Critical Evaluation of Perioperative Complications in Laparoscopic Partial Nephrectomy

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OBJECTIVES To analyze our experience with laparoscopic partial nephrectomy (LPN) to detail postoperative adverse events and identify factors that may contribute to adverse surgical outcomes. Complications from LPN result from a variety of factors, both technical and inherent.

METHODS Single-center review of 144 consecutive LPN (4 surgeons) performed between November 2002 and January 2008 was conducted. Identified complications were graded using standard reporting criteria. Univariate and multivariate statistical analysis of variables and their association with complication event and blood loss was performed.

RESULTS A total of 39 complications occurred in 29 (20%) cases. Of these, 20 (51%) were urologic and 19 (49%) were nonurologic. Individual adverse events by grade were as follows: grade I, 6 (15.4%); grade II, 19 (48.7%), grade III, 11 (28.2%), and grade IV, 3 (7.7%). No grade V complications occurred. The median tumor size and ischemia time were 2.7 cm and 35 minutes, respectively. Univariate analysis identified increased American Society of Anesthesiologists risk score (odds ratio 2.99, 95% confidence interval [CI] 1.28, 6.94) and ischemia time (odds ratio 1.31; 95% CI 1.00, 1.71) as associated with complication risk. On multivariate analysis, longer ischemia time was associated with increased estimated blood loss (95% CI 3, 57; P = .03). Hospital readmission and reintervention was required in 15 (10.4%) and 9 (6.2%) patients, respectively.

CONCLUSIONS Complications from LPN occur in a meaningful proportion of procedures although the majority does not require reintervention and half are not urologic. Increasing ischemia time and American Society of Anesthesiologists score are associated with risk for unfavorable surgical outcomes. UROLOGY 75: 288–294, 2010.

In 2007, an estimated 51 190 Americans were diagnosed with renal cancer and 12 890 died of their disease.[1,2] Widespread use of imaging identifies smaller, incidental renal tumors and a concordant decrease in tumor size at the time of diagnosis, with half of the patients found harboring stage I disease.[3] The management of small renal masses has grown increasingly challenging with the development of new techniques and treatment options.

Nephron-sparing surgery (NSS) is currently considered the standard for most T1a kidney tumors that are treated electively.[4] NSS is a safe and effective procedure for small tumors and an acceptable alternative to radical nephrectomy for select T1b renal tumors.[5]

NSS can be performed by conventional open (OPN) or minimally invasive laparoscopic surgery (LPN). Proponents of the laparoscopic approach contend that oncologic and safety outcomes are comparable to open surgery while providing a convalescence benefit through a less invasive procedure.[6-8] Both OPN and LPN are technically challenging operations, which may be responsible for their limited use. Complications from these procedures have been well documented and may be comparatively higher with LPN.[7,8] Aside from surgeon experience,[9] additional factors, as ischemia time, are likely to contribute to complication risk, which warrant further critical evaluation. We hypothesized that preoperative and intraoperative parameters may have an effect on the risk of complications during LPN. By using a standardized reporting system we examined our complete LPN series to identify and classify procedure-associated complications, allowing follow-up for 6 months or more after

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surgery. Preoperative and intraoperative features were evaluated to isolate variables that were associated with adverse events.

MATERIAL AND METHODS

Detailed review was conducted from all 144 consecutive LPN procedures performed at our center by 4 experienced, fellowship-trained surgeons with expertise in laparoscopy, from the first procedure in November 2002 to January 2008 after institutional review board's approval. Case selection was preferentially by laparoscopic means for this group of surgeons although open partial nephrectomy was also contemporaneously performed within the institution by other surgeons.

Our LPN techniques have been described previously.[10,11] Retroperitoneal or transperitoneal approaches were selected based on tumor location, and surgeon preference. Intraoperative ultrasound was performed in all cases to confirm tumor location. Lesions were sharply excised using cold scissors. Recognized pelvicaliceal entry was reconstructed with absorbable suture. Hemostasis was performed with 2-0 or 3-0 suture when necessary. Hemostatic agents and sections of oxidized cellulose were used to improve hemostasis based on surgeon's description. Vascular control was based on particular surgeon's preference. In 43 patients (30%) renal hypothermia was attempted by retrograde cold saline injection through a ureteral catheter ($n = 35$), infusion of cold isotonic crystalloid in the renal artery ($n = 7$), or use of ice slush ($n = 1$). When the procedure was performed without vascular clamping, the ischemia time was recorded as zero.

