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Covered vs bare stent for distal malignant biliary obstruction due to primary common biliary cancer

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Abstract

This study was designed as a means of comparing the clinical efficacy and long-term outcomes of covered vs bare stent insertion as a treatment for distal malignant biliary obstruction (DMBO) caused by primary common biliary cancer (PCBC).

This retrospective study was designed using data collected between January 2012 and December 2019 to assess the short- and long-term outcomes in patients with DMBO caused by PCBC treated by inserting either bare or covered stents were compared.

Ninety two patients with DMBO caused by PCBC were divided between bare (n = 51) or covered (n = 41) stent groups. Technical success rates in both groups were 100%. Clinical success of bare vs covered stent use were 96.1% and 97.6% ($P = 1.00$). Stent dysfunction was seen in 17 and 6 patients in the bare and covered stent groups, respectively ($P = .04$). The median stent patency for bare and covered stents was 177 and 195 days, respectively ($P = .51$). The median survival was 188 and 200 days in the bare and covered stent groups, respectively ($P = .85$).

For patients with DMBO caused by PCBC, using bare vs covered stents yields similar clinical efficacy and long term outcomes.

Abbreviations: CI = confidence intervals, DMBO = distal malignant biliary obstruction, HR = hazard ratios, MBO = malignant biliary obstruction, OR = odds ratio, PCBC = primary common biliary cancer.

Keywords: bare, common biliary obstruction, covered, stent

1. Introduction

Malignant biliary obstruction (MBO) frequently develops in patients suffering from primary or secondary tumors that have affected the hepato–biliary–pancreatic system.[1–4] MBO not only limits the patients' survival, but also causes the jaundice, which decreases the patients' quality of life.[1–4] Stent insertion remains the most common palliative intervention toward relieving the symptoms related to cholangitis, pain, and jaundice.[1–4] However, stent dysfunction remains a major postoperative problem.

Tumor in-growth is a major cause of stent dysfunction. Covered stents had been designed to prevent the tumor in-growth occurring with bare stents.[5–11] At present, the covered stents were usually used for patients with distal MBO (DMBO).[5–11] A randomized controlled trial had demonstrated that covered stents had a longer duration of patency (219 d vs 167 d, $P < .05$) than bare stents for patients with DMBO.[7] However, another randomized controlled trial had demonstrated that covered stents failed to prolong the stent patency (395 d vs 365 d, $P = .47$) for patients with DMBO.[8] Therefore, the clinical effectiveness of covered stents was still controversial.

Some previous studies regarding of covered vs bare stenting for DMBO contained biliary cancer, pancreatic cancer, and metastases.[8–11] Therefore, the potential bias might be caused by the multiple cancer types. To overcome this disadvantage, the studies which only contain the unique disease are needed to reduce the risk of bias. Some studies have focused on the DMBO caused by pancreatic carcinoma.[5,7] However, there lacks the study which focus on the DMBO caused by primary common biliary cancer (PCBC).

Herein, we aimed to assess the clinical efficacy and long-term outcomes of covered stenting for patients with DMBO caused by PCBC.

2. Materials and methods

This retrospective study was approved by the Institutional Review Board of The Fourth People's Hospital of Taizhou. As the study was retrospective, patient written informed consent requirements were waived.

2.1. Study design

Consecutive patients with DMBO caused by PCBC were treated via either bare or covered stenting between January 2012 and

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December 2019. The patients who were treated before January 2016 underwent bare stenting, while those who were treated thereafter underwent covered stenting.

The patient inclusion criteria were:

1. a confirmed diagnosis of DMBO caused by PCBC,
2. inoperable cases or patients who unwilling to undergo surgery, and
3. Eastern Cooperative Oncology Group performance status (ECOG PS) < 4.

Patient exclusion criteria were:

1. DMBO caused by pancreatic cancer or metastasis lymph nodules, and
2. patients who experienced severe cardiac, renal, lung, or coagulatory dysfunctions.

