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Original Article

Efficacy and safety of transurethral resection of bladder tumor for superficial bladder cancer

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Abstract: The purpose of this study was to explore the efficacy and safety of transurethral resection of bladder tumor (TURBT) in the treatment of superficial bladder cancer (SBC). In this retrospective study, we included 103 patients with SBC who were admitted to the Hebei Yanda Hospital from March 2015 to May 2019. Among them, 53 patients were treated by TURBT and assigned to the research group. The rest, 50 patients, were treated by partial cystectomy (PC) and were included in the control group. The two groups were compared in terms of curative efficacy, complications, operation-related indexes, 2-year recurrence and survival, quality of life, and serum tumor markers. The operation-related indexes mainly included intraoperative blood loss, the time of operation, bladder flushing, catheter indwelling, and hospitalization. The quality of life of patients was assessed by the 36-Item Short-Form Health Survey (SF-36). The data revealed that compared with the control group, the overall response rate and the scores of various dimensions of the SF-36 were significantly higher in the research group. The complication rate, surgical indicators, and 2-year recurrence were significantly lower in the research group, with a better survival. Serum levels of tumor marker cancer antigen 125 (CA125), carcinoembryonic antigen (CEA), and neuron specific enolase (NSE) in the research group were significantly lower than those in the control group after treatment. TURBT is effective and safe in the treatment of patients with SBC.

Keywords: Transurethral resection of bladder tumor, superficial bladder cancer, efficacy, safety

Introduction

Bladder cancer (BC) is a disease of the genitourinary organs and the 14th most common malignancy, with pathogenic factors including smoking and aniline dyes [1, 2]. Superficial bladder cancer (SBC), also known as non-muscle invasive bladder cancer (NMIBC), is a typical representative of BC, accounting for 70% of all BC cases [3]. The 5-year survival rate can be as high as 90%. It has a high risk of recurrence and metastasis [4]. Once the lesion metastases, the survival rate of patients will be greatly reduced [5]. Currently, the treatment modalities for SBC include surgery, local or systemic immunotherapy, chemotherapy, and radiotherapy, with varying therapeutic efficacy [6]. This study mainly analyzed and compared the effects of partial cystectomy (PC) and transurethral resection of bladder tumor (TURBT) on the efficacy and safety of patients with SBC. This can provide references for clinical treatment options for SBC patients, and may be beneficial to improve the treatment safety and prognosis of patients.

PC is a common surgical method for SBC, which is mainly used to remove the tumor and its surrounding tissues according to pathological conditions such as lesion size and infiltration range [7, 8]. This is an invasive procedure that causes great damage to patients. With the disadvantage of high complication and recurrence rate, this results in unsatisfactory overall efficacy and reduced rehabilitation effect [9, 10]. Optimizing the selection of surgical methods carries huge implications for patients with SBC, which is conducive to improving safety and reducing the risk of recurrence. TURBT, is to place the endoscope into the bladder through the urethra for lesion removal. This has the advantages of smaller trauma and less intraoperative bleeding [11-13]. Pak [14] reported that TURBT can not only improve the chemotherapy

sensitivity of patients with muscle-invasive bladder cancer (MIBC), but also improve the 5-year survival rate.

In this study, 103 patients with SBC were enrolled to compare the clinical advantages of TURBT over PC for SBC. The innovation of our study mainly lies in the comprehensive and reliable results obtained from the evaluation of efficacy, safety, surgical indicators, prognosis, quality of life (QOL), and serum tumor markers of the two surgical methods.

Materials and methods

General data

In this retrospective study, 103 patients with SBC admitted to the Hebei Yanda Hospital from March 2015 to May 2019 were selected Fifty-three patients were assigned to the research group and all underwent TURBT. The other 50 patients were treated with PC and were included in the control group. The study protocol was approved by the Ethics Committee of Hebei Yanda Hospital (1003-55). All the participants and their guardians were notified and signed the informed consent form. Inclusion criteria: All the included patients were diagnosed with SBC by pathological examination [15], with primary and single tumor, normal communication, no mental disease/severe visceral, or systemic disease nor contraindication to surgery, and were able to complete the 2-year follow-up. The exclusion criteria were the presence of severe urinary tract infection and/or lesion metastasis, infectious diseases, coagulation disorders, severe hypovolemia, and chemotherapy and radiotherapy before admission.

