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ORIGINAL ARTICLE

Retrospective Cohort Study

Safety and feasibility of modified duct-to-mucosa pancreaticojejunostomy during pancreatoduodenectomy: A retrospective cohort study

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Abstract

BACKGROUND

Pancreatoduodenectomy (PD) is the most effective surgical procedure to remove a pancreatic tumor, but the prevalent postoperative complications, including postoperative pancreatic fistula (POPF), can be life-threatening. Thus far, there is no consensus about the prevention of POPF.

AIM

To determine possible prognostic factors and investigate the clinical effects of modified duct-to-mucosa pancreaticojejunostomy (PJ) on POPF development.

METHODS

We retrospectively collected and analyzed the data of 215 patients who underwent PD between January 2017 and February 2022 in our surgery center. The risk factors for POPF were analyzed by univariate analysis and multivariate logistic regression analysis. Then, we stratified patients by anastomotic technique (end-to-side invagination PJ *vs* modified duct-to-mucosa PJ) to conduct a comparative study.

RESULTS

A total of 108 patients received traditional end-to-side invagination PJ, and 107 received modified duct-to-mucosa PJ. Overall, 58.6% of patients had various complications, and 0.9% of patients died after PD. Univariate and multivariate logistic regression analyses showed that anastomotic approaches, main pancreatic duct (MPD) diameter and pancreatic texture were significantly associated with the incidence of POPF. Additionally, the POPF incidence and operation time in patients receiving modified duct-to-mucosa PJ were 11.2% and 283.4 min, respectively, which were significantly lower than those in patients receiving traditional end-to-side invagination PJ (27.8% and 333.2 minutes).

CONCLUSION
Anastomotic approach, MPD diameter and pancreatic texture are major risk factors for POPF development. Compared with traditional end-to-side invagination PJ, modified duct-to-mucosa PJ is a simpler and more efficient technique that results in a lower incidence of POPF. Further studies are needed to validate our findings and explore the clinical applicability of our technique for laparoscopic and robotic PD.

Key Words: Pancreaticojejunostomy; Pancreatoduodenectomy; Suture technique; Pancreatic fistula

Core Tip: We evaluated the safety and feasibility of modified duct-to-mucosa pancreaticojejunostomy (PJ) during pancreatoduodenectomy (PD) by analyzing the data of 215 patients who underwent PD in our surgery center. Compared with traditional end-to-side invagination PJ, modified duct-to-mucosa PJ was a simpler and more efficient technique that resulted in a lower incidence of postoperative pancreatic fistula (11.2%). Meanwhile, we found that anastomotic approach, main pancreatic duct diameter and pancreatic texture were major risk factors for postoperative pancreatic fistula development.

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INTRODUCTION

Pancreatoduodenectomy (PD) is widely performed as the standard treatment for resectable tumors in the pancreas and periampullary region. Despite recent advances in surgical techniques and perioperative management, the incidence of postoperative complications and overall mortality remain high[1]. Specifically, a postoperative pancreatic fistula (POPF), the most common and potentially deadly postoperative complication, develops in 5% to 26% of patients[2]. To improve the operation efficacy, effective prevention of POPF can be crucial. Therefore, proper assessment of relevant risk factors for POPF is necessary, and anastomosis has proven to be an effective treatment approach[3]. The intention of this retrospective, single-center study is to explore the risk factors for POPF and further determine the effects of modified duct-to-mucosa pancreaticojejunostomy (PJ) on POPF prevention.