Collected data included clinical parameters, comorbidities, and renal function. Cross-sectional imaging studies were used to measure the number, location, and largest diameter of the tumor. Location included classification of upper, mid, or lower pole; medial or lateral; and anterior or posterior. Tumor depth was classified as exophytic, subcortical (>50% of the tumor within the renal cortex), or hilar (sinus fat involvement).

Complication and hospitalization information was obtained from a prospectively maintained database, and was verified or augmented retrospectively for every patient in the series by detailed review of patient records, including outpatient visits. All intraoperative and postoperative complications were tabulated from the date of surgery until last follow-up visit. Early postoperative complications were defined as those occurring within 30 days of the procedure.

Complications were categorized using predefined criteria for 11 system domains.[12] Drain management varied among surgeons and included routine discharge home with drain removal in the outpatient clinic within 1 week. Urinary fistula was therefore considered prolonged when urine output beyond postoperative day 7 was identified or a urinoma required percutaneous drain placement. Enteric function was characterized by number of days until resumption of diet and use of nasogastric tube postoperatively. Acute renal failure was defined as any requirement for hemodialysis within 30 days of surgery or medical management of hyperkalemia. Hemorrhage was defined as clinically meaningful, surgery-related blood loss requiring treatment and included the following: hemoglobin levels <8 mg/dL, hemodynamic instability, or requirement of procedural intervention or reoperation. Blood transfusion was reported separately because some patients received blood products for unrelated indications including pre-existing blood dyscrasias.

Complications were graded using the modified Clavien classification system establishing as grade I—oral medication or bedside care; grade II—intravenous therapy or thoracostomy tube; grade III—intubation, interventional radiology, endoscopy, or reoperation; grade IV—major organ resection or chronic disability; and grade V—death.[12] Renal function was calculated using estimated glomerular filtration rate (eGFR) using the abbreviated Modification of Diet in Renal Disease study equation, eGFR in millilitres per minute per 1.73 m^2 = $186 \times SCr - 1.154 \times age - 0.203 \times (0.742 \text{ if female}) \times (1.210 \text{ if African American})$.[13]

We analyzed baseline and perioperative variables to identify risk factors associated with postoperative complications. Because of the limited number of events, predictors were analyzed with univariate logistic regression analysis, and included age, American Society of Anesthesiologists (ASA) risk score, body mass index, tumor size, tumor location, tumor depth, estimated blood loss, ischemia time and method, approach, caliceal entry, and NSS indication. Additional analysis using multivariate linear regression evaluated predictors of blood loss as a surrogate for intraoperative hemorrhage. Multivariate predictors for this analysis included tumor depth, tumor size, age, ASA score, body mass index, ischemia method, and ischemia time. Statistical analyses were conducted using Stata 10.0 (StataCorp LP, College Station, TX).

RESULTS

LPN was performed successfully in 141 (98%) cases and required open conversion in 3 patients. Demographics and preoperative data are listed in Table 1. Tumors were identified as a solid renal mass in 134 patients (93.1%) or complex renal cyst in 10 patients (6.9%). Median follow-up was 52 weeks (interquartile range [IQR] 27, 94).

One or more postoperative complications occurred in 29 patients (20%). Single complication events occurred in 20 patients, whereas multiple adverse events occurred in 9 patients for a total of 39 postoperative complications. Of the 39 complications, 20 (51%) were urological. Graded events included 6 (15.4%) grade I, 19 (48.7%) grade II, 11 (28.2%) grade III, and 3 (7.7%) as grade IV. No deaths occurred.

Surgical Events

Perioperative data are summarized in Table 1. Median ischemia time was 35 minutes (IQR 25, 43). There were 5 (3.5%) intraoperative complications. Two patients developed bleeding from the surgical resection site requiring secondary measures during the surgery. One received transfusion and additional reconstruction to achieve hemostasis. The other required open conversion and radical nephrectomy. Two additional conversions to OPN occurred due to difficulties in maintaining the pneumoperitonium. Spleen puncture by Veress needle occurred in 1 patient managed by monopolar cautery.