Treatment methods

Patients in both groups received continuous epidural anesthesia or lumbar anesthesia before surgery. Patients in the control group were treated with PC. A surgical approach was performed in the middle of the bladder in the lower abdomen of the patient. The bladder was opened and the tumor tissue at 2-3 cm around the tumor was removed until the bladder wall. After surgery, the abdominal wall was sutured after flushing with mannitol (Chineway Pharma Tech Co., Ltd., Shanghai, China, Granutol) and placing drainage tubes.

Patients in the research group received TURBT. After general anesthesia, the patient was placed in the bladder lithotomy position with the bladder volume controlled at 200 mL. The tranurethral electroresection (Fangda Hezhong Technology Development Co., Ltd., Beijing, China) was placed for resection. Before surgery, the size, nature, shape, and location of the tumor were carefully observed, and a reasonable and effective resection plan was formulated accordingly. Normal saline was delivered to the bladder before surgery to keep it in a semi-filled state. Tumors larger than 2 cm in diameter were excised from the base. One side of the tumor was removed to the base of the tumor. For tumor removal, a cut was made from the root until the superficial muscle layer, followed by an electrical resection of 2 cm of normal tissue around the base. A urinary catheter was placed after the bladder was flushed with mannitol.

Patients in both groups were reexamined by B ultrasound every three months and cystoscopy every six months.

Efficacy evaluation

The pathological changes were evaluated by B-ultrasound and cystoscopy. Complete response (CR) was considered the complete disappearance of lesions after surgery, without recurrence one month after operation. Partial response (PR) corresponded to at least a 50% decrease in the lesion volume compared with that before surgery. Stable disease (SD) was indicated if the lesion volume was reduced by 10%-50% compared with that before surgery. Progressive disease (PD) was translated in a less than 10% decrease in the lesion volume compared with that before surgery.

Outcome measures

Clinical efficacy: The efficacy evaluation criteria were described above. The overall response rate was calculated as the percentage of the number of patients with CR, PR, and SD to the total number of patients. Incidence of complications: The incidence of complications, which mainly included cystospasm, urethrostenosis, cysthemorrhagia, and postoperative infection, was calculated. Operation-related indexes: The surgical indexes, including intraoperative blood loss, the time of operation, bladder flushing,

Table 1. General data [n (%), mean ± SD]

Variable	n	Control group (n=50)	Research group (n=53)	χ^2/t	P
Gender				1.983	0.159
Male	65	35 (70.00)	30 (56.60)		
Female	38	15 (30.00)	23 (43.40)		
Age (year)				0.734	0.392
<50	45	24 (48.00)	21 (39.62)		
≥50	58	26 (52.00)	32 (60.38)		
Average age (years)	103	52.68±12.66	53.95±15.83	0.448	0.655
Tumor staging (stage)				0.230	0.632
I	49	25 (50.00)	24 (45.28)		
II	54	25 (50.00)	29 (54.72)		
Pathological grading (grade)				0.182	0.670
G1	66	31 (62.00)	35 (66.04)		
G2	37	19 (38.00)	18 (33.96)		
Tumor diameter (cm)				0.195	0.659
<2	41	21 (42.00)	20 (37.74)		
≥2	62	29 (58.00)	33 (62.26)		
Smoking history				0.391	0.532
No	26	14 (28.00)	12 (22.64)		
Yes	77	36 (72.00)	41 (77.36)		
Drinking history				1.098	0.295
No	42	23 (46.00)	19 (35.85)		
Yes	61	27 (54.00)	34 (64.15)		
Residence				0.163	0.686
Urban	74	35 (70.00)	39 (73.58)		
Rural	29	15 (30.00)	14 (26.42)		
Marital status				0.393	0.531
Single	34	18 (36.00)	16 (30.19)		
Married	69	32 (64.00)	37 (69.81)		

catheter indwelling, and hospitalization, were observed and compared.

The patients were followed up with once every 3 months for 2 years, mainly through telephone interviews and visits, to record their 2-year recurrence and survival.

