

Bare-metal stents across the Vater's ampulla is a safe method for patients with lower bile duct obstruction

Xiao-Nan Mao, MD, Zai-Ming Lu, MD, Feng Wen, MD, Hong-Yuan Liang, MD, Qi-Yong Guo, MD*

Abstract

This study explored the effect of the implant position of stents across the Vater's ampulla on treatment outcomes in patients with lower bile duct obstruction.

In the retrospective study, 41 patients with malignant obstruction of the lower bile duct and obstructive jaundice received percutaneous transhepatic biliary placement of bare-metal stents. Basic demographic data on patients, such as sex, age, and primary diseases, and follow-up data, including postoperative complications and jaundice-free survival, were recorded. The follow-up data on patients with an involved ampulla, patients with an uninvolved ampulla, patients with a stent across the ampulla, and patients with a stent at a site other than the ampulla were compared. Furthermore, prognostic factors for jaundice-free survival were investigated using Cox proportional hazards regression analysis.

Among the 41 patients, 38 patients experienced subsiding of jaundice, whereas 3 cases had unsuccessful stent patency. Whether or not the ampulla was involved did not influence the incidence rates of postoperative complications and the jaundice-free survival time. Notably, when stents were placed across the ampulla, the jaundice-free survival time was significantly longer than when stents were placed at sites other than across the ampulla ($P < .05$). Furthermore, placement of the stent across the ampulla or at other sites was an independent prognostic factor (hazard ratio=0.154, 95% confidence interval 0.042–0.560, $P = .005$) for jaundice-free survival of patients.

The current study revealed that the implant position of a stent across the ampulla resulted in maintenance of stent patency and prolongation of the jaundice-free survival time.

Abbreviations: CI = confidence intervals, HR = hazard ratio.

Keywords: implant position of biliary stents, jaundice-free survival, malignant lower bile duct obstruction, postoperative complications, stents across ampulla

1. Introduction

Malignant obstructive jaundice caused by lower bile duct obstruction is the main symptom of periampullary cancers, such as pancreatic carcinoma, cholangiocarcinoma, and ampullary carcinoma.^[1] Long-term cholestasis in the intrahepatic or extrahepatic duct can seriously impair liver function, thereby

resulting in liver failure and death.^[1,2] Although technological advances have been achieved, radical surgery for periampullary cancers may cause the significant injury, and jaundice caused by biliary obstruction is closely related to high morbidity and mortality.^[3,4] Thus, relieving jaundice is a prime concern during the palliative treatment of patients with malignant obstruction of the lower bile duct.^[5]

Biliary drainage is considered an effective method for diminution of potentially life-threatening obstructive jaundice by discharging bile from the intrahepatic or extrahepatic duct.^[6] Currently, a drainage tube usually is implanted via the nose, esophagus, stomach, and major duodenal papilla under endoscopy, or via a percutaneous transhepatic biliary approach.^[7,8] However, because of long-term retention of the drainage tube, all these approaches can lead to loss of the bile and severe reduction in patients' quality of life.^[8]

Notably, a biliary stent may avoid these disadvantages, and a stent can provide drainage of the biliary tree across the obstructing mass.^[9] Currently, metal stents have been applied widely in clinical practice, because of the advantages in preventing the growth of bacteria and maintaining stent patency.^[10,11]

Although the placement of bare-metal stents has an obvious therapeutic effect for malignant biliary obstruction, potential complications, such as stent restenosis, attract much clinical attention.^[12,13] Because lesions may be involved in obstruction of the ampulla of Vater, the placement of stents may influence the structure or function of Vater's ampulla, and increase the

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This study was approved by the Ethics Committee of Shengjing Hospital affiliated with China Medical University. Informed consent was obtained from the included patients. The authors declare no conflicts of interests.

Department of Radiology, Shengjing Hospital, China Medical University, Shenyang, Liaoning, China.

* Correspondence: Qi-Yong Guo, Department of Radiology, Shengjing Hospital, China Medical University, No. 36, Sanhao Street, Heping District, Shenyang, Liaoning 110004, China (e-mail: guoqy_med@163.com).