MATERIALS AND METHODS

The data of a series of 215 consecutive patients who underwent elective PD for benign or malignant pathologies in our center between January 2017 and February 2022 were analyzed. Patients were then stratified into two groups according to the anastomotic method for further analysis. Patients with a pathological diagnosis of periampullary lesions, with an American Society of Anesthesiologists score I-III, and who provided informed consent were included in the study. Patients with incomplete medical records, who underwent neoadjuvant treatment preoperatively, who had undergone emergency surgery, or with synchronous cancer were excluded from the study. The primary outcome measure was the POPF rate, and the secondary outcome measures were mortality rates, operative time, blood loss and length of hospital stay. Other outcomes of interest included demographic characteristics (age, sex, anamnesis, concomitant disease, biochemical indices) and intraoperative data (main pancreatic duct (MPD) diameter, pancreas texture, type of anastomosis). According to the International Study Group on Pancreatic Surgery 2016 consensus statement, POPD was strictly defined as “any measurable volume of drained fluid on or after postoperative Day 3 with an amylase level more than 3 times the upper limit of the normal amylase range and having an impact on clinical outcome”[4]. A grade A pancreatic fistula was defined as a "biochemical leak", a grade B fistula required changes in postoperative management, and a grade C fistula needed reoperation or led to organ failure and/or mortality[4]. Mortality specifically referred to the death of inpatients within 3 mo after surgery.

Surgical procedure

Experienced hepato-bilio-pancreatic surgeons performed standard PD (Child's procedure) on all the patients, and there were no differences between the two groups except for the PJ procedure. The routine procedures for placing the pancreatic stent tube were as follows: After suturing the posterior wall of the pancreatic stump, a right-sized stent tube (8-10 cm in length) with side holes was inserted 3-5 cm into the pancreatic duct, and the other end was placed approximately 5 cm into the small intestine. Then, a stitch was placed to suture and fix the stent tube on the posterior side of the pancreas. Classic end-to-side invagination PJ was implemented as previously reported[5], and the key steps are shown in Figure 1. The procedures of modified duct-to-mucosa PJ were as follows: (1) After enterotomy was performed according

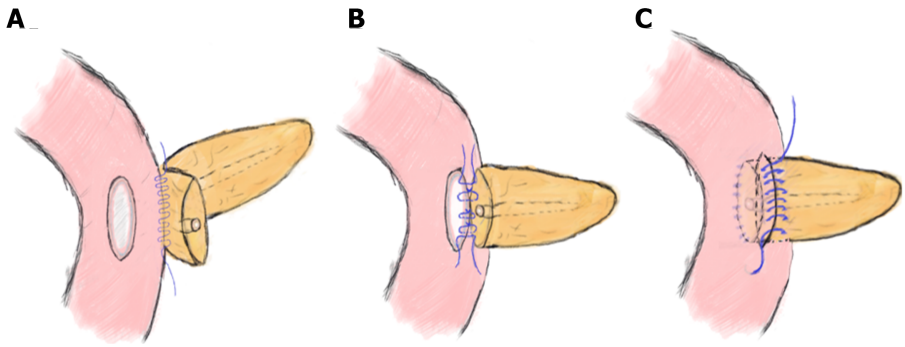

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Figure 1 Schematic diagram of end-to-side invagination pancreaticojejunostomy. A: Continuous suturing was performed between the rear side of the pancreatic stump (approximately 1.5 cm from its edge) and the jejunal seromuscular layer with a 3-0 Prolene slip line; B: Suture of the pancreatic margin and seromuscular layer of the jejunum intermittently; C: The pancreatic stump was inserted into the jejunum, and the anterior side of the pancreas and jejunal seromuscular layer were continuously sutured.

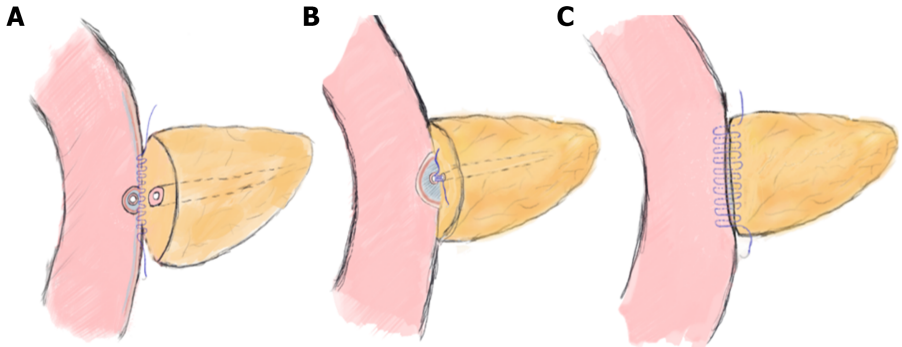

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Figure 2 Schematic diagram of modified duct-to-mucosa pancreaticojejunostomy. A: Perform continuous suturing between the rear edge of the pancreatic stump and jejunal seromuscular layer with a 3-0 Prolene suture; B: Sew 3-4 stiches continuously in the posterior wall of the pancreatic duct and the jejunal mucosa with 4-0 Prolene sutures; C: Continuous suturing was performed between the front edge of the pancreatic stump and the whole layer of the jejunum.

