Original Article

Predictors for Occlusion of the First Inserted Metallic Stent in Patients with Malignant Biliary Obstruction

Wandong Hong, Yunfei Zhu[1], Yanyan Dong[2], Yanqing Wu[3], Mengtao Zhou[4], Haizhen Ni[5]

Departments of Gastroenterology and Hepatology, [4]Hepatobiliary Surgery and [5]Vascular Surgery, The First Affiliated Hospital, [2]Ultrasound, The Second Affiliated Hospital, Wenzhou Medical University, Wenzhou, Zhejiang, [1]Department of Emergency Surgery, The First Affiliated Hospital, Zhejiang Chinese Medical University, Hangzhou, Zhejiang, [3]Department of Reproductive Medicine, Family Planning Research Institute, Tongji Medical College, Wuhan, Hubei, PR China

Address for correspondence:
Dr. Wandong Hong, Department of Gastroenterology and Hepatology, The First Affiliated Hospital, Wenzhou Medical University, No 2, Fu Xue Road, Wenzhou, Zhejiang - 325 000, PR China.
E-mail: xhnk-hwd@163.com

ABSTRACT

Background/Aims: Endoscopic biliary stent drainage plays an important role in the palliative treatment of malignant biliary obstruction. The aim of this study was to investigate predictors of occlusion of first metal inserted stent in patients with malignant biliary obstruction. **Patients and Methods:** The retrospective analysis was performed in 178 patients with malignant biliary obstruction. Factors associated with stent occlusion were analyzed by Cox regression analysis. **Results:** Median overall stent patency was 178 days. Total cumulative obstruction rate of the first stents during the follow up was 33%, 57%, 83%, and 96% at 90, 180, 360, and 720 days. Multivariate analysis revealed that hilar obstruction (hazard ratio [HR] =3.26, 95% confidence interval [CI, 2.31–4.61), metastasis cancer (HR = 2.61, 95% CI, 1.79–3.80), and length of stent (HR = 1.74, 95% CI, 1.24–2.46) were independent predictors of stent occlusion. **Conclusions:** Hilar biliary stricture, metastatic cancer, and length of stent were important predictors of occlusion of first-inserted metal stent in patients with malignant biliary obstruction.

Key Words: Biliary stent, endoscopic retrograde cholangiopancreatography, predictor, malignant biliary obstruction, stent occlusion

Received: 15.12.2014, Accepted: 09.02.2015

How to cite this article: Hong W, Zhu Y, Dong Y, Wu Y, Zhou M, Ni H. Predictors for occlusion of the first inserted metallic stent in patients with malignant biliary obstruction. Saudi J Gastroenterol 2015;21:386-90.

Endoscopic biliary stent placement is a well-established palliative treatment for patients with malignant biliary obstruction.[1,2] The patency period of stents is of paramount importance for the patient with a short life expectancy.[3,4] Stent occlusion can occur and drainage has to be re-established in patients with expected long survival. Therefore, it is important to identify patients with malignant biliary obstruction at high risk for stent occlusion, which may be helpful for clinicians to identify patients who would most likely need early elective stent exchange or subsequent stent insertion.

Access this article online

Quick Response Code:

Website: www.saudijgastro.com

DOI: 10.4103/1319-3767.164204

There is no consensus on which factors would significantly affect the patency of biliary stent, although several studies on this subject have been published.[3,5-7] Matsuda *et al*.[5] reported that age and serum total bilirubin level are the important factors affecting the patency of implanted plastic stent in patients with malignant biliary obstruction. Khashab *et al*.[6] suggested that only male gender and hilar stricture are predictors of early stent occlusion among plastic biliary stents. Kim *et al*.[3] suggested that early expansion of the stent and easy passage of larger-caliber instruments through the stricture were favorable factors for long-term patency of the metal stent. Recently, van Boeckel *et al*.[7] reported that a score model consisted of stent type, bilirubin level, and a biliary stricture preceding dilation can predict early stent occlusion. Such predictive factors may be expected to vary in different populations because of differences in the etiologies of malignant biliary obstructions. In addition, to our best knowledge, predictors of occlusion of the first inserted metal stent in patients with malignant biliary obstruction have not been fully investigated and data from China are scarce. For

above-mentioned reasons, we aimed to investigate predictors of occlusion of first implanted metal stent in patients with malignant biliary obstruction.

