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Brief communication (Original)

Predictive factors for postoperative complications in radical nephrectomy for renal cell carcinoma

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Background: Radical nephrectomy is the treatment of choice for large renal cell carcinoma (RCC).
Objectives: To describe the complications after radical nephrectomy for suspected or proven RCC and analyze the risk factors.
Materials and methods: We retrospectively reviewed medical records from 110 patients who underwent radical nephrectomy for RCC in our institution between January 2007 and December 2013. The clinicopathological data of all patients were recorded and complications were graded using modified Clavien classification. Univariate and multivariate analysis was made of the predictive factors for complications.
Results: Fifty postoperative complications occurred in 34 patients (31%) within 30 days, including 11% transfusion related complications. There were 22% minor complications (6% grade 1, 16% grade 2) and 9% major complication (5% grade 3, 2% grade 4, and 2% grade 5). The most common complications were transfusion-related, re-laparotomy because of bleeding, and prolong ileus. In univariate analysis, pathological T-stage (P = 0.001), American Society of Anesthesiologists (ASA) score (P = 0.007), tumor size (P = 0.01), and tumor diameter >4 cm (P = 0.03) were significant predicting factors. Major Charlson comorbidity index (CCI >2) was the only significant factor for major complications (P = 0.04). In multivariate analysis, ASA score was a significant independent predictor for overall complications (odds ratio 4.83, P = 0.01).
Conclusions: ASA score was a significant predictive factor for overall postoperative complications. Comorbidities was also a predictor for major complications in radical nephrectomy. Preoperative risk stratification for complications should be considered during decision-making and for proper counseling of patients.

Keywords: Complication, radical nephrectomy, renal cancer

Renal cell carcinoma (RCC) comprises approximately 2% of all cancer diagnoses [1]. The incidence, particularly in asymptomatic patients, has increased because of the development of imaging techniques and widespread use of the cross-sectional imaging studies [2]. Radical nephrectomy (RN), first described by Robson [3], is still the treatment of choice for large RCC. With the increasing incidence of RCC in elderly populations, the age of the patient and their comorbidities are the important factors for predicting surgical outcomes besides tumor characteristics [4, 5]. This strengthens the importance of preoperative decision-making for those who might benefit from surgical treatment of RCC.

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Although complication rates are often used to compare the success of renal surgical techniques, there is no definition for complications or guidelines for reporting surgical outcomes. Martin et al. [6] proposed 10-standard criteria that should be incorporated into the analysis of data for surgical complications in pancreatectomy, esophagectomy, and hepatectomy. These criteria included the method of accruing data, duration of follow-up, inclusion of outpatient information, definition of complications, mortality and morbidity rates, procedure-specific complications, grading system, length of stay data, and risk factor analysis. More recently in 2007, Donat [7] modified the reporting criteria for procedure-specific complications in urologic oncologic surgery including RN.

One standardized system, that systematically scores the severity of surgical complications, is the Clavien–Dindo system (CCSC) [8]. The CCSC has

been developed and validated for complication assessment in general surgery; however, it can be adjusted to any surgical procedures.

There were several studies that analyzed the correlation between preoperative predictive factors and postoperative complications in RN [9-13]. The purpose of this study was to describe the postoperative complications after RN in a single-center experience and identify the risk factors for complications by using standardized reporting criteria in Thai patients treated in a university referral hospital.

Materials and methods

We retrospectively reviewed medical records of all patients who underwent RN (by either open or laparoscopic approach) in our institution from January 2007 to December 2013. One hundred and ten patients were identified and included in this study.

Indication for surgery in all patients was a large enhancing renal mass suspicious for RCC on preoperative computed tomography (CT) or magnetic resonance imaging (MRI). All operations were performed under general anesthesia. The kidney was totally removed with Gerota's fascia in standardized fashion. The ipsilateral adrenal gland was concomitantly removed in case of upper pole tumor and lymph node dissection was performed when lymphadenopathy was detected.

The choice of surgical approach was chosen based on tumor size, patient, and surgeon preference. In the open approach, either a subcostal incision or midline incision was made. In the laparoscopic approach, all cases were performed with the transperitoneal approach with 3 or 4 laparoscopic trocars.

Postoperative management included removal of the close-suction drain when the content was clear and the amount less than 30 ml/day. The patient was discharged once able to walk and tolerate food.

The study was approved by the Institution Review Board (IRB) of King Chulalongkorn Memorial Hospital Ethics Committees. Data are based on chart reviews. All patients operated on had given informed consent before being treated (IRB No.129/57).

