Complications of radical nephrectomy for renal cell carcinoma: a retrospective study comparing transperitoneal and retroperitoneal approaches using a standardized reporting methodology in two Chinese centers

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Abstract

The reporting of complications following transperitoneal and retroperitoneal open radical nephrectomy (RN) is nonstandardized. This study aimed to compare early complications between the two approaches using a standardized reporting methodology in a large contemporary cohort. Between 1996 and 2009, 558 patients underwent open RN for renal cell carcinoma (RCC) in our two centers (424 from Sun Yat-sen University Cancer Center and 134 from the First Affiliated Hospital of Sun Yat-sen University). Records were reviewed for clinicopathologic features and complications. Complications were graded using the Clavien system based on the severity of impact. One hundred and five patients (18.8%) had one or more early complications (168 complications overall). The overall rates of grades I to V complications were 5.6%, 10.8%, 2.2%, 0.4%, and 0.2%, respectively. Patients who underwent transperitoneal RN did not experience more overall or procedure-related complications than those who underwent retroperitoneal RN ($P = 0.911$ and $P = 0.851$, respectively). On subgroup analysis, neither grade I/II nor grades III–V complications were significantly different between the transperitonal RN and retroperitoneal RN groups. Multivariate analysis showed that for any grade of complication, age ($P = 0.016$) and estimated blood loss ($P = 0.001$) were significant predictors. We concluded that open RN is a safe procedure associated with low rates of serious morbidity and mortality. Compared with retroperitoneal RN, transperitoneal RN was not associated with more complications. Older patient and more blood loss at surgery were independent predictors for higher early postoperative complication rates.

Keywords Radical nephrectomy, complication, standardized reporting methodology

Renal cell carcinoma (RCC) accounts for approximately 3% of all adult malignancies and is the most lethal genitourinary tumor. More than 40% of RCC patients die of the disease¹². Nephrectomy, either partial or radical, is the most effective treatment for this disease. Although laparoscopic or partial nephrectomy is widely used in early stage RCC, a large proportion of patients with RCC undergo open radical nephrectomy (RN). In recent years, only approximately 44.9% RN³ have been performed with laparoscopy and 25.1%–32.2% RCC patients undergo partial nephrectomy (PN)⁴,⁵, according to data from Surveillance, Epidemiology, and End Results (SEER), Nationwide Inpatient Sample, and National Cancer Data Base. On reviewing the literature, we found morbidity of open RN ranged from 3.3% to 54%⁶–¹⁰. As a result of the lack of rigorous reporting using standardized methodologies, the reported complication rates vary widely between medical centers. This makes it difficult to assess surgical techniques and preoperative patient education.

In the past, several studies have tried to compare the complications of open transperitoneal and retroperitoneal RN⁸,¹⁷,¹⁸ but were limited by small sample size or nonstandardized reporting methods. Recently, researchers have compared complication rates between the two approaches in patients undergoing laparoscopic RN, although none used standardized reporting methodology. Thus, it remains unclear whether transperitoneal RN is associated with more
Complications of radical nephrectomy

Zhi-Ling Zhang et al.

Complications were categorized principally according to the literature of the early complications of procedures and/or the intensity of the treatment required. Recently, 10 criteria complications are graded according to the severity of their impact from our renal tumor database. After reviewing the charts, outpatient notes, and correspondence with local physicians, we retrospectively recorded the complication rate. Early complications were defined as any deviation from the normal postoperative course occurring within 90 days after surgery, and graded according to the five-tier modified Clavien system. Martin et al.’s 10 criteria for accurate and comprehensive reporting of surgical complications were applied. Complications were categorized principally according to the organ and/or system involved. Ileus was defined as nil by mouth status maintained beyond postoperative day 5 or the postoperative placement of a nasogastric tube. Acute renal failure was defined as an elevation in serum creatinine greater than 50% from baseline or hemodialysis requirement. A postoperative hemorrhagic episode was defined as any postoperative acute bleeding that resulted in a decrease in serum hemoglobin below 80 g/L, hemodynamic instability, or reoperation. Chylous ascites was suspected when there was increased drain output of milky-colored fluid after the start of oral intake food and was confirmed by analysis of ascitic fluid obtained from the drain. Other specific conditions were verified based on routine diagnostic studies.