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incidence rates of complications in patients with lower bile duct obstruction.^[14–16] In addition, several studies have reported that stents across the ampulla could lead to stent restenosis and cholangitis because of the intestinal-biliary backflow, thereby reducing the curative effect.^[16–18] Therefore, it is important to investigate further whether stents should be placed across the ampulla.

The current study focused on the relationships of the site of biliary obstruction and Vater's ampulla, and the implant position of the stent and Vater's ampulla. Determining the long-term therapeutic effects and the incidence rates of complications were aimed at investigating the efficacy and safety of stents across the ampulla in patients with lower bile duct obstruction and obstructive jaundice.

2. Materials and methods

2.1. Study population

This retrospective study was approved by the Ethics Committee of Shengjing Hospital affiliated with China Medical University. In total, 54 patients with malignant lower bile duct obstruction and obstructive jaundice who received percutaneous transhepatic biliary placement of bare-metal stents from January 2013 to December 2015 at Shengjing Hospital affiliated with China Medical University were recruited in the study. Lower biliary obstruction was confirmed according to preoperative imaging examinations and intraoperative cholangiography. Electronic medical records were available for all patients, and telephone follow up was performed for all patients. Patients without a follow-up visit were excluded from the study. The final study population included 41 patients. Basic demographic information on patients, such as sex, age, and primary diseases, were recorded. Because all patients received palliative therapy, but not surgery for the malignancies, primary diseases such as pancreatic carcinoma, cholangiocarcinoma, ampullary cancer, and postoperative lymph node metastasis were diagnosed according to laboratory and imaging examinations.

2.2. Clinical treatment

All patients received implantation of a bare-metal stent on the distal common bile duct via a percutaneous transhepatic biliary approach. After the DLPN trocar was punctured into the intrahepatic bile duct under the guidance of ultrasonography, the 0.035-inch guidewire was inserted along the catheter and advanced over the stenosis of the common bile duct to the intracavity of the duodenum. Next, a 5F angiographic catheter was advanced through the guidewire to determine the stenosis of the common bile duct and ampulla, followed by the removal of the catheter. For a one-step method, the bare-metal stent (Angiomed GmbH & Co. Medizintechnik KG, Germany; diameter, 10mm; length, 4–10cm) was placed along the guidewire to pass through the stenosis. When lesions were involved in the ampulla, the bare-metal stent was placed across the ampulla into the intracavity of the duodenum. The length of the stent was longer than 1 cm beyond the stenosis. For a 2-step method, the drainage catheter was inserted along the guidewire, and then the biliary stent was implanted until resolution of jaundice occurred. After implantation of the bare-metal stents, the drainage catheter was placed in the biliary tract to confirm the stent patency by cholangiography, followed by closure.

Patients received conventional anti-inflammation, liver protection, and rehydration treatments during the perioperative period.

Meanwhile, perioperative symptoms, such as bile leakage, abdominal pain, and fever, were observed. Hemogram analysis of blood cells and measurement of hepatic function via level of serum bilirubin were performed at 3 to 5 days after the operation. The daily bile flux was recorded. After the drainage catheter was closed for 48 hours, the yellowing of the skin and eyes had faded, the level of serum bilirubin was reduced, and no complications were found, cholangiography was performed again to confirm stent patency. Ultimately, the drainage catheter was removed, and patients were discharged from the hospital.

2.3. Grouping of patients

All patients were classified into ampulla involved (group A) and ampulla not involved (group B), based on the preoperative imaging examinations and intraoperative cholangiography. No clear boundary was found between common bile duct stenosis and ampulla region in patients in group A (Fig. 1), whereas a normal biliary tract was observed between common bile duct stenosis and ampulla region in patients in group B (Figs. 2 and 3). According to whether some stents were placed across the ampulla into the duodenum, patients were classified into stent across ampulla (group C) (Figs. 1 and 3) and stent not across ampulla (group D) (Fig. 2). In addition, patients in group B were further classified into uninvolved ampulla + stent across ampulla (group E) and uninvolved ampulla + stent not across ampulla (group F). In the following sections of this article, groups A–F denote the 6 groups of patients.

