



# Risk Factors for Postoperative Hemorrhage After Partial Nephrectomy

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**Purpose:** To evaluate the frequency and clinical characteristics of postoperative hemorrhage as a complication of partial nephrectomy.

**Materials and Methods:** The demographics, physical statistics, tumor size, R.E.N.A.L. nephrometry score, operative method, warm ischemic time, and presence of postoperative hemorrhage and its severity and method of intervention were examined in 300 partial nephrectomy patients in two medical centers (Stanford Medical Center and Kyung Hee University Medical Center) between March 2000 and March 2012.

**Results:** Of the 300 subjects, 13 (4.3%) experienced postoperative hemorrhage severe enough to require intervention more invasive than transfusion (Clavien grade III or higher). Univariate analysis of the bleeding and nonbleeding groups showed that whereas age, ischemic time, tumor size and stage, body mass index, American Society of Anesthesiologists class, and operative method did not differ significantly, the exophytic (E) score was significantly higher for severe postoperative hemorrhage ( $p=0.04$ ). However, multivariate analysis showed none of the factors to differ significantly. In most of the cases requiring intervention, selective embolization was sufficient, but in one case explorative laparotomy and nephrectomy were required. Clinical characteristics varied significantly among severe hemorrhage cases, with time of onset ranging from the first to the 30th postoperative day and symptoms presenting in a diverse manner, such as gross hematuria and pleuritic chest pain. Computed tomography and angiographic findings were consistent with either arteriovenous fistula or pseudoaneurysms.

**Conclusions:** Severe hemorrhage after partial nephrectomy is rare. Nonetheless, with the great variability in presenting symptoms and time of onset after surgery, surgeons should exercise great vigilance during the postoperative care of partial nephrectomy patients.

**Keywords:** Nephrectomy; Postoperative hemorrhage; Renal cell carcinoma

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**Article History:**

received 3 February, 2013

accepted 8 October, 2013

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## INTRODUCTION

Renal cell carcinoma is a relatively prevalent urologic malignancy, involving over 50,000 new cases in the United States alone each year [1]. Developments in imaging modalities and their increasing availability have led to an increasing proportion of the cases being incidentally diagnosed. With recent advances in surgical technique, partial

nephrectomy has become the treatment of choice for localized lesions [2]. Nephron sparing through partial nephrectomy has proven advantageous for T1a lesions not only for the non-cancer-related death rate but also for overall survival [3], and the oncologic safety of partial nephrectomy for T1b disease has also been shown not to differ significantly from that of radical nephrectomy [4]. Nevertheless, partial nephrectomy remains far more technically

challenging than radical nephrectomy, a problem that is amplified when minimally invasive techniques, such as laparoscopy or robot assistance, are involved, with a consequent increase in surgery-associated morbidity, such as urinary fistulas, postoperative bleeding, and pleural entry [5].

Arguably, the most important surgery-associated morbidity following partial nephrectomy is postoperative bleeding. Despite the relatively low incidence of bleeding after partial nephrectomy (reported to be in the range of 4.2% to 6% for laparoscopic partial nephrectomy [6] and 6% and 8.1% for open and robot-assisted procedures, respectively [7]), it remains one of the most serious complications, and this is especially so for centrally located tumors [8-10]. Several studies have examined different factors in relation to hemorrhage following partial nephrectomy, including patient and demographic factors, operative method, and tumor parameters [9]. Van Poppel et al. [11], in their study on open partial nephrectomy in 76 patients, suggested that larger tumor size and central tumor location correlated with increased risk of postoperative hemorrhage. Likewise, Ramani et al. [9] reported that the incidence of postoperative bleeding was higher in patients with central tumors and deeper infiltration.

The R.E.N.A.L. nephrometry scoring system is a system for quantification of the salient anatomy of renal masses developed by Kutikov and Uzzo [12]. It is divided into 5 categories, R (for radius, based on a scale between 1 and 3), E (for exophyticity, again on a scale from 1 to 3), N (for nearness of the tumor to the collecting system, on a scale from 1 to 3), A (for anterior/posterior location of the tumor), and L (for location relative to the polar and middle lines of the kidney, on a scale from 1 to 3); the aggregate figure is used as a quantification of the salient anatomy of a renal mass [12]. The scoring system is increasingly being used as a clinical tool for guiding management decisions for small renal masses and for comparison of clinical outcomes of certain treatment methods, such as partial nephrectomy [13,14]. In particular, the tool is seeing widespread use in assessing the complexity of planned surgical procedures, such as laparoscopic partial nephrectomy. However, no study to date has reported on postoperative bleeding in relation to R.E.N.A.L. nephrometry scores. In the present study, the authors examined patients who underwent partial nephrectomy in two centers to identify factors associated with increased risk of postoperative bleeding after partial nephrectomy.