PATIENTS AND METHODS

Data of patients who underwent therapeutic endoscopic retrograde cholangiopancreatography for malignant biliary obstruction from January 2009 to January 2012 were reviewed. Each patient's status was classified according to the physical status classification of the American Society of Anesthesiologists (ASA).[8,9] Patients with successful endoscopic metal stent implantation were enrolled. Exclusion criteria from the study included previous biliary stent, previous percutaneous transhepatic biliary drainage, previous surgery, no follow-up information available, surgically resectable case, and possible benign case. Endoscopic sphincterotomy was performed to facilitate stent placements. All metallic biliary stents used in the current study were uncovered, 1 cm in diameter, and ranging from 6 to 8 cm in length. The metallic stents mainly come from Taewoong (Seoul, Korea) and Sewoon Medical (Seoul, Korea) manufacturers. All patients with hilar strictures underwent unilateral stent placement irrespective of Bismuch classification, in whom magnetic resonance cholangiopancreatography and/or computed tomography was used to plan drainage only of the largest intercommunicating ductal segments, with avoidance of ducts draining atrophic lobes.[10] This study protocol was approved by the Ethics Committee of the First Affiliated Hospital of Wenzhou Medical University.

Occlusion of the stent was considered if patients had recurrent jaundice or cholangitis. If stent occlusion occurred, mechanical cleaning with a balloon and "stent-in-stent" placement with a plastic stent were used as an endoscopic treatment modality. As described by Raju *et al.*,[11] Stent patency was determined as the period between first stent placement and stent occlusion and was calculated for each patient using the data from the initial inserted stent.

The duration of stent patency was analyzed by Kaplan–Meier method and compared by using the log rank test. All variables that were found to be significantly correlated to the stent patency on univariate analysis were selected as candidates for multivariate Cox regression analysis. Hazard ratio (HR) with 95% confidence interval (CI) was calculated. The equality of cumulative incidence of stent obstruction across groups was evaluated by Gray's test.[12] If a patient succumbs to the disease without stent occlusion, we considered the patency time was equal to the survival period and considered both stent obstruction and death as the events when performing univariate and multivariate analysis. However, the patient's death was considered as a competing risk when we analyzed the cumulative incidence of stent obstruction.[12] *P* values below 0.05 were considered significant. All analyses were performed using STATA version 12.0.

RESULTS

Patient characteristics

The clinical characteristics of patients are shown in Table 1. A total of 178 patients (116 male; median age 71) were included in the current study. Only two patients received radiotherapy and one patient received a combination of chemotherapy and radiotherapy. The leading cause of biliary obstruction was cholangiocarcinoma (42.6%). Seventy-four (41.6%) patients had hilar biliary obstruction (4 Bismuth type I, 10 type II, 24 type III, and 36 type IV). Distal metastasis was found in 72 (40.5%) patients. All patients had jaundice and 140 (78.6%) patients had fever. The median initial total bilirubin level before stenting was 13.2 mg/dL. One hundred and seventy-one patients underwent stent occlusion during the follow up and only seven patients died without stent clogging. Of the 171 patients, 44 patients underwent "stent-in-stent" procedures, whereas the remainder received palliative medicine (122 patients) or percutaneous transhepatic cholangial drainage (five patients) before death. Median overall patency of the first stent was 178 days (128–180 days). As shown in Figure 1, total cumulative obstruction rate of the first inserted stents during

Table 1: Baseline patient characteristics (*n*=178)

Parameter	Results
Age (year)	71 (63-78)
Male	116 (65.2%)
ASA status (number)	
I	6
II	34
III	72
IV	64
V	2
Bilirubin level (mg/dL)	13.2 (8.6-18.4)
Alkaline phosphatase (U/L)	441 (307-705)
Gamma GT (U/L)	424 (223-811)
Etiology, %	
Cholangiocarcinoma	42.6
Pancreatic cancer	18.9
Liver cancer	13.5
Others	25.0
Location of strictures (number)	
Hilar (Bismuth type)	74 (4 I, 10 II, 24 III, 36 IV)
No-hilar	104
Cholecystectomy, %	17.4
Length of stent (number)	
6 cm	59
8 cm	119

Data are shown as percentages, medians, and interquartile ranges

the follow up was 33%, 57%, 83%, and 96% at 90, 180, 360, and 720 days.

