Scientific Research

Partial Nephrectomy for Renal Cell Carcinoma: Risk Factors for Acute Post-Operative Hemorrhage and Impact on Subsequent Hospital Course and Complete Nephrectomy Rate. An Analysis of 200 Consecutive Cases

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ABSTRACT

Purpose: Clinical guidelines recommend partial nephrectomy (PN) as the preferred method of surgical excision of the small renal tumor whenever feasible. PN has comparable cancer cure rates to that of radical nephrectomy in this setting, and decreased risk of chronic kidney disease. A recognized devastating complication following partial nephrectomy is acute post-operative hemorrhage (APOH) from the reconstructed kidney. Risk factors for hemorrhage following partial nephrectomy remain poorly elucidated, as does the impact of hemorrhage on subsequent hospital stay. Identification of risk factors for hemorrhage may lead to a better understanding of and reduction of this complication. **Material and Methods:** We utilized a prospectively managed database comprised of patients undergoing open partial nephrectomy at our institution by the same surgical team from January 2006 to July 2012. Clinicopathologic factors assessed APOH for their relationships, including patient age, gender, diabetes, smoking, hypertension, coronary artery disease, American Society of Anesthesia Score (ASA), tumor size, RENAL nephrotomy score, pathologic result, cancer margin status, operative time, and intra-operative blood loss. The impact of APOH on subsequent hospital course was evaluated and compared with the entire cohort. **Results:** Data were analyzed from 200 consecutive patients. We identified 7 patients (3.5%) who experienced APOH. Compared with the entire cohort, APOH resulted in an increased hospital length of stay (median, 5 days; range, 2 - 11 days, p = 0.001), an increased transfusion requirement (median, 6 units; range, 1 - 16 units. p = 0.001), a greater risk of selective angiographic embolization (median, 2 procedures; range, 0 - 3, p = 0.001), and completion nephrectomy (n = 2, p = 0.001). One patient in the APOH group experienced cardiac arrest and was resuscitated. Clinicopathologic factors associated with the increased risk of APOH in the present cohort were male gender (p = 0.03) and hypertension (p = 0.006). **Conclusion:** In the present analysis, APOH was associated with extended hospitalization, the increased transfusion requirement and the need for more ancillary procedures. APOH patients were at significantly increased risk of renal loss. Male gender and hypertension were associated with increased risk for APOH. We have incorporated this information into an APOH risk reduction program at our institution.

Keywords: Kidney Neoplasms; Partial Nephrectomy; Renal Cell Carcinoma

1. Introduction

Clinical guidelines recommend partial nephrectomy (PN) as the preferred method of surgical excision of the small renal tumor whenever feasible [1]. PN has comparable cancer cure rates to that of radical nephrectomy in this setting [2], and decreased risk of chronic kidney disease [3]. A recognized devastating complication following partial nephrectomy is acute post-operative hemorrhage (APOH) from the reconstructed kidney. Risk factors for hemorrhage following partial nephrectomy remain poorly elucidated, as does the impact of hemorrhage on subsequent hospital stay. Identification of risk factors for he-

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morrhage may lead to a better understanding of and reduction of this complication. In the present investigation, we sought to determine risk factors for acute post-operative hemorrhage after partial nephrectomy utilizing a prospectively managed patient database. We also evaluated the impact of APOH on subsequent hospital stay.

2. Material and Methods

A prospectively managed database was utilized comprised of patients undergoing open partial nephrectomy at our institution. The current investigation includes all patients operated from January 2006 to July 2012 by a single surgical team. Clinicopathologic factors assessed for their relationship to APOH included patient age, gender, diabetes, smoking, hypertension, coronary artery disease, American Society of Anesthesia Score (ASA), R.E.N.A.L. nephrotomy score [4], tumor size, pathologic result, cancer margin status, operative time, and intra-operative blood loss. The impact of APOH on subsequent hospital course was evaluated and compared to the entire cohort.