Surgical margins were positive in 6 (4.2%) cases, of which 5 were pathologically benign lesions. Cancer was present at the surgical margin in 1 patient (0.7%). One patient (0.7%) with surgically negative margin had local tumor recurrence adjacent to the resection area approx-

Table 1. Preoperative patient characteristics and operative data

Variable	All Patients	Patients With No Complications	Patients With Complications
No. patients (%)	144 (100)	115 (80)	29 (20)
Median age, y (IQR)	62 (54, 71)	62 (54, 70)	65 (55, 72)
Male, n (%)	102 (71)	80 (70)	22 (76)
Body mass index (IQR)	28.6 (25.3, 32.6)	28.5 (25.2, 31.9)	28.6 (26.1, 33.4)
ASA score ≥3, n (%)	58 (40)	40 (35)	18 (62)
Tumor size, cm (IQR)	2.7 (2, 3.6)	2.6 (2, 3.5)	3.4 (2, 4.2)
Tumor size >4 cm, n (%)	25 (17)	16 (14)	9 (31)
Left-sided tumor, n (%)	71 (49)	56 (49)	15 (55)
Depth, n (%)			
Exophytic	88 (61)	73 (63)	15 (52)
Subcortical	28 (19)	18 (16)	10 (34)
Sinus involvement	28 (19)	24 (21)	4 (14)
Symptomatic, n (%)	19 (13)	17 (15)	2 (7)
Location, n (%)			
Lower pole	58 (40)	45 (39)	13 (45)
Middle pole	37 (19)	33 (29)	4 (14)
Upper pole	59 (41)	37 (32)	12 (41)
Operative time, min	219 (177, 274)	217 (177, 265)	236 (177, 306)
Estimated blood loss, cc	200 (100, 300)	200 (100, 300)	200 (100, 400)
Approach, n (%)			
Retroperitoneal	16 (11)	13 (11)	3 (10)
Transperitoneal	128 (89)	102 (89)	26 (90)
Ischemia, n (%)			
None	7 (5)	7 (6)	0 (0)
Hypothermic	43 (30)	33 (29)	11 (35)
Normothermic	94 (65)	75 (65)	19 (65)
Median ischemia time, min	35 (25, 43)	34 (23, 41)	40 (34, 45)
Length of stay, days	3 (2, 4)	3 (2, 3)	4 (2, 6)

All values are median (IQR) or frequency (proportion).
ASA score = American Society of Anesthesiologists risk score; IQR, interquartile range.

imately 27 months after surgery. This was a 1.3-cm exophytic conventional renal cell carcinoma. No cases with a positive surgical margin have experienced recurrence at a median follow-up of 41 weeks (IQR 28, 52).

Hemorrhage and Transfusion

Hemorrhage events occurred in 9 patients (6.2%), all of which had vascular control intraoperatively. Two patients were intraoperative (described previously). One patient demonstrated persistent bloody drain output with hemodynamic instability in the postanesthetic unit managed by reoperative open repair. Six bleeding events occurred after hospital discharge. Two patients with gross hematuria, occurring at 8 and 21 days, underwent radical nephrectomy. Arteriovenous fistula was identified in 3 patients successfully treated with angioembolization. These patients demonstrated gross hematuria 8, 25, and 49 days after the procedure. One patient experienced self-limited gross hematuria 24 days after LPN requiring blood transfusion alone without subsequent episode. Blood transfusion was necessary in 12 (8.3%) patients overall. Overall, radical nephrectomy was performed in 3 (2.1%) patients, all related to bleeding events, 2 of which were delayed.

The multivariate analysis examined age, ASA score, ischemia (type and time), tumor depth, and tumor size as related to blood loss used as a surrogate for operative trauma. Only increased ischemia time was significantly associated with higher levels of blood loss (P = .03; 95% confidence interval [CI] 3, 57).

Urinary Fistula

A perinephric drain was used in 139 patients (96%). Creatinine levels from the drain fluid were measured postoperatively in 117 cases (81%). Median drain creatinine level was 1.2 mg/dL (IQR, 1, 1.5). Median time to drain removal was 2 days (IQR 2, 4), which occurred before hospital discharge in 114 (82%) patients.

