Single-docking robotic assisted proctectomy for rectal cancer below peritoneal reflection: a propensity score matching analysis

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Background: The aim of this study was to compare the short and long-term outcomes of robotic assisted proctectomy (RP) and laparoscopic assisted proctectomy (LP) for rectal cancer below the peritoneal reflection using propensity score matching (PSM) analysis.

Methods: We evaluated the medical records of 200 patients who underwent proctectomy for rectal cancer below the peritoneal reflection through a robotic (n=81) or laparoscopic (n=119) approach between Jan 2015 and Dec 2017. The data were prospectively collected, and the patients were matched at a ratio of 1:1 according to age, sex, body mass index (BMI), previous abdominal surgeries, comorbidities, American Society of Anesthesiologist score ($\leq 2/>2$), and pathologic stage.

Results: After matching, each group included 74 patients. Compared to the LP group, the RP group showed shorter postoperative hospital stays (PHS) [7 (\pm 2) *vs.* 9 (\pm 2.3) d, P=0.003], shorter time to liquid diet [3 (\pm 2) *vs.* 5 (\pm 3) d, P<0.001], and shorter time to removal of catheter [6 (\pm 2) *vs.* 7 (\pm 2.3) d, p=0.014]. The operative expense was higher in the RP group [8,365 (\pm 1,600) *vs.* 6,922 (\pm 1,220) RMB, P<0.001]. The operation time, estimated blood loss, postoperative complications, and pathologic outcomes were similar between the two groups. No conversion to laparotomy, readmission, or mortality was observed in either group within 30 days after surgery. The 3-year disease-free survival (DFS) were 75.2% and 88.3% (P=0.070), and overall survival (OS) were 92.9% and 93.7% (P=0.810) in the RP and the LP groups, respectively and the risk of low anterior resection syndrome (LARS) was lower in the RP group (OR =0.304, 95% CI: 0.124–0.745, P=0.009).

Conclusions: Compared to LP, RP is worth recommending as it has long-term survival, faster postoperative recovery, and a lower risk of LARS in patients with rectal cancer below the peritoneal reflection.

Keywords: Rectal cancer; robotic assisted proctectomy (RP); laparoscopic assisted proctectomy (LP); short-term outcomes; long-term outcomes

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Introduction

Colorectal cancer (CRC) is the third most common malignancy in the world. The proportion of new cancer cases and cancer death of CRC was 10% and 9.4% according to Global Cancer Statistics 2020 (1). Among the different locations, mid-low rectal cancer is known as requiring a relatively high level of surgical expertise, as both the resection margin (distal margin and circumferential margin) and lymph node dissection in a relatively narrow space.

Through almost two decades of development, robotic surgery has been increasingly applied in rectal surgery owing to its stability and dexterity, 3-dimensional highdefinition display, and precision and accuracy in anatomical dissection. However, robotic surgery is expensive and private insurers may not fully reimburse its cost. Despite this, robotic surgery for rectal cancer has continued to gain global utilization, and some clinical analyses report robotic rectal resection is a safe and adequate technique for the treatment of rectal cancer. Further, it was strongly associated with better short-term outcomes over laparoscopic surgery, and even allowed for the preservation of urinary and sexual functions in patients with mid-low rectal cancer (2,3).

In the present study, we used a propensity score match (PSM) method with real world data from a single center, those who with T stage under T3 and received no neoadjuvant radiotherapy were included, with the aim of retrospectively comparing the short-term and longterm outcomes of robotic assisted proctectomy (RP) and laparoscopic assisted proctectomy (LP) for rectal cancer below the peritoneal reflection.

We present the following article in accordance with the STROBE reporting checklist (available at https://dx.doi. org/10.21037/atm-21-2744).

Methods

Patients and data collection

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). It was approved by institutional ethics board of Ruijin Hospital, Shanghai Jiao Tong University School of Medicine. (No.: 109/2017) and informed consent was taken from all individual participants. Following institutional review board approval, a retrospective chart review was performed on consecutive patients who underwent RP and LP for rectal adenocarcinoma from Jan 2015 to Dec 2017 at the Department of General Surgery, Ruijin Hospital, Shanghai

Jiao Tong University School of Medicine in Shanghai, China. The exclusion criteria were abdominal perineal resection, the use of new adjuvant chemoradiotherapy, stage IV rectal cancer, T4 tumors, tumors above the peritoneal reflection, the concomitant presence of other malignant tumors, and incomplete records for review. After screening, 200 patients (RP:81; LP:119) were included in the study.