Date collection and statistical analysis

Studied parameters included age, sex, body mass index (BMI), American Society of Anesthesiologists (ASA) score, Charlson Comorbidity Index (CCI), tumor size, tumor laterality, previous abdominal surgery, operative approach, metastasis at time of diagnosis, 2002 TNM classification, Fuhrman nuclear grade and subtype of renal mass.

The CCI is a validated comorbidity measurement based on relative risks of mortality for 19 conditions observed during a longitudinal study of 559 internal medicine cases [14]. The CCI was categorized as described by Santos et al. [15], by which minor comorbidity is defined as a CCI score of ≤2 and major comorbidity is defined as a CCI score of >2.

Postoperative complications within 30 days of surgery were categorized according to the CCSC. Minor complication are defined as grade 2 and major complication are defined as grade >2. Complication that was expected after nephrectomy, such as a decline of renal function but not leading to dialysis, was not included in this study. In patients with multiple complications, all complications were graded and the highest grade was used for statistical analysis.

Categorical data were reported as count (%) and continuous data were reported as median (IQR). Patient parameters in univariate analysis for predicting postoperative complications include age, sex, body mass index (BMI), ASA score, CCI, tumor size, tumor laterality, previous abdominal surgery, surgical approach, metastasis at time of diagnosis, pathological T stage, Fuhrman nuclear grade, and subtype of renal mass.

The Chi-square and Fisher exact tests were used to compare the difference among the categorical variables. A Student *t* test was used for continuous variables. $P < 0.05$ was considered statistically significant in comparison. Variables with $P < 0.05$ in univariate analysis were selected in a multivariate logistic regression model to assess the independent predictive factors for postoperative complications. All statistical analyses were performed using SPSS version 16.0.

Results

Patient's demographic data and pathological reports are presented in **Table 1**. RN was mostly performed using an open approach (83%). Median patient age was 60 years. Median tumor size was 8.3 cm. Fifty patients (46%) had major comorbidities (CCI >2) and 11 patients (10%) had metastasis at the time of diagnosis.

Pathology reports showed RCC in 91 patients (83%) and clear cell cancer was the most common subtype (56%). Eleven patients (10%) were diagnosed

as benign disease including 5 angiomyolipoma, 2 chronic pyelonephritis, 1 oncocytoma, 1 cystic nephroma, 1 xanthogranulomatous pyelonephritis and 1 hemorrhagic cyst. Eight patients (7%) had other types of cancer (3 urothelial carcinoma, 3 malignant spindle cell tumor, 1 metastatic adenoma, and 1 malignant epithelioid angiomyolipoma).

Table 1. Patient's demographic data and pathological reports (N = 110)

Variables	n (%)
Age, years, mean (SD)	60 (13.3)
BMI, kg/m^2, mean (SD)	24.3 (4.7)
Male sex, n (%)	63 (57)
Operative approach, n (%)	
Laparoscopic	19 (17)
Open	91 (83)
Metastasis at time of diagnosis, n (%)	11 (10)
ASA score, n (%)	
1–2	89 (81)
3–4	21 (19)
Tumor diameter, cm. , mean (SD)	8.3 (4.9)
Tumor diameter, n (%)	
<4cm	28 (26)
>4cm	82 (75)
Charlson's comorbidity index, n (%)	
0	18 (16)
1	16 (15)
2	26 (24)
3	24 (22)
4	17 (16)
5	2 (2)
≥6	7 (6)
Previous abdominal surgery, n (%)	9 (8)
Renal cell carcinoma pathological stage, n (%)	
pT1	34 (31)
pT2	19 (17)
pT3	33 (30)
pT4	5 (5)
Benign tumor	11 (10)
Other malignancy	8 (7)
Tumor subtype, n (%)	
Clear cell RCC	62 (56)
Papillary RCC	18 (16)
Chromophobe RCC	4 (4)
RCC, not otherwise specified	7 (6)
Benign and other malignancy	19 (17)
Fuhrman nuclear grade, n (%)	
1–2	47 (43)
3–4	34 (31)
Unclassified	29 (26)

BMI = body mass index, ASA = American Society of Anesthesiologists, RCC = renal cell carcinoma, SD = standard deviation

Complications

There were 50 postoperative complications occurring in 34 patients (31%) within 30 days after surgery. The distribution of patients according to the grade of complication as per Clavien–Dindo classification is presented in **Table 2**. There were 22% of patients with minor complications (Clavien grade 1–2) and 10% of patients with major complication (Clavien 3–5). There were two (2%) fatal complications leading to perioperative deaths (Clavien grade 5).

