Am J Transl Res 2021;13(3):1817-1824
www.ajtr.org /ISSN:1943-8141/AJTR0106640

Original Article

Effect of percutaneous transhepatic cholangial drainag + radiofrequency ablation combined with biliary stent implantation on the liver function of patients with cholangiocarcinoma complicated with malignant obstructive jaundice

Shuangyu Qi, Huijun Yan

Department of Hepatobiliary and Pancreatic Surgery, Hengshui People's Hospital, Hengshui, Hebei Province, China

Received December 19, 2019; Accepted January 15, 2020; Epub March 15, 2021; Published March 30, 2021

Abstract: Objective: To investigate the effect of percutaneous transhepatic cholangial drainage (PTCD) + radiofrequency ablation (RFA) combined with biliary stent implantation on the liver function of patients with cholangiocarcinoma complicated with malignant obstructive jaundice. Methods: Retrospective analysis of 120 patients with cholangiocarcinoma complicated with malignant obstructive jaundice were divided into the research group (n=60) and the control group (n=60) according to different treatments. The research group received PTCD + RFA combined with biliary stent implantation, while the control group received only PTCD combined with biliary stent implantation. The changes of liver function indexes before and after treatment, the condition of postoperative jaundice in different periods after operation, toxicity and survival time were observed. Results: There was no statistically significant difference between the two groups in general data (P>0.05). Before treatment, there was no statistically significant difference between the two groups in albumin (ALB), alkaline phosphatase (ALP), glutamyltranspeptidase (GGT), total bilirubin (TBil) and direct bilirubin (DBil) (all P>0.05). After treatment, the above indicators were all decreased (all P<0.05), and the patient's condition improved, but there was no significant difference between the research group and the control group (P>0.05). There were patients with postoperative jaundice in the two groups at 1 month, 3 months, and 6 months after surgery. The total incidence of postoperative jaundice in the research group and the control group within 6 months was 11.67% and 30.00%, respectively (P<0.05). After treatment, the aftereffects were observed in the research group (15.00%) and the control group (25.00%), including infection, cholangitis, and biliary bleeding, without statistical significance (P>0.05). There was no statistical significant difference in progression-free survival between the two groups (P>0.05), while patients in the research group had higher median survival and 1-year survival rates than those of the control group (both P<0.05). Conclusion: After PTCD + RFA combined with biliary stent implantation was performed on the patients with cholangiocarcinoma complicated with malignant obstructive jaundice, the number of patients with postoperative jaundice at different time points was reduced; 1-year survival rate and median survival were increased; patents' liver function and condition were improved. Thus, this method is worthy of promotion and application.

Keywords: Cholangiocarcinoma complicated with malignant obstructive jaundice, percutaneous transhepatic cholangial drainage, radiofrequency ablation, biliary stent implantation, liver function

Introduction

Malignant obstructive jaundice, which occurs in elderly patients easily, is a bile duct obstruction induced by lesions of the biliopancreatic system. Cholangiocarcinoma complicated with malignant obstructive jaundice are mostly caused by biliary tumors, which presents jaundice on the body surface. The formation of jaundice is closely related to the high expression of bilirubin [1]. The incidence of malignant obstructive jaundice in extrahepatic biliary tract and pancreatic tumors accounts for more than 70% of the incidence of surgical malignant obstructive jaundice, and malignant obstructive jaundice can also be induced by lymphatic metastasis of

other cancers. A large number of studies have shown that the incidence of other organ lesions in patients with cholangiocarcinoma complicated with malignant obstructive jaundice is more than twice that of healthy people, which is a great threat to human life [2, 3].

At present, surgery, a direct way to cure this disease, is one of the main clinical methods. Palliative surgery will be adopted for patients who cannot be cured by removing the lesion. Besides, for patients with cholangiocarcinoma and malignant obstructive jaundice, preoperative biliary drainage should be carefully used. Traditional biliary stent implantation has no effect on malignant tumors, and the probability of recurrent bile duct stricture increases with the passing time. Some scholars have proposed that patients with cholangiocarcinoma complicated with malignant obstructive jaundice are directly related to recurrent bile duct stricture, and it is vital to find a suitable treatment [4]. Currently, percutaneous transhepatic cholangial drainage (PTCD) is commonly used in the diagnosis and treatment of this disease, and new bipolar radiofrequency ablation (RFA) is a nice tool to treat bile duct stricture [5]. However, it is rare of the literature on the combined use of the two treatment options. Therefore, this study explored the effects of PTCD and RFA combined with biliary stent implantation on the liver function, aftereffects and survival rates of such patients.