## MATERIALS AND METHODS

A total of 300 patients who underwent partial nephrectomy in two medical centers (Stanford Medical Center, Stanford, CA, USA; Kyung Hee University Medical Center, Seoul, Korea) between March 2000 and July 2012 were enrolled in the present study. The partial nephrectomy procedures consisted of open, laparoscopic, and robot-assisted surgeries and were undertaken by multiple surgeons.

For the surgical procedures, the open method exclusively utilized cold ischemia. The laparoscopic procedures, which used transperitoneal approaches for anteriorly or laterally located tumors and retroperitoneal approaches for posteriorly located tumors, and the robot-assisted procedures, which exclusively used transperitoneal approaches, utilized only warm ischemia. Cold ischemia times were excluded from comparative evaluation of warm ischemia times to allow for more accurate analysis of the effect of warm ischemia. For arterial and venous clamping during surgery, only the renal artery was clamped for peripheral or small (< 4 cm) tumors. For central/hilar or large tumors, both the renal artery and vein were clamped. Bulldog clamps were mostly used for vascular clamping, although in select laparoscopic surgery cases Satinsky clamps were used for en bloc clamping of both renal artery and vein. On the other hand, only bulldog clamps were used during robot-assisted surgery. Resection of the tumor was carried out by using scalpels and scissors, without application of electrosurgical coagulation devices. Intraoperative bleeding was addressed conservatively through transfusion or administration of intravenous fluids, and bleeding at resection margins was addressed through meticulous renorrhaphy, consisting of application of Surgicel absorbable hemostats (Ethicon, Somerville, NJ, USA) or Flo-Seal hemostasis matrix (Baxter Healthcare, Hayward, CA, USA) for filling in resection defects followed by closure of the defect by use of Vicryl sutures with Surgicel buttresses. The operative procedure in general did not differ between the two centers.

Following the operation, each of the patients underwent postoperative care, including close observation of vital signs and daily evaluation of the complete blood count (CBC) and blood chemistry. If patients did not exhibit any problems, they were discharged on the third or fourth postoperative day following removal of drains. On the other hand, computerized tomography (CT) evaluation was carried out when significant decline in the hemoglobin level or persistent bloody discharge through drains of large amounts (> 400 mL/d) was observed. Discharged patients were also evaluated by use of CT if they visited the Emergency Department for symptoms warranting a high degree of suspicion, such as flank pain or gross hematuria. Patients whose CT results revealed postoperative bleeding foci, such as pseudoaneurysms (arterial wall defect visible as extrusive masses on segmental arteries with communicating vascular lumen on contrast-enhanced CT) or arteriovenous (AV) fistulas (direct artery-vein communication visible as direct confluence between segmental arteries and veins on CT), and those who were stable subsequently underwent angiographic intervention (Clavien grade IIIa), whereas those whose vital signs were unstable underwent surgical exploration (Clavien grade IIIb). Patients whose CT images did not show signs of active bleeding foci underwent conservative treatment, including transfusion and CBC follow-up (Clavien grade II). Postoperative hemorrhage was judged to be significant if measures more

**TABLE 1.** Comparison of baseline characteristics, R.E.N.A.L. nephrometry score, tumor stages, and operative methods between the bleeding and nonbleeding groups