Statistical analysis

Continuous variables were compared using Student’s t test for normally distributed data and the Mann-Whitney U test for non-normally distributed data. Categorical variables were compared using the chi-square and Fisher’s exact tests. Logistic regression analysis was used to identify variables that were associated with complications using a stepwise forward selection procedure. All statistical analyses were conducted using the SPSS v.13.0 statistical software package (SPSS, Chicago, IL, USA). In all cases, P < 0.05 was considered statistically significant.

Results

Patient information and clinicopathologic features

A total of 360 male and 198 female RCC patients were included in this study, with a median age of 52 years (range, 4–83 years). Median follow-up was 45 months (range, 3–147 months). The patients’ clinicopathologic parameters are listed in Table 1.

Transperitoneal RN was used more often in RCC patients with high American Society of Anesthesiologists scores (P = 0.001), larger tumors (P < 0.001), higher N category (P < 0.001), higher M category (P = 0.001), and lower body-mass index (P = 0.008). However, transperitoneal RN was associated with higher volumes of estimated blood loss (P = 0.001). Other clinicopathologic parameters, including age, sex, operative time, length of hospital stay, and transfusion rate, were not significantly different between the two groups.

Complications

The details of complications are listed in Table 2. Of the 558 patients, 105 (18.8%) had one or more postoperative complications. Thirty-eight patients had multiple adverse events (101 complications) and 67 patients had a single adverse event (67 complications), resulting in a total of 168 postoperative complications. The overall rates of grades I to V complications were 5.6%, 10.8%, 2.2%, 0.4%, and 0.2%, respectively.

In the transperitoneal RN group, the complication rate was...
19.0% (66/347), of which 4.6% were grade I, 11.8% were grade II, 2.0% were grade III, 0.3% were grade IV, and 0.3% were grade V. In the retroperitoneal RN group, the complication rate was 18.5% (39/211); the overall rates of grades I to V complications were 7.1%, 9.0%, 1.9%, 0.5%, and 0, respectively. Patients who underwent transperitoneal RN did not experience more complications than those who underwent retroperitoneal RN (P = 0.911). On subgroup analysis, neither grade I/II nor grades III–V complications showed any significant differences between the transperitoneal RN and retroperitoneal RN groups.

There were 41 procedure-related complications in 32 patients (Table 3). The procedure-related complication rate did not differ significantly between the transperitoneal RN and retroperitoneal RN groups (6.1% vs. 5.2%, P = 0.851). No grade V procedure-related complications occurred. Ileus and chylous ascites occurred in 2.3% and 1.4% of patients who underwent transperitoneal RN, respectively. No ileus or chylous ascites occurred in those who underwent retroperitoneal RN.

One patient died of congestive heart failure, and 6 patients needed reoperations for severe complications. The most common complication categories were gastrointestinal (23.8%), bleeding (15.5%), pulmonary (13.7%), genitourinary (11.3%), cardiac (10.7%), and infectious (10.7%). Table 2 shows the frequency of individual complications within each category.

Predictors of postoperative complications

Univariate analysis showed age (P = 0.008), American Society of Anesthesiologists score (P = 0.013), operative time (P = 0.012), and estimated blood loss (P = 0.001) to be significant in predicting the occurrence of a complication. On multivariate analysis for any grade of complication, age (P = 0.016) and estimated blood loss (P = 0.001) were significant predictors (Table 4).