We identified patients with and without APOH. For the purposes of this investigation, APOH was defined as acute post-operative drop in hemoglobin (<8 mg/dl) and radiographic CT scan evidence of either peri-nephric retroperitoneal hematoma or blood within the renal collecting system of the operated kidney. APOH could be associated with acute hypotension (*i.e.*, systolic BP < 100 mmHg), gross hematuria and increasing flank pain, but this was not required for the diagnosis of APOH. Evaluated subsequent hospital course outcome measures included blood transfusion, renal angiography procedure with or without selective renal embolization, and completion nephrectomy.

Univariate statistical analysis was performed using the X^2 test and Fisher's exact test as appropriate for categorical data [5]. These included gender, hypertension, smoking, diabetes, coronary artery disease, American Society of Anesthesiologists (ASA) score (dichotomized as 1 and 2 versus 3, 4 and 5), tumor laterality, pathologic result (cancer versus benign), surgical margin status (*i.e.*, cancer at margin versus not). The Mann-Whitney test [5] was utilized for continuous data including age, tumor size, R.E.N.A.L. nephrotomy score, operative time, renal artery clamp time, and intra-operative blood loss.

In assessing the impact of APOH on subsequent hospital course, measured variables were dichotomized as length of stay (LOS) ≤3 days versus >3 days; transfusion as none versus ≥1 unit of packed red blood cell (PRBC); no angiographic embolization versus angiographic embolization regardless of number of procedures performed

for each patient; completion nephrectomy as either performed or not performed.

3. Results

Data were analyzed from 200 consecutive patients operated from January 1st, 2006 to July 30th 2012. **Table 1** presents the clinicopathologic features for the APOH cohort and the non-APOH cohort.

APOH was identified in 7 patients. The only clinicopathologic factor associated with increased risk of APOH in the present cohort were male gender (p = 0.03) and hypertension (p = 0.006). This data is shown in **Table 1**. Only a subset of the current cohort had calculation of R.E.N.A.L. nephrotomy score following its description in 2009. In the present investigation, R.E.N.A.L. nephrotomy score did not correlate with APOH in the subset evaluated. Age, diabetes, smoking, coronary artery disease, American Society of Anesthesia Score (ASA), tumor size, pathologic result, cancer margin status, operative time, and intra-operative blood loss did not correlate with APOH.

Table 2 illustrates the impact of APOH on subsequent hospital course. Compared to the entire cohort, APOH resulted an increased hospital length of stay (median, 5 days; range, 2 - 11 days, p = 0.001), increased transfusion requirement (median 6 units; range, 1 - 16 units, p = 0.001), greater risk of selective angiographic embolization (median, 2 procedures; range, 0 - 3, p = 0.001), and greater risk of completion nephrectomy (n = 2, p = 0.001). One patient in the APOH group experienced cardiac arrest and was resuscitated. There were no deaths in either cohort.

4. Discussion

It is estimated that there will be 65,140 new cases of kidney cancer in the United States in 2013, and the incidence is increasing [6,7]. Greater than 70% of newly detected renal tumors are incidentally detected, often less than 4 cm [8], and potentially amenable to either surveillance (lesions ≤ 2 cm), emerging percutaneous treatments (*i.e.*, radiofrequency ablation; cryosurgery), compete nephrectomy and partial nephrectomy [9]. For those patients felt best to be managed with surgical excision, clinical guidelines recommend partial nephrectomy (PN) as the preferred method of surgical excision of the small renal tumor whenever feasible [1]. PN has comparable cancer cure rates to that of radical nephrectomy in this setting [2], and decreased risk of chronic kidney disease [3]. Despite this, investigators have reported that PN appears to be underutilized in the United States, even in

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Table 1. Clinical features of patient with and without acute post-operative hemorrhage.

	APOH Cohort	Non-APOH Cohort	
Pt. No.	7	193	
Age (years)	60 (54 - 73)	58 (28 - 84)	p = NS
Tumor Size (cm)	3.1 (2.2 - 7.5)	2.8 (0.6 - 11)	p = NS
Gender			p = 0.03
Male	7 (100%)	115 (59%)	
Female	-	78 (41%)	
Tumor Side			p = NS
Left	3 (42%)	92 (48%)	
Right	4 (57%)	101 (52%)	
Hypertension	7 (100%)	96 (49%)	p = 0.006
Diabetes	1 (14%)	23 (12%)	p = NS
Smoking	3 (42%)	84 (43%)	p = NS
CAD	1 (14%)	22 (11%)	p = NS
ASA	2 (2 - 3)	2 (2 - 3)	p = NS

APOH = acute post-operative hemorrhage; Pt. No. = patient number; ASA = American Society of Anesthesiology score; age, tumor size and ASA are expressed as the median and range; NS = statistically not significantly different.