Six (4.2%) patients had persistent urine drainage beyond postoperative day 7. All were initially managed by observation. In 4 patients, the urinary fistula spontaneously healed after 21, 23, 34, and 40 days allowing drain removal. Additional drainage was needed in the other 2 patients for infected retroperitoneal urinoma.

Renal Function

Median preoperative creatinine and eGFR were respectively 1.2 mg/dL (IQR 1, 1.2) and 65 mL/min per 1.73 m^2 (IQR 57, 93). Preoperatively, 39% of patients had eGFR <60 mL/min per 1.73 m^2. At 1 day, 2 months, 6 months, and 12 months postoperatively the mean overall percentage decrease in eGFR was 9.9%, 7.5%, 6.9%, and 2.9%, respectively. One patient (0.7%) developed acute renal failure postoperatively and required temporary dialysis, with subsequent return of adequate renal function (serum creatinine level 1.5 mg/dL, 18 weeks post-LPN).

Infection

Three patients (2.1%) developed a perinephric abscess. Two had prolonged urinary fistula, which consequently progressed to infected urinoma (noted previously). Another patient presented with clinical signs of infection and purulent percutaneous discharge at 12 days requiring drainage. Computed tomography scan confirmed a perinephric abscess in all cases, which were successfully managed with antibiotics and drain placement. Two patients (1.4%) experienced wound infections that responded to local care. Two other patients (1.4%) developed pneumonia, as described later in the text.

Thromboembolic and Pulmonary Complications

Clinically recognized pulmonary complications occurred in 5 patients (3.5%). Perioperative pulmonary embolism occurred in 3 patients (2%) discovered on postoperative day 3 (2 patients) and day 4. All patients were managed with anticoagulation without further sequelae. One patient (0.7%) developed an apical pneumothorax after subclavian vein central venous line insertion that was performed postoperatively. Further sequelae in this patient included pulmonary edema and pneumonia, all of which resolved with medical therapy. An additional patient was diagnosed with postoperative pneumonia, which was treated successfully with antibiotics. One patient had imaging evidence of renal vein thrombosis presenting as acute flank pain and normal serum creatinine on postoperative day 7. Supportive care was provided with image confirmation of normal renal vascularization at 6 months.

Gastrointestinal Function

Mean time to resumption of diet was 2 days (IQR 2, 2). All but 2 patients (1.4%) resumed diet by the fourth postoperative day; both required nasogastric tube decompression, with regular diet resuming on days 9 and 12 after surgery.

In 1 patient (0.7%), an upper gastrointestinal bleed occurred 24 days after the procedure requiring transfusion. Despite thorough investigation, no cause was identified nor recurrence experienced.

Cardiovascular Complications

Cardiovascular complications were recorded in 3 patients (2.1%). Atrial fibrillation occurred in 2 patients before discharge and was managed medically. One patient with a history of ischemic heart disease and an intraoperative bleeding event developed postoperative angina, along with elevated cardiac enzyme levels, which responded to medical therapy.

Postoperative Incisional Hernias

Five (3.5%) incisional hernias were detected. Hernias occurred in the umbilical (2), epigastric (1), and retrieval (2) port sites. The diagnosis was made at a median of 36 weeks (IQR 35, 46) after the procedure. All hernias were surgically repaired.

Table 2. Causes of readmissions and reinterventions

	Total (N = 144)
Readmission, n (%)	
Abscess	3 (2.1)
Bleeding	6 (6.2)
GI bleeding	1 (0.7)
Dehydration	2 (1.4)
Pain	1 (0.7)
Pneumonia	1 (0.7)
Ileus	1 (0.7)
Total	15 (10.4)
Reintervention, n (%)	
Percutaneous drainage of abscess	3 (2.1)
Angioembolization	3 (2.1)
Nephrectomy	2 (1.4)
Renorrhaphy	1 (0.7)
Total	9 (6.2)

GI = gastrointestinal.