Stage (P = 0.013), operative time (P = 0.007), and estimated
### Table 2. Overall postoperative complication data of 568 patients with renal cell cancer

| Complication                                      | Total   | TPRN (n = 347) | RTPRN (n = 211) | P       |
|---------------------------------------------------|---------|----------------|-----------------|---------|
| Patients with complications (n, %)                | 105 (18.8) | 66 (19.0)       | 39 (18.5)        | 0.911   |
| Total number of complications                     | 168     | 108            | 60              | 0.568   |
| Grade I/II complications (n, %)                   | 91 (16.3) | 57 (16.4)       | 34 (16.1)        | 1.000   |
| Grade I                                           | 31 (5.6)  | 16 (4.6)        | 15 (7.1)         |         |
| Grade II                                          | 60 (10.8) | 41 (11.8)       | 19 (9.0)         |         |
| Grades III–V complications (n, %)                 | 14 (2.5)  | 9 (2.6)         | 5 (2.4)          | 1.000   |
| Grade III                                         | 11 (2.2)  | 7 (2.0)         | 4 (1.9)          |         |
| Grade IV                                          | 2 (0.4)   | 1 (0.3)         | 1 (0.5)          |         |
| Grade V                                           | 1 (0.2)   | 1 (0.3)         | 0               |         |
| Gastrointestinal (23.8%, n = 40)                  | 40       | 27             | 13              | 0.504   |
| Ileus                                             | 8        | 8              | 0               |         |
| SBO                                               | 1        | 1              | 0               |         |
| Diarrhea                                          | 9        | 5              | 4               |         |
| Fistula, intestinal                               | 2        | 1              | 1               |         |
| Constipation                                      | 5        | 2              | 3               |         |
| Emesis                                            | 7        | 4              | 3               |         |
| Colitis                                           | 3        | 1              | 2               |         |
| Chylos ascites                                    | 5        | 5              | 0               |         |
| Infectious (10.7%, n = 18)                        | 18       | 15             | 3               | 0.082   |
| Fever                                             | 15       | 14             | 1               |         |
| Sepsin                                            | 1        | 0              | 1               |         |
| Cholecystitis                                     | 2        | 1              | 1               |         |
| Wound (3.6%, n = 6)                               | 6        | 4              | 2               | 0.312   |
| Seroma                                            | 6        | 4              | 2               |         |
| Genitourinary (11.3%, n = 19)                     | 19       | 9              | 10              | 0.228   |
| Renal failure                                     | 16       | 9              | 7               |         |
| Urinary retention                                 | 3        | 0              | 3               |         |
| Cardiac (10.7%, n = 18)                           | 18       | 11             | 7               | 1.000   |
| Arrhythmia                                        | 8        | 5              | 3               |         |
| Hypotension                                       | 6        | 2              | 4               |         |
| Congestive heart failure                          | 3        | 3              | 0               |         |
| Angina                                            | 1        | 1              | 0               |         |
| Pulmonary (13.7%, n = 23)                         | 23       | 12             | 11              | 0.380   |
| Atelectasis                                       | 1        | 1              | 0               |         |
| Pneumonia                                         | 7        | 3              | 4               |         |
| Respiratory distress                              | 3        | 2              | 1               |         |
| Pneumothorax                                      | 4        | 2              | 2               |         |
| Pleural effusion                                  | 8        | 4              | 4               |         |
| Bleeding (15.5%, n = 26)                          | 26       | 19             | 7               | 0.302   |
| Postoperative bleed other than gastrointestinal    | 6        | 4              | 2               |         |
| Anemia requiring transfusion                      | 20       | 15             | 5               |         |
| Thromboembolic (5.4%, n = 9)                      | 9        | 8              | 1               | 0.164   |
| Deep venous thrombosis                            | 1        | 1              | 0               |         |
| Pulmonary embolus                                 | 1        | 1              | 0               |         |
| Superficial phlebitis                             | 1        | 1              | 0               |         |
| Thrombocytopenia                                  | 6        | 5              | 1               |         |
| Neurological (2.4%, n = 4)                        | 4        | 2              | 2               | 0.635   |
| Vertigo                                           | 1        | 0              | 1               |         |
| Loss of consciousness                            | 1        | 1              | 0               |         |
| Seizure                                           | 2        | 1              | 1               |         |
| Others (3.0%, n = 5)                              | 5        | 1              | 4               | 0.070   |
| Acidosis                                          | 1        | 0              | 1               |         |
| Rash                                              | 4        | 1              | 3               |         |