Characteristic	No bleeding (n=287)	Bleeding (n=13)	p-value
Age (y)	58.2±12.9	57.1±12.3	0.770
Sex			0.546
Male	183	8	
Female	104	5	
Side			0.600
Right	137	8	
Left	150	5	
Body mass index (kg/m <sup>2</sup> )	27.7±7.4	25.9±9.2	0.440
ASA score	2.3±0.7	2.6±0.5	0.240
Tumor size (cm)	2.8±1.3	2.7±1.5	0.810
R	1.2±0.4	1.1±0.3	0.370
E	1.7±0.7	2.1±0.7	0.040 <sup>a</sup>
N	2.1±0.8	2.2±0.7	0.700
L	1.8±0.7	2.2±0.8	0.060
Nephrometry score	7.1±6.1	7.6±1.0	0.760
WIT (min)	25.6±15.0	34.8±12.0	0.080
EBL (mL)	376.1±476.0	312.5±217.6	0.650
Tumor stage <sup>b</sup>			0.375
T1a	231 (80.5)	11 (84.6)	
T1b	36 (12.5)	1 (7.7)	
T2	0 (0)	0 (0)	
T3	10 (3.5)	0 (0)	
N/A <sup>c</sup>	10 (3.5)	1 (7.7)	
Operative method			0.538
Open	188 (65.5)	7 (53.8)	
Laparoscopic	71 (24.7)	5 (38.5)	
Robot-assisted	28 (9.8)	1 (7.7)	

Values are presented as mean±standard deviation or number (%).

ASA, American Society of Anesthesiologists; WIT, warm ischemic time; EBL, estimated blood loss.

<sup>a</sup>:p-value < 0.05 from Student t-test for age, body mass index, ASA, tumor size, R, E, N, L, nephrometry score, WIT, and EBL and Pearson chi-square test for sex, tumor stage, and operative method. <sup>b</sup>:No. of pT2 lesions observed in the present study. <sup>c</sup>:Pathologically determined as benign tumors after operation.

invasive than transfusion were required to stabilize the hemoglobin level.

The demographics, physical statistics, tumor size, R.E.N.A.L. nephrometry score, operative method and parameters (warm ischemic time [WIT] and estimated blood loss), presence of postoperative hemorrhage, and, if present, the severity and method of intervention were investigated.

The study was carried out with Institutional Review Board approval, and all of the subjects were given guarantees of confidentiality and provided written informed consent.

Statistical analyses were carried out by using SPSS ver. 12.0 (SPSS Inc., Chicago, IL, USA). For Student t-test, Pearson chi-square test, and univariate and multivariate analyses using logistic regression,  $p < 0.05$  was considered to be indicative of statistical significance.

## RESULTS

Of the 300 patients examined, clinically significant post-

operative hemorrhage (i.e., hemorrhage for which measures more invasive than transfusion were required to stabilize the hemoglobin level) occurred in 13 patients (4.3%). The general characteristics, R.E.N.A.L. nephrometry parameters, and operative parameters of the patients are as listed in Table 1. The average R.E.N.A.L. nephrometry scores were 7.1 and 7.6 for the nonbleeding and bleeding groups, respectively, with no statistically significant difference between the two groups. Of the individual nephrometry parameters, only the E category (exophyticity) of the R.E.N.A.L. scoring system was shown to differ between the two groups with any statistical significance ( $p=0.04$ ). In addition, although the L parameter, with average values of 1.8 and 2.2 for the nonbleeding and bleeding groups, respectively, differed between the two groups, the difference was not significant. Likewise, the WIT, with an average of 25.6 minutes and 34.8 minutes for the nonbleeding and the bleeding groups, respectively, also differed between these groups, although again without statistical significance. As for the tumor stage distribution, no pT2 lesion was identified in the present study, and the two groups did not differ

significantly ( $p=0.375$ ). Similarly, the bleeding and non-bleeding groups did not differ in terms of the operative method used ( $p=0.538$ ). In the univariate and multivariate analyses using logistic regression (with a confidence interval of 95%), although the univariate analysis showed the E score to be significant ( $p=0.033$ ; odds ratio, 0.727), the multivariate analyses failed to show any of the factors to have statistical significance (Table 2).

Although not provided in a separate table, whereas 13 of the patients required invasive procedures for control of postoperative bleeding, another 14 patients experienced bleeding not requiring treatment greater than transfusion. Of these, 9 patients (3.0% of all patients) recovered after close observation only, whereas 5 patients (1.7%) re-

quired transfusion.