QOL: Patients' QOL was evaluated using the 36-Item Short-Form Health Survey (SF-36) from the dimensions of physical functioning (PF), role-physical (RP), bodily pain (BP), general health (GH), vitality (VT), social functioning (SF), role-emotional (RE), and mental health (MH). Each dimension scores 0-100 points. Higher scores indicate better QOL [16].

Before and after treatment, 3 mL of fasting peripheral venous blood was sampled from all the patients, and centrifuged to collect the supernatant. The levels of serum cancer antigen 125 (CA125), carcinoembryonic antigen (CEA), and neuron specific enolase (NSE) were detected by electrochemiluminescence immunoassay with the kits all purchased from Shanghai Wa Lan Biotechnology Co., Ltd. (Cat. Nos. E01788, E01791, E01289).

Statistical analysis

The statistical analysis and image rendering of the collected data were performed by GraphPad Prism 6 and SPSS17.0, respectively. Categorical and continuous variables were recorded as number/percentage (n/%) and mean ± SEM, respectively. Categorical variables were compared between groups using the Chi-square test, or the Chi-square continuity correction when the theoretical frequency in the Chi-square was <5. For continuous variables, the inter-group comparison was performed by independent samples T-test, and the intra-group comparison before and after treatment was conducted by paired T-test. The Kaplan-Meier method was used to draw the survival curve to calculate the survival rate. The Log-rank test was used for survival analysis. Differences with *p*-values <0.05 were considered significant.

Results

General data

The two groups were not statistically different in general data such as gender, average age, tumor staging, pathological grading, tumor diameter, smoking history, drinking history, residence, and marital status (P>0.05) **Table 1**.

Table 2. Therapeutic effect of transurethral resection of bladder tumor [n (%)]

Group	n	Complete response	Partial response	Stable disease	Progressive disease	Overall response rate (%)
Control group	50	16 (32.00)	12 (24.00)	8 (16.00)	14 (28.00)	72.00
Research group	53	22 (41.51)	21 (39.62)	4 (7.55)	6 (11.32)	88.68
χ^2 value	-	-	-	-	-	4.574
P value	-	-	-	-	-	0.033

Table 3. Complications of transurethral resection of bladder tumor [n (%)]

Categories	Control group (n=50)	Research group (n=53)	χ^2 value	*P* value
Cystospasm	3 (6.00)	0 (0.00)	-	-
Urethrostenosis	2 (4.00)	0 (0.00)	-	-
Cysthemorrhagia	7 (14.00)	1 (1.89)	-	-
Postoperative infection	4 (8.00)	3 (5.66)	-	-
Total	16 (32.00)	4 (7.55)	9.832	0.002

Curative effect of TURBT

PC was performed in the control group and TURBT was performed in the research group. The observation of the treatment efficacy showed that the overall response rate of the research group was significantly higher than that of the control group (88.68% *vs.* 72.00%, P<0.05) **Table 2**.

Complications of TURBT

We recorded the complications (cystospasm, urethrostenosis, cysthemorrhagia, and postoperative infection) in both groups. The data identified a lower complication rate in the research group compared with the control group (7.55% *vs.* 32.00%, P<0.05) **Table 3**.

Operation-related indexes of TURBT

We observed and compared operation-related indexes between the two groups. The data revealed significantly less intraoperative blood loss and shorter time of operation, bladder flushing, catheter indwelling, and hospitalization in the research group, versus the control group (P<0.05) **Figure 1**.

Two-year recurrence and survival of patients

We evaluated the two-year recurrence and survival rates of patients after operation to analyze their outcomes under different treatment modalities. The results revealed that the two-year recurrence rate of the research group was significantly lower than that of the control group (15.09% *vs.* 36.00%, P<0.05). Kaplan-Meier analysis revealed that the 2-year survival of the research group was significantly better than that of the control group (P<0.05) **Figure 2**.

QOL of patients

We assessed the QOL of the two groups using the SF-36. The results showed that there was no significant difference in the SF-36 score between the two groups before treatment (P>0.05). The SF-36 scores assessed from 8 dimensions all elevated after treatment and the score of each dimension was higher in the research group compared with the control group (P<0.05) **Figure 3**.

Changes of serum tumor markers in patients

We detected the levels of CA125, CEA, and NSE in the serum of patients. The data identified no distinct difference in the above serum tumor markers between the two groups before treatment (P>0.05). After treatment, CA125, CEA, and NSE all reduced significantly in both groups (P<0.05), with lower levels in the research group (P<0.05) **Figure 4**.