2.2. Diagnosis

DMBO was confirmed based on patients' clinical symptoms, liver function tests, computed tomography (CT), and magnetic resonance imaging (MRI) results. The pathological diagnoses of PCBC were confirmed via biopsy.

2.3. Bare and covered stents

A bare stent was a normal self-expanded metal stent (Micro-Tech, Nanjing, China). The stent diameter and length were 8 mm and 60 to 80 mm, respectively.

A covered stent had a silicone membrane which is loaded internally to the stent skeleton (Micro-Tech). The stent diameter and length were 8 mm and 60 to 80 mm, respectively.

2.4. Stent insertion

Both bare and covered stents were inserted under the fluoroscopic guidance. The methods of bare and covered stents insertion were same. A 21G Chiba needle (Cook, Bloomington, IN) was punctured into the intrahepatic biliary tract via the right approach. The contrast-medium was injected into the biliary tract to confirm the DMBO site and the length of obstruction. A 4F angiographic catheter (Cordis, Warren, FL) with a 0.035-inch normal guide wire (Terumo, Tokyo, Japan) was then employed to pass through the obstruction. When the catheter and guide wire entered the duodenum, a 0.035-inch stiff guide wire (Cook) was used to replace the normal guide wire. The stent introducer sheaths were sent to the DMBO site via the stiff guide-wire and the stents were released to recanalize the obstruction.

All patients were placed an 8.5F temporary biliary drainage catheter (Cook) and administered preventive anti-inflammatory medications and hemostasis for 5 days.

2.5. Assessment

Stent insertion technical success was verified by assessing the smoothness of contrast-medium flow through the stent as a surrogate for obstruction elimination.[6,7] The definition of clinical success was a 30% or greater reduction in total bilirubin levels after 2 weeks post insertion.[1–3] Stent dysfunction included stent reobstruction and migration. In-growth was defined as in-stent stenosis which balloon sweep or biliary drainage were unable to eliminate.[3] Sludge was also defined as in-stent stenosis which balloon sweep or biliary drainage were unable to eliminate.[3] Stenosis below or above the stent was defined as overgrowth.[3] Patient survival was defined as the duration between stent insertion and death.

All patients had a postoperative physical examination, a CT examination, and liver function tests after 2 weeks, and after 1, 3, and 6 months, as well as every 6 months thereafter.

2.6. Statistical analysis

SPSS v16.0 (SPSS, Inc., IL) was employed for statistical testing. Continuous variables are given as means ± standard deviations and were analyzed via t tests. Categorical variables were presented as a percentage (number/total) and analyzed using χ^2 tests. Duration of patient survival and stent patency were compared using Kaplan–Meier curves and log-rank tests. Factors associated with patient survival were identified through the use of multivariate Cox regression analyses. All variables achieving a P value <.1 in the initial univariate analysis were incorporated into the subsequent multivariate model. $P < .05$ was the significance threshold.

3. Results

3.1. Patients

During the study period, ninety two patients with DMBO caused by PCBC were divided into bare (n = 51) and covered (n = 41) stent groups (Fig. 1). All patients had common biliary adenocarcinoma. The baseline data were comparable between the 2 groups (Table 1). There were no differences regarding the poststent chemotherapy instituted in both groups (bare stent group: 25; covered stent group: 22, $P = .66$). No patient was lost to follow up.

3.2. Technical success

Technical success of stent insertion in both groups was 100% (Table 2, Fig. 2). Neither group exhibited procedure-related complications. Each patient received 1 stent.

3.3. Clinical success

Clinical success was 96.1% (49/51) in the bare stent group and 97.6% (40/41) in the covered stent group ($P = 1.00$). Both groups saw a significant decrease in total bilirubin, aspartate transaminase, and alanine aminotransferase levels after treatment (see Table 1).

