Original Article

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 = 0.911and 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.

Key words 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 disease^[1,2]. 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% RN^[3] 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%^[6-16]. 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 RN^[8,9,17,18] 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

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complications than retroperitoneal RN.

Clavien defined a grading system for surgical complications in 1992^[19] and renewed it in 2004^[20]. In this five-tier system, complications are graded according to the severity of their impact and/or the intensity of the treatment required. Recently, 10 criteria have been proposed to standardize reporting in the surgical literature of the early complications of procedures^[21]. In radical cystectomy patients, this standardized reporting methodology is used widely and accepted as an objective tool to characterize complications^[22,23]. Stephenson et al.^[6] and Joudi et al.^[8] used this methodology to report the complications of nephrectomy, with rates of 16% and 18.2%, respectively. In the present study, we aimed to report the clinicopathologic characteristics and early postoperative complications in a large contemporary RCC patient cohort. By comparing the complication rates between the transperitoneal RN and retroperitoneal RN groups using standardized reporting methodology, we aimed to determine the approach associated with more complications and the predictive factors for early postoperative complications.

Patients and Methods

Patients and surgical approach

Between 1996 and 2009, 1,068 RCC patients were treated surgically for RCC in our two centers. Prior patient consent and approval from the Institutional Research Ethics Committee were obtained for the use of these clinical materials for research purposes. We excluded 201 patients who received laparoscopic RN and 206 patients who received PN from the study. Overall, 103 patients whose records lacked sufficient follow-up data were excluded. The remaining 558 patients (424 from Sun Yat-sen University Cancer Center and 134 from the First Affiliated Hospital of Sun Yat-sen University) who underwent RN were enrolled in this study. A total of 347 patients (62.2%) underwent transperitoneal RN and 211 (37.8%) underwent retroperitoneal RN. Transperitoneal RN and retroperitoneal RN were performed as described by Hinman^[24]. The decision to use a retroperitoneal or transperitoneal approach was influenced predominantly by clinical TNM stage. In general, we chose transperitoneal RN for large tumors with local progression. For localized tumors, either transperitoneal RN or retroperitoneal RN was the preferred option, according to the surgeon's discretion.

Defining and grading complications

We retrospectively reviewed hospitalization information obtained 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^[6]. Martin *et al.*'s 10 criteria for accurate and comprehensive reporting of surgical complications^[21] 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 nonnormally 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 T categroy (P < 0.001), higher N categroy (P < 0.001), higher M categroy (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

Characteristic	Total	TPRN (n = 347)	RTPRN (n = 211)	Р
Median age (years, range)	52 (4–83)	53 (4-83)	52 (12–79)	0.476
Male patients (n, %)	360 (64.5)	220 (63.4)	140 (66.4)	0.523
Left-sided tumors (n, %)	281 (50.4)	176 (50.7)	105 (49.8)	0.914
ASA score (n, %)				0.001
1	243 (43.5)	150 (43.2)	93 (44.1)	
2	137 (24.6)	69 (19.9)	68 (32.2)	
3	146 (26.2)	103 (29.7)	43 (20.4)	
4	32 (5.7)	25 (7.2)	7 (3.3)	
Patients with prior abdominal surgery (n, %)	41 (7.3)	26 (7.5)	15 (7.1)	1.000
Mean body-mass index (kg/m², range)	23.3 (14.0-39.0)	23.0 (14.0-39.0)	23.9 (16.9-36.2)	0.008
Overweight (body-mass index >25 kg/m ²) (n, %)	168 (30.1)	92 (26.5)	76 (36.0)	0.022
Median tumor size (cm, interquartile range)	5.5 (4.0-8.0)	6.0 (5.0-9.0)	4.9 (3.0-6.0)	< 0.001
T category (n, %)				< 0.001
T1a	151 (27.1)	62 (17.9)	89 (42.2)	
T1b	198 (35.5)	113 (32.6)	85 (40.3)	
T2	125 (22.4)	96 (27.7)	29 (13.7)	
T3-T4	84 (15.1)	76 (21.9)	8 (3.8)	
N category (n, %)				<0.001
NO	329 (59.0)	234 (67.4)	95 (45.0)	
N1+2	53 (9.5)	43 (12.4)	10 (4.7)	
Nx	176 (31.5)	70 (20.2)	106 (50.2)	
M category (n, %)				0.001
MO	504 (90.3)	302 (87.0)	202 (95.7)	
M1	54 (10.4)	45 (13.0)	9 (4.3)	
Median operative time (min, interquartile range)	155 (120–185)	155 (121–189)	150 (120–185)	0.915
Median length of hospital stay (days, interquartile range)	9 (7–11)	9 (7–12)	9 (8–11)	0.910
Reoperation (n, %)	6 (1.1)	4 (1.2)	2 (0.9)	1.000
Complication-related deaths (n, %)	1 (0.2)	1 (0.3)	0 (0)	1.000
Median estimated blood loss (mL, interquartile range)	150 (100-300)	200 (100-350)	150 (100-200)	0.001
Transfusion required (n, %)	40 (7.2)	28 (8.1)	12 (5.7)	0.315