Materials and methods

General data

From January 2016 to February 2018, 120 patients with cholangiocarcinoma complicated with malignant obstructive jaundice treated in Hengshui People's Hospital were retrospectively analyzed. They were divided into the research group (n=60) and the control group (n=60) according to different treatments. This study was approved by the Ethics Committee of Hengshui People's Hospital. There were no significant differences in gender, age, course of disease and weight between the two groups.

Inclusion and exclusion criteria

Inclusion criteria: All patients were diagnosed as cholangiocarcinoma with malignant obstructive jaundice by B-ultrasound and computed tomography (CT) imaging; all patients met biliary obstruction criteria; all patients signed the consent form.

Exclusion criteria: Patients had bile duct stones and benign obstructive jaundice; patients showed weak compliance; patients did not have complete clinical information.

Methods

The research group received PTCD + RFA combined with biliary stent implantation. Patients were in a supine position. After disinfection, the needle insertion point was selected, and the patient was put to anesthesia status. The needle was inserted in the right place to extract bile at the 11th thoracic spine, and contrast agent was injected (Shanghai New Hualian Pharmaceutical Co. Ltd., China). According to the radiographic display, a guide wire was inserted through the narrow part of bile duct, and then external and internal drainage were performed. External drainage was indwelled at proximal obstruction, such as the duodenum. Then, the internal drainage was performed and anti-infective treatment was prepared. One week later, RFA and biliary stent implantation were performed. First, the degree of stenosis was determined. Then, the drainage catheter was withdrawn and the guide wire was replaced. The RFA catheter was placed into distant biliary stenosis. Multiple ablations were performed based on stenosis, and the range was 4-8 mm on the left and right sides of the narrow end. The stent release was put after the RFA catheter was unplugged. Then, 6 mm biliary stent was put in, with 60 mm in length, covering more than 12 mm on both sides of the narrow part. The successful passage of the contrast agent was regarded as a successful implantation, and then patients took oral inflammation-resolving gall-bladder-excreting tablet (Jilin Aodong Yanbian Pharmaceutical Co. Ltd., China). After 7 d, the drainage tube was unplugged. The control group received only PTCD combined with biliary stent implantation. And the method details were the same as above.

Outcome measures

Liver function indexes: Before and after treatment, 3 mL of venous blood from the patient was collected overnight, and the serum was separated. Then, the following indexes were detected. Albumin (ALB) was detected by bromcresol green method (Shanghai Xinyu Biote-

Table 1. Comparison of general data

	Gender		Average age/year	Course of disease/month	BMI
	Male	Female			
Research group (n=60)	35	25	66.12±7.51	1.64±1.33	19.35±2.39
Control group (n=60)	38	22	67.08±7.02	1.71±1.23	19.44±2.69
χ^2/t	0.534		0.278	0.029	0.193
P	0.766		0.759	0.972	0.846

Note: BMI, body mass index.

chnology, China). Alkaline phosphatase (ALP) and glutamyltranspeptidase (GGT) levels were tested using rate method (the kit from Shanghai Xinfan Biotechnology, China). Total bilirubin (TBil) and direct bilirubin (DBil) were detected by vanadate kit (Xiamen Haifei Biotechnology Company, China). Criterion: ALB: 40-55 g/L; TBil: 3.4-2.0 μmol/L; DBil: 0.0-6.8 μmol/L; ALP: 9-50 U/L; GGT: 15-40 U/L.

Postoperative jaundice changes: Patients in the two groups were re-examined to observe the recurrence of postoperative jaundice at 1 month, 3 months, and 6 months after surgery. New patients with jaundice were considered to be caused by inflammation and treated with hormones. For traditional Chinese medicine, liver-relieving and choleretic method could be adopted. After 1-4 months, the patients recovered well.

Aftereffects: After treatment, the aftereffects were observed in both groups, including infection, cholangitis, and biliary bleeding. Hydrogen peroxide flushing with antibiotics (Shanghai Xinyu Biotechnology Co. Ltd., China) was adopted for biliary tract bleeding; cholangitis is treated with inflammation-resolving gall-bladder-excreting drug; antibiotics were used for biliary infection immediately.

Follow-up survival rate: Patients in the research group and the control group were followed up for 12 months to observe their survival rate.

