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Management of Unresectable Hilar Biliary Obstruction: Plastic Stents versus Metallic Stents and Unilateral versus Bilateral Biliary Drainage

Hirotoshi Iwano,[1] *Shomei Ryozawa,*[1] *Megumi Harano,*[1] *Sayaka Iwamoto,*[1] *Noriko Ishigaki,*[1] *Kumiko Taba*[1] *and Isao Sakaida*[1]

[1] Department of Gastroenterology and Hepatology, Yamaguchi University Graduate School of Medicine, 1-1-1 Minami-Kogushi, Ube, Yamaguchi 755-8505, Japan
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Abstract **Background and aim:** Consensus regarding stenting for hilar biliary obstruction has not yet been established. The aim of this study was to compare the patency of plastic stents (PS) and metallic stents (MS), and to determine the ideal management for hilar biliary obstruction. **Patients and methods:** We retrospectively reviewed 126 patients with unresectable, malignant hilar/upper biliary obstruction treated with placement of plastic stent (PS, 19 patients), bared metallic stent (bMS, 98 patients), or covered metallic stent (cMS, 9 patients) and compared their the survival period, duration of stent patency and complications. We also compared patients who underwent unilateral biliary drainage (unilateral group, 50 patients) with those who underwent bilateral biliary drainage (bilateral group, 17 patients) for biliary obstruction. **Results:** Median survival time, cumulative patency duration, and median event-free survival time were all longer in the bMS group than in the PS group ($p<0.01$). There was no significant difference in them between the unilateral group and bilateral group. Liver abscess was observed at a higher frequency in the bilateral group (17.6%) than in the unilateral group (2%) ($P<0.05$). **Conclusions:** Unilateral placement of bMS is recommended for patients with malignant biliary obstruction, and bilateral biliary drainage is only indicated for patients who developed contralateral cholangitis or those with poor relief of jaundice.

Key words: hilar biliary obstruction, unilateral biliary drainage, bilateral biliary drainage, plastic stents, metallic stents

Introduction

Internal drainage for malignant biliary obstruction is a palliative treatment. Currently used stents consist of two basic types -- plastic stents (PS) and metallic stents (MS) -- but both are associated with complications therefore require maintenance. No meta analyses or randomized controlled trials (RCTs) comparing PS and MS in patients with hilar biliary obstruction have been reported to date and no consensus on their use has yet been established. We investigated outcomes with PS, bared metallic stents (bMS), and covered metallic stents (cMS) placed in patients with unresectable, malignant hilar biliary obstruction in order to determine to the ideal indications for their use and associated complications.

Patients and methods

We retrospectively reviewed 126 patients who underwent stenting for unresectable, malignant hilar/upper biliary obstruction at our institution and affiliated institutions

from September 1981 to July 2005. To exclude the possibility of bias, i.e. choosing MS or PS according to the expected prognosis at the time of stenting, the PS group consisted of patients who had stents placed in or prior to 1990. Among the patients treated with MS for biliary obstruction (grade II or higher according to Bismuth's classification), those who underwent unilateral biliary drainage (Uni group) and those who underwent bilateral biliary drainage (Bi group) were compared. The parameters investigated included the survival period, duration of stent patency, complications, time to occurrence of the first complication (event free survival; EFS). Twenty-three PS were placed in 19 patients, 138 bMS were placed in 98 patients, and 12 cMS were placed in 9 patients. The sex ratio, age, and diseases in each group are shown in Tables, 1 and 3. We used 10-12 Fr straight type tube stents for PS and 8-10 mm stents for MS. For cMS, a partially covered stent was used for so as not to block the branches.

For statistical analyses, we performed log-rank test and Breslow-Gehan-Wilcoxon test using the Kaplan-Meier method for survival period, duration of stent patency, and EFS. Any patients who died within 30 days without stent occlusion or event were excluded. The distribution of age was analyzed using Bartlett test or F-test. Sex ratio, diseases, and complications were analyzed using Chi-square test or Fisher's exact test, with Yates' correction if necessary. Comparisons between groups were always done with Bonferroni correction. A *p*-value less than 0.05 was considered statistically significant.

