Published in final edited form as:

World J Urol. 2015 December ; 33(12): 2023–2029. doi:10.1007/s00345-015-1581-9.

Partial nephrectomy for renal tumors in solitary kidneys: postoperative renal function dynamics

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Abstract

Objective—To describe renal functional outcomes after partial nephrectomy (PN) for a tumor in a solitary kidney using the estimated glomerular filtration rate eGFR (MDRD equation).

Patients and methods—A retrospective review of 103 cases of PN in a solitary kidney at Memorial Sloan-Kettering Cancer Center from December 1989 to July 2010 was conducted. The postoperative eGFR measurements were broken into three timeframes: 1–10 days after PN, 10 days–8 weeks after PN, and 4–12 months after PN. Several factors were analyzed for their impact on postoperative eGFR on univariate and multivariable analyses. To illustrate the change in eGFR after surgery over time, a univariate generalized estimating equation (GEE) model was constructed.

Results—Median preoperative eGFR was 47 ml/min/1.72 m² (IQR 39, 58). Higher preoperative eGFR, younger age at the time of PN, less estimated blood loss during PN, increased time between PN and previous radical nephrectomy, and decreased arterial clamp (ischemia) time were all significantly associated with increased post-operative eGFR in the early postoperative period on multivariable analysis. Younger age and higher preoperative eGFR were the only variables significantly associated with increased postoperative eGFR at all three time points. From the GEE model, postoperative eGFR continues to rise after PN until it reaches a plateau approximately 1 month after PN without attaining preoperative levels.

Conclusion—PN for tumors in a solitary kidney is feasible and safe. In our model, non-modifiable factors predict the long-term postoperative eGFR: Young patients with healthy kidneys have superior renal functional results.

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Conflict of interest The authors declare that they have no conflict of interests.

Ethical standard This study has been approved by the appropriate ethics committee (IRB) and has therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

Keywords

Carcinoma; Outcome assessment; Partial nephrectomy; Postoperative complications; Renal cell; Renal function

Introduction

Partial nephrectomy (PN) is an imperative operation for patients with a renal tumor in a functional or anatomic solitary kidney. Over the last decade, in the elective setting, mounting evidence indicates that when technically feasible, PN provides equivalent oncological results to RN while at the same time maximally preserving renal function, preventing or delaying the onset of chronic kidney disease (CKD) and associated cardiovascular morbidity and potential mortality [1–4]. Despite strong evidence supporting PN for both oncological control and renal functional preservation, RN remains over-utilized in the management of small renal masses. The exception to this over-utilization may be at high-volume medical centers with a research and clinical interest in the management of kidney tumors [1, 5]. A difficult surgical problem relates to the management of a renal tumor in a solitary kidney. PN, if safely executed, can achieve local tumor control and maintain sufficient renal function to keep the patient off hemodialysis. In addition, PN in a patient with a solitary kidney provides a unique opportunity to study the adverse impact of this operation on immediate and long-term renal function, without the intervention of the compensating contralateral kidney. In this study, we evaluate clinical factors associated with renal functional outcomes for patients undergoing PN in a solitary kidney.

Materials and methods

Patient selection

Between 1989 and 2010, 103 patients from Memorial Sloan-Kettering Cancer Center with a renal tumor in a solitary kidney underwent PN for a renal cortical tumor. Two (2 %) patients had a solitary kidney due to kidney atrophy and 101 (98 %) as a result of a previous RN. An Institutional Review Board-approved and Health Insurance Portability and Accountability Act-compliant review of Medical records was conducted. None of the patients of this study had a hereditary or familial renal cancer syndrome. The PN technique has been previously described [6]. For endophytic and larger renal tumors, renal artery clamping allowed for surgical resection in a relatively bloodless surgical field. Intravenous mannitol (12.5 g/200 ml of normal saline) was administered within 30 min of arterial cross-clamping. After arterial cross-clamping, renoprotective ice slush was applied to the kidney. For small exophytic tumors, excision without arterial cross-clamping using renal parenchymal compression was utilized in selected cases. In highly selected more complex cases, resection of the renal tumor in the solitary kidney was performed without arterial cross-clamping with the acceptance of more blood loss and possibly the need to transfuse in lieu of acute renal failure and the need for temporary dialysis.