Discussion

SBC is a disease that may be accompanied by repeated recurrence, which adversely affects the QOL of patients and increases the burden of social medical care [17, 18]. The purpose of this study was to optimize the clinical treatment options for patients with SBC. This is helpful to improve their QOL and reduce the risk of recurrence and medical burden.

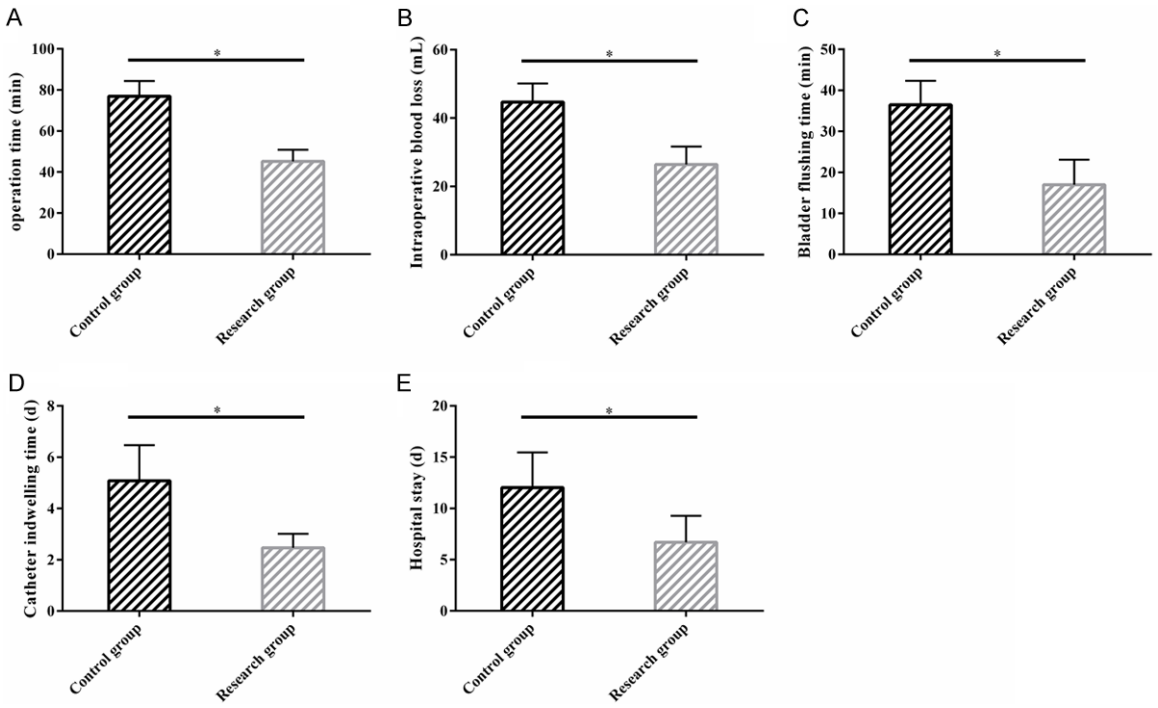

Figure 1. Operation-related indexes of transurethral resection of bladder tumor. A. The operation time of the research group was significantly shorter than that of the control group. B. The intraoperative blood loss in the research group was significantly less than that in the control group. C. The bladder flushing time of the research group was significantly shorter than that of the control group. D. The catheter indwelling time of the research group was significantly shorter than that in the control group. E. The hospital stay in the research group was significantly shorter than that in the control group. Note: **P<0.01.

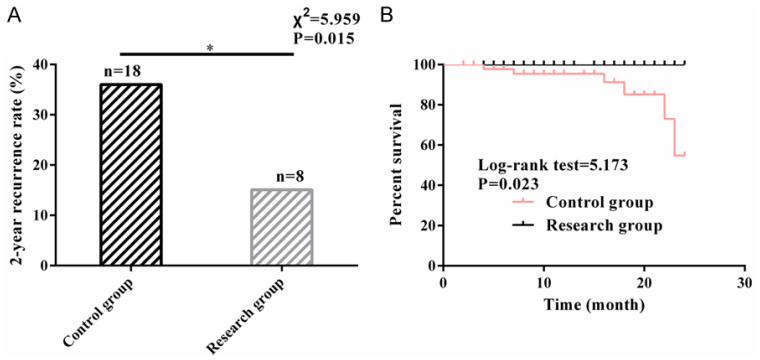

Figure 2. Two-year recurrence and survival of patients. Compared with the control group, the two-year recurrence rate (A) of the research group was significantly lower and the 2-year survival (B) was significantly better. Note: *P<0.05.