TPRN, transperitoneal radical nephrectomy; RTPRN, retroperitoneal radical nephrectomy; ASA, American Society of Anesthesiologists.
### Table 3. Procedure-related complications in patients treated with TPRN and RTPRN

| Complication                          | Total   | Grade |
|---------------------------------------|---------|-------|
|                                       |         | I     | II    | III   | IV    |
| **TPRN (n, %)**                       |         |       |       |       |       |
| Retroperitoneal hemorrhage            | 21 (6.1)| 6 (1.7)| 9 (2.6)| 5 (1.4)| 1 (0.3)|
| Fistula, intestinal                   | 4       | 0     | 0     | 3     | 1     |
| Bowel obstruction                     | 8       | 0     | 8     | 0     | 0     |
| Acute renal failure                   | 9       | 8     | 0     | 1     | 0     |
| Chylous ascites                       | 5       | 0     | 4     | 1     | 0     |
| Pneumothorax                          | 2       | 0     | 0     | 2     | 0     |
| **Total**                             | 29      | 8     | 12    | 8     | 1     |
| **RTPRN (n, %)**                      |         |       |       |       |       |
| Retroperitoneal hemorrhage            | 11 (5.2)| 7 (3.3)| 1 (0.5)| 2 (0.9)| 1 (0.5)|
| Fistula, intestinal                   | 2       | 0     | 1     | 1     | 0     |
| Acute renal failure                   | 7       | 7     | 0     | 0     | 0     |
| Pneumothorax                          | 2       | 1     | 0     | 1     | 0     |
| **Total**                             | 12      | 8     | 1     | 2     | 1     |

TPRN, transperitoneal radical nephrectomy; RTPRN, retroperitoneal radical nephrectomy. All values are presented as the number of patients.

### Table 4. Logistic regression analysis of variables associated with early complications

| Variable                          | Univariate analysis | Multivariate analysis |
|-----------------------------------|---------------------|-----------------------|
|                                   | OR 95% CI P         | OR 95% CI P           |
| **Early postoperative complications** |                     |                       |
| Age                               | 1.023 1.006–1.040 0.008 | 1.021 1.004–1.038 0.016 |
| Sex                               | 1.250 0.794–1.969 0.336 | 1.064 0.664–1.705 0.797 |
| ASA score                         | 1.316 1.060–1.633 0.013 | 1.129 0.853–1.494 0.396 |
| Body-mass index                   | 1.045 0.986–1.108 0.138 | 1.038 0.976–1.104 0.241 |
| Prior abdominal surgery           | 0.579 0.222–1.513 0.265 | 0.495 0.182–1.350 0.170 |
| Tumor size                        | 1.004 0.998–1.010 0.204 | 1.002 0.994–1.010 0.650 |
| Tumor side                        | 1.000 0.728–1.374 0.999 | 1.003 0.723–1.392 0.985 |
| Stage                             | 1.131 0.931–1.375 0.215 | 0.943 0.721–1.235 0.671 |
| Operative time                    | 1.004 1.001–1.008 0.012 | 1.002 0.998–1.006 0.411 |
| Estimated blood loss              | 1.001 1.000–1.001 0.001 | 1.001 1.000–1.001 0.001 |
| Surgical approach                 | 1.036 0.668–1.607 0.875 | 0.904 0.556–1.470 0.685 |
| **Procedure-related complications** |                     |                       |
| Age                               | 1.011 0.984–1.038 0.443 | 1.007 0.974–1.041 0.686 |
| Sex                               | 1.053 0.497–2.232 0.893 | 0.807 0.367–1.774 0.594 |
| ASA score                         | 1.311 0.917–1.876 0.138 | 1.110 0.691–1.783 0.666 |
| Body-mass index                   | 1.011 0.916–1.116 0.823 | 1.020 0.922–1.128 0.706 |
| Prior abdominal surgery           | 0.392 0.052–2.946 0.363 | 0.376 0.048–2.925 0.350 |
| Tumor size                        | 1.003 0.992–1.014 0.584 | 0.991 0.977–1.005 0.198 |
| Tumor side                        | 0.593 0.284–1.236 0.163 | 0.583 0.270–1.260 0.170 |
| Stage                             | 1.464 1.083–1.979 0.013 | 1.351 0.905–2.016 0.141 |
| Operative time                    | 1.007 1.002–1.013 0.007 | 1.002 0.995–1.008 0.628 |
| Estimated blood loss              | 1.001 1.000–1.001 0.001 | 1.001 1.000–1.001 0.001 |
| Surgical approach                 | 1.171 0.553–2.481 0.680 | 0.850 0.364–1.985 0.707 |