Methods

Our first aim was to estimate postoperative eGFR. The postoperative eGFR measurements were broken into three timeframes: 1–10 days after PN, 10 days–8 weeks after PN, and 4–12 months after PN. A multivariable linear regression model was constructed to predict eGFR within each time-frame. The following factors were analyzed for their impact on postoperative eGFR: preoperative eGFR, age, ASA category (1/2 vs. 3/4), coronary artery disease, hypertension, diabetes, estimated blood loss during PN, time between PN and prior RN, ischemia time, use of arterial clamping, and tumor size. Significant factors associated (p value <0.10) with postoperative eGFR in a univariate linear regression model were added to the multivariable model. If a patient had multiple eGFR measurements in one timeframe, the eGFR measurement closest to the center of the timeframe was utilized for the analyses. To illustrate the change in eGFR after surgery over time, a univariate generalized estimating equation (GEE) model was constructed. Time since PN was added with restricted cubic splines (knots at 15 days and 2 months after PN) allowing for a nonlinear relationship between postoperative eGFR and time since PN.

Our second aim was to describe the complications patients experienced after PN. Complications are summarized by the complication category according to Clavien scale [7] and by the highest grade complication for each patient (see Table 1).

Our third aim was to describe overall survival and survival from kidney cancer. Each of these measures was summarized with a Kaplan–Meier curve. Five patients with non-malignant tumors were excluded from the survival analyses (three oncocytoma and two with renal oncocytosis without chromophobe carcinoma components). All analyses were conducted using Stata statistical software (version 11.1; Stata Corp, College Station, TX).

Results

In total, 103 patients with a solitary kidney underwent a PN at MSKCC between 1989 and 2010. The median age was 62 years, and 74 patients (72 %) were male. Additional characteristics of these patients are found in Table 2.

Median preoperative eGFR was 47 ml/min/1.73 m² (IQR 39, 58). Multivariable linear regression models were constructed to predict postoperative eGFR in three time-frames: 1–10 days, 10 days–8 weeks, and 4–12 months after surgery. Patients without eGFR measurements within the three timeframes or missing data on predictors were not included in the models. The models included 103, 68, and 75 patients in the timeframes 1–10 days, 10 days–8 weeks, and 4–12 months, respectively. Higher preoperative eGFR, younger age at surgery, less estimated blood loss during surgery, increased time between PN and previous nephrectomy, and decreased clamp time were all significantly associated with increased immediate postoperative eGFR. Younger age at surgery and higher preoperative eGFR were the only variables significantly associated with increased postoperative eGFR at all three time points (see Tables 3, 4). Figure 1 illustrates the mean eGFR after surgery, which demonstrates that the postoperative eGFR continues to rise after PN until it reaches a plateau at approximately 1 month after PN.

Eight patients experienced acute kidney failure after PN, three of whom required temporary dialysis (2.9 %).

Most patients did not experience any complications within 90 days of surgery (70 %), and only 16 (15 %) experienced a significant complication (grade 3–5). The most common complications occurred in the genitourinary system in 19 patients (18 %), including 15 urinary leaks. The next most frequent complication category was infectious, which occurred in 7 patients (7 %) (Tables 5, 6).

Overall, 39 patients (38 %) with malignant renal tumors died, 19 (18.4 %) from kidney cancer. In Figs. 2 and 3, Kaplan–Meier curves summarize overall survival and kidney cancer-specific survival. The 5-year probability of being alive (overall survival) and being free from kidney cancer death was 64 % (95 % CI 52 %, 74 %) and 81 % (95 % CI 68 %, 89 %), respectively.

Discussion

In this report, we update our previous study on PN for the treatment of a renal tumor in a solitary kidney [6]. This report included more patients and provided a renal functional assessment by using eGFR as determined by the MDRD equation [8], and the statistical methods allowed an attempt to identify independent predictors of postoperative eGFR.