Risk factors related to stent occlusion: Univariate and multivariate analysis

Eight variables considered relevant to stent patency were tested using univariate analyses. As shown in Table 2, the log-rank test revealed that age, ASA status, biliary stricture location, metastasis cancer, and length of stent were significantly associated with the duration of stent patency. Variables significantly linked to the duration of stent patency were assessed by multivariate Cox regression analysis. As shown in Figure 2, multivariate analysis confirmed that hilar obstruction (HR = 3.26, 95% CI, 2.31–4.61; $P < 0.001$), metastasis cancer (HR = 2.61, 95% CI, 1.79–3.80; $P < 0.001$), and length of stent (HR = 1.74, 95% CI, 1.24–2.46; $P < 0.001$) were independent risk factors to stent occlusion.

With respect to cumulative obstruction rate of inserted stents, it was 55%, 82%, and 93% at 90, 180, and 360 days in patients with hilar obstruction compared with 17%, 40%, and 75% in patients without hilar obstruction (Gray's test: $P < 0.001$) [Figure 3]. Patients with metastasis cancer had a cumulative obstruction rate of 62%, 82%, and 90% at 90, 180, and 360 days, whereas it was 13%, 41%, and 77% in patients without metastasis cancer (Gray's test: $P < 0.001$) [Figure 4]. Patients with 8 cm length stents had a higher cumulative obstruction rate of 39%, 63%, and 85% at 90,180, and 360 days compared with 20%, 47%, and 76% for patients with 6 cm length stents (Gray's test: $P = 0.04$) [Figure 5].

DISCUSSION

As expected, our data showed that patients with hilar strictures had a shorter duration of patency than that of distal obstruction (90 vs 210 days) [Table 2]. Multivariate

Table 2: Univariate analysis of stent patency time

Variable	Patients	Median patency time (95% CI)	*P*
Age (year)			0.002
≦71	90	122 (90-150)	
>71	88	180 (151-240)	
Gender			0.966
Female	62	177 (128-210)	
Male	116	150 (95-181)	
Advance ASA status			<0.001
Yes (IV-V)	64	98 (68-128)	
No (I-III)	114	180 (164-210)	
Bilirubin (mg/dL)			0.77
>13.2	89	177 (128-210)	
≦13.2	89	150 (95-180)	
Alkaline phosphatase (U/L)			0.968
>441	88	150 (95-202)	
≦441	90	151 (128-180)	
Gamma GT (U/L)			0.711
>424	88	122 (95-181)	
≦ 424	90	164 (150-202)	
Fever			0.70
Yes	38	150 (120-238)	
No	140	151 (106-180)	
Abdominal pain			0.188
Yes	64	151 (106-180)	
No	114	164 (120-202)	
Stricture location			<0.001
Hilar	74	90 (60-95)	
No-hilar	104	210 (180-240)	
Metastatic cancer			<0.001
Yes	72	60 (37-92)	
No	106	181 (180-240)	
Length of stent			0.01
8 cm	119	150 (117-169)	
6 cm	59	181 (120-247)	

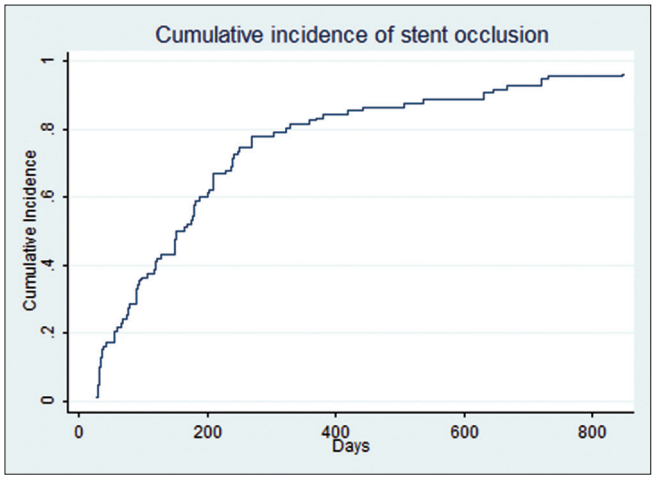

Figure 1: Cumulative incidence of stent obstruction in 178 patients during the follow up