2.4. Clinical follow-up

All patients were followed up to June 2016. The electronic medical records were analyzed, telephone follow up was performed, and complications such as stent restenosis, biliary infection, and gastrointestinal bleeding were recorded. The jaundice-free survival of patients was calculated. For patients without stent restenosis, the follow up endpoint was death or survival. For patients with stent restenosis, the follow up endpoint was defined at the day of stent restenosis.

2.5. Statistical analysis

SPSS 17.0 software (SPSS Inc., Chicago, IL) was used to perform statistical analysis of data. The rates of stent restenosis, biliary infection, and gastrointestinal bleeding between groups A and B, C and D, or E and F were compared by χ^2 test. The Kaplan–Meier method was used to construct the survival curves. The difference in jaundice-free survival rates was analyzed using the Gehan–Breslow–Wilcoxon test. To confirm the prognostic roles of the following factors: age, sex, types of primary disease, lesions involving ampulla or not, and stent across ampulla or at other sites, the Cox proportional hazards regression multivariate analysis was used to calculate the hazard ratio (HR) and 95% confidence intervals (CI). $P > .05$ were considered statistically significant.

3. Results

3.1. Patient characteristics

A total of 41 patients with malignant lower biliary obstructive jaundice who received percutaneous placement of bare-metal stents were included in this study. Baseline characteristics of

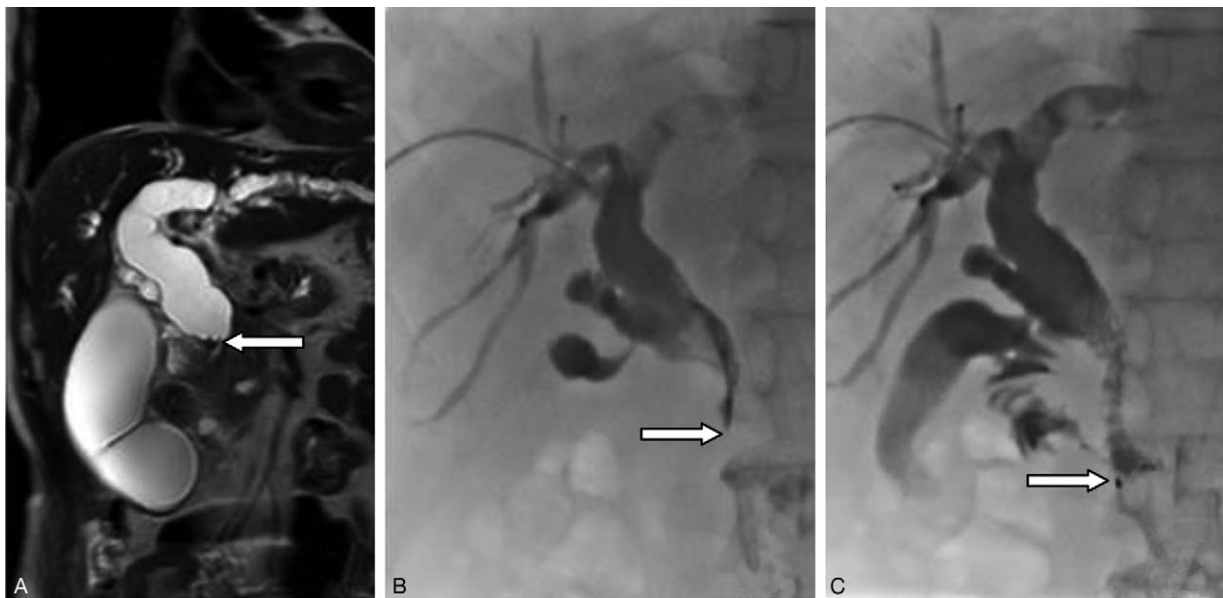


Figure 1. The preoperative imaging examinations and intraoperative cholangiography of a patient (male, 73 years old) with pancreatic carcinoma. A, The preoperative MR imaging of the common bile duct. The arrow indicates the distal common bile duct. B, The intraoperative cholangiography image before stent implantation. The arrow indicates the involved ampulla. C, The intraoperative cholangiography image after stent implantation. The arrow indicates the distal stent across the ampulla into the duodenum.

patients are shown in Table 1. The mean age of the patients was 71.3 years, with a range of 48 to 94 years. Of the patients, 24 were males, and 17 were females. In the study, there were 23 cases with pancreatic carcinoma, 6 cases with cholangiocarcinoma, 5 cases with ampullary cancer, 4 cases with postoperative lymph node metastasis, and 3 cases with other primary diseases.