Table 3. Univariate analyses for predictors of complications

Predictor	OR	95% CI	*P*
Age, y	1.02	0.98, 1.05	.4
ASA score	2.99	1.28, 6.94	.011
Tumor size	1.16	0.91, 1.49	.2
Depth			.067
Exophytic	Ref	Ref	
Subcortical	2.86	1.10, 7.47	
Sinus invasion	0.846	0.255, 2.81	
Location			.3
Upper pole	Ref	Ref	
Lower pole	0.911	0.371, 2.24	
Middle pole	0.385	0.113, 1.31	
Elective indication	0.21	0.07, 0.65	.007
Estimated blood loss	1.13	0.99, 1.28	.066
Ischemia time	1.31	1.00, 1.71	.047
Ischemia method	0.71	0.30, 1.67	.4
Approach	1.13	0.30, 4.25	.9
Caliceal open	2.06	0.90, 4.73	.087

ASA score = American Society of Anesthesiologists risk score; CI = confidence interval.

Readmission and Reintervention

Fifteen patients (10.4%) were readmitted after hospital discharge and 9 (6.2%) required an additional procedure postoperatively (Table 2). Hemorrhage was the leading cause of readmission, prompting intervention in 6 patients. Three patients with abscess underwent drain placement procedures.

Risk Factors Associated With Postoperative Complications

Table 3 shows the univariate analyses of complications. ASA score (odds ratio [OR] 2.99; 95% CI 1.28, 6.94; P = .011) and greater ischemia time (OR 1.31; 95% CI 1.00, 1.71; P = .047) were significant factors associated with risk for complication. Elective indication for NSS showed a significant inverse relationship (OR 0.21; 95% CI .07, .65; $P = .007$).

COMMENT

Management of small renal masses is a new challenge in oncology care. Although small incidental renal tumors are benign in 20% of cases, the majority will represent curable primary cancers.[14] Advances in biological and image characterization hold great prognostic potential yet surgical resection remains the best curative option, whether with open or minimally invasive approaches. Advances in surgical techniques now employ smaller incisions focused on maintaining excellent oncologic results while minimizing the unwanted side effects of surgery including pain and prolonged convalescence.[15] LPN has shown satisfactory oncologic outcomes compared with OPN for stage T1a tumors.[16] The role of LPN in management of more complex renal masses is an evolving experience at selected centers.

Despite benefits of laparoscopic surgery,[7] acceptance has been slow to develop. The first reports on LPN-related adverse events reflected the technical challenges of the operation in demonstrating complication rates as high as 33%, raising issues of safety.[17,18] Gained expertise and technical developments have since refined the procedure and improved outcomes. Simmons and Gill[9] reported on complication rates from an updated series of 200 LPN and comparison made to an initial experience with 200 cases noting a reduction in the severity and number of complications over time. This improvement was believed to be related to the procedure's learning curve, technical modifications, and the use of hemostatic agents. Comparative analysis of contemporary LPN and OPN series in a single institution indicated similar complications rates between these groups.

Turna et al[19] described complications in 507 LPN procedures. A total of 107 complications occurred in 93 patients (19.7%). Forty-nine complications (46%) were urologic. Hemorrhage, urinary fistula, and acute renal failure occurred in 29 (5.7%), 12 (2.4%), and 5 (1%) patients, respectively. Of total complications, 22 (20.6%) were grade I, 48 (45%) grade II, 32 (30%) grade III, 5 (4.7%) grade IV, and none were grade V. Multivariate analysis identified increased ischemia time, presence of solitary kidney, and increased estimated blood loss as significant predictors of postoperative complications. Interestingly, there is a higher incidence of arteriovenous fistula in LPN. It may reflect the LPN renorrhaphy techniques, in which the entire resection bed is oversewn to limit the duration of warm ischemia.[20]

In the present study, clinical, surgical, and pathologic features were assessed to identify any predictor of procedure-related complications. Although this review suffers from the retrospective design, the observed results appear consistent with those of similar reports. Increased ASA score and ischemia time were significantly associated with complication, whereas an elective NSS indication carried lower risk. Blood loss, calyceal opening, and increased depth of the tumor demonstrated a trend toward increased complication risk in line with expectations from deeper resection. Lengthy ischemia time seemingly reflects the technical requirements of intracorporeal suturing for hemostasis and collecting system closure, capturing some degree of the variables for vascular involvement, and calyceal entry and the predisposition for bleeding or urinary fistula. In the nonelective setting, the pressing need for surgical expediency to strike a balance for adequate resection, minimal ischemia, and maximal renal preservation creates a setting for heightened though manageable morbidity.