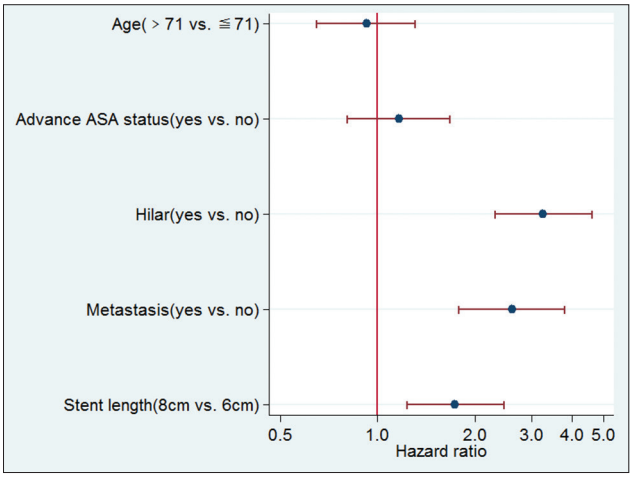

Figure 2: Cox regression plot of hazard ratios and 95% confidence intervals. Significant predictors of stent occlusion included hilar obstruction, metastasis cancer, and stent length

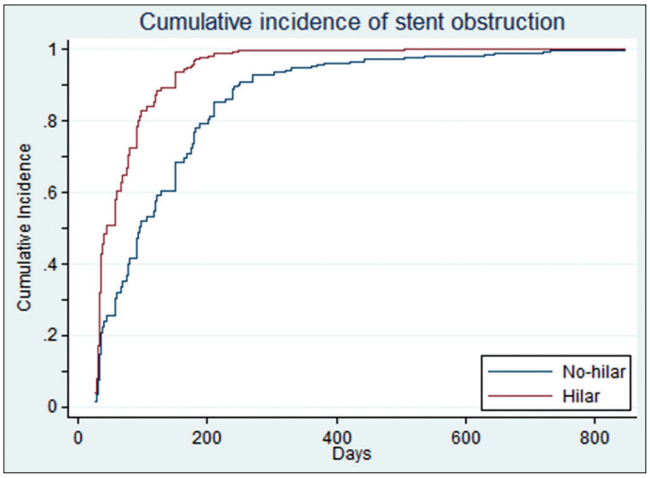

Figure 3: Cumulative incidence of stent obstruction in patients with or without hilar obstruction during the follow up

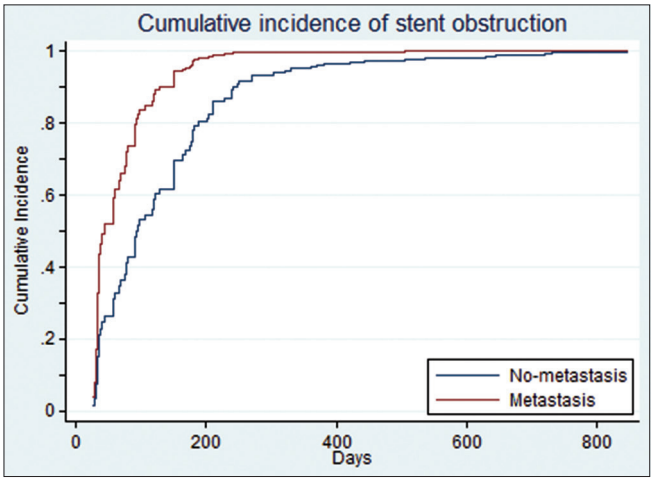

Figure 4: Cumulative incidence of stent obstruction in patients with or without metastasis cancer during the follow up

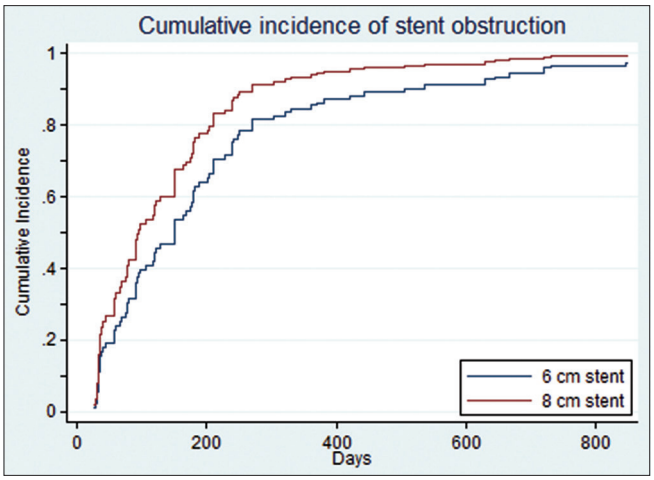

Figure 5: Cumulative incidence of stent obstruction in patients with different lengths of stent during the follow up