The characteristics of the patients of the hemorrhage group are shown in Table 3. The presenting symptoms, including gross hematuria and pleuritic chest pain, varied greatly among the patients. Likewise, the time of onset also differed greatly, from the first to the 30th day after operation, with only 7 of 13 patients presenting with symptoms within the first postoperative week. Of these patients, 7 underwent open procedures, whereas 5 underwent laparoscopic surgery and 1 underwent robot-assisted surgery. The nephrometry score was 6 on CT, and angiographic findings were consistent with either renal artery pseudoaneurysm or AV fistula. In most of the cases that required intervention, selective embolization was sufficient, but in one case explorative laparotomy and nephrectomy was required.

**TABLE 2.** Univariate analysis of factors associated with postoperative bleeding following partial nephrectomy

Factor	Postoperative bleeding	
	Odds ratio (95% CI)	p-value
Univariate analysis		
Age	0.873 (0.726-1.050)	0.148
Sex (male vs. female)	0.341 (0.012-9.734)	0.529
Body mass index	0.848 (0.248-2.898)	0.793
Weight	1.041 (0.646-1.679)	0.868
Tumor size	0.261 (0.033-2.041)	0.201
R score	0.718 (0.417-1.518)	0.426
E score	0.727 (0.598-0.952)	0.033 <sup>a</sup>
N score	0.473 (0.287-0.966)	0.305
L score	0.750 (0.426-1.006)	0.638
Operative method (open vs. laparoscopic vs. robot)	0.104 (0.067-0.191)	0.140
Warm ischemic time	0.919 (0.898-0.941)	0.209
Estimated blood loss	0.989 (0.986-0.991)	0.102

CI, confidence interval.

<sup>a</sup>: $p < 0.05$  considered to indicate statistical significance.

## DISCUSSION

The number of newly diagnosed cases of RCC is on the rise, due much to developments in and increased availability of advanced imaging modalities. For this same reason, the number of cases with small localized lesions has also risen. With recent advances in surgical techniques, partial nephrectomy has become the treatment of choice for localized lesions [2]. Nephron sparing through partial nephrectomy has proven advantageous not only for preservation of renal function but also for overall survival for T1a lesions [3]. Furthermore, the oncologic safety for partial nephrectomy has been shown to be comparable to that for radical nephrectomy [3,4].

On the other hand, partial nephrectomy remains far more technically challenging than radical nephrectomy, especially with the use of minimally invasive techniques, with a consequent increase in surgery-associated morbidity. To standardize the classification or grading of renal tumors and as a means of assessing the technical complex-

**TABLE 3.** Clinical characteristics of patients with postoperative bleeding after partial nephrectomy

Patient no.	Age/sex	Presented symptom	Onset (POD)	Tumor size (cm)	Operative method	Nephrometry	EBL	Treatment
1	61/M	Gross hematuria	18	2.0	OPN	8	250	Angioembolization
2	45/F	Gross hematuria	17	3.2	OPN	8	200	Angioembolization
3	48/M	Gross hematuria	30	2.5	OPN	8	400	Angioembolization
4	54/F	Acute flank pain	8	3.1	LPN	7	200	Angioembolization
5	52/M	Bleeding from drain	5	3.1	OPN	8	100	Exploration
6	64/F	Bleeding from drain	1	2.2	OPN	9	300	Angioembolization
7	64/M	Acute flank pain	15	1.5	LPN	7	100	Angioembolization
8	40/M	Gross hematuria	11	6.5	OPN	9	500	Angioembolization
9	73/M	Bleeding from drain	7	1.4	RAPN	8	200	Angioembolization
10	40/F	Pleuritic chest pain	13	1.4	LPN	6	700	Angioembolization
11	74/F	Gross hematuria	4	2.4	OPN	8	100	Angioembolization
12	70/M	Gross hematuria	7	3.5	LPN	6	250	Angioembolization
13	68/M	Gross hematuria	2	1.3	LPN	6	700	Angioembolization

POD, postoperative day; EBL, estimated blood loss; OPN, open partial nephrectomy; LPN, laparoscopic partial nephrectomy; RAPN, robot-assisted laparoscopic partial nephrectomy.

ity of nephron-saving procedures, several classification systems, most notably the R.E.N.A.L. [12,13], preoperative aspects and dimensions used for an anatomical [14], and centrality index (C-index) [15,16] systems, have been proposed.