3.4. Stent dysfunction

Seventeen and 6 patients in the bare and covered stent groups suffered stent dysfunction (33.3% vs 14.6%, $P = .04$, Table 2). In bare stent group, the causes of stent dysfunction included tumor in-growth (n = 13), tumor over-growth (n = 3), and sludge (n = 1). In covered stent group, the causes of stent dysfunction included tumor over-growth (n = 4) and sludge (n = 2). The covered stent group saw no tumor in-growth in contrast to 25.5% in the bare stent group ($P < .01$). The incidence of tumor over-growth or sludge did not significantly differ between the 2 groups (Table 2).

In the bare stent group, 17 stent dysfunctions were remedied by inserting a second stent (n = 11) or a biliary drainage catheter (n =

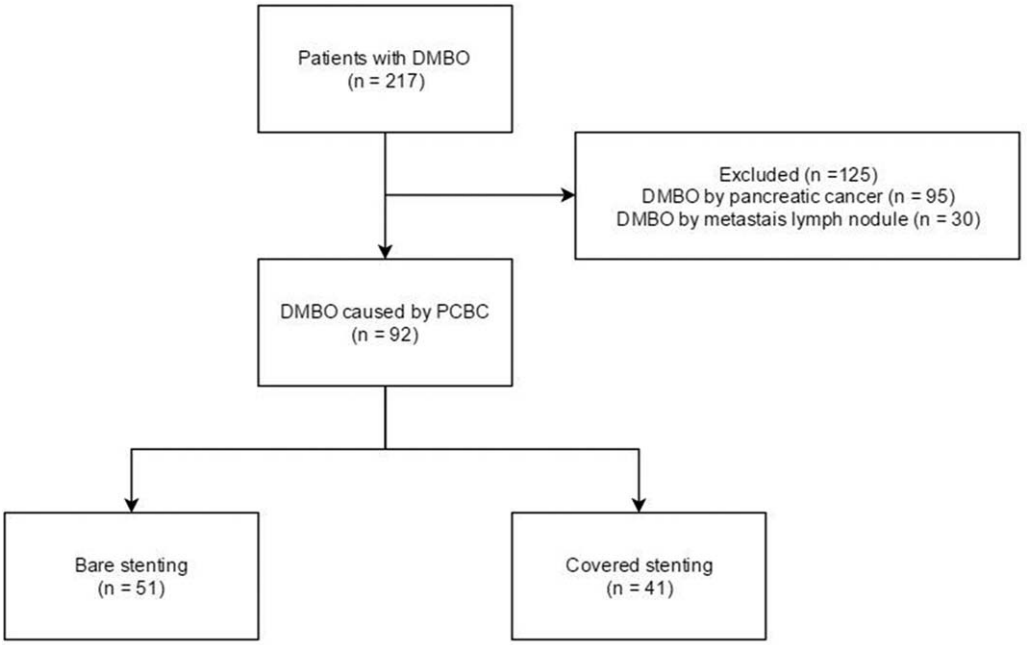

Figure 1. The flowchart of this study.

6). In the covered stent group, all stent dysfunctions were remedied by inserting a biliary drainage catheter.

3.5. Patency

Median stent patency was 177 and 195 days in the bare and covered stent groups ($P=.51$, Fig. 3a). The risk factor of stent dysfunction was evaluated for all stents (both bare and covered stents) by using the Cox-regression analysis. Using univariate Cox-regression analysis, only postoperative chemotherapy predicted prevention of stent dysfunction (hazard ratio: 0.49; 95% confidence interval: 0.31–0.75; $P<.01$). Median stent patency was 198 days in patients that underwent post-operative chemotherapy and 156 days in patients without postoperative chemotherapy ($P<.01$). Use of covered stents was not associated with stent dysfunction ($P=.52$).

3.6. Survival

The cause of death of all patients in the study was tumor progression. Median patient survival in the bare and covered stent groups was 188 and 200 days, respectively ($P=.85$, Fig. 3b).