analysis indicated that hilar stricture was associated with a significantly increased risk of stent occlusion (HR = 3.26; 95% CI: 2.31–4.61) [Figure 2]. The cumulative obstruction rate of inserted stents in patients with hilar obstruction was 55%, 82%, and 93% at 90,180, and 360 days [Figure 3]. These results are consistent with previous reports.[6,11,13] It may be explained that tortuous hilar anatomy and atrophic lobes with diminished volume of parenchyma in patients with hilar obstruction may limit sufficient drainage of secondary or tertiary branches of ducts.

Patients with unrespectable metastasis hilar obstruction often have a median life expectancy of 2–4 months compared with 6 months or more in patients without metastasis cancer.[14,15] Raju *et al*.[11] suggested that presence of metastasis and absence of treatment with chemotherapy, radiotherapy, or chemo-radiation were independent prognostic factors for survival. In addition, Eum *et al*.[16] suggested that a higher cancer stage (tumors involving the celiac axis or superior mesenteric artery or tumors having distant metastasis) was associated with shorter patency of metal stent in unrespectable pancreatic cancers. As expected, multivariate analysis indicated that metastatic tumors were associated with a significantly increased risk of stent occlusion (HR = 2.61; 95% CI: 1.79–3.81) [Figure 2]. Patients with metastasis cancer had a cumulative obstruction rate of 62%, 82%, and 90% at 90, 180, and 360 days [Figure 4].

Few studies investigated the relationship between length of stent and duration of stent patency. Kim *et al*.[3] suggested that length of stent did not affect the patency of metal stents. However, our data indicated that length of stent may be associated with stent occlusion (HR = 1.74, 95% CI, 1.24–2.46) [Figure 2]. Patients with a longer-length stent (8 cm) had a higher cumulative obstruction rate of 39%, 63%, 85% at 90, 180, and 360 days compared with 20%, 47%, and 76% for patients with short-length stent (6 cm) [Figure 5]. The difference may be partly explained that the small sample (68 patients) of study by Kim *et al*. does not lead to a statistically significant result. Presumably, flow velocity of bile may be decreased in these longer-length stents secondary to fluid dynamics when compared with short-length stents.

It should be mentioned that there were more than 10% patients who survived 1–2 years and 4% patients who survived more than 2 years after stent insertion in the present study [Figure 1]. We were not sure whether a palliative surgery would be a better option for these patients. However, a cost-effective study by Raikar *et al*.[17] reported that compared with palliative surgery, endoscopic stenting for unresectable pancreatic cancer could provide equivalent duration of survival at reduced cost and shortened hospital stay, although subsequent stent changes were necessary.

The median overall stent patency (178 days) in our study appeared a little shorter than that reported by Kim *et al.*[3] (189 days). This difference may in part be due to the higher proportion of patients with metastatic cancer or hilar obstruction enrolled in our study, where unilateral drainage was performed even where advanced Bismuth-type hilar strictures existed. Vienne *et al.*[18] suggested that draining more than 50% of liver volume, which often requires bilateral drainage, was an important predictor of successful drainage for advanced Bismuth-type hilar strictures. In addition, it must be noted that only a few patients received adjuvant treatment in our study, which in turn may also influence the duration of stent patency. Other limitations of our study include the retrospective nature of our study, which may produce a population bias and also prevent us to investigate other potential predictors such as the type of metal stent (different manufacturers) and severity of the bile duct stricture.[3] It will be interesting to analyze and compare these parameters in the future. However, compared to previous studies, we only analyzed the patency of the first inserted stent and also two lengths of stents with the same diameter, and this renders homogeneity to the study population.

In conclusion, we have shown in this study that a hilar biliary stricture, metastatic cancer, and length of stent were important predictors of occlusion of first inserted metal stent in patients with malignant biliary obstruction.

ACKNOWLEDGMENTS

We are very thankful to two anonymous reviewers for their thoughtful and precise critiques, observing which has helped us to improve the quality of the manuscript substantially.