The details of complications classified by event and management are summarized in **Table 3**. The most common minor complications were anemia requiring blood transfusion (n = 12) and prolonged ileus requiring total parenteral nutrition (n = 4). The most common major complication was relaparotomy because of bleeding (n = 5).

Table 2. Thirty-day postoperative complications classified by Clavien Classification* (N = 110)

Clavien Classification	Number of patients (%)
No complications	76 (69)
Grade 1	7 (6)
Grade 2	17 (16)
Grade 3a	1 (1)
Grade 3b	5 (5)
Grade 4a	2 (2)
Grade 4b	0 (0)
Grade 5	2 (2)

*Highest grade of complication was used to classify in patient with more than one complication

Table 3. Detail of complications and managements by events (n = 50)

Clavien grade	Number	Complication (n)	Management
1	7	Prolonged ileus (1)	Conservative
		Wound infection (1)	Wound dressing
		Prolonged fever (1)	Conservative
		Atelectasis (1)	Chest physiotherapy
		Vertigo (1)	Conservative
		Prolonged drain leakage (1)	Conservative
		Acute Tubular necrosis (1)	Conservative
2	27	Anemia (12)	Transfusion
		Prolonged ileus (4)	TPN
		Pneumonia (2)	Antibiotic
		Urinary tract infection (2)	Antibiotic
		Pulmonary embolism (2)	Anticoagulant
		Hypertensive urgency (2)	Antihypertensive
		Atrial fibrillation (1)	Anticoagulant
		Transient ischemic attack (1)	Anticoagulant
		Partial small bowel obstruction (1)	TPN
3a	3	Pleural effusion (1)	PCD
		Congestive heart failure (1)	Central line insertion
		Intraabdominal collection (1)	PCD
3b	6	Postoperative bleeding (5)	Relaparotomy
		Wound dehiscence (1)	Secondary wound closure
4a	5	Acute renal failure (2)	Hemodialysis
		Epilepsy (1)	Admission to ICU
		Ischemic stroke (1)	Admission to ICU
		Septic shock (1)	Admission to ICU
5	2	Rupture aortic aneurysm (1)	-
		Multi-organ failure leading to death (1)	-

TPN = total parenteral nutrition, PCD = percutaneous drainage, ICU= intensive care unit

Predictive factors for postoperative complications

All analyzed data are shown in **Table 4**. In univariate analysis, pathological T-stage ($P = 0.001$), ASA score ($P = 0.007$), tumor size ($P = 0.01$), and tumor diameter >4 cm ($P = 0.03$) were significant parameters predicting overall postoperative complications. In multivariate analysis, ASA score was the only significant independent predictor for overall complications; odds ratio 4.83 (1.4–16.66), $P = 0.01$.

For major complication, major comorbidity (CCI >2) was the only significant parameter that increased the risk of complication compared with minor comorbidity (CCI ≤2); 16% vs. 3%, $P = 0.04$. (Data is not shown in the Table).

Table 4. Univariate and multivariate analysis between all predictive factors and overall postoperative complications

Parameters	Univariate			Multivariate	
	Without complications (n = 76)	With complications (n = 34)	*P*	OR (95% CI)	*P*
Age, years, mean (SD)	59.76 (11.97)	59.82 (16.10)	0.98	–	–
BMI, kg/m^2, mean (SD)	24.84 (4.76)	22.91 (4.49)	0.05	–	–
Sex, n (%)			0.54	–	–
Male	42 (66.7)	21 (33.3)			
Female	34 (72.3)	13 (27.7)			
Operative approach, n (%)			0.17	–	–
Laparoscopic	16 (84.2)	3 (15.8)			
Open	60 (65.9)	31 (34.1)			
Metastasis at diagnosis, n (%)			0.09	–	–
Mx/M 0	71 (71.7)	28 (28.3)			
M 1	5 (45.5)	6 (54.5)			
ASA score, n (%)			0.007*		0.01*
1–2	67 (75.3)	22 (24.7)		–	
3–4	9 (42.9)	12 (57.1)		4.83(1.4–16.66)	
Tumor diameter, cm, mean (SD)	7.47 (4.6)	10.06 (5.25)	0.01*	1.07(0.93–1.23)	0.33
Tumor diameter, n (%)			0.03*		0.18
≤4 cm	24 (85.7)	4 (14.3)		–	
>4 cm	52 (63.4)	30 (36.6)		3.77(0.54–26.22)	
Tumor subtype, n (%)			0.13	–	–
Clear cell RCC	47 (75.8)	15 (24.2)			
Papillary RCC	9 (50)	9 (50)			
Chromophobe RCC	3 (75)	1 (25)			
RCC, not otherwise specified	3 (42.9)	4 (57.1)			
Benign tumor	9 (81.8)	2 (18.2)			
Other malignancy	5 (62.5)	3 (37.5)			
Fuhrman nuclear grade, n (%)			0.09	–	–
1–2	36 (76.6)	11 (23.4)			
3–4	20 (58.8)	14 (41.2)			
Pathological T-stage, n (%)			0.001*		0.586
pT1	27 (79.4)	7 (20.6)		–	Ref
pT2	16 (84.2)	3 (15.8)		0.25(0.33–1.93)	0.184
pT3	20 (60.6)	13 (39.4)		0.55(0.88–3.42)	0.521
pT4	0 (0)	5 (100)		1.297x10^9	0.999
Charlson's comorbidity index, n (%)			0.29	–	–
<2	44 (73.3)	16 (26.7)			
≥2	32 (64)	18 (36)			
Previous abdominal surgery, n (%)			0.27	–	–
No	68 (67.3)	33 (32.7)			
Yes	8 (88.9)	1 (11.1)			