Results

Plastic stents versus metallic stents

Sex ratio, age, and diseases did not differ significantly between groups (Table 1). The 50% survival time was 60 days (8-285 days) in the PS group, 223 days (16-821 days) in the bMS group, and 390 days (12-427 days) in the cMS group (Fig. 1A). The 50% stent patency duration was 49 days (8-165 days) in the PS group, 165 days (6-616 days) in the bMS group, and 104 days (12-180 days) in the cMS group (Fig. 1B). The survival time and patency period were both significantly longer in the bMS group than in the PS group ($p<0.01$). Stent occlusion/migration was the most frequent complication and was found to occur 8 times (42.1%) in the PS group, 28 times (28.6%) in the bMS group, and 4 times (44.4%) in the cMS group. Other complications included cholangitis, liver abscess, perforation, hemobilia, duodenal ulcer and pancreatitis. The main cause of occlusion was sludge (7 times, 36.8%) in the PS group, tumor growth (19 times, 19.4%; ingrowth 15 times and overgrowth 4 times) in the bMS group, and tumor growth (3 times, 33.3%; ingrowth twice and overgrowth once) in the cMS group. Sludge occurred more commonly in the PS group than in the bMS group ($p<0.01$). Serious com-

Table 1 Patient characteristics of the three stent groups

	PS	bMS	cMS
No. of patients	19	98	9
Sex (M/F)	15/4	57/41	4/5
Age (yr)	67.0	68.7	74.7
(mean (range))	(41-88)	(29-93)	(59-91)
Diagnosis			
Pancreatic cancer	1	0	0
Bile duct cancer	8	52	5
Gallbladder cancer	6	23	2
Lymph metastasis	1	8	2
Others	3	15	0

PS, Plastic stent group. bMS, bared metallic stent group. cMS, covered metallic stent group.

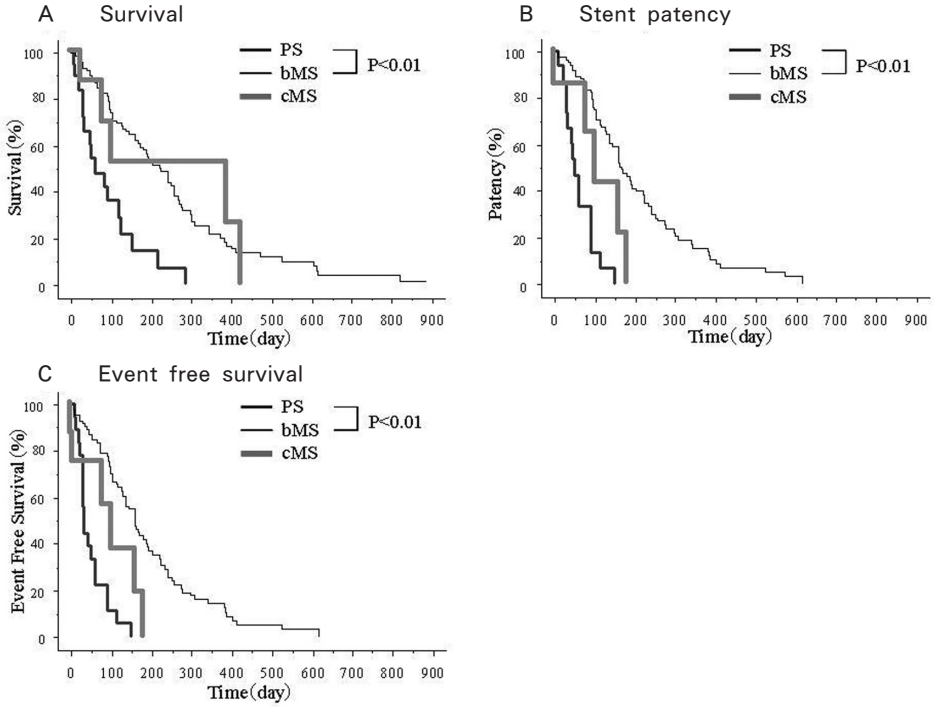

Fig. 1 (A) Kaplan-Meier graph showing survival of patients. Survival was significantly higher (P<0.01) in the bMS group than in the PS group. No significant difference was observed among the other groups. (B) Kaplan-Meier graph showing cumulative patency. Stent patency was significantly higher (P<0.01) in the bMS group than in the PS group. No significant difference was observed among the other groups. (C) Kaplan-Meier graph showing event free survival. Event free survival was significantly higher (P<0.01) in the bMS group than in the PS group. No significant difference was observed among the other groups.

plications directly related to death included liver abscess in 7 cases, cholangitis in 4 cases, bile duct perforation in 1 case and hemobilia in 1 case. The 50% EFS was 32 days (11-150 days) in the PS group, 159 days (5-616 days) in the bMS group, and 104 days (1-180 days) in the cMS group (Fig. 1C). EFS was longer in the bMS group than in the PS group (p<0.01). An excellent QOL was achieved without any adverse events in 7 cases (36.8%) for the PS group, 65 cases (66.3%) for the bMS group, and in 5 cases (55.6%) for the cMS group. When each of the events occurring at the time of stent placement was analyzed separately, sludge was found more commonly in the PS group than in the bMS group (p<0.01) (Table 2).