Clinicopathologic information and perioperative outcomes were obtained from medical records, including sex, age, body mass index (BMI), ASA grade, comorbidities, previous abdominal surgery, operation time, estimated blood loss, time to liquid diet, length of postoperative hospital stay (PHS), conversion to laparotomy, temporary terminal ileostomy, postoperative complications, perioperative mortality, tumor size, histology, lymph nodes harvest, proximal and distal resection margins, circumferential resection margin (CRM), metastatic lymph node, neurovascular invasion, anastomotic height, and pathologic stage according to the 8th Edition of the AJCC Cancer Staging Manual. Postoperative complications were graded according to the Clavien-Dindo classification.

Follow-up surveillance was consistent with the National Comprehensive Cancer Network (NCCN) guidelines, and recurrence was confirmed by radiological or histological methods. Patients with Stage III or Stage II lesions with high risk were routinely sent to chemotherapy or radiotherapy for further treatment according to the guidelines. A low anterior resection syndrome (LARS) questionnaire was collected 18 months after surgery.

Surgical procedure

All operations were carried out by the same wellexperienced and qualified surgical team, who performed more than 400 RP or LP surgeries per year. Bowel preparation was the same between the two groups including 1–2 days of liquid diet and polyethylene glycol electrolyte solution, and prophylactic antibiotics the day before operation.

In the RP group, a single-docking technique with five ports to fulfill the whole process was performed (*Figure 1*). As the tumor was located below the peritoneal reflection, the anastomosis could be quite low, and high ligation for lymph node dissection was required, which resulted in the left colic artery not being preserved in most patients. The splenic flexure of the colon was not routinely mobilized, depending on the tension of the anastomosis. Following the principle of total mesorectal excision (TME),

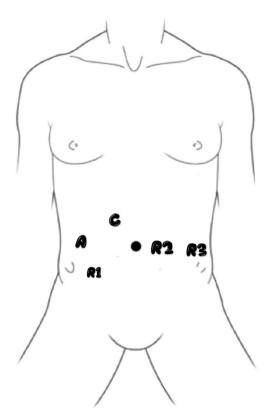


Figure 1 Port sites in the RP group. A, assistant; R1, 2, 3, robotic 1, 2, 3; C, camera. RP, robotic assisted proctectomy.

anterior resection (AR) with a double-staple technique was performed accordingly. The tumor specimen was extracted through a small hypogastric midline incision with protection of the incision (*Figure 2*).

A temporary terminal ileostomy was not routinely performed except in cases in which the surgeon considered the patient had a substantial risk of anastomotic leakage. The dissected pelvic peritoneum was not sutured, and one or two drainage cannulas were placed near the anastomosis for detecting leakage. Once leakage occurred, the cannula was flushed, and the faeces drained to prevent local infection.

As the laparoscopic procedure was similar to the robotic procedure and is well documented elsewhere, it is not described in this paper. All patients were supervised by the same treatment team according to unified standards.

Matching

Propensity Score Matching (PSM) is a statistical method used to process observational study data. Due to various reasons, there are many data biases and confounding variables in observational study. The method of propensity score matching is to reduce the influence of these biases and confounding variables, so as to make more reasonable comparison between the experimental group and the control group. We applied 1:1 PSM by using bivariate logistic regression, and age, sex, BMI, ASA grade, comorbidities, previous abdominal surgery, and pathologic stage were selected as covariates.

Statistical analysis

Statistical analysis was performed with SPSS (version 23.0, SPSS Inc. Chicago, IL, USA), and statistically significant differences were evaluated using the Student's *t*-test, Mann-Whitney U test, χ^2 test, and Fisher exact test, as appropriate. Disease-free survival (DFS) rates and overall survival (OS) were estimated by the Kaplan-Meier method and compared by the log-rank test. LARS was predicted by binary logistic regression analyses and a P value <0.05 was considered statistically significant.