to the MPD diameter, the rear edge of the pancreatic stump and the posterior jejunal seromuscular layer were continuously sutured with 3-0 Prolene sutures. The needle was inserted vertically into the pancreas 1.5 cm from the rear edge of the pancreatic stump and passed through the posterior wall of the jejunum after passing through its seromuscular layers. The spacing was approximately 8–10 mm, and the margin was greater than 10 mm (Figure 2A); (2) The posterior wall of the pancreatic duct and the jejunal mucosa were continuously sutured with three to four 4-0 Prolene sutures. The spacing and margin were adjusted according to the MPD diameter (Figure 2B); and (3) After the stent was inserted, the front edges of the pancreatic stump and whole-layer of the jejunum were anastomosed with 3-0 Prolene running sutures. The spacing and margin were similar to those of the first stitch. Although the depth of needle entry was controlled at approximately 1 cm to avoid damaging the MPD on the pancreatic side, it was deeper on the jejunal side to ensure suturing of the whole layer (Figure 2C). In our modified method, tension-free sutures were applied, and no dead space was left between the pancreatic stump and jejunum.

Perioperative management

During the perioperative period, most treatment measures were the same for each patient. The preoperative management included smoking and drinking cessation, weight control, skin preparation and antibiotic prophylaxis. Epidural analgesia and gastrointestinal decompression were administered during the operation. Drain amylase levels were routinely measured on the 1st, 3rd and 5th days after surgery, while octreotide was used simultaneously for 7-10 d. Other postoperative management included thromboprophylaxis, nutritional support and controlled fluid infusion. The patients were followed up for 3 mo after discharge.

Statistical analysis

SPSS 21.0 statistical software was used for data description and analysis. Continuous variables are expressed as the mean ± SD, and Student's t test was used for comparisons where appropriate. Categorical variables were analyzed by using Fisher's exact test and the χ^2 test. Univariate analysis was used to evaluate the factors associated with POPF development, and multivariate regression analysis was performed to determine the independent risk factors.

RESULTS

Of the 215 patients with an average age of 54.5±13.3 years, 112 patients were male and 103 were female. The percentages of patients with diabetes mellitus, smoking history and previous abdominal surgery were 23.7%, 42.8% and 22.3%, respectively. Preoperative blood tests showed that the respective values of total bilirubin and albumin were 186.9 (μmol/L) and 35.4 (g/L). More than half of the patients (57.2%) had undergone biliary drainage preoperatively. According to the pathological results, the most prevalent conditions were ampullary carcinoma, pancreatic head carcinoma and distal cholangiocarcinoma. The average total operative time was 308.4 min, while the average intraoperative blood loss was 555.1 mL. The overall complication rate was 53.5% (115/215), and the mortality rate was 0.9% (2/215). Specifically, POPF was the most common complication (19.5%), followed by peritoneal infection (13%), abdominal bleeding (11.6%) and bile leakage (9.3%). Additionally, the two cases of death were due to abdominal bleeding associated with POPF development (Table 1).

As the most common postoperative complication, POPF can also increase the risks of abdominal infection and hemorrhage[6]. Consequently, we further explored possible factors correlated with POPF development through univariate analysis. As shown in Table 2, POPF development had no significant correlation with the following factors: Age, sex, smoking history, preoperative bilirubin and albumin, preoperative biliary drainage, previous abdominal surgery, blood loss, or operative time. Anastomotic techniques (P = 0.0015), MPD diameter (P = 0.0015) and pancreatic texture (P = 0.0386) were significantly correlated with POPF development in the multivariate logistic regression analysis.