Using univariate Cox-regression analysis, only postoperative chemotherapy predicted prolonged survival (hazard ratio: 0.35; 95% confidential interval: 0.22–0.56; $P<.01$). Median survival was 242 days in patients with postoperative chemotherapy and

Table 1

Patient characteristics.

	Bare stent	Covered stent	*P* value
Patients number	51	41	–
Age (years)	63.2±10.1	66.1±13.4	.25
Male/Female	32/19	23/18	.52
ECOG PS			.99
II	20	16	
III	31	25	
Tumor stage			.77
II	16	12	
III	20	19	
IV	15	10	
TBIL (μmol/L)			
Before	203.6±115.1	204.8±105.1	.96
After	98.4±59.7	98.7±54.7	.98
AST (U/L)			
Before	154.9±113.5	147.0±102.3	.73
After	67.3±34.5	66.4±46.0	.91
ALT (U/L)			
Before	146.5±101.8	148.8±103.4	.92
After	71.0±36.7	64.2±47.7	.44
Post-stent chemotherapy	25	22	.66

ALT = alanine aminotransferase, AST = aspartate transaminase, ECOG PS = Eastern Cooperative Oncology Group performance status, TBIL = total bilirubin.

Table 2

Comparison of outcomes between 2 groups.

	Bare stent	Covered stent	*P* value
Technical success	51 (100%)	41 (100%)	–
Clinical success	49 (96.1%)	40 (97.6%)	1.00
Stent dysfunction	17 (33.3%)	6 (14.6%)	.04
Tumor in-growth	13 (25.5%)	0 (0%)	<.01
Tumor over-growth	3 (5.9%)	4 (9.8%)	.76
Sludge	1 (2.0%)	2 (4.9%)	.58
Migration	0 (0%)	0 (0%)	–
Adverse events	7 (13.7%)	6 (14.6%)	.90
Cholangitis	7 (13.7%)	5 (12.2%)	.83
Pancreatitis	0 (0%)	1 (2.4%)	.45
Patency (days)	177	195	.51
Overall survival (days)	188	200	.85

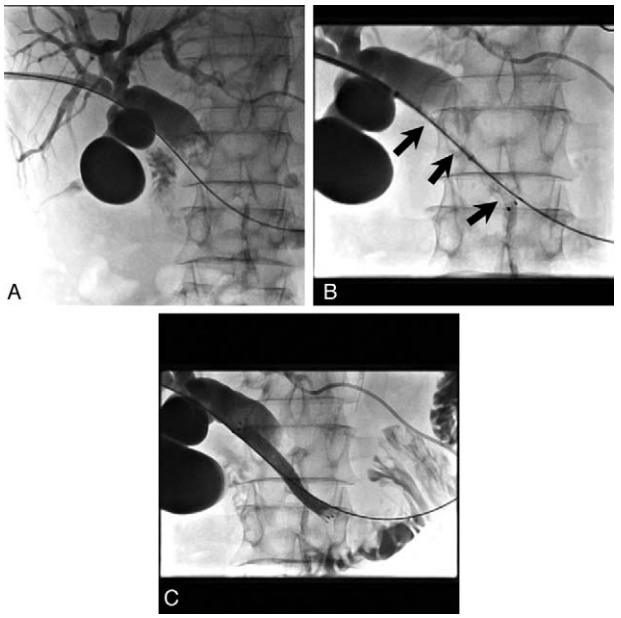

Figure 2. (A) Percutaneous cholangiography demonstrated a low common biliary obstruction. The intrahepatic and upper common biliary tracts expanded. (B) A covered stent was placed at the obstructed site (arrows). (C) The contrast-medium flowed into the duodenum smoothly via the stent.

156 days in patients without postoperative chemotherapy ($P < .01$).