PC, a traditional surgical method extensively applied in clinic for the treatment of SBC, which to a certain extent, can timely control the disease and relieve patients' clinical symptoms [19]. TURBT is a common surgical approach for SBC, which is not only well tolerated by patients, but also has relatively high efficacy [20]. In the present study, the control group was treated with PC, and the research group was treated by TURBT. It was found that TURBT had outstanding performance in terms of treatment efficiency and safety. According to the study of Wei [21], TURBT is not only safe, efficient, and effective, but can correctly determine the pathological staging of patients, which is consistent with the results of our study. The underlying reason may be that TURBT only removes the focus itself with a small surgical incision. It is less detrimental to bladder tissue and urethral tissue. As such, the bladder and urethral function of patients can be effectively preserved, and the risk of adverse events such as cystospasm, urethrostenosis, cysthemorrhagia, and postoperative infection can be significantly reduced. According to the research of Gregg [22], the common complications of patients undergoing TURBT are cystospasm

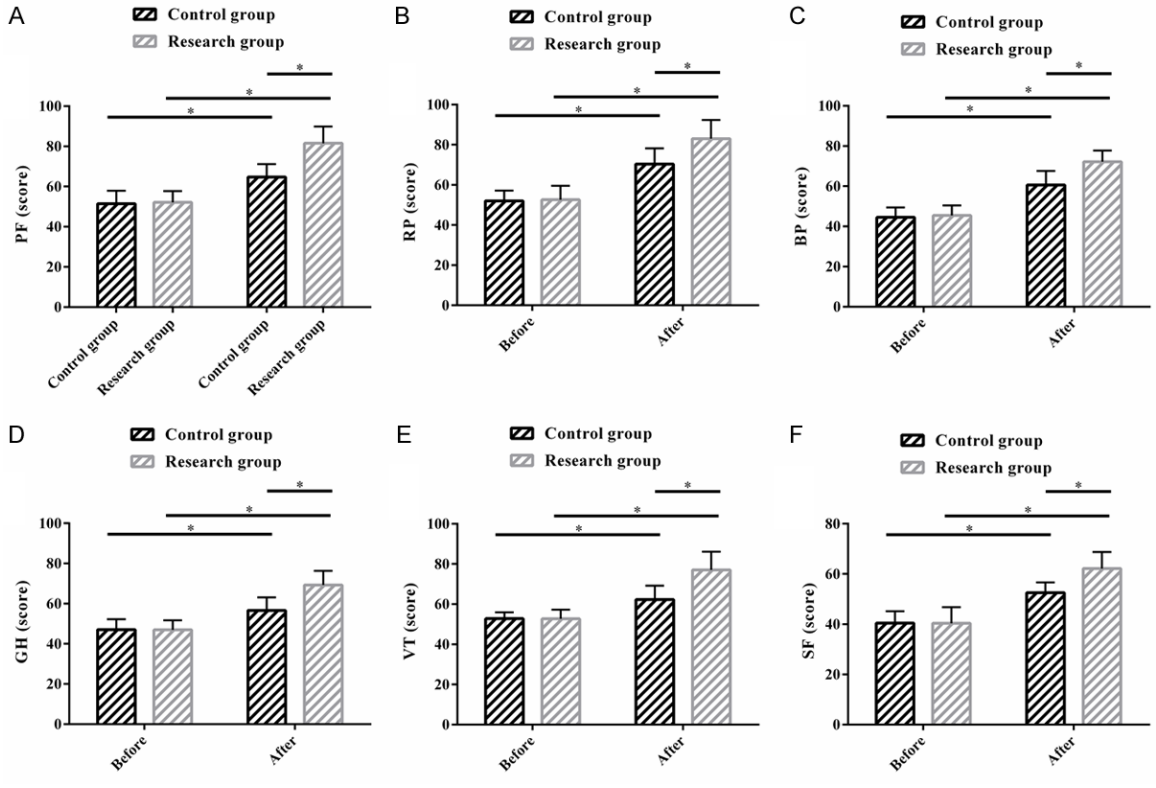

Figure 3. Quality of life of patients. The scores of PF (A), RP (B), BP (C), GH (D), VT (E), SF (F), RE (G), and MH (H) of the research group after treatment were significantly higher than those before treatment and the control group. Note: PF, physical functioning; RP, role-physical; BP, bodily pain; GH, general health; VT, vitality; SF, social functioning; RE, role-emotional; MH, mental health; **P<0.01.

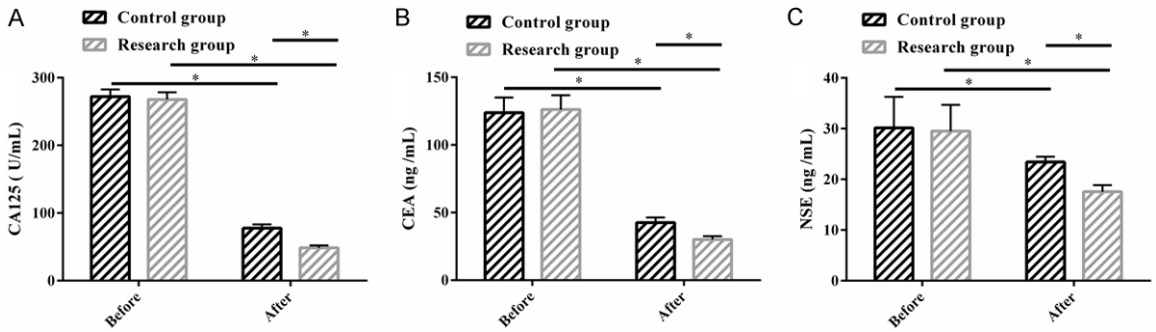

Figure 4. Changes of serum tumor markers in two groups. The serum levels of CA125 (A), CEA (B), and NSE (C) in the research group were significantly lower than those in the control group after treatment. Note: CA125, cancer antigen 125; CEA, carcinoembryonic antigen; NSE, neuron specific enolase; **P<0.01.

and postoperative infection, with an overall complication rate of 8.1%, which is similar to our research results.

Although the effect of TURBT for SBC is remarkable, there are some considerations that should be paid attention to during the actual operation.