Table 2. Impact of acute post-operative hemorrhage on subsequent hospital course.

	APOH Cohort	Non-APOH Cohort	
Length of Stay			p = 0.001
≤3 days	1 (14%)	140 (72%)	
>3 day	6 (85%)	53 (27%)	
Transfusion			p = 0.001
none	1 (14%)	184 (95%)	
≥1 unit PRBC	6 (85%)	9 (5%)	
Renal Angiography			p = 0.001
none	2 (28%)	-	
≥1 procedure	5 (72%)	193 (100%)	
Completion Nephrectomy			p = 0.001
yes	2 (28%)	4 (2%)	
no	5 (72%)	189 (98%)	

APOH = acute post-operative hemorrhage; PRBC = packed red blood cells; renal angiography denotes angiogram of the bleeding kidney with or without attempted embolization.

patients with pre-existing renal insufficiency who may benefit most from PN [9]. Investigators utilizing the National Cancer Database recently reported a decrease in the median tumor size of stage 1 tumors from 4.1 to 3.6 cm between 1993 and 2004 [10], indicating that many of these tumors may be amenable to partial nephrectomy.

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However, a recent analysis utilizing the Surveillance, Epidemiology ad End Results program during that same time period showed that in the US only 35.2% of patients with T1a (≤4 cm) renal masses received partial nephrectomy between 1999 and 2006 [11]. That same study revealed that only 50% of tumors <2 cm were treated with partial nephrectomy, and 48% of tumors between 2 and 4 cm were treated with partial nephrectomy [12].

There is increasing evidence that surgically induced chronic kidney disease [13,14] following complete nephrectomy is associated with increased risk of cardiovascular disease including death [15,16] and metabolic adverse consequences including anemia, acidosis, and osteoporosis [17,18] and associated significant adverse health consequences.

The reason for underutilization of partial nephrectomy compared to radical nephrectomy for management of the T1a (<4 cm) and select T1b 4 - 7 cm) renal mass is unclear, and is beyond the scope of the current investigation. Investigators have suggested that the explanation may be multifactorial, including physician and patient factors, and that the decision making requires complex multi perspective reasoning [19]. It is generally recognized that partial nephrectomy is a complex procedure requiring surgical expertise, a dedicated operating room team and advanced surgical technology, and that partial nephrectomy is associated with increased surgical risk both intra-operative and post-operative, the most devastating being post-operative hemorrhage. The present study sought to identify risk factors for APOH after partial nephrectomy. Though a rare event, APOH increased the hospital length of stay, the transfusion rate, the need for ancillary procedures and most importantly, the complete nephrectomy rate which was 29% in the APOH cohort compared to 2% in the non-APOH group. Furthermore, we sought to identify risk factors associated with APOH. So that such knowledge may allow preemptive risk reduction. At our institution all hypertensive males are treated under the care of a cardiologist to maximize hypertension management for at least 1 month prior to partial nephrectomy. In addition, we have instituted a peri-operative protocol to maintain normotensive status throughout the intra-operative and post-operative period. Whereas in the past all patients received PRN supplemental meds for hypertension, now our protocol administers that medication (usually beta-blockade) as standing order with hold parameter (*i.e.* Systolic BP < 100 mmHg or HR < 60 bpm). We attempt to maintain a mean arterial pressure of 70 - 80. Since the institution of this protocol in October 2011 we have not experienced an APOH. During this period, our patient criteria, volume, surgical technique and post-operative pathway [20] remain constant.

5. Conclusion

In the present analysis, APOH was associated with extended hospitalization, the increased transfusion requirement and the need for more ancillary procedures. APOH patients were at significantly increased risk of renal loss. Male gender and hypertension were associated with increased risk for APOH. We have incorporated this information into an APOH risk reduction program at our institution.

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