3.7. Complications

Seven and 5 patients in the bare and covered stent groups experienced cholangitis following stent dysfunction ($P = .83$), which was relieved with remediation of stent dysfunction. One patient in the covered stent group suffered from pancreatitis. The patient was successfully managed through gastrointestinal decompression and drug treatment.

4. Discussion

In this study, we compared the clinical efficacy and long-term outcomes in patients with DMBO caused by PCBC receiving bare vs covered stenting. First of all, high and comparable technical (100% and 100%) and clinical (96.1% vs 97.6%, $P = 1.00$) success were found in bare and covered groups, suggesting different stent types do not interfere with the immediate palliative relief of patients with DMBO caused by PCBC.

In this study, we performed percutaneous transhepatic biliary stenting for patients with DMBO. The high technical success rates were comparable to those in previous studies regarding of percutaneous transhepatic biliary stenting for patients with DMBO.[12–15] Although endoscopic stenting were usually used for DMBO,[5–9] percutaneous transhepatic biliary stenting remains an essential interventional radiological procedure.[16] Percutaneous transhepatic biliary stenting plays an important role in cases where endoscopic procedures failed due to altered anatomy (congenital, traumatic, or postsurgical), and thus, percutaneous stenting has also been widely used for treating DMBO.[12–15] A previous randomized controlled trial had also demonstrated that percutaneous transhepatic biliary drainage provided better biliary drainage and had lower complication rates in patients with MBO.[17]

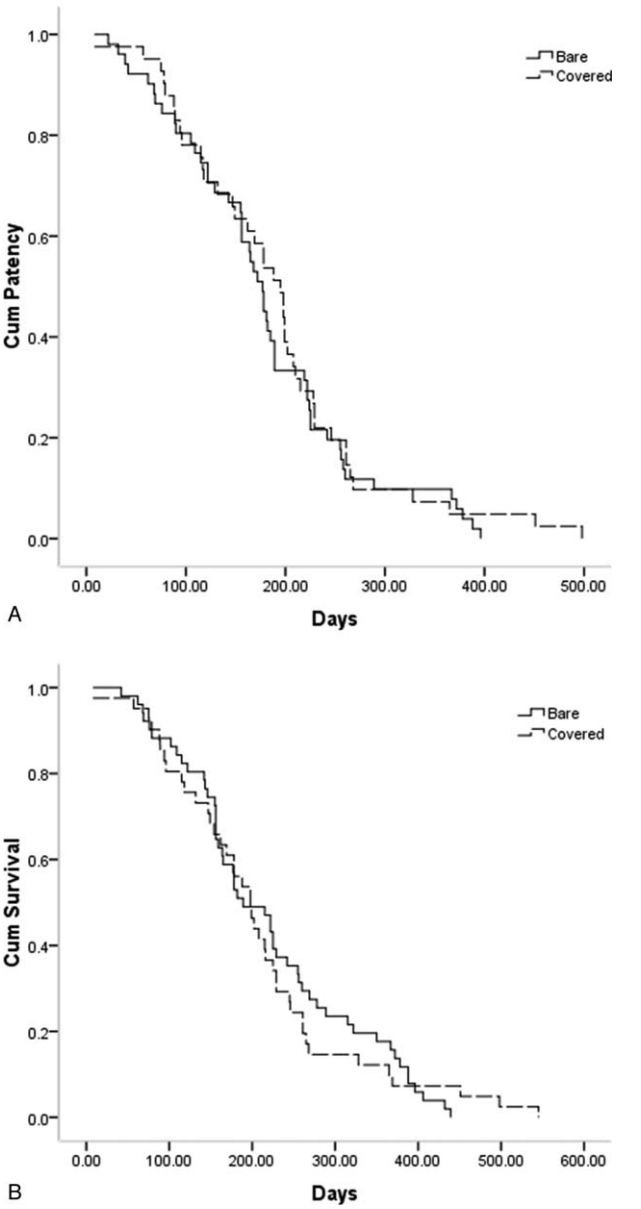

Figure 3. There were no significant variations in patency (A) and overall survival (B) as shown through Kaplan–Meier curves between 2 groups.