3.2. Treatment outcomes

The success rate of biliary stent placement was 100% in terms of resolution of jaundice. Only one patient received a one-step method of implantation, whereas 40 patients received a 2-step method of implantation. During cholangiography, in addition to the lack of an imaging result in one case, 20 cases received intercostal puncture at the right axillary midline, and 20 cases

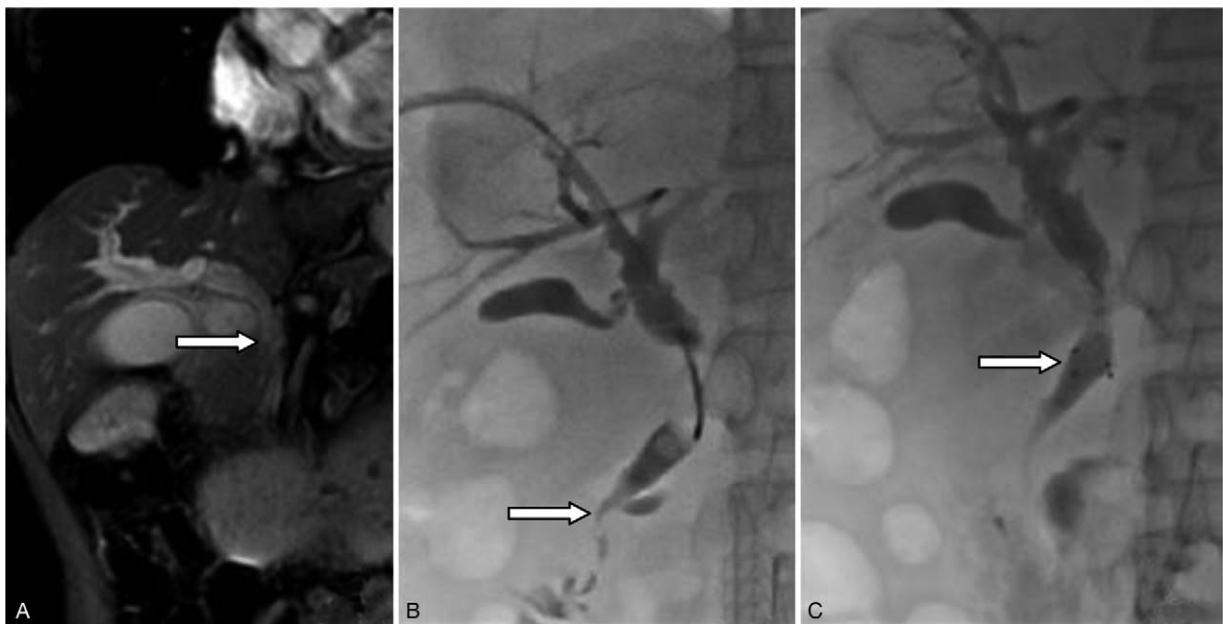


Figure 2. The preoperative imaging examinations and intraoperative cholangiography of a patient (female, 72-years old) with pancreatic carcinoma. A, The preoperative MR imaging of the common bile duct. The arrow indicates the distal common bile duct. B, The intraoperative cholangiography image before stent implantation. The arrow indicates the uninvolved ampulla and the normal common bile duct. C, The intraoperative cholangiography image after stent implantation. The arrow indicates the distal stent, which is not across the ampulla.