BMI = body mass index, ASA = American Society of Anesthesiologists, RCC = renal cell carcinoma.

Discussion

Currently, RN is the treatment of choice for large renal tumors. Studies specifically looking at the complications associated with RN have been reported, but not all of them were using standardized reporting criteria. Thus, additional literature adopting rigorous methodology for reporting of surgical complications following RN is needed.

The range of complication rates after RN in patients with RCC were 6%–51%. There were many predictive factors for complications after RN. From previous studies, ASA classification, weight loss >10%, CCI, pathological stage, patient age, operative time, higher volume surgeon, and chronic pulmonary disease were associated with complication rates after RN [5, 9, 12, 16-22]. Postoperative complication rates and predictive factors in selected series are summarized in **Table 5**.

In our study, the overall complication rate was 31%, with 9% being major complications. Blood transfusion is the most common complication in our study (11%). All of our Clavien grade 4 complications were medical complications.

Two deaths occurred in our study cohort (2%). The first patient was a 76-year old man with history of brain infarction who presented with 20-cm renal tumor. He had aspiration pneumonia, and died from septicemia. The second patient was a 50-year old man with a chronic dissecting aortic aneurysm type B and end stage renal disease. He presented with a ruptured 3-cm renal tumor and underwent laparoscopic RN. He had postoperative bleeding and required laparotomy to stop bleeding. The immediate postoperative period was uneventful; however, the patient died because of a ruptured dissecting aorta 1 week after surgery.

Although complication rates are often used to compare the success of renal surgery, there is no consensus about the criteria for reporting postoperative complications. Therefore, comparison cannot be made directly between studies. The present study shows the CCSC is feasible and easy to apply for grading complications after surgery. Moreover the advantage of CCSC, the grading system, is followed by the therapeutic consequences of complications, which is important for the patient's outcome.

Limitations of our study include its retrospective, nonrandomized study design. The procedures were performed by multiple surgeons, which can affect surgical outcomes. Long term oncological outcomes and renal function study were not specifically assessed and interpreted in this study.

Conclusion

RN represents safe surgical treatment for large renal tumors. It offers an acceptable perioperative complication rate which, mostly, can be effectively managed conservatively. ASA score was a significant predictive factor for overall postoperative complications and major comorbidities was the predictor for major complications. Our analysis consists of accurate information that can represent a useful tool for counseling patients before surgery.

No authors have any conflict of interest to declare.

Table 5. Postoperative complication rate and predictive factors of radical nephrectomy in selected series

Study	Year	Patients (n)	Complication rate	Standard system	Risk factors
Tan et al. [17]	2011	8,003	Open 5.3% Lap 36.9%	No	high volume surgeon and hospital
Stephenson et al. [18]	2004	688	16%	5-tiered scale	age, operative time, pathological stage
Dunn et al. [20]	2000	33	Open 55% Lap 37%	No	–
Joudi et al. [22]	2007	18,575	18.2%	ICD-9	age, male gender, comorbidity, hospital location
Hennus et al. [9]	2012	158	34%	CCSC	comorbidity, tumor stage
Abouassaly et al. [16]	2011	20,286	34.1%	ICD-9 and 10	age, comorbidity

ICD = International Classification of Diseases, CCSC = Clavien Classification of Surgical complications

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