Statistical analysis

SPSS 22.0 was used for statistical analysis. Liver function, age and course of disease were indicated by mean ± standard deviation ($\overline{x}$ ± sd). Independent sample t-test was used to compare between groups; paired t-test was used to compare before and after treatment in the same group; X^2 test was adopted for gender and other enumeration data; log-rank test was used to compare the survival rates between the two groups. P<0.05 was considered statistically significant.

Results

Comparison of general data

There were no significant differences between the research group and the control group in terms of average age (66.12±7.51 vs 67.08± 7.02 years), history of jaundice (1.64±1.33 vs 1.71±1.23 months) and body mass index (19.35±2.39 vs 19.44±2.69) (all P>0.05). See **Table 1**.

Comparison of liver function indexes

Before treatment, there were no statistically significant differences between the two groups in albumin (ALB), alkaline phosphatase (ALP), glutamyltranspeptidase (GGT), total bilirubin (TBil) and direct bilirubin (DBil) (all P>0.05). Compared with before treatment, there was significant difference after treatment (all P< 0.05). After treatment, patients' condition was improved, without statistically significant difference between the two groups (P>0.05). See **Table 2**.

Comparison of postoperative jaundice at different time points after surgery

There were patients with postoperative jaundice in the research group and the control group at 1 month, 3 months, and 6 months after surgery. The total incidence of postoperative jaundice in the research group and the control group within 6 months was 11.67% and 30.00%, respectively, with a statistically significant difference (P<0.05). See **Table 3**.

Comparison of incidence of postoperative aftereffect

There were aftereffects in the research group (15.00%) and the control group (25.00%) after

Table 2. Comparison of liver function indexes

Group		Research group (n=60)	Control group (n=60)	t	P
ALB	Before treatment	226.49±90.38	225.31±91.03	0.014	0.986
	After treatment	56.28±22.91	57.22±23.34	0.054	0.946
t		14.14	13.86		
P		<0.001	<0.001		
ALP	Before treatment	835.37±412.59	833.15±411.99	0.002	0.998
	After treatment	200.14±75.29	201.78±77.28	0.033	0.948
t		11.73	11.67		
P		<0.001	<0.001		
GGT	Before treatment	785.36±355.39	780.48±360.32	0.005	0.995
	After treatment	175.09±80.83	174.33±81.24	0.046	0.982
t		12.97	12.71		
P		<0.001	<0.001		
TBil	Before treatment	210.49±47.47	211.31±47.39	0.044	0.957
	After treatment	78.48±15.83	77.03±16.48	0.035	0.965
t		20.49	20.73		
P		<0.001	<0.001		
DBil	Before treatment	160.21±35.26	157.33±36.17	0.166	0.837
	After treatment	66.39±10.59	67.17±11.03	0.283	0.816
t		19.74	18.47		
P		<0.001	<0.001		

Note: ALB, albumin; ALP, alkaline phosphatase; GGT, glutamyltranspeptidase; TBil, total bilirubin; DBil, direct bilirubin.

Table 3. Comparison of postoperative jaundice at different time points after surgery

Group	1 month after surgery	3 month after surgery	6 month after surgery	Total incidence
Research group (n=60)	1 (1.67%)	2 (3.33%)	4 (6.67%)	7 (11.67%)
Control group (n=60)	3 (5.00%)	5 (8.33%)	10 (16.67%)	18 (30.00%)
χ^2	0.968	1.216	2.307	4.029
P	0.325	0.270	0.128	0.044

Table 4. Comparison of incidence of postoperative aftereffect

Group	Infection	Cholangitis	Biliary bleeding	Incidence rate
Research group (n=60)	1	2	6	9 (15.00)
Control group (n=60)	2	3	10	15 (25.00)
χ^2				2.500
P				0.114

surgery, without statistically significant difference (P>0.05). See **Table 4**.

Comparison of survival rates

The median survival and 1-year survival rate of patients in the research group were higher than those in the control group (both P<0.05), and the progression-free survival between the research group and the control group showed no statistical significance (P>0.05). See **Table 5** and **Figure 1**.

Case study

A patient, female, 58 years old, was admitted to hospital due to jaundice for 14 days. CT images showed that lesions appeared in the head of pancreas, and the common bile duct and gallbladder were dilated. The disease was considered to be pancreatic head carcinoma involving the duodenum. CT images during the treatment process were shown in **Figure 2**.