The R.E.N.A.L. nephrometry scoring system, developed by Kutikov and Uzzo [12], is a system for quantification of the salient anatomy of renal masses. It is seeing increasing use as a clinical tool for guiding management decisions for small renal masses and comparison of clinical outcomes of certain treatment methods, such as partial nephrectomy [13-15]. In particular, it is seeing widespread use in assessing the complexity of planned surgical procedures, such as laparoscopic partial nephrectomy. However, no study to date has reported on postoperative bleeding in relation to R.E.N.A.L. nephrometry scores. In the present study, Student t-test and Pearson chi-square test (for tumor stage and operative method) showed that the E category of the R.E.N.A.L. scoring system was the only parameter to differ between the bleeding and the nonbleeding groups with any statistical significance. That the E category is associated with postoperative bleeding in itself is not surprising, given the method of approach and excision inherent in partial nephrectomy. What is unexpected, nonetheless, is that other parameters, namely the R, N, and L scores and the total R.E.N.A.L. nephrometry score, which were thought to bear some relevance, were found not to differ between the groups with any statistical significance. This may have been due to several factors, one of which may have been the exclusion bias against larger masses less suitable for partial nephrectomy. On the other hand, whereas the univariate analysis showed the E score to bear statistically significant relevance to postoperative bleeding, the multivariate analysis showed that none of the factors was significant. It is possible that the scarcity of cases with significant postoperative bleeding in the present study (13 of 300 cases) may have limited the statistical strength of the parameters. Additionally, the proximity of segmental arteries to the resection margin, anticoagulation/antithrombotic therapy, and presence of coagulopathies, which were not examined in the present study, may have been pertinent factors. Overall, these results suggest that the R.E.N.A.L. nephrometry scores may not be significant predictors of postoperative bleeding.

Whereas Mayer et al. [17] reported that the total nephrometry score, as well as the N and R scores, is predictive for extended warm ischemia time and collecting system entry, Hayn et al. [18] showed that higher total nephrometry scores are associated with increased intraoperative estimated blood loss, warm ischemia time, and length of hospital stay. Furthermore, Liu et al. [19] showed that the N score is the single predictive factor for overall complications and postoperative hemorrhage following minimally invasive nephron-sparing surgery. The difference between these studies and the findings of the present study may be due to several factors. First, the present study included cases involving open partial nephrectomy. Second, a possible

selection bias may have been included in one or more studies in terms of the nature of the renal masses considered for partial nephrectomy.

In the present study, 13 patients out of a total subject population of 300 (4.3%) experienced postoperative bleeding significant enough to require intervention greater than transfusion. Postoperative bleeding after partial nephrectomy has been reported to be in the range of 4.2% to 6% for laparoscopic partial nephrectomy [5]. In the present study, however, the patients included those who underwent partial nephrectomy by any of the three modalities: open, laparoscopic, and robot-assisted. Of these, 7 underwent open procedures, 5 underwent laparoscopic procedures, and 1 underwent robot-assisted partial nephrectomy. Although it was shown in previous studies that minimally invasive procedures yield better postoperative outcomes in terms of complications for partial nephrectomy [20,21], the number of patients succumbing to significant postoperative bleeding was almost equal between the laparoscopic and the open surgery groups. Further analysis of the patients who developed significant postoperative bleeding would be necessary to explain this unexpected finding.

In the present study, the presenting symptom of postoperative bleeding varied from increased drain output to persistent gross hematuria to acute flank pain, and the time of onset also varied from the second postoperative day to the 30th postoperative day. As was reported in previous studies [5], although the presenting symptoms were diverse, CT and percutaneous angiography showed the presence of either renal artery pseudoaneurysms or AV fistulas. Again, as was reported in several previous studies [6,22,23], selective angioembolism was sufficient in 12 of the 13 cases in the present study. However, in one of the cases, explorative laparotomy was necessary to identify and control the bleeding focus.

## CONCLUSIONS

The findings of this study show that whereas higher E scores in the R.E.N.A.L. nephrometry system are associated with significant postoperative bleeding by Student t-test, the univariate and multivariate analyses showed otherwise. Although such bleeding as a whole is a rare occurrence following partial nephrectomy, selective angioembolization in most cases was sufficient for treatment. Nevertheless, owing to significant disparities in the time of onset and presenting symptoms, great vigilance on the part of the surgeon should be practiced for timely identification and intervention.

## CONFLICTS OF INTEREST

The authors have nothing to disclose.

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