Table 3 shows the differences between traditional end-to-side invagination PJ and modified duct-to-mucosa PJ. Of these patients, 108 received traditional end-to-side invagination PJ, and 107 received modified duct-to-mucosa PJ. The results indicated no difference between the groups in terms of age, sex, pancreatic texture, postoperative hospital stay or mortality. However, patients subjected to modified duct-to-mucosa PJ had a lower incidence of POPF (11.2%) than the other group (27.8%). Further analysis indicated that there were 7 cases of grade A POPFs, 4 cases of grade B POPFs, and 1 case of grade C POPF in the modified PJ group. However, in the traditional group, the number of cases at each grade was 20, 7 and 3, respectively. Obviously, modified PJ might attenuate POPF severity based on the comparison results. Similarly, the modified anastomotic method demonstrated its superiority in terms of operative time (end-to-side invagination PJ: modified duct-to-mucosa PJ: 333.2 min vs. 283.4 min). Contrary to expectations, there were more patients with MPD diameters less than 3 mm in the modified method group, a factor that was previously found to be significantly correlated with POPF development.

DISCUSSION

With the advancements in surgical techniques and perioperative care, the mortality of patients subjected to PD has gradually decreased, while the incidence of POPF remains high[7,8]. As the most frequent lethal complication, POPF has been heavily discussed to reach a consensus on its prevention. Our research preliminarily found that the independent risk factors for POPF included PJ method, MPD diameter and pancreatic texture. Our result was partially consistent with the result of a recent meta-analysis evaluating pancreatic texture and MPD size as risk factors for POPF development[9]. Other factors, including sex, body mass index, anastomotic techniques, intraoperative blood loss, operative time and drain fluid amylase, have also been reported to be related to POPF development[10-12]. Obviously, numerous studies on the risk factors for POPF have indicated seemingly conflicting and perplexing results. Ecker *et al*[13] believed that attempting to create a reliable prediction model based on the risk factors for POPF development seemed to be unrealistic and had limited effectiveness. Nevertheless, we believe that the abovementioned factors are valuable references that can help surgeons improve the therapeutic efficacy during the perioperative period.

In clinical practice, various surgical techniques have been applied to prevent POPF development, such as reconstruction methods [PJ, pancreaticogastrostomy (PG)], anastomotic techniques (Blumgart's method[14], Kakita's method[15], Peng's binding PJ[16] and end-to-side invagination anastomosis) and stent placement. Debates about the pros and cons of the various surgical techniques are ongoing. A multicenter randomized trial conducted between June 2009 and August 2012 showed that PG was more efficient than PJ in reducing the incidence of POPF development[17]. Conversely, in another single-center, phase 3, randomized clinical trial, researchers recommended PJ for patients at high risk for POPF development[18]. In the present study, all the patients were subjected to PJ because surgeons were more skilled and experienced in performing this surgical technique. Two PJ anastomotic techniques were used here: end-to-side invagination anastomosis and modified duct-to-mucosa anastomosis. The operation time (283.4 minutes) and POPF (11.2%) incidence of the modified method group were significantly lower than those of the comparison group. Our results were roughly consistent with some other surgical center reports[19,20]. Classic invagination PJ can completely drain pancreatic juice from the main pancreatic duct and pancreatic stump into the intestinal cavity, but there are risks of pancreatic stump hemorrhage, pancreatic duct obstruction, and pancreatitis[16,21]. Many scholars have conducted comparative studies of various anastomosis methods. Wang *et al*[22] found no significant differences among duct-to-mucosa PJ, invagination PJ and binding PJ in the prevention of postoperative complications and death. While Ratnayake's research favored duct-to-mucosa PG[23], Peng's and Berger's studies indicated that invagination could reduce the incidence of POPF development more significantly[16,21]. Compared with traditional duct-to-mucosa PJ, our technique used double-layer continuous suturing of posterior tissues and single-layer continuous suturing of anterior tissues, namely, "semicontact continuous anastomosis". Our modified method had several advantages: first, the procedure better ensured the continuity between the pancreatic duct and the jejunal mucosa; second, tension-free and continuous anastomosis prevented cutting of the pancreas parenchyma; and third, convenient procedures helped reduce

Table 1 Clinical characteristics of the patients, *n* (%)