Unilateral versus bilateral drainage

Of the 67 patients with biliary obstruction (grade II or higher according to Bismuth's classification) who had MS placed at the time of first admission, unilateral biliary drainage was performed in 50 patients (Uni group, 74.6%) and bilateral biliary drainage was performed in 17 patients (Bi group, 25.4%) (Table 3). The 50% survival time was 248 days (21-887 days) in the Uni group and 223 days (28-399 days) in the Bi group. The 50% stent patency duration was 188 days (7-616 days) in the Uni group and 158 days (64-399 days) in the Bi group. There was no significant difference in survival time and stent patency time between the groups. Stent occlusion was the most frequent complication, which occurred 18 times (36.0%) in the Uni group and 5 times (29.4%) in the Bi group. Cholangitis was the second most frequent complication, which occurred 4 times (8.0%) in the Uni group and twice (11.8%) in the Bi group. Liver abscess was observed once (2.0%) in the Uni group and 3 times (17.6%) in the Bi group, showing a

Table 2 Patient survival, stent patency, event-free survival and complications in the three stent groups

	PS	bMS	cMS	p Value
No. of patients	19	98	9	
Survival (days)	60	223	390	<0.01 (PS vs. bMS)
(median (range))	(8-285)	(16-821)	(12-427)	
Stent patency (days)	49	165	104	<0.01 (PS vs. bMS)
(median (range))	(8-165)	(6-616)	(12-180)	
Event free survival (days)	32	159	104	<0.01 (PS vs. bMS)
(median (range))	(11-150)	(5-616)	(1-180)	
Complications (Severe)				
Obstruction	7 (0)	28 (0)	4 (0)	NS (NS)
Sludge	7	8	1	<0.01 (PS vs. bMS)
Ingrowth	0	15	2	NS
Overgrowth	0	4	0	NS
In & Overgrowth	0	0	1	NS
Hemobilia	0	1	0	NS
Migration	1 (0)	0 (0)	0 (0)	NS (NS)
Cholangitis	3 (0)	8 (3)	1 (1)	NS (NS)
Perforation	1 (0)	1 (1)	0 (0)	NS (NS)
Duodenul ulcer	1 (0)	0 (0)	0 (0)	NS (NS)
Hemobilia	0 (0)	0 (0)	1 (1)	NS (NS)
Liver abscess	2 (2)	6 (5)	0 (0)	NS (NS)
Pancreatitis	0 (0)	0 (0)	1 (0)	NS (NS)
First complications after stenting				
Cholangitis	2	7	1	NS
Sludge	7	7	1	<0.01 (PS vs. bMS)
Ingrowth	0	13	1	NS
Overgrowth	0	3	0	NS
Perforation	1	1	0	NS
Duodenul ulcer	1	0	0	NS
Hemobilia	0	1	0	NS
Liver abscess	1	1	0	NS
Pancreatitis	0	0	1	NS
None	7	65	5	NS

PS, Plastic stent. bMS, bared metallic stent. cMS, covered metallic stent.

Table 3 Patient characteristics of unilateral and bilateral groups

	Uni	Bi
No. of patients	50	17
Sex (M/F)	27/23	11/6
Age (yr)	71.9	66.6
(mean (range))	(29-93)	(43-82)
Diagnosis		
Pancreatic cancer	0	0
Bile duct cancer	36	10
Gallbladder cancer	5	5
Lymph metastasis	4	0
Others	5	2

Uni, unilateral drainage group. Bi, bilateral drainage group.

significantly higher rate in the Bi group ($p<0.05$). The main cause of occlusion was tumor growth (14 times, 28.0%; ingrowth 11 times and overgrowth 3 times) in the Uni group and was sludge (3 times, 17.6%) in the Bi group. Serious complications directly related to death included liver abscess in 1 case and cholangitis in 1 case in each group. The 50% EFS was 159 days (5-616 days) in the Uni group and 129 days (64-399 days) in the Bi group, and did not differ significantly between groups (Table 4). An excellent QOL was achieved without any adverse events in 33 cases (66.0%) in the Uni group and in 10 cases (58.8%) in the Bi group.