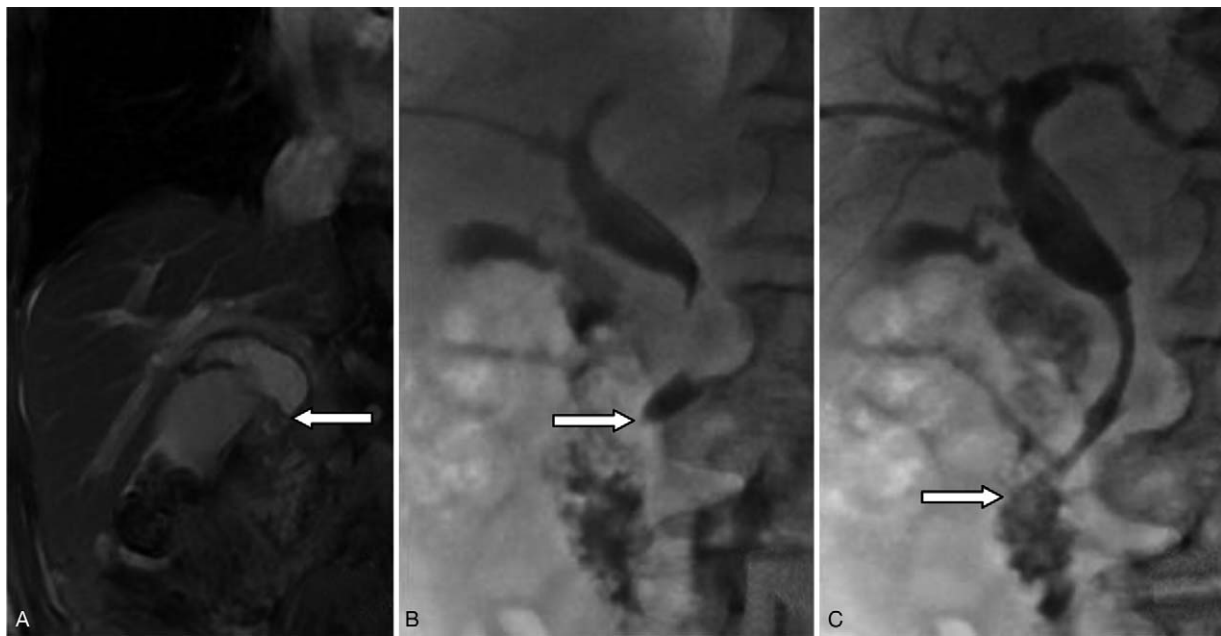


Figure 3. The preoperative imaging examinations and intraoperative cholangiography of a patient (male, 86 years old) with pancreatic carcinoma. A, The preoperative MR imaging of the common bile duct. The arrow indicates the distal common bile duct. B, The intraoperative cholangiography image before stent implantation. The arrow indicates the uninvolved ampulla and the normal common bile duct. C, The intraoperative cholangiography image after stent implantation. The arrow indicates the distal stent across the ampulla into the duodenum.

received the puncture below the xiphoid. As the imaging examinations and cholangiography results revealed that the lesions were involved in the ampullar region in 9 patients, all the stents in these 9 patients were placed across the ampulla. For the 32 patients lacking lesions in the ampullar region, 25 cases received a stent across the ampulla, and 7 cases received a stent at a site other than across the ampulla.

Five patients had unsuccessful stent patency. For these 5 patients, balloon dilatation was performed in 3 cases performed

balloon dilatation; only 2 of these cases receiving balloon dilatation showed stent patency. Drain removal was performed in 38 cases in which jaundice subsided. However, the drains were not removed from the remaining 3 cases in which stent patency was unsuccessful.

3.3. Postoperative complications

Postoperative complications were recorded. The results revealed 15 cases with stent restenosis, 16 cases with biliary infection, and 7 cases with gastrointestinal bleeding. No significant difference was found in the incidence rates of these postoperative complications between group A and group B, group C and group D, or group E and group F (Table 2).

3.4. Prognostic factors for jaundice-free survival of patients

Only one of the 41 patients was lost to the follow-up visit. At the end of the follow-up period, 38 of the 40 patients died of stent restenosis and the rest 2 patients are still alive.

Table 1

The baseline characteristics of patients.