It has been shown that a large proportion of patients with renal cortical diagnosed tumors have low eGFRs before the surgery; in a study from Huang et al. [3], at least 26 % of patients with small renal tumor (<4 cm), a serum creatinine within normal limits, and a normal contra lateral kidney had an eGFR < 60 ml/min/1.73 m² consistent with stage 3 CKD [9]. In this report of patients with renal tumors in a solitary kidney, the median preoperative eGFR was only 47 ml/min/1.73 m², indicating the vulnerability of this high-risk population to further loss of kidney function as a result of an attempt by the surgeon to perform a PN in a solitary kidney.

In a different study [10] of 89 partial nephrectomies on solitary kidneys, LaRochelle and colleagues suggested that cold ischemia time and the presence of all following vascular risk factors (diabetes, hypertension, and cardiovascular disease) were the only variables predicting the decrease in immediate postoperative eGFR. No variables were associated with a decrease in late eGFR. In this report, a significant proportion of the patients presented with medical risk factors for CKD including hypertension (62 %), diabetes (18 %), or a previous RN (98 %). However, none of these cardiovascular risk factors appeared as independent predictors for impairment of renal function after PN in their solitary kidney. Interestingly, we also did not find evidence that tumor size, which partly correlates with the amount of renal parenchyma that will be removed by surgery (along with tumor location), was associated with postoperative eGFR. Yet, if a tumor is exophytic and large, very little normal renal parenchyma could be lost during the resection. However, the wide confidence intervals associated with tumor size did not completely exclude a clinically meaningful effect of tumor size on postoperative eGFR. For the immediate postoperative period, it appeared that the surgeon did have influence on renal function since estimated blood loss and renal artery

clamp time, which can be considered as surrogates for a more difficult PN, were significant predictors of postoperative eGFR in the multivariable model.

More surprisingly, we did not see evidence that any modifiable factor, such as ischemia time, was associated with long-term postoperative eGFR, although median ischemia time was relatively long among patients (40 min). The common notion that a threshold of 20 min of ischemia must be respected [11] or “that every minute” of ischemia counts [12] does not appear to affect eGFR on the long term in our series where the use of renoprotective maneuvers, particularly ice slush, may have been effective. One could argue that our series has several limitations and that our results are in contrast to most of the literature, but the same group that proposed that each minute counts more recently suggested that in fact only preexisting CKD, age, and percentage of parenchyma preserved predicted independently for long-term postoperative eGFR [13]. Also, a recent single-center study from Ching et al. [14] found that only patient age, tumor size, percentage of parenchyma spared, and preoperative renal function predicted ultimate renal function. Our data would indicate that the quality and the quantity of remaining renal parenchyma matter more than the time of the arterial cross-clamping.

For the early timeframe, the longer the patient had a solitary kidney, the better the early postoperative renal function, but we did not observe a significant association between years between RN and PN and eGFR in the midterm or long-term timeframes. This suggests that the compensatory glomerular hypertrophy of the remaining kidney after a radical nephrectomy (RN) provides a resistance to renal injury though it is known that aging induces a physiological decrease in creatinine clearance of 0.75 ml/min/year [15].

Figure 1 demonstrates an immediate drop in postoperative eGFR following PN in a solitary kidney, which appears to plateau a month after PN. However, the post-operative eGFR never returns to the preoperative eGFR level. Consistent with the findings of La Rochelle et al. [10], we did not observe a trend in a marked decrease in eGFR during the postoperative period (median follow-up of 14 months). Interestingly, in the study from Ching et al. [14] assessing renal function after PN on solitary kidney with a much longer follow-up (mean 175 months), it is suggested that “after an initial decrease due to surgical resection, renal function remains relatively stable,” with 35.1 ml/min/1.73 m² at 5-year follow-up and 34.5 ml/min/1.73 m² at 10 years.