Variables	Total patients, *n* = 215
Gender (male/female)	112/103
Age (yr)	54.5 ± 13.3
Diabetes mellitus	51 (23.7)
Smoking history	92 (42.8)
History of abdominal operation	48 (22.3)
Preoperative total bilirubin (μmol/L)	186.9 ± 74.4
Preoperative biliary drainage	123 (57.2)
Albumin (g/L)	35.4 ± 4.8
Pathological types	
Ampullary carcinoma	102 (47.4)
Pancreatic head carcinoma	51 (23.7)
Distal cholangiocarcinoma	35 (16.3)
Duodenal papillary carcinoma	22 (10.2)
Ampullary benign diseases	2 (0.9)
Other rare diseases	3 (1.4)
Anastomotic method	
End-to-side invagination pancreatoduodenectomy	108 (50.2)
Modified duct-to-mucosa pancreatoduodenectomy	107 (47.8)
Main pancreatic duct diameter	
≤ 3 mm	121 (56.3)
> 3 mm	94 (43.7)
Pancreatic texture	
Hard	112 (52.1)
Soft	103 (47.9)
Postoperative complications	
Postoperative pancreatic fistula	42 (19.5)
Grade A	27 (12.6)
Grade B	11 (5.1)
Grade C	4 (1.9)
Operative time (min)	308.4 ± 57.3
Blood loss (mL)	555.1 ± 228.7
Peritoneal infection	28 (13)
Intra-abdominal hemorrhage	25 (11.6)
Biliary fistula	20 (9.3)
Re-operation	4 (1.9)
Mortality	2 (0.9)
Length of stay (d)	15.7 ± 2.7

the difficulty of PD and the surgeon's training time. With the popularity of laparoscopic and robotic PD, the advantages of our modified anastomotic approach might better meet the strict requirements of these operations. Although more high-quality evidence is required to demonstrate the benefits of modified duct-to-mucosa anastomosis, our present study indicated that it was a feasible and effective method for reducing the incidence of POPF development.

Table 2 Univariate and Multivariate logistic regression analysis of risk factors associated with postoperative pancreatic fistula

	Univariate		Multivariate	
	OR (95%CI)	*P* value	OR (95%CI)	*P* value
Age (≤ 60 *vs* > 60 yr)	1.603 (0.800-3.203)	0.188		
Gender (male *vs* female)	1.143 (0.594-2.266)	0.7		
Diabetes mellitus	0.711 (0.324-1.585)	0.427		
Smoking history	1.275 (0.649-2.470)	0.481		
History of abdominal operation	0.782 (0.355-1.757)	0.57		
Preoperative total bilirubin (≤ 171 *vs* > 171 μmol/L)	1.295 (0.654-2.700)	0.475		
Preoperative biliary drainage (yes *vs* no)	1.444 (0.740-2.894)	0.385		
Serum albumin (≤ 35 *vs* > 35 g/L)	0.665 (0.322-1.359)	0.275		
Anastomotic method (End-to-side invagination pancreaticojejunostomy *vs* Modified duct-to-mucosa pancreaticojejunostomy)	3.045 (1.500-6.248)	0.002[a]	0.288 (0.129-0.606)	0.0015[a]
Main pancreatic duct diameter (≤ 3 *vs* > 3 mm)	2.599 (1.255-5.676)	0.011[a]	3.608 (1.678-8.302)	0.0015[a]
Operative time (≤ 300 *vs* > 300 min)	1.125 (0.583-2.181)	0.735		
Blood loss (≤ 600 *vs* > 600 mL)	0.855 (0.431-1.645)	0.651		
Pancreatic texture (Hard *vs* Soft)	0.494 (0.253-0.956)	0.043[a]	2.171 (1.051-4.602)	0.0386[a]

[a]Statistically significant.