Results

Baseline characteristics

Prior to matching, patients in the two groups showed great significance in comorbidity [20 (24.7%) vs. 50 (42%) P=0.015] and previous abdominal surgery [4 (4.9%) vs. 18 (15.1%) P=0.036]. However, after matching, each group comprised of 74 patients, and differences in patient characteristic were eliminated (*Table 1*).

Intraoperative and perioperative outcomes

Robotic surgery was superior to laparoscopic surgery in time to liquid diet [3 (\pm 2) vs. 5 (\pm 3), P<0.001], removal of catheters [6 (\pm 2) vs. 7 (\pm 2.3), P=0.014], and the length of PHS [7 (\pm 2) vs. 9 (\pm 2.3), P=0.003] (*Table 2*). There were no significant differences between the RP and LP groups in operation time, estimated blood loss, temporary terminal ileostomy, anastomotic height, and postoperative complications. No cases were converted to laparotomy, and there were neither readmissions nor mortality within 30 days after surgery in either group. The operation time was measured from the beginning of anesthesia until the end of all surgical procedures, and since draping and docking commenced when the anesthesiologist started infusion, this added no extra time. Most complications Page 4 of 10

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Figure 2 A typical total mesorectal excision specimen.

Table 1 Baseline characteristics

	Overall			After matching		
Characteristics	RP (n=81)	LP (n=119)	Р	RP (n=74)	LP (n=74)	Р
Age, median [IQR], years	64 [15]	63 [16]	0.364	64 [14]	61.5 [13]	0.594
Sex, n (%)			1			1
Male	53 (65.4)	77 (64.7)		48 (64.9)	48 (64.9)	
Female	28 (34.6)	42 (35.3)		26 (35.1)	26 (35.1)	
BMI, median [IQR], kg/m ²	23.30 [4.53]	23.84 [4.22]	0.511	23.17 [4.18]	23.28 [3.59]	0.798
ASA grade, n (%)			0.128			1
≤2	79 (97.5)	109 (91.6)		72 (97.3)	72 (97.3)	
>2	2 (2.5)	10 (8.4)		2 (2.7)	2 (2.7)	
Comorbidities, n (%)	20 (24.7)	50 (42.0)	0.015	19 (25.7)	18 (24.3)	1
Previous abdominal surgery, n (%)	4 (4.9)	18 (15.1)	0.036	4 (5.4)	3 (4.1)	1
Pathologic stage, n (%)			0.232			0.868
0, I	15 (18.5)	31 (26.0)		14 (18.9)	17 (23.0)	
II	34 (42.0)	37 (31.1)		28 (37.8)	26 (35.1)	
III	32 (39.5)	51 (42.9)		32 (43.2)	31 (41.9)	

IQR, interquartile range; BMI, body mass index; ASA, The American Society of Anesthesiologists.

Table 2 Intraoperative and perioperative outcomes

Variable	RP (n=74)	LP (n=74)	Р
Operation time, median [IQR], min	140 [51.3]	140 [51.3]	0.185
Estimated blood loss, median [IQR], mL	50 [50]	50 [76]	0.057
Intraoperative morbidity, n (%)	0	0	-
Vascular injury	0	0	
Adjacent organ injury	0	0	
Conversion to laparotomy, n (%)	0	0	-
Temporary terminal ileostomy, n (%)	10 (13.5)	18 (24.3)	0.141
Anastomotic height, median [IQR], cm	1.25 [1]	1.00 [1]	0.313
Time to liquid diet, median [IQR], d	3 [2]	5 [3]	<0.001
Time to removal of catheter, median [IQR], d	6 [2]	7 [2.3]	0.014
_ength of PHS, median [IQR], d	7 [2]	9 [2.3]	0.003
Postoperative complications, n (%)	13 (17.6)	10 (13.5)	0.651
Anastomotic leakage	4	6	
Pulmonary infection	1	0	
lleus	1	0	
Urinary retention	6	2	
Ascites	0	1	
Arrhythmia/HF	1	1	
Grade of complications, n (%)			1
1/11	12 (16.2)	9 (12.2)	
III/IV	1 (1.4)	1 (1.4)	
Readmission within 30 days of surgery, n (%)	0	0	-
Mortality within 30 days of surgery, n (%)	0	0	-
Operation expenses, median [IQR], RMB	8,365 [1,600]	6,922 [1,220]	<0.001
Materials expenses, median [IQR], RMB	20,509 [4,780]	21,010 [5,788]	0.275
_ARS level, n (%)			0.032
No	59 (86.8)	44 (67.7)	
Minor	5 (7.4)	12 (18.5)	
Major	4 (5.9)	9 (13.8)	