Table 1. Clinical features, intraoperative data, and hospitalization duration of 568 patients with renal cell cancer

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 cases of ileus or chylous ascites occured 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

Complication	Total	TPRN (n = 347)	RTPRN (n = 211)	Р
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
lleus	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	
Chylous ascites	5	5	0	
Infectious (10.7%, n = 18)	18	15	3	0.082
Fever	15	14	1	
Sepsis	1	0	1	
Cholecystitis	2	1	1	
Wound (3.6%, n = 6)	6	4	2	0.312
Seroma	6	4	2	0.0.1
Genitourinary (11.3%, n = 19)	19	9	10	0 228
Renal failure	16	9	7	0.220
Urinary retention	3	0	3	
Cardiac (10.7%, n = 18)	18	11	7	1 000
Arrhythmia	8	5	3	1.000
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	0.000
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	0.002
Anemia requiring transfusion	20	15	5	
Thromboembolic $(5.4\%, n = 9)$	9	8	1	0 164
Deep venous thrombosis	1	1	0	0.104
Pulmonary embolus	1	1	0	
Superficial phlebitis	1	1	0	
Thrombocytopenia	6	5	1	
Neurological $(2.4\%, n = 4)$	4	2	2	0.605
Vertigo	1	0	1	0.035
Loss of consciousness	1	1	n n	
Seizure	2	1	1	
Others (3.0% $n = 5$)	5	1	Λ	0.070
Acidosis	J 1	0	4	0.070
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Complication	Total	Grade				
Complication	TOTAL	I			IV	
TPRN (n, %)	21 (6.1)	6 (1.7)	9 (2.6)	5 (1.4)	1 (0.3)	
Retroperitoneal hemorrhage	4	0	0	3	1 1	
Fistula, intestinal	1	0	0	1	0	
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, %)	11 (5.2)	7 (3.3)	1 (0.5)	2 (0.9)	1 (0.5)	
Retroperitoneal hemorrhage	2	0	1	1	0	
Fistula, intestinal	1	0	0	0	1	
Acute renal failure	7	7	0	0	0	
Pneumothorax	2	1	0	1	0	
Total	12	8	1	2	1	

Table 3. Procedure-related complications in patients treated with TPRN and RTPRN

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

.,	Univariate analysis			Multivariate analysis			
Variable	OR	95% CI	Р	OR	95% CI	Р	
Early postoperative complication	ons						
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 complication	ns						
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	

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^[11,25] or PN^[26-28] 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^[3,29], and only 32.2% of patients with stage I RCC underwent PN in recent years^[4]. 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^[21], 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 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^[20]. 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^[6,8]. 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^[20]. This grading system has been widely accepted for reporting the severity of complications^[8,22,23]. Stephenson *et al.*^[6] 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

Investigator	Country	Year	Number of patients	Laparoscopic	Complication rate	TPRN	RTPRN	Standard system
Shekarriz <i>et al.</i> ^[7]	USA	1991–1997	60	No	3.3%	NA	NA	No
Shuford et al. [9]	USA	1999–2001	41	No	10.0%	NA	NA	No
Mejean et al. [10]	France	1986–1997	656	No	20.9%	NA	NA	No
Dunn <i>et al</i> . ^[11]	Egypt	1990–1999	33	No	54.0%	NA	NA	No
Hemal <i>et al</i> . ^{12]}	India	1998-2006	71	No	15.5%	NA	NA	No
Gill et al. [13]	USA	1997-2000	34	No	24.0%	NA	NA	No
Herranz Amo <i>et al</i> . ^[14]	Spanish	NA	109	No	24.8%	NA	NA	No
Stephenson et al.[6]	USA	1995-2002	688	No	16.0%	NA	NA	Yes
Joudi <i>et al</i> . ^[8]	USA	2000-2003	18575	No	18.2%	NA	NA	Yes
Desai <i>et al</i> . ^[32]	USA	1999–2001	102	Yes	16.7%	20.0%	13.5%	No
Taue <i>et al</i> . ^[15]	Japan	NA	100	Yes	9.0%	4.5%	9.1%	No
Berdjis <i>et al</i> . ^[16]	Germany	1999–2003	63	Yes	9.5%	11.8%	7.0%	No
Zhang <i>et al</i> .	China	1999–2009	558	No	18.8%	19.0%	18.5%	Yes

that the retroperitoneal approach provides quicker access to the renal hilum without the need for mobilization and retraction of the bowel^[30]. Moreover, in obese patients, the panniculus falls forward. Retroperitoneal incision is not straightforward and is easy to perform. Although two prospective randomized studies^[31,32] have suggested that the transperitoneal 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 transperitoneal 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

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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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