ASA, American Society of Anesthesiologists; BMI, body-mass index; OR, odds ratio; CI, confidence interval.
blood loss \((P < 0.001)\) were associated with procedure-related complications on univariate analysis. However, multivariate analysis revealed that estimated blood loss \((P < 0.001)\) is the sole independent predictor for procedure-related complications (Table 4).

**Discussion**

The complication of open RN could be perceived as outdated due to the rise in popularity of laparoscopic RN or PN for early-stage RCC. Several large-scale studies with long-term follow-up durations have confirmed that laparoscopic RN\(^{11,23}\) or PN\(^{24-28}\) can achieve similar oncological outcomes to open RN in the treatment of localized RCC. However, even in the USA, less than half of the RNs were performed by laparoscopy\(^{23,24}\), and only 32.2% of patients with stage I RCC underwent PN in recent years\(^{11}\). Under the present conditions, a large portion of patients with RCC still undergo open RN. Furthermore, there is a lack of rigorous reporting to compare the complication rate between transperitoneal and retroperitoneal open RN using standardized methodology. Hence, our study has important clinical significance.

The reporting of complications after surgery is often confusing, making it difficult to compare complications between different centers and evaluate patient counseling. To solve this problem, Martin et al.\(^{21}\) proposed 10 criteria for reporting early postoperative complications. Detailed reporting is suggested\(^{27}\), but even with these criteria, two issues continue to puzzle surgeons. The first is that there is no consensus on how to define a complication; in other words, opinions vary on which types of event should be considered complications. This disagreement has led to extreme variations in the reported incidences of complications. Table 5 lists some examples. The reported incidence of complications of RN ranges from 3.3% to 54.0%. Complications should be defined as any deviation from the normal postoperative course, which means that asymptomatic complications such as arrhythmia and atelectasis should also be taken into account\(^{21}\). According to this principle, complications should be listed in detail and classified by system. The second problem is that we also lack the conventional use of a standard grading system to stratify complications by severity. On reviewing urological literature focused on complications, we found that few studies graded complications\(^{8,28}\). Some researchers use “major” or “minor” to stratify the severity of complications, but there is no unambiguous definition of these terms. In 1992, Clavien et al.\(^{19}\) defined a system to grade surgical complications, classifying them into five grades according to their severity. The system was later modified and simplified for convenience\(^{29}\). This grading system has been widely accepted for reporting the severity of complications\(^{8,22,23}\). Stephenson et al.\(^{8}\) reported complications in a group of 688 patients who underwent open RN. In that study, 16% experienced a postoperative complication, and only 2.5% experienced grades III to V complications; the perioperative mortality rate was 0.4%, and only a few patients (0.6%) required re-exploration. In the present study, we used the same standard method to categorize and grade complications. We report a complication rate of 18.8% for the whole group and a rate of 2.5% for grades III to V complications. The mortality rate was 0.2%, and the reoperation rate was 1.1%. Using this standard method, complication rates were found to be comparable between different medical centers. Our study also confirmed that RN is a safe procedure that is associated with low rates of serious morbidity and mortality.