Discussion

The onset of malignant obstructive jaundice is uneasy to be found; thus, the golden treatment time is often missed. Malignant obstructive jaundice is a narrow obstruction somewhere in

Table 5. Comparison of long-term survival rates

Group	Progression-free survival/month	Median survival/month	1-year survival rate (%)
Research group (n=60)	5.46±0.28	11.06±3.25	14 (23.33)
Control group (n=60)	5.47±0.25	8.18±3.12	7 (11.67)
t/χ^2	0.173	9.026	4.235
P	0.863	<0.001	0.040

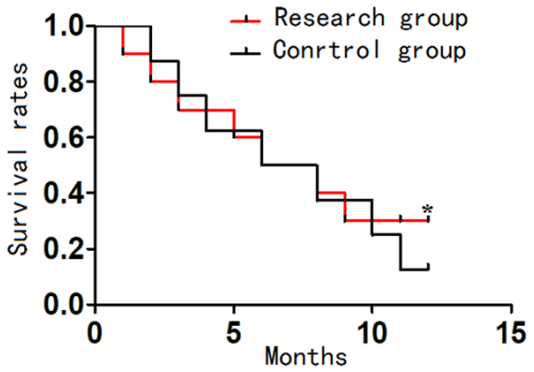

Figure 1. Survival rates of the research and control groups. Compared with the control group, *P<0.05.

the extrahepatic bile duct caused by diseases such as cholangiocarcinoma. Patients with biliary obstruction have abnormal liver function, poor nutritional absorption, and low protein levels, which can lead to a series of aftereffects [6]. If the condition worsens, it will induce bilirubin to enter the blood, affect multiple organ systems and threaten life [7, 8].

In this study, patients in the research group and the control group treated with PTCD + biliary stent implantation + intra-cavity RFA or PTCD + biliary stent implantation had changed liver function indexes before and after surgery and improved liver function, but without difference after surgery between the two groups. For patients with cholangiocarcinoma jaundice, bile duct incision is commonly used to reduce pressure and perform drainage, but with high incidence of postoperative infection. PTCD and RFA are new minimally invasive technologies in recent years that can help patients with bile circulation [9, 10]. ALP, TBil and DBil all improve significantly in patients with cholangiocarcinoma complicated with malignant obstructive jaundice; harmful substances in bile flow back into the body, inducing heart and kidney damage [11]. The success of PTCD puncture was able to accurately report the extent of bile duct dilatation, and its combination with ablation and stent could prevent reflux and jaundice recurrence and have a significant effect on patients with malignant jaundice in the middle and advanced stages, which was consistent with the results in studies of Alkawas [12, 13]. This showed that PTCD and RFA combined with biliary stent could improve the lesion, reduce bile duct pressure, and promote the return of liver cells to normal, which was consistent with the results of Zhang [14].

In this study, postoperative jaundice in the research group was less than that in the control group within 6 months. Hsien-Tzu found that patients with cholangiocarcinoma complicated with malignant obstructive jaundice used bile duct puncture drainage combined with RFA and stent implantation to relieve jaundice, which reduced bile duct pressure, promoted bile to enter the intestinal tract, participated in metabolic absorption, restored the immune capacity, and reduced endotoxin production, flora imbalance and postoperative jaundice recurrence [15]. Kinoshita found that the use of PTCD to puncture patients with cholangiocarcinoma and malignant obstructive jaundice, followed by ablation combined with stent, reduced tumor cell regeneration, improved treatment effect, and prevented jaundice regeneration, which was consistent with the results of Hashim [16-18]. Therefore, this study revealed that the use of PTCD, RFA combined with bile duct stent reduced jaundice recurrence and improved the condition. In this study, the incidence of infection, cholangitis and biliary bleeding in the control group was higher, and the survival rate and median survival of patients in the research group were higher. Nakai found that in patients with malignant biliary jaundice treated with PTCD combined with ablation, inflammatory response occurred in the bile duct of 2 patients; however, after treatment with biliary medicine, the symptom alleviated, and the condition, 1-year survival rate as well as survival time improved [19, 20]. In the study by Dai, patients with cholangiocarcinoma complicated with