PHS, postoperative hospital stay; HF, heart failure; IQR, interquartile range; LARS, low anterior resection syndrome; RP, robotic assisted proctectomy; LP, laparoscopic assisted proctectomy.

were grade I/II and included urinary retention with a delay of Foley catheter removal in less than a week, pulmonary infection, ileus, and arrythmias, while ascites occurred in one patient pre-comorbid with cirrhosis. There were four cases (5.4%) of anastomotic leakage in the RP group and six (8.1%) in the LP group, while one patient (1.4%) in the LP group required an extra diversion stoma to control the leakage and was considered a grade IIIb case. Other cases were cured by flush and drainage through the catheter. One aged patient (1.4%) in the RP group with poor preoperative

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Table 3 Pathologic and oncologic outcomes

Variable	RP (n=74)	LP (n=74)	Р
Tumor size, median [IQR], cm	4 [2]	4 [2]	0.627
Proximal resection margins, median [IQR], cm	11 [1.3]	7 [2]	<0.001
Distal resection margins, median [IQR], cm	3 [1]	3 [0.5]	0.370
Lymph nodes Harvest, median [IQR], n	15 [5]	15 [5]	0.606
Positive circumferential resection margin, n (%)	0	0	-
Cell type, n (%)			0.824
WD/MD	63 (85.1)	61 (82.4)	
PD/others	11 (14.9)	13 (17.6)	
Metastatic Lymph node, n (%)	32 (43.2)	31 (41.9)	1
Vascular invasion, n (%)	8 (10.8)	2 (2.7)	0.097
Perineural invasion, n (%)	12 (16.2)	2 (2.7)	0.009
Follow-up period, median [IQR], months	39 [8.3]	57 [25.3]	<0.001
Recurrence, n (%)	17 (23.0)	10 (13.5)	0.201
Stage 0/I	None	None	
Stage II	Liver: 3	Lung & liver: 1	
	Lung: 2	Liver: 2	
Stage III	Liver: 1	Liver: 2	
	Lung: 4	Lung: 2	
	Lung & liver: 3	Lung & liver: 1	
	Local: 3; peritoneal seeding: 1	Local: 2	
Death, n (%)	5 (6.8)	4 (5.4)	1
LARS level, n (%)			0.032
No	59 (86.8)	44 (67.7)	
Minor	5 (7.4)	12 (18.5)	
Major	4 (5.9)	9 (13.8)	

IQR, interquartile range; WD, well differentiated; MD, moderately differentiated; PD, poorly differentiated; LARS, low anterior resection syndrome; RP, robotic assisted proctectomy; LP, laparoscopic assisted proctectomy.

heart function suffered heart failure after surgery and was sent to Intensive Care Unit to rehabilitate. While the operative material expense, including disposable instruments and staplers, was not different between the groups, the operative ongoing maintenance was higher in the RP group with statistical significance [8,365 (\pm 1,600) vs. 6,922 (\pm 1,220) RMB, P<0.001]. The extra expense associated with the machine running fee in robotic surgery amounted to about 30,000 RMB (4,200 US dollars), although private insurance covered this cost for some patients.

