statistics to identify those patients who had undergone radical or partial nephrectomy between 1999 and 2013 using OPCS codes. Data was collected on cardiac-related admissions and deaths in nephrectomy patients. Equivalent data was also collected for the general population to allow age-standardized comparison. Charlson score was used as a proxy for pre-operative co-morbidity.

Results: Radical/partial nephrectomy patients had a greater risk of cardiac-related admissions compared with the general population (relative risk (RR) 3.32, 95% confidence interval (CI) 3.24–3.40), but with no increase in cardiac-related deaths (RR 0.84, 95% CI 0.70–1.01). There was no difference in the admission risk, or death, comparing radical or partial nephrectomy for T1 renal tumours (RR 1.02, 95% CI 0.88–1.17) using ‘time to event’ analysis. There was no difference in the comorbidity index between radical nephrectomy and partial nephrectomy patients.

Conclusion: The higher incidence of cardiac-related admissions seen for radical/partial nephrectomy patients may be explained by a higher proportion of patients with medical illnesses including cardiovascular risk factors (hypertension, diabetes) undergoing renal imaging. The absence of a difference between the radical nephrectomy and partial nephrectomy groups supports the phenomenon of surgically-induced chronic kidney disease, which may not have the same morbidity implications as medically-induced chronic kidney disease.

Keywords

Renal cancer, chronic kidney disease, surgically-induced CKD, cardiovascular disease, nephrectomy

Date received: 20 June 2016; accepted: 27 November 2016

Introduction

The more frequent use of both abdominal ultrasound and computed tomography as primary diagnostic tools in healthcare has led to an increase in the detection of small renal masses. These are usually reported incidentally or through screening of patients with chronic renal impairment with risk factors including cardiovascular disease,

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diabetes and hypertension. The TNM classification may be used to classify renal tumours based on size and extent of the primary tumour.¹ T1 renal tumours are tumours ≤ 7 cm in greatest dimension and are confined to the kidney. They are subdivided into T1a (≤ 4 cm) and T1b (≥ 4 cm but ≤ 7 cm). When small renal tumours are managed surgically, current guidelines recommend that partial nephrectomy should be the preferred option wherever possible in this patient population.¹ These guidelines are based on evidence suggesting improved quality of life outcomes, morbidity and mortality and equivalent oncological outcomes when compared with radical nephrectomy.^{2,3}

Over time the incidence of kidney cancer has increased, small renal masses contribute the majority of this increase. Simultaneously the all-cause mortality for this group of patients has continued to increase despite a high curative treatment rate for small renal masses.⁴ Further examination of non-oncological factors that may be contributing to adverse mortality in these patients has identified chronic kidney disease and cardiovascular disease as prominent factors in this regard.⁵

Chronic kidney disease is known to be a significant risk factor for cardiovascular disease and subsequent mortality. Radical nephrectomy is associated with a higher risk of chronic kidney disease compared with partial nephrectomy and thus studies have investigated whether there are differences in cardiovascular outcomes in patients undergoing radical or partial nephrectomy.⁶ Some studies have reported an increased risk of cardiovascular deaths in patients undergoing radical nephrectomy compared with partial nephrectomy.⁷ Other studies have shown that although cardiovascular events are more common in patients undergoing radical as opposed to partial nephrectomy, cardiovascular deaths remained equivalent between the two groups.⁶ A confounder is that, as a result of the 'screen' detected nature of small renal masses, many patients undergoing radical or partial nephrectomy already have a degree of chronic renal impairment and cardiovascular disease or at least cardiovascular risk factors. These non-oncological factors may influence the case selection in deciding whether to offer radical or partial nephrectomy to patients. The objectives of this present study were threefold:

1. Is there a higher incidence of cardiac-related events in patients with T1 tumours ('screen' detected/incidental renal mass) undergoing nephrectomy (partial and radical) when compared with the general population?
2. Is there a difference in the co-morbidity profile between patients with T1 tumours undergoing partial versus radical nephrectomy?
3. Is there a difference in the incidence of cardiac-related events between patients undergoing partial versus radical nephrectomy?