Whether RN should be performed using transperitoneal or retroperitoneal approach remains controversial. Proponents for the transperitoneal approach claim that this approach provides a great space in which to work, especially when the tumor is very large or there is accidental bleeding. However, advocates for the retroperitoneal approach can also use this argument. They believe

### Table 5. Reported incidence of postoperative complications of radical nephrectomy

| Investigator       | Country | Year         | Number of patients | Laparoscopic | Complication rate | TPRN | RTPRN | Standard system |
|--------------------|---------|--------------|--------------------|--------------|-------------------|------|-------|-----------------|
| Shekarriz et al.   | USA     | 1991–1997    | 60                 | No           | 3.3%              | NA   | NA    | No              |
| Shuford et al.     | USA     | 1999–2001    | 41                 | No           | 10.0%             | NA   | NA    | No              |
| Mejean et al.      | France  | 1986–1997    | 656                | No           | 20.9%             | NA   | NA    | No              |
| Dunn et al.        | Egypt   | 1990–1999    | 33                 | No           | 54.0%             | NA   | NA    | No              |
| Hemal et al.       | India   | 1998–2006    | 71                 | No           | 15.5%             | NA   | NA    | No              |
| Gill et al.        | USA     | 1997–2000    | 34                 | No           | 24.0%             | NA   | NA    | No              |
| Herranz Amo et al. | Spanish | NA           | 109                | No           | 24.8%             | NA   | NA    | No              |
| Stephenson et al.  | USA     | 1995–2002    | 688                | No           | 16.0%             | NA   | NA    | Yes             |
| Joudi et al.       | USA     | 2000–2003    | 18575              | No           | 18.2%             | NA   | NA    | Yes             |
| Desai et al.       | USA     | 1999–2001    | 102                | Yes          | 16.7%             | 20.0%| 13.5% | No              |
| Taue et al.        | Japan   | NA           | 100                | Yes          | 9.0%              | 4.5% | 9.1%  | No              |
| Berdjis et al.     | Germany | 1999–2003    | 63                 | Yes          | 9.5%              | 11.8%| 7.0%  | No              |
| Zhang et al.       | China   | 1999–2009    | 558                | No           | 18.8%             | 19.0%| 18.5% | Yes             |

TPRN, transperitoneal radical nephrectomy; RTPRN, retroperitoneal radical nephrectomy; NA, not available.
that the retroperitoneal approach provides quicker access to the renal hilum without the need for mobilization and retraction of the bowel\textsuperscript{[10,11]. Moreover, in obese patients, the panniculus falls forward. Retroperitoneal incision is not straightforward and is easy to perform. Although two prospective randomized studies\textsuperscript{[6,12] have suggested that the laparoscopic approach does not lead to more complications than the retroperitoneal approach in RN for RCC, this conclusion has not been confirmed by rigorous reporting using standardized methodology. In our present study, we compared early postoperative complications between transperitoneal RN and retroperitoneal RN for RCC, using standardized reporting methodology, and found that the complication rate between transperitoneal RN and retroperitoneal RN group was similar (19.0% vs. 18.5%, \(P = 0.911\)). Our result confirmed the above-mentioned conclusion.

We also found that transperitoneal RN was used more often in RCC patients with high ASA scores, larger tumors, and higher stage disease. However, patients in the retroperitoneal RN group did not show a significantly higher incidence of complications than those in the retroperitoneal RN group, although the estimated blood loss was greater in the transperitoneal RN group. It should be noted that certain complications, including bowel obstruction and chylous ascites, only occurred in the transperitoneal RN group. The careful mobilization and retraction of bowel with the ligation of every suspicious lymphatic vessel may help to reduce this kind of complication.

Patient age and estimated blood loss were significant predictors of postoperative complications on multivariate analysis. The approach (transperitoneal vs. retroperitoneal) did not influence the rate of postoperative complications. Thus, regardless of which surgical approach is chosen, reducing bleeding is the key to reducing the complication rate, especially in elderly patients.

The limitations of this study include the fact that it is a retrospective study, and thus some bias is inevitable. Another limitation is the relative small number of cases in the retroperitoneal RN group. Verification of the results using a larger cohort is needed.

Conclusions

Open RN is a safe procedure that is associated with low rates of serious morbidity and mortality. Using a standardized reporting methodology, we found the complications in this cohort were comparable with previous reports. Compared with retroperitoneal RN, transperitoneal RN was not associated with more complications. Older patient age and more blood loss at surgery were independent predictors for higher early postoperative complication rates.

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Complications of radical nephrectomy

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