Characteristics	N (41)
Age, yrs (range)	71.3 (48–94)
Sex (male/female)	24/17
Primary diseases	
Pancreatic carcinoma	23
Cholangiocarcinoma	6
Ampullary cancer	5
postoperative lymph node metastasis	4
Others	3

Table 2

Postoperative complications of patients.

Group	N	Stent restenosis	P	Biliary infection	P	Gastrointestinal bleeding	P
Group A	9	4	NS	4	NS	1	NS
Group B	32	11		12		16	
Group C	34	11	NS	14	NS	6	NS
Group D	7	4		2		1	
Group E	25	7	NS	10	NS	5	NS
Group F	7	4		2		1	

Group A, ampulla involved; Group B, ampulla not involved; Group C, stent across; Group D, stent not across; Group E, ampulla not involved + stent across; Group F, ampulla not involved + stent not across; NS = not significant.

Table 3

The jaundice free survival time of patients.

Group	N	Range (month)	Mean survival time (month)	P
Group A	9	0–20	6.676 ± 2.865	.206
Group B	32	0–31	6.563 ± 1.183	
Group C	34	0–31	7.563 ± 1.624	.013
Group D	7	0–5	2.429 ± 0.685	
Group E	25	0–31	7.485 ± 1.246	.006
Group F	7	0–5	2.429 ± 0.685	

Group A, ampulla involved; Group B, ampulla not involved; Group C, stent across; Group D, stent not across; Group E, ampulla not involved + stent across; Group F, ampulla not involved + stent not across.

Only 2 of the 40 patients were still jaundice-free for 8 months and 15 months, respectively. The mean jaundice-free survival time of the 40 patients was 5.950 months, with a range of 0 to 31 months; the median jaundice-free survival time was 4 months. There was no significant difference in the jaundice-free survival

time between group A and group B (Table 3, Fig. 4A). Compared with group C, patients in group D had reduced jaundice-free survival time (2.429 ± 0.685 vs 7.563 ± 1.624, P = .013, Table 3, Fig. 4B). In addition, a lower jaundice-free survival time was found in group F than in group E (2.429 ± 0.685 vs 7.854 ± 1.452, P = .006, Table 3, Fig. 4C). To explore the prognostic factors, the Cox proportional hazards regression models were analyzed. The multivariate analyses demonstrated that stent placement across ampulla or at other sites (HR = 0.154, 95% CI 0.042–0.560, P = .005) was an independent prognostic factor for jaundice-free survival of patients (Table 4).

4. Discussion

In the current study, 41 patients with malignant obstruction of the lower bile duct and obstructive jaundice who received implantation of stents were followed. The results revealed that 38 patients experienced resolution of jaundice, whereas 3 cases had unsuccessful stent patency. In addition, no significant difference was observed in the incidence rates of postoperative complications and the jaundice-free survival time between group A and group B. This result suggested that the impaired structure or function of Vater’s ampulla prior to stent placement did not increase the incidence rates of postoperative complications, as well as did not decrease the jaundice-free survival time.

We then focused on the influence of placement of stents across the ampulla in terms of postoperative complications and jaundice-free survival. The results demonstrated that there was no significant difference in the incidence rates of postoperative complications. Thus regardless of whether or not the structure or function of Vater’s ampulla was impaired, the open ampulla caused by stent placement across ampulla also did not increase the incidence rates of postoperative complications.

These 2 results showed that the implantation of a stent across the ampulla was a safe method, which was consistent with the results of Feng^[19] and Hu.^[20] An animal experiment of Wen et al^[21] had shown that implantation of a stent across the ampulla