Methods

Data from the National Cancer Registration Service was searched to identify T1 renal cancer diagnoses between 1999 and 2012. This data was then matched against hospital episode statistics (HES) to identify those patients who had undergone radical or partial nephrectomy between 1999 and 2013 using OPCS codes M021–M025 (radical nephrectomy) and M028–M029 (partial nephrectomy).

Data was collected on cardiac-related admissions and deaths in nephrectomy patients. Equivalent data was also collected for the general population to allow age-standardized comparison. Expected and actual cardiac-related admissions and deaths were calculated using age-standardized ratios of admissions and death based on age specific rates in the population. Cardiac diagnoses were defined using the ICD-10 codes I11 – hypertensive heart disease, I13 – hypertensive heart and renal disease, I20–I25 – ischaemic heart diseases, I26–I28 – pulmonary heart disease, I30–I52 – other forms of heart disease.

Charlson co-morbidity score (a validated tool used for assessing the burden of disease and estimating mortality⁸) was calculated from HES admissions data and cancer registry data for independent primaries and used as a proxy for pre-operative co-morbidity.

Results

A total of 11,769 patients with T1 renal tumours were identified with 7518 patients having undergone surgical management either as radical or partial nephrectomy (Table 1). For those patients with T1 renal tumours undergoing either radical or partial nephrectomy there was a higher incidence of cardiac-related admissions compared with the general population (Table 2), although this was not reflected in a statistically significant difference in cardiac-related deaths (Table 3). Overall, in the radical/partial nephrectomy cohort, 1.6% had a cardiac-related mortality.

There was no difference in the co-morbidity profile between patients with T1 tumours undergoing partial versus radical nephrectomy (Table 4).

When comparing partial with radical nephrectomy, there was no difference in the cardiac-related admission rates (Table 5). Using a 'time-to-event' analysis the timing of those admissions after radical or partial nephrectomy did not differ; 7% had their cardiac event during the same admission as their partial or radical nephrectomy (Figure 1).

Discussion

This study, which used linked registry data for over 11,000 patients, showed that patients undergoing nephrectomy

Table 1. Patients with T1 renal tumours undergoing nephrectomy (1999–2013).

Year of diagnosis	Partial	Radical	Total
1999	2	75	77
2000	4	137	141
2001	4	196	200
2002	10	249	259
2003	7	281	288
2004	7	343	350
2005	10	376	386
2006	10	472	482
2007	9	578	587
2008	28	744	772
2009	18	788	806
2010	20	862	882
2011	21	1131	1152
2012	28	1108	1136

Table 2. Comparison of age-standardized admissions relating to cardiac causes, all nephrectomy patients compared with general population.

Expected admissions	Actual admissions	Ratio	95% CI
2360	7842	3.32	3.24–3.40

CI: confidence interval.

Table 3. Comparison of age-standardized deaths relating to cardiac causes, all nephrectomy patients compared with general population (based on 2001–2011 data).

Expected deaths	Actual deaths	Ratio	95% CI
140	118	0.84	0.70–1.01

CI: confidence interval.

(radical or partial) for T1 renal tumours had a greater incidence of cardiovascular events when compared with the general population. This did not, however, result in an increased risk of cardiovascular deaths in this population. In line with the findings of previous studies,⁶ there was no difference in pre-operative comorbidity or post-operative cardiovascular events in radical nephrectomy patients as compared with partial nephrectomy patients.

Table 4. Charlson score of patients with T1 renal tumours undergoing radical or partial nephrectomy.

Score	Partial	Radical
0	46%	45%
1	17%	19%
2	18%	17%
3+	18%	19%

Table 5. Comparison of age-standardized admissions relating to cardiac causes, partial nephrectomy patients compared with radical nephrectomy patients.

Expected admissions	Actual admissions	Ratio	95% CI
188	191	1.02	0.88–1.17

CI: confidence interval.

The higher incidence of cardiac-related admissions seen for radical/partial nephrectomy patients may be explained by a higher proportion of patients with medical illnesses such as hypertension and diabetes undergoing renal imaging as part of their routine assessment. These patients are predisposed with cardiovascular pathology and therefore the cardiovascular events seen in nephrectomy patients are unlikely to be purely treatment (surgically-induced renal impairment) effect but rather a reflection of the pre-existing cardiovascular risk. Furthermore, it is not surprising that cardiovascular disease is often encountered in patients undergoing nephrectomy as diabetes and hypertension are known to be independent risk factors for the development of renal cell carcinoma.⁹ Of note, the risk of cardiac-related death after radical/partial nephrectomy was low in our series at 1.6%.