Pathologic and long-term outcomes

The tumor size, CRM, distal resection margins, lymph nodes harvest, histology, metastatic lymph node, and vascular invasion did not differ significantly between the two groups (*Table 3*). A longer proximal resection margin [11 (\pm 1.3) *vs.* 7 (\pm 2) cm, P<0.001] and more perineural invasion [12 (\pm 16.2) *vs.* 2 (\pm 2.7), P=0.009] were found in the RP group. The median follow-up period was 39 months in the RP group and 57 months in the LP group (P<0.001), the 3-year DFS

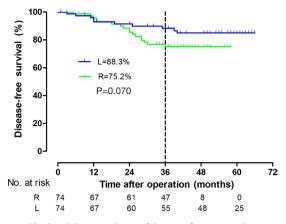


Figure 3 Kaplan-Meier analysis of disease-free survival.

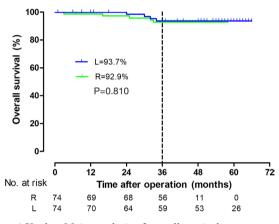


Figure 4 Kaplan-Meier analysis of overall survival.

were 75.2% and 88.3% (P=0.070, *Figure 3*), and the OS were 92.9% and 93.7% (P=0.810, *Figure 4*) in the RP and the LP groups, respectively. The total LARS incidence (assessed 18 months after surgery) was higher in the LP group [RP: minor 5 (7.1%), major 4 (5.7%); LP: minor 12 (17.9%), major 9 (13.4%), P=0.032], evaluated by LARS score. After univariate analysis was performed (*Table 4*), surgical approach (RP or LP), T stage (Tis/T1/T2 or T3), and age were selected as covariates in the binary logistic regression to evaluate the predictors of LARS. The results (*Table 5*) showed that RP patients had a lower risk of LARS than LP patients (OR =0.304, 95% CI: 0.124–0.745, P=0.009).

Discussion

Although the question of whether laparoscopic surgery is equivalent to open procedures in the treatment of mid or low proctectomy remains controversial, several well-known multicentral randomized trials had proven the noninferiority of laparoscopic proctectomy compared to open procedures in recent years (4-8). In 2009, the UK Medical Research Council and National Institute of Health Research, through the Efficacy and Mechanism Evaluation Program, funded the Robotic vs. Laparoscopic Resection for Rectal Cancer (ROLARR) trial to undertake an evaluation of the safety, efficacy, and short- and long-term outcomes of roboticassisted vs. conventional laparoscopic rectal cancer surgery (9). No difference between the treatment groups was observed for longer-term outcomes, disease-free, and OS, and the short-term outcomes were complicated. This demonstrated that among patients with rectal adenocarcinoma suitable for curative resection, robotic-assisted laparoscopic surgery, as compared with conventional laparoscopic surgery, did not significantly reduce the risk of conversion to open laparotomy. These findings suggest that when performed by surgeons with varying experience, robotic-assisted laparoscopic surgery does not confer an advantage in rectal cancer resection (3,10,11).

In our study, we focused on surgical procedures for rectal cancer below the peritoneal reflection, which guaranteed it to be a study of true mid-low rectal surgery. We found robotic assisted surgery manifested an overall faster recovery when compared to laparoscopic procedures, in the time of catheter removal, time to liquid diet, and length of PHS. Robotic assisted surgery did not increase the incidence of conversion to laparotomy, postoperative complications, operation time, intraoperative blood loss, readmission, or mortality within 30 days of surgery.

RP could also reach the standard of TME and showed no difference to laparoscopic procedures. Other studies have reported that the CRM had an overall positive rate of around 5% (9), with no difference in robotic and laparoscopic groups. However, in the present study, there were no positive CRM patients in either group, which may be due to the fine-selection of patients who received robotic surgery (T1-T3) and the PSM statistical process. The OS were quite promising in demonstrating equivalent longterm outcomes of the surgical methods. However, in the 3-year DFS, although there's no statistic difference between 2 groups, the curve seemed separated after 24 months. Looking into the data, we found a higher occurrence of perineural invasion, this may cause more lung metastasis in robotic group.