There is wide variation in the classification and reporting of complications data. We identified 2 other published series with reporting methods similar to the present study (Table 4). Across these series LPN appears associated with less intraoperative blood loss, blood transfusion, and length of stay when compared with OPN; however, a higher readmission and reintervention rate is notable. Both LPN series had similar postoperative hemorrhage and transfusion rates, whereas proportionally fewer patients in the OPN series developed postoperative hemorrhage although a higher transfusion rate is evident. Plausible mechanisms include gas pressure tamponade effect over the surgical field during laparoscopic procedures, which limits some forms of blood loss during surgery yet may mask areas that can subsequently bleed. Supporting this explanation is the finding of comparable urine leakage rates across the LPN and OPN series, an area that would be less affected. Graded complication rates among the series reflected the management requirements dictated by these differences although overall rates of complications were comparable.

The organizational methods used for this study help in highlighting the important need for procedure-specific standardized measures and reporting systems. In the absence of randomized prospective surgical trials, such systems would allow balanced and consistent evaluation of adaptations in surgical approach, improving the ability to gauge progress in the field. Not uncommonly, complications of surgery are under-reported due to a variety of factors.[22] Detailed record review and follow-up in this study helped identify and characterize some of the events and outcomes. Standardized grading criteria were used, which allow comparison to other series. Other outcomes data affecting all patients, including duration of perinephric drains, time to recovery of enteric function, and renal function were reported as raw data whenever possible. The utility and clinical relevance of endpoints such as renal failure and hemorrhage as used here may not accurately reflect meaningful outcomes just as distinguishing a positive cancer margin from any positive margin may create an arbitrary boundary of questionable significance. Ideally, clinical databases and reporting would have objective standards for prospective data entry and format to simplify the study of outcomes analysis.

Table 4. Patient characteristics compared with those of other large contemporary series of LPN or OPN

Characteristic	Current Series (LPN)	Turna et al[19] (LPN)	Stephenson et al[21] (OPN)
No. patients	144	507	361
Age, y	62	60 (mean)	60 (mean)
BMI	28.6	29.2 (mean)	NA
ASA score >2	41	44	37
Tumor size, cm	2.7	2.9 (mean)	2.5
Pathologic stage T1	97	NA	89
Patients with preoperative serum creatinine level >1.5 mg/dL	4.9	7.7	NA
Blood loss, cm^3	200	237 (mean)	350
Length of stay, days	3	3.4 (mean)	5
Operation time, h	3.6	3.6 (mean)	3.1
Solitary kidney	3.5	4.9	11
WIT, min	35	32 (mean)	NA
Pelvicaliceal repair	44	83	NA
Positive margins	6.2	NA	NA
Cancer-positive margins (%)	1 (0.6)	1 (0.2)	NA
No. patients with complications (%)	29 (20)	93 (19.7)	68 (19)
Index of total complications/patient	1.3	1.2	1.4
Worst complication/patient, %			
Grade I	4.2	4.4	9
Grade II	10.4	9.5	5
Grade III	4.2	6.3	4
Grade IV	2.1	1	0.2
Grade V	0	0	0
Readmissions	10.4	NA	6
Reoperation	2.8	1.8	0.2
Reintervention	6.2	NA	2.5
Transfusion	8.3	7.1	18
Hemorrhage	6.2	NA	NA
Intraoperative	1.4	NA	NA
Postoperative	4.8	5.7	1.1
Urine leakage	4.2	2.4	5.5
Patients requiring dialysis	0.7	NA	0.5
Ileus	1.4	1.2	2

All values are median or percentages unless otherwise noted.

ASA score = American Society of Anesthesiologists risk score; BMI = body mass index; DM = diabetes mellitus; HT = hypertension; LPN = laparoscopic partial nephrectomy; N/A = not applicable, OPN = open partial nephrectomy; WIT = warm ischemia time.

This study is limited by the restrospective design and variability in technique and experience among the 4 surgeons evaluated.

CONCLUSIONS

Overall LPN complications rates at our institution were similar to those of other large contemporary series of LPN or OPN. Increasing ASA score, greater ischemia time, and imperative indication were significant predictors of complication. Prospective randomized study of LPN and OPN are needed to characterize the comparative advantages and limitations of these nephron-sparing surgical approaches with regard to adverse events, renal function, and convalescence.

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