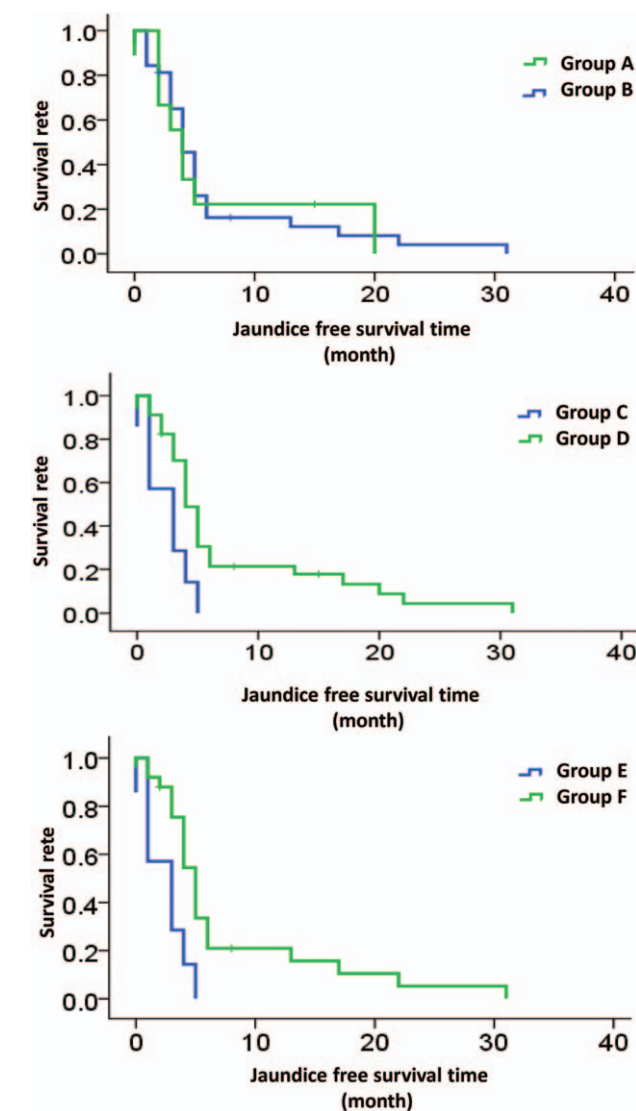


Figure 4. The jaundice-free survival curves of patients by the Kaplan-Meier method. A, The jaundice-free survival curves of patients between Group A and Group B. B, The jaundice-free survival curves of patients between Group C and Group D. C, The jaundice-free survival curves of patients between Group E and Group F.

Table 4

Cox proportional hazard regression model analyses of whole cohort.

Factors	HR	95% CI		P
		Low	High	
Age	1.013	0.979	1.048	.465
Sex	0.631	0.314	1.267	.195
Primary disease types	2.113	0.863	5.170	.101
Lesions involved ampulla or not	1.735	0.692	4.348	.240
Stent across ampulla or not	0.154	0.042	0.560	.005

CI = confidence intervals, HR = hazard ratio.

could only reduce the functional contraction of the sphincter, but not the basic contraction of the sphincter. Therefore, although the open ampulla in the animal study by Wen et al was induced by implantation of a stent across the ampulla, the basic pressure gradient could be maintained and intestinal-biliary backflow and consequent side effects were inhibited effectively.

Although stent restenosis can be caused by multiple factors, the continuous progression of a tumor has been considered as a key factor in stent restenosis.^[22,23] However, our study found that when stents were placed across the ampulla, the jaundice-free survival time was significantly longer than when stents were placed at other sites. In the current study, stent placement across the ampulla or at other sites was considered to be an independent prognostic factor for jaundice-free survival of patients. The reasons might be that (1) the coverage of stent across the ampulla was greater than when stents are placed at other sites, so the longitudinal growth of tumor might result in longer time needed for stent restenosis to be induced; and (2) after the short-term damage and inflammation caused by stent implantation, the proliferation of bile duct endothelial cells was decreased in a shorter period of time,^[24] and the expression of tumor suppressor genes was higher in an area covered by a stent across the ampulla than in another area covered by a stent at a different site.^[25] Thus, we speculated that the area covered by a stent might have a stronger role in inhibiting tumor proliferation, which might lead to the longer jaundice-free survival time of patients. Further studies should be performed to investigate this possibility.

5. Conclusions

The current study reveals that the implant position of a stent across the ampulla of Vater in patients with malignant obstruction of the lower bile duct may not increase the incidence rates of postoperative complications, and may represent a benefit in maintaining stent patency and prolonging the jaundice-free survival time. Therefore, we suggest that an implant position of a stent across the ampulla be considered as one of the optimizing treatments for patients with malignant lower bile duct obstruction and obstructive jaundice.

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