A robotic surgical system provides outstanding dexterity, stability, and accuracy. Accordingly, it is particularly useful

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Table 4 Univariate analysis of LARS after AR in 137 patients

Factor	Total	No/minor LARS	Major LARS	Statistics	P value
Surgical approach					
Robotic	70	61	9		
Laparoscopic	67	46	21	χ²=6.840	0.009
Sex					
Male	90	71	19		
Female	47	11	36	χ²=0.095	0.758
Age	137	60.79	63.57	T=-1.188	0.237
BMI	137	23.17	23.54	T=-0.611	0.542
Surgical history					
No	131	103	28		
Yes	6	4	2	χ²=0.480	0.489
Pathological stage					
I	30	22	8		
II	53	41	12		
III	54	44	10	χ²=0.777	0.678
T stage					
1	14	7	7		
2	20	16	4		
3	103	83	19	χ²=7.224	0.027
Vascular invasion					
No	127	98	29		
Yes	10	9	1	χ²=0.893	0.345
Nerve invasion					
No	123	95	28		
Yes	14	12	2	χ²=0.528	0.467
Blood loss (mL)	137	73.87	54.00	T=1.265	0.208
Operation time (min)	137	148.12	148.67	T=-0.059	0.953
Anastomotic height (cm)	137	1.360	1.317	T=0.338	0.736

LARS, low anterior resection syndrome; AR, anterior resection.

			1
Factor	OR	95% CI	P value
Surgical approach	0.311	0.125–0.772	0.012
T stage	-	-	0.073
1	Ref	-	-
2	0.255	0.053-1.221	0.087
3	0.252	0.076–0.834	0.024
Age	1.030	0.991-1.072	0.137

LARS, low anterior resection syndrome; AR, anterior resection.

in dissecting tissue in a narrow space such as the pelvis, and in the protection of important nerves and vessels. It is reported that scores of the European Organization for Research and Treatment of Cancer Quality of Life (EORTC QLQ C30) and EORTC QLQ CR38 were similar in both robotic and laparoscopic groups, but in the EORTC QLQ CR38 questionnaire, sexual function 12 months postoperatively was better in the robot-assisted group than in the laparoscopic group (12). Similarly, Chang *et al.* (3) found urinary function and general sexual satisfaction

decreased significantly 1 month after robotic surgery for both sexes. However, both parameters subsequently increased progressively, and the values 1 year after surgery were comparable to those measured before. Some studies (13-19), found a significant prevalence of LARS following oncological rectal resection, and a low anastomotic height or history of radiotherapy were major risk factors. Patients with LARS often experience either a pattern of urgency and incontinence, or alternately, obstructed defecation. Bowel adaptation is thought to occur by about 18 months post operatively, after which, further improvement with time is unlikely, and there is no effective medical treatment. In reviewing the charts of patients in our cohort, we found the incidence of LARS was much higher in laparoscopic groups, and the univariant analysis and multivariant analysis confirmed that the risk of LARS in robotic assisted surgery was lower than that in laparoscopic assisted surgery. Combined with the above studies, we found that RP had better long-term postoperative functional recovery for patients with rectal cancer below peritoneal reflection and is worthy of recommendation.

The only limitation of robotic rectal surgery could be the relatively high expense. Some patients could not accept the extra expense due to their economic situation. However, a new policy is announced this year in some city of China, i.e., almost 80% of the surgical expense of robotic rectal surgery can be reimbursed by the national health insurance. So, in the near future, more patients would choose robotic surgery.

This study had several limitations, including its small sample size and that it was conducted at a single center. In addition, patients with stage IV rectal cancer, T4 tumor, and those receiving new adjuvant chemoradiotherapy were not included, which could possibly influence the DFS and OS results and although the follow-up period of both groups exceeded 36 months, the median followup period of robotic surgery was shorter than laparoscopic surgery. Finally, as this is a retrospective study, the potential selection bias and confounding bias could not be completely excluded despite the use of PSM.

Conclusions

RP below the peritoneal reflection has the advantage of fast recovery compared to laparoscopic assisted surgery. The risk of LARS in robotic assisted surgery was lower than that in laparoscopic assisted surgery and the long-term survival of both was equivalent. The results of this study suggest RP is worthy of recommendation in patients with rectal cancer below the peritoneal reflection.

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Footnote

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki 2013. The study was approved by institutional ethics board of Ruijin Hospital, Shanghai Jiao Tong University School of Medicine (No.: 109/2017) and informed consent was taken from all individual participants.

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