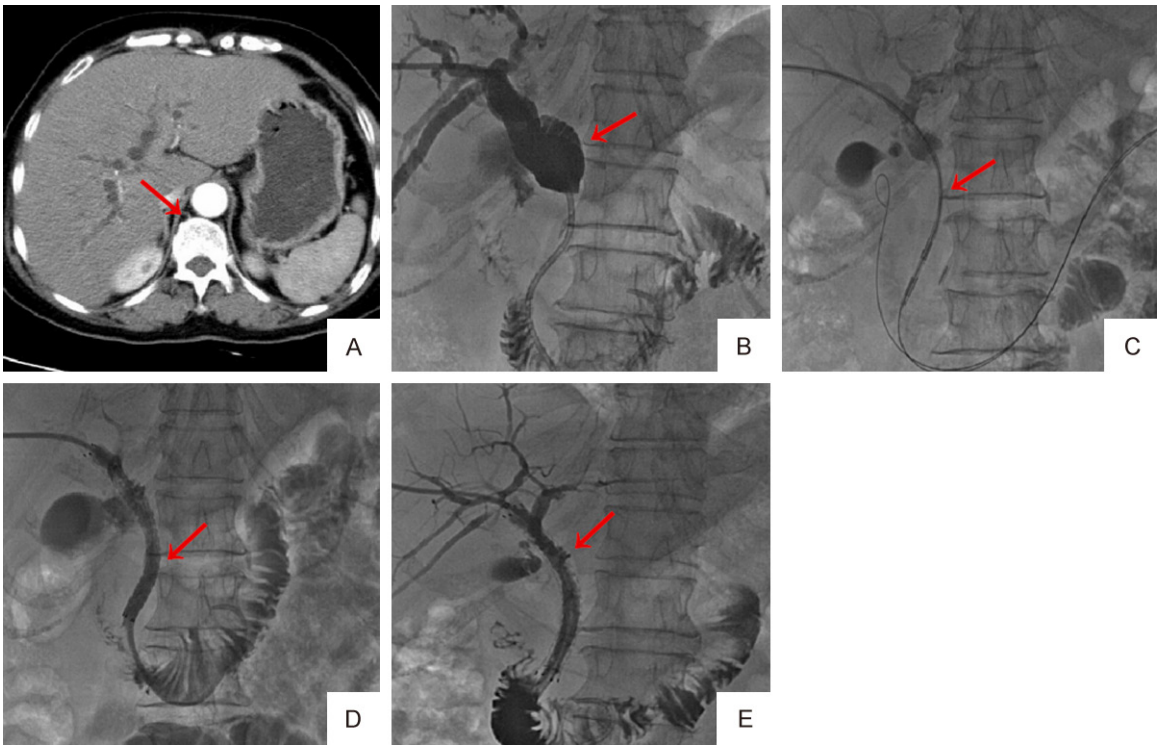

Figure 2. Case study. Note: (A) The arrow showed that the patient had common bile duct dilatation, cholangiocarcinoma complicated with malignant obstructive jaundice by CT examination at admission. (B) The arrow showed that at PTCD cholangiography by puncturing, it found intrahepatic bile duct dilation, and rhamphoid lower end of the common bile duct. (C) The arrow showed that in PTCD combined with RFA method, the ablation catheter was put along the hard exchanged guide wire to perform radiofrequency ablation in the stricture part of the common bile duct. (D) The arrow showed the implantation of biliary stent. (E) The arrow showed that a metal stent was implanted after balloon dilation, and the cholangiography found well expanded stent and reopen of the common bile duct.

malignant obstruction treated with bile duct puncture and ablation had reduced aftereffects, quicker recovery, increased survival time and median survival, and good stent unblocked effect [21, 22]. It indicated that PTCD + RFA + biliary stent implantation in the research group could increase survival time of the patient and reduce complications, which was of great significance to improve patient's condition and quality of life.

In summary, PTCD + RFA + biliary stent implantation in patients with cholangiocarcinoma complicated with malignant obstructive jaundice reduce postoperative jaundice at different time points after surgery, increase the survival rate and median survival, and improve liver function and condition, which are worthy of promotion and application. However, there were shortcomings in this study. During the surgery, the positioning of biliary stent and the position of obstruction were not accurate enough; a small number of patients had complications after the surgery. In this study, PTCD + RFA combined with biliary stent implantation have a good treatment effect and promote the quick recovery of patients. However, whether biliary stent implantation practice and ablation zone should be expanded needs to be further studied.

Disclosure of conflict of interest

None.

Address correspondence to: Shuangyu Qi, Department of Hepatobiliary and Pancreatic Surgery, Hengshui People's Hospital, No. 180 Renmin East Road, Taocheng District, Hengshui 053000, Hebei Province, China. Tel: +86-15610836325; E-mail: qishuangyu4hs7@163.com

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