Of the eight patients who suffered acute kidney failure after surgery, most (seven patients) had significant preexisting CKD and eGFR between 28 and 38 ml/min/1.73 m²; the remaining patient had a preoperative eGFR of 45 ml/min/1.73 m². Only three patients required temporary dialysis. These findings are consistent with those of most recent studies that report that PN in a solitary kidney seldom requires chronic hemodialysis [10, 12, 14]. Regarding other complications, only 16 patients (6.5 %) had complication grade 3 or 4 mostly in the genitourinary system (13 out of 16). The only grade 4 complication was a cerebrovascular accident that ended in a chronic neurological deficit.

The cancer-specific survival at 5 years was 81 % with 19 patients (18.4 %) dying of their kidney cancer, which is similar to our previous report (88 %) [5] as well as other contemporary studies: 77.5–81 % [16, 17].

It is our opinion that for a patient with a tumor in a solitary kidney, referral to a major center with a large experience in renal sparing surgery is preferable. In planning operations in this setting, the surgeon must decide whether the tumor is exophytic and in a location amenable to parenchymal compression (a form of regional ischemia) such that resection can be executed with minimal blood loss and allowing continued perfusion and function of the solitary kidney throughout the operation. For endophytic tumors or those involving the renal sinus, a dialysis catheter is placed in anticipation for perioperative dialysis. In this setting, renal artery cross-clamping with cold ischemia, rapid tumor resection, and reconstruction are performed. Rapid surgical resection and repair, with good vision and minimal blood loss, is preferable to massive blood loss, sloppy repair, and hypotension-induced acute tubular necrosis (ATN). Often-times, there is temporary ATN that reverses prior to the patient requiring temporary dialysis. If short-term dialysis is required, most patients will recover sufficiently to ultimately be dialysis free. It is essential for the urologist and nephrologist to have a close working relationship that is established long before the operation is performed.

This study is limited by its retrospective nature with biases inherent to this approach as well as by the relatively small number of patients (though it is from a single institution). Also, the calculated percentage of parenchymal loss was not available as a data for assessment, yet this factor appeared to be the most important determinant of long-term eGFR after PN in recent studies [13, 14, 18]. Tumor location and nephrometry scores, which account for surgical complexity, were also not available for the assessment.

Conclusion

PN is a safe and feasible operation for renal tumors in a solitary kidney. The solitary kidney can effectively be operated upon using contemporary renoprotective techniques with sufficient renal preservation to avoid long-term dialysis despite the fact that most patients had CKD prior to PN. Non-modifiable factors predict the long-term postoperative eGFR, with younger and healthier kidneys able to retain higher postoperative eGFR after PN. Ischemia time, possibly because of renoprotective measures, did not influence eGFR postoperatively in the long term. PN also allows for effective local tumor control.

Acknowledgments

Supported by: The Sidney Kimmel Center for Prostate and Urologic Cancers.

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Fig. 1.
Estimated postoperative eGFR by months since surgery estimated from GEE model

Fig. 2.
Kaplan–Meier curve for overall survival with 95 % CI

Fig. 3.
Kaplan–Meier curve for CSS with 95 % CI

Table 1

Postoperative complication grading system

Grade	Definition
Grade 0	No event observed beyond 90 days postoperatively
Grade 1	Use of oral medications or bedside intervention
Grade 2	Use of intravenous medications, total parenteral nutrition (TPN), enteral nutrition, or blood transfusion
Grade 3	Interventional radiology, therapeutic endoscopy, intubation, angiography, or operation
Grade 4	Residual and lasting disability requiring major rehabilitation or organ resection
Grade 5	Death of patient

Table 2

Patient characteristics

N = 103	
Age at surgery (years)	62 (58, 72)
Male	74 (72 %)
ASA category	
I	4 (4 %)
II	33 (33 %)
III	64 (63 %)
IV	0 (0 %)
Tumor size (cm)	3.0 (2.0, 4.0)
Ischemia	71 (69 %)
Ischemia time (min)	40 (32, 49)
Ice slush	64 (63 %)
Previous nephrectomy	101 (98 %)
Years between nephrectomies	5.4 (1.0, 11.6)
Hypertension	64 (62 %)
Diabetes	19 (18 %)
Coronary artery disease	7 (7 %)
Estimated blood loss (cc)	575 (300, 1000)
Metastasis prior to PN	15 (15 %)
Malignant tumor	98 (95 %)
Preoperative eGFR	47 (39, 58)