Discussion

In our present analysis, survival time, stent patency time, and EFS were significantly longer in the bMS group than in the PS group. In addition, stent occlusion by sludge was less commonly observed in the bMS group than in the PS group. RCTs have been conducted comparing survival time between PS and MS for middle and lower biliary obstruction,[1] between bMS and cMS for lower biliary obstruction,[2] and between unilateral biliary drainage and bilateral biliary drainage in patients with PS for hilar biliary obstruction.[3] However, all of these reports showed no significant difference in survival times. On the other hand, our study demonstrated a significantly longer survival time in the bMS group as compared with the PS group. Since the PS group only included patients who had stents placed prior to the time when MS became commercially available, this is very likely to reflect prolongation of survival time due to subsequent advances in anticancer therapy.

Previous RCTs[1)4)5)] in patients with lower biliary obstruction reported longer stent patency time and EFS in patients with MS than in those with PS. However, these RCTs were performed in patients with lower biliary obstruction. The stent patency time and EFS in our analysis were affected by survival time. Moreover, bMS may be superior in stent patency time and EFS, since PS was associated with a higher complication rate (63.2% in the PS group, 33.7% in the bMS group, and 44.4% in the cMS group) despite its shorter survival time, and the main complication was stent occlusion.

De Palma et al[3] conducted a RCT using PS to compare the outcome of unilateral versus bilateral drainage in patients with biliary obstruction at the hilum. They showed that unilateral stent insertion had a significantly higher rate of technical success and successful drainage compared with bilateral stent inser-

Table 4 Patient survival, stent patency, event-free survival and complications in the unilateral and bilateral groups

	Uni	Bi	p Value
No. of patients	50	17	
Survival (days) (median (range))	248 (21-887)	223 (28-399)	NS
Stent patency (days) (median (range))	188 (7-616)	158 (64-399)	NS
Event free survival (days) (median (range))	159 (5-616)	129 (64-399)	NS
Complications (Severe)			
Obstruction	18 (0)	5 (0)	NS (NS)
Sludge	4	3	NS
Ingrowth	11	2	NS
Overgrowth	3	0	NS
Cholangitis	4 (1)	2 (1)	NS (NS)
Liver abscess	1 (1)	3 (1)	<0.05 (NS)
First complications after stenting			
Cholangitis	3	2	NS
Sludge	3	3	NS
Ingrowth	9	2	NS
Overgrowth	2	0	NS
None	33	10	NS

Uni, unilateral drainage group. Bi, bilateral drainage group.

tion, while a higher rate of complications was evident in bilateral stent group. The investigators concluded that single stent insertion is effective and avoids the risk of further procedure-related complication and mortality. Furthermore, Dowett et al[6] reported that drainage from 25% of the total volume of the liver can improve hepatic function and achieve biliary decompression, thereby improving QOL. In our analysis, there was no significant difference in survival time, stent patency time, or EFS between the Uni and Bi groups. Regarding complications, liver abscess was more common in the Bi group. It is possible that by crossing multiple stents at the hepatic hilum, stasis of bile flow can occur and sludge can be easily formed. As bilateral drainage is associated with a higher rate of liver abscess and complicated crossing of multiple stents make subsequent intervention difficult, we conclude that bilateral drainage is not necessarily required for all patients. Therefore, unilateral placement of bMS is primarily recommended for patients with hilar biliary obstruction, and bilateral biliary drainage is only indicated for patients who develop cholangitis at non-drained segments or for those who do not achieve relief of jaundice.

However, if bMS cannot be removed, attention should be paid on possible future complications in long term survivors. In addition, PS is applicable for patients with poor prognosis of approximately 1 month. After placement of bMS, the local control to suppress tumor ingrowth by radiotherapy or chemotherapy and to prevent tumor overgrowth by choosing long stent as possible are important. Reducing a load of the stent against biliary wall by releasing an extension power of it and improving a flexibility of the stent could decrease the incidence of cholangitis and liver abscess. For further improvement of QOL, further studies of treatment of the bile duct cancer and refinements on the stent are required. As this study is a retrospective trial, a large-scale randomized prospective one among some institutions is expected.

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