Table 3 Comparison results between End-to-side invagination pancreatoduodenectomy and Modified duct-to-mucosa pancreatoduodenectomy, *n* (%)

	End-to-side invagination pancreatoduodenectomy (*n* = 108)	Modified duct-to-mucosa pancreatoduodenectomy (*n* = 107)	*P* value
Age (yr)	53.6 ± 13.7	55.3 ± 12.8	0.336
Male	50 (46.3)	62 (57.9)	0.088
Pancreatic texture			0.152
Hard	51 (47.2)	61 (57.0)	
Soft	57 (52.8)	46 (43.0)	
Main pancreatic duct diameter			0.033[a]
≤ 3 mm	53 (49.1)	68 (63.6)	
> 3 mm	55 (50.9)	39 (36.4)	
Operative time (min)	333.2 ± 48.9	283.4 ± 54.2	< 0.0001[a]
Blood loss (mL)	571.4 ± 257.3	538.7 ± 195.4	0.295
Postoperative complications			

Postoperative pancreatic fistula	30 (27.8)	12 (11.2)	0.002[a]
Grade A	20 (18.5)	7 (15.9)	
Grade B	7 (6.5)	4 (3.7)	
Grade C	3 (2.8)	1 (0.9)	
Peritoneal infection	13 (12.0)	15 (13.9)	0.38
Intra-abdominal hemorrhage	15 (13.9)	10 (9.3)	0.299
Biliary fistula	11 (10.2)	9 (8.3)	0.654
Re-operation	3 (2.8)	1 (0.9)	0.622
Mortality	2 (1.9)	0 (0)	0.498
Length of stay (d)	16 ± 2.6	15.5 ± 2.8	0.187

[a]Statistically significant.

This study also has some limitations that might weaken the persuasiveness of the evidence. First, our study is a single-center retrospective study with a limited sample size. Second, the limited follow-up time may not accurately reflect the patient's long-term clinical outcome. Therefore, large-scale randomized studies with long-term follow-up are desperately needed.

CONCLUSION

In conclusion, we found that anastomotic approaches, MPD diameter and pancreatic texture were major risk factors for POPF development. In addition, modified duct-to-mucosa PJ had advantages of shorter operation time and lower POPF incidence over classic end-to-side invagination PJ. Although the findings need to be further validated with more high-quality evidence, this modified method could be considered for some patients undergoing PD.

ARTICLE HIGHLIGHTS

Research background

Pancreatoduodenectomy (PD) is widely used as an effective surgical treatment for pancreatic tumors, but there is currently no consensus on how to effectively prevent postoperative complications, especially pancreatic fistula. How to prevent postoperative pancreatic fistula (POPF) is a current research hotspot and our research focuses on how to solve this problem by improving surgical methods

Research motivation

To demonstrate the safety and feasibility of modified duct-to-mucosa pancreaticojejunostomy (PJ) during PD, especially in the terms of preventing POPF.

Research objectives

To identify independent risk factors for POPF and evaluate the clinical outcomes of two anastomotic techniques (end-to-side invagination PJ *versus* modified duct-to-mucosa PJ).

Research methods

This stud was a retrospective cohort study which collected and analyzed the information of patients undergoing PD in our hospital. Univariate analysis and multivariate logistic regression analysis were used to analyze the risk factors of POPF and subgroup analysis were conducted to compare the different outcomes between end-to-side invagination PJ and modified duct-to-mucosa PJ.

Research results

Anastomotic approaches, main pancreatic duct (MPD) diameter and pancreatic texture were proven to be significantly associated with the incidence of POPF. And modified duct-to-mucosa PJ could significantly decrease the POPF incidence (11.2%) and operation time (283.4 min) in patients compared with traditional end-to-side invagination.

Research conclusions

Modified duct-to-mucosa PJ had advantages of shorter operation time and lower POPF incidence over classic end-to-side invagination PJ. Additionally, we found that anastomotic approaches, MPD diameter and pancreatic texture were major risk factors for POPF development.

Research perspectives

Modified duct-to-mucosa PJ is effective and safe according to preliminary outcomes. It is an innovative anastomotic technique with great application prospects in PD and also has broad application prospects in future robotic or minimally invasive operations of pancreatic tumors.

FOOTNOTES

Author contributions: Sun Y and Chai C contributed to conceptualization; Yao H and Yu XF contributed to investigation; Ma YQ and Xu S contributed to data curation; Sun Y contributed to writing – original draft preparation; Sun Y and Chai C contributed to writing – review & editing; All authors read and approved the final manuscript.

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Informed consent statement: Written informed consent was obtained from all the subjects involved in this study.

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Data sharing statement: The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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