Stent dysfunction and patency are important clinical endpoints when comparing bare vs covered stenting for DMBO.[6–11] We found that covered stents decreased stent dysfunction by 18.7% by preventing tumor in-growth in this present study. This result is similar to previous studies of bare vs covered stenting for DMBO due to pancreatic carcinoma.[5,7] Krokidis et al[5] and Kitano et al[7] reported that covered stents decreased stent dysfunction by 14% to 20%. However, Yang et al[8] found a similar stent dysfunction rate (28.8% vs 33.3%, $P = .62$) in bare and covered stenting for DMBO. This may be due to bias caused by the multiple cancer types evaluated by the Yang study.[8]

Stent migration did not occur in either group. Migration is a risk associated with covered stents. In prior work,[7] Wallstent (Boston Scientific) covered stents were used; they are prone to

migration because the smooth membrane is located outside of the Wallstent stent skeleton. This problem was not encountered with our choice of covered stents (Micro-Tech, Nanjing, China). The design of the covered stents in this present study is different from the Wallstent stents. The silicone membrane is located inside of the stent skeleton. This design can not only prevent the tumor ingrowth, but also prevent the stent migration because the better attachment between the tumor and stent skeleton.[5]

The duration of stent patency did not differ significantly, although covered stents had longer patency: 195 days vs 177 days ($P = .51$). However, in a previous study regarding of bare vs covered stenting for DMBO secondary to pancreatic head cancer, the mean patency was significant longer in covered group (234d vs 166d, $P < .01$).[5] This may result from both groups having approximately 50% of patients undergoing post-operative chemotherapy in this study. Although chemotherapy could not completely prevent tumor growth, it may slow tumor growth. In addition, all patients also had postoperative temporary biliary drainage, which may decrease the incidence of sludge. Krokidis et al[5] used postoperative temporary biliary drainage, but did not mention any postoperative anticancer treatment.

The overall survival was similar in both groups (188 d vs 200 d, $P = .85$). This is consistent with previous studies regarding of bare vs covered stenting for DMBO.[5–9] Neither bare nor covered stents have any direct anticancer effect. Thus, only additional anticancer treatments can increase stent patency and overall survival.[7,12–15] We found that stent patency (198 d vs 156 d, $P < .01$) and survival (242 d vs 156 d, $P < .01$) were both higher in patients who received chemotherapy.

Recently, some researchers have designed a radioactive stent to simultaneously provide palliative treatment and intraluminal brachytherapy for MBO patients.[12–14] The previous results also demonstrated that radioactive stents achieved both longer patency and overall survival in MBO patient as compared with normal stenting.[12–14] However, some major complications, including massive hemorrhage or the formation of fistulas, might limit the use of radioactive stents.[18]

No significant difference in complication rates between groups was seen, suggesting covered stents do not lead to additional complications. Moreover, pancreatitis was only found in 1 patient in the covered group. Using covered stents proximal to the papilla of Vater was not inherently associated with acute pancreatitis, likely due to the distal portion of the duct already having undergone tumor infiltration and obstruction.[5]

The present study has certain limitations. It was a retrospective study, and thus susceptible to selection bias. Chemotherapy depended on the condition of patients, possibly introducing additional selective bias. Our study was also singlecenter; thus other prospective, multicenter studies are needed to support and extend the findings presented here.

In conclusion, our data suggests that the use of bare and covered stents offers similar clinical efficacy and long term outcomes for patients with DMBO caused by PCBC. Furthermore, added chemotherapy might increase patient survival following stent insertion.

Author contributions

Data curation: Ling Tang.
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Methodology: Kai-Hu Bao, Peng-Hui Liu.
Supervision: Yuan-Shun Xu.
Writing – original draft: Ling Tang.
Writing – review & editing: Yuan-Shun Xu.

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