All values are median (IQR) or frequency (proportion)

Table 3

Univariate linear regression model with postoperative eGFR as outcome

	1–10 days after surgery			10 days–8 weeks after surgery			4–12 months after surgery		
	Coefficient	95 % CI	<i>p</i> value	Coefficient	95 % CI	<i>p</i> value	Coefficient	95 % CI	<i>p</i> value
Tumor size (cm)	–1.3	–3.7, 1.1	0.3	1.1	–1.3, 3.4	0.4	–0.7	–2.4, 1.1	0.4
Clamp time (min)	–0.24	–0.41, –0.06	0.008	–0.07	–0.23, 0.08	0.3	–0.09	–0.22, 0.05	0.2
Years between nephrectomies	0.36	–0.04, 0.76	0.074	0.26	–0.09, 0.60	0.14	0.13	–0.22, 0.48	0.5
Age (10 years increments)	–5.9	–9.5, –2.4	0.001	–7.2	–10.5, –4.0	<0.0005	–4.2	–6.9, –1.5	0.003
Preoperative eGFR	0.9	0.7, 1.1	<0.0005	0.8	0.6, 1.0	<0.0005	0.7	0.6, 0.9	<0.0005
Estimated blood loss (100-cc increments)	–0.49	–0.97, –0.01	0.047	–0.30	–0.72, 0.12	0.16	–0.26	–0.71, 0.20	0.3
Hypertension	–2.1	–10.6, 6.4	0.6	–1.0	–9.4, 7.4	0.8	0.9	–5.9, 7.8	0.8
Coronary artery disease	–1.0	–17.4, 15.5	0.9	0.2	–13.9, 14.4	1	–1.7	–13.7, 10.3	0.8
Diabetes	0.1	–10.6, 10.8	1	1.7	–8.5, 11.9	0.7	–0.9	–9.3, 7.4	0.8
ASA category (1/2 vs. 3/4)	–8.7	–17.2, –0.2	0.045	–10.7	–18.6, –2.8	0.009	–6.0	–12.9, 0.9	0.088
Ischemia	–6.9	–15.7, 2.0	0.13	–4.0	–12.6, 4.7	0.4	–5.0	–12.0, 1.9	0.15

p values <0.05 are in bold

Table 4

Multivariable linear regression model with postoperative eGFR as outcome

	1–10 days after surgery			10 days–8 weeks after surgery			4–12 months after surgery		
	Coefficient	95 % CI	<i>p</i> value	Coefficient	95 % CI	<i>p</i> value	Coefficient	95 % CI	<i>p</i> value
Preoperative eGFR	0.8	0.6, 1.0	<0.0005	0.7	0.5, 0.9	<0.0005	0.7	0.5, 0.8	<0.0005
Age (10-year increments)	–3.5	–6.3, –0.8	0.012	–4.2	–7.0, –1.4	0.004	–2.3	–4.3, –0.4	0.02
ASA category (1/2 v. 3/4)	–2.4	–8.8, 3.9	0.4	–1.3	–7.5, 4.9	0.7	–3.4	–8.2, 1.3	0.15
Clamp time (min)	–0.29	–0.42, –0.16	<0.0005						
Years between nephrectomies	0.44	0.15, 0.73	0.004						
Estimated blood loss (100 cc increments)	–0.75	–1.10, –0.39	<0.0005						

p values <0.05 are in bold

Table 5

Highest complication grade

Grade 0	72 (70 %)
Grade 1	11 (11 %)
Grade 2	4 (4 %)
Grade 3	15 (15 %)
Grade 4	1 (1 %)
Grade 5	0 (0 %)

Table 6

Complications by category

Cardiovascular system	3 (3 %)
Endocrine system	1 (1 %)
Genitourinary system	19 (18 %)
Hematologic or vascular system	2 (2 %)
Infection	7 (7 %)
Nervous system	3 (3 %)
Pulmonary system	1 (1 %)
Wound or skin	6 (6 %)