The absence of a difference between the radical and partial nephrectomy groups is interesting and supports the phenomenon of surgically-induced chronic kidney disease (CKD). Nephrectomy is known to be a cause of CKD, which is in turn associated with cardiovascular disease and morbidity.³ Emerging evidence suggests that distinguishing the aetiology of CKD, be it medical or surgical, is important due to differing implications. Surgical CKD which occurs as a result of nephron loss secondary to nephrectomy may not have the same morbidity implications as medically-induced CKD. Medically-induced CKD, caused by conditions such as hypertension and diabetes, is associated with a progressive decline in renal function and the underlying cause in addition to causing nephron damage often also affects other systems as part of general cardiovascular dysfunction. Surgically-induced

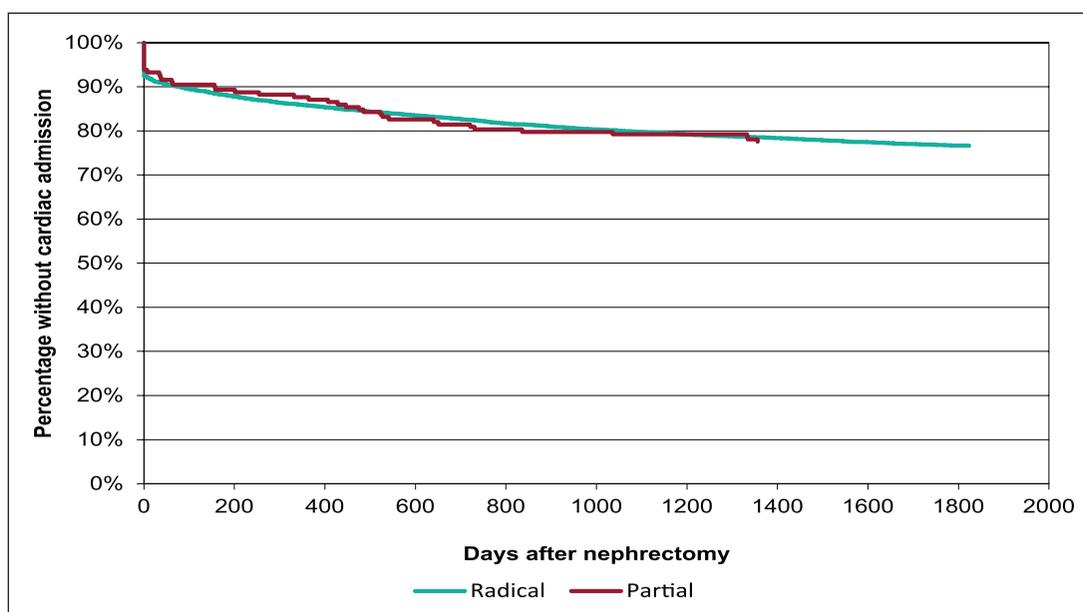


Figure 1. Time to event analysis for cardiac admissions after nephrectomy (followed up to five years).

CKD, however, is due to a single event and has a much lower risk of progression.¹⁰ It therefore has fewer morbidity implications over time particularly in the presence of a normal contralateral kidney.

It is clear, however, that a significant proportion of patients being diagnosed with renal tumours and subsequently requiring surgical treatment will have underlying cardiovascular disease or risk factors. It is therefore prudent to undertake nephron sparing surgery whenever possible, not because the surgically-induced CKD from a radical nephrectomy appears to have adverse cardiovascular implications, but rather because their underlying pre-operative cardiovascular risk factors/medically-induced CKD will have on-going progressive effects on morbidity.

Conflicting interests

The authors declare that there is no conflict of interest.

Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Ethical approval

Not applicable.

Informed consent

Not applicable.

Guarantor

The guarantor for this paper: EM.

Contributorship

EM, LH and RK conceived the study. EEM and LH researched the literature. LH and EEM performed the data analysis. EEM and EM prepared the first draft of this paper. All authors have reviewed and edited the manuscript and approved the final version of this paper.

Acknowledgements

None.

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