The first is to thoroughly flush the patient's urethra and bladder before surgery to ensure the best surgical field of vision [23]. Second, normal bladder tissue should be protected as much as possible during lesion resection to avoid surgical trauma [24]. Third, when the extent of the lesion is not clear, the resection scope should be expanded as much as possible to avoid postoperative recurrence [25]. In our study, the surgical indexes and recovery time of patients in the research group undergoing TURBT were significantly shorter/lower than those in the control group receiving PC, suggesting that TURBT was superior to PC in terms of convenience and safety of the operation and the recovery speed of patients. Patients who underwent surgery had a better prognosis, with a lower recurrence rate and a higher survival rate at two years after surgery. Through the evaluation of various dimensions of the SF-36, we found that the research group treated with TURBT had a better QOL, due to the preservation of bladder and urethral functions and a lower complication rate. Dellabella [26] pointed out that simultaneous transurethral resection of bladder tumor and prostate can significantly improve the treatment safety and the QOL of patients with benign prostatic hyperplasia. This was similar to our results. We also found that the improvement of serum tumor markers CA125, CEA, and NSE in patients treated with TURBT as more significant, which indirectly proved the effectiveness of this treatment.

In this study, we demonstrated that TURBT is effective in the treatment of SBC, and can be recommended as the preferred treatment for patients compared with PC. Our research still has some limitations. The sample size can be expanded to improve the accuracy of the experimental results. An increased scope of evaluation from other dimensions such as stress and inflammation to study the application value of TURBT in the treatment of SBC should be considered. In the future, we will gradually improve the research based on the above points.

To sum up, TURBT has more clinical advantages in treating patients with SBC than PC, which is worthy of extensive promotion.

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Disclosure of conflict of interest

None.

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