REFERENCES

1. Hong WD, Chen XW, Wu WZ, Zhu QH, Chen XR. Metal versus plastic stents for malignant biliary obstruction: An update meta-analysis. Clin Res Hepatol Gastroenterol 2013;37:496-500.
2. Hong W, Sun X, Zhu Q. Endoscopic stenting for malignant hilar biliary obstruction: Should it be metal or plastic and unilateral or bilateral? Eur J Gastroenterol Hepatol 2013;25:1105-12.
3. Kim HS, Lee DK, Kim HG, Park JJ, Park SH, Kim JH, *et al*. Features of malignant biliary obstruction affecting the patency of metallic stents: A multicenter study. Gastrointest Endosc 2002;55:359-65.
4. Pola S, Muralimohan R, Cohen B, Fehmi SM, Savides TJ. Long-term risk of cholangitis in patients with metal stents for malignant biliary obstruction. Dig Dis Sci 2012;57:2693-6.
5. Matsuda Y, Shimakura K, Akamatsu T. Factors affecting the patency of stents in malignant biliary obstructive disease: Univariate and multivariate analysis. Am J Gastroenterol 1991;86:843-9.
6. Khashab MA, Kim K, Hutfless S, Lennon AM, Kalloo AN, Singh VK. Predictors of early stent occlusion among plastic biliary stents. Dig Dis Sci 2012;57:2446-50.
7. van Boeckel PG, Steyerberg EW, Vleggaar FP, Groenen MJ, Witteman BJ, Weusten BL, *et al*. Multicenter study evaluating factors for stent patency in patients with malignant biliary strictures: Development of a simple score model. J Gastroenterol 2011;46:1104-10.
8. Katsinelos P, Paroutoglou G, Kountouras J, Zavos C, Beltsis A, Tzovaras G. Efficacy and safety of therapeutic ERCP in patients 90 years of age and older. Gastrointest Endosc 2006;63:417-23.
9. Owens WD, Felts JA, Spitznagel EL Jr. ASA physical status classifications: A study of consistency of ratings. Anesthesiology 1978;49:239-43.
10. Freeman ML, Overby C. Selective MRCP and CT-targeted drainage of malignant hilar biliary obstruction with self-expanding metallic stents. Gastrointest Endosc 2003;58:41-9.
11. Raju RP, Jaganmohan SR, Ross WA, Davila ML, Javle M, Raju GS, *et al*. Optimum palliation of inoperable hilar cholangiocarcinoma: Comparative assessment of the efficacy of plastic and self-expanding metal stents. Dig Dis Sci 2011;56:1557-64.
12. Gray RJ. A class of K-sample tests for comparing the cumulative incidence of a competing risk. Ann Stat 1988;16:1141-54.
13. Bueno JT, Gerdes H, Kurtz RC. Endoscopic management of occluded biliary wallstents: A cancer center experience. Gastrointest Endosc 2003;58:879-84.
14. Van Laethem JL, De Broux S, Eisendrath P, Cremer M, Le Moine O, Devière J. Clinical impact of biliary drainage and jaundice resolution in patients with obstructive metastases at the hilum. Am J Gastroenterol 2003;98:1271-7.
15. De Palma GD, Galloro G, Siciliano S, Iovino P, Catanzano C. Unilateral versus bilateral endoscopic hepatic duct drainage in patients with malignant hilar biliary obstruction: Results of a prospective, randomized, and controlled study. Gastrointest Endosc 2001;53:547-53.
16. Eum YO, Kim YT, Lee SH, Park SW, Hwang JH, Yoon WJ, *et al*. Stent patency using competing risk model in unresectable pancreatic cancers inserted with biliary self-expandable metallic stent. Dig Endosc 2013;25:67-75.
17. Raikar GV, Melin MM, Ress A, Lettieri SZ, Poterucha JJ, Nagorney DM, *et al*. Cost-effective analysis of surgical palliation versus endoscopic stenting in the management of unresectable pancreatic cancer. Ann Surg Oncol 1996;3:470-5.
18. Vienne A, Hobeika E, Gouya H, Lapidus N, Fritsch J, Choury AD, *et al*. Prediction of drainage effectiveness during endoscopic stenting of malignant hilar strictures: The role of liver volume assessment. Gastrointest Endosc 2010;72:728-35.

Source of Support: Nil, **Conflict of Interest:** The authors declare that they have no potential conflicts of interest.