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Triple metallic stenting in hilar malignant biliary obstructions

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PURPOSE
To research the effects of triple stenting on primary patency rates and on clinical and biochemical findings in patients with high-level malignant biliary obstruction.

MATERIALS AND METHODS
We analyzed eight patients who had undergone triple stenting for hilar malignant biliary obstruction, mainly with the percutaneous approach, between January 2009, and September 2009. Pre-interventional bilirubin levels and the existence of pruritus or cholangitis were recorded. Patients were examined 15 days and three months post-intervention. Procedure-related mortality and 30-day mortality rates were recorded. Changes in the serum bilirubin levels, pruritis and cholangitis were examined. Primary patency rates were calculated with the Kaplan-Meier method.

RESULTS
Pruritis and cholangitis improved within 15 days. There was a significant decrease in serum bilirubin levels, which were very near to normal limits. Two patients died: one in the fourth month and the other in the eighth month. The mean patency rate was 179±18.81 days. There were no procedure-related or 30-day mortalities in the study group.

CONCLUSION
Triple metallic stenting did not significantly improve primary patency rates in hilar malignant biliary obstructions. However, the beneficial effects of triple stenting included the rapid improvement in clinical and biochemical signs in select patients. Triple stenting will be beneficial in preventing isolation that might cause cholangitis. Malignant biliary obstruction in patients with a trifurcation anomaly in the hilar region may necessitate triple stenting.

Key words: • *bile duct obstruction* • *biliary tract neoplasms* • *stents*

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The majority of patients with malignant biliary obstructions has unresectable tumors or is at high risk for surgery when they are admitted to the hospital. Alternative treatment methods secondary to palliative bypass surgery include percutaneous transhepatic and endoscopic biliary interventions. Both of these methods are safe and effective for palliation of the obstructive symptoms. The percutaneous transhepatic approach is the choice for palliative treatment in patients with high-level obstructions and in patients with low-level obstructions in whom previous endoscopic intervention has failed (1–7).

There are some advantages of palliative metallic stenting in patients with malignant biliary obstruction: ductal patency will be maintained, and patients avoid having a catheter extend outside of their bodies (2, 4, 5). There are several previous reports about single- or double-metallic stenting in hilar malignant biliary obstructions (2, 5, 8–12). When metallic stenting is considered in patients with cholangitis, all of the infected ducts must be drained (3–5).

Concomitant effective or impending isolation and cholangitis may require triple stenting in patients with a high-level malignant biliary obstruction. Few reports about triple stenting or trisector drainage exist in the literature (10, 13–15). Thus, the efficacy, safety and indications for triple stenting need to be discussed in detail. In this study, we research the effects of triple stenting on primary patency rates and on the clinical and biochemical findings of patients with high-level malignant biliary obstructions.

Materials and methods

We analyzed patients admitted to our hospital who had been triple-stented for hilar malignant biliary obstruction. Written informed consent was obtained from all patients. Patients in which multiple stents were deployed in different ducts, but not in the same duct coaxially, were included in the study. We found eight patients that had undergone triple stenting; all of them had a histopathologic diagnosis established by either percutaneous liver biopsy or percutaneous intrabiliary brush biopsy, and all were accepted as inoperable at the time of referral. Bile duct obstructions were evaluated with ultrasonography, computed tomography and magnetic resonance imaging before the intervention. The decision to proceed with triple stenting in these patients was made after a mutual consensus of interventional radiologists, gastroenterologists and gastroenterologic surgeons. The main indications for palliative stenting were cholangitis (in seven patients, 87.5%), pruritus (in eight patients, 100%) and the need to lower serum bilirubin levels before chemotherapy (in one patient, 12.5%). All of the patients had high-level obstructions (above the level where the cystic duct joins the common hepatic duct) (3). Six of the eight patients (75%) had a Bismuth-Corlette Type 3A ma-

lignant biliary obstruction and two of the eight patients (25%) had hilar malignant biliary obstructions with trifurcation variance. All patients underwent percutaneous transhepatic cholangiography (PTC). The techniques for PTC and drainage were the same as previously reported in detail (2, 4, 5, 7, 16). In most of the patients three sessions were required for treatment. Because most of the patients had acute cholangitis before the intervention, all of the patients underwent biliary decompression with external-internal drainage of one or more ducts until the second session. In the second session, the remaining ducts were catheterized under fluoroscopy and ultrasonography and external-internal drainage catheters were put in place. After treatment with antibiotics and decompression, cholangitis improved in the patients. In subsequent sessions, guide wires were placed simultaneously on all three intervention tracts. After placement of 7F sheaths, different-sized and various-branded nitinol, self-expandable, uncovered metallic stents were placed concomitantly (three stents for each of the eight patients, total count was 24 stents), and balloon dilatations were performed. Stent sizes were chosen with the consideration to not overexpand the common hepatic duct or choledochus (the widest diameter used was 8 mm). The stent-in-stent technique, in which side-branch stenting extends through the struts of the main stent, was not used. The majority of the stents were placed percutaneously; however, in two patients, left hepatic ducts were stented with an endoscopic approach. In these patients, the left hepatic ducts were previously drained with an endoscopic intervention.

Pre-interventional bilirubin levels, as well as the existence of pruritus and cholangitis, were recorded. Scaling of the pruritus was done from 0 to 4 as previously defined by Whitington and Whitington (17). Patients were examined on the 15th day and third month after the interventions. These control periods were determined arbitrarily as they approximated early and midterm follow-ups. Procedure-related mortality and 30-day mortality rates were recorded. Improvement or worsening of the serum bilirubin levels, pruritus and symptoms of cholangitis were analyzed. The primary patency of the stents was recorded. Primary patency was evaluated as the time from stent deployment to occlusion or death. During follow-up periods, elevation of cholestatic markers [serum bilirubin, alkaline phosphatase (ALP), and gamma glutamyl transpeptidase (GGT)], recurrence of the obstructive symptoms (jaundice, pruritus) or dilatation in the bile ducts compared to previous studies suggested stent obstruction; these patients were evaluated with PTC. When one of three stents occluded, all stents were assumed to be occluded: we considered the set of three stents as a uniform system. All of the data that were obtained was transferred into the statistical analysis program SPSS 14 for Windows (2005, SPSS Inc., Chicago, USA) for statistical analysis. Primary patency rates were calculated according to the Kaplan-Meier method. The Wilcoxon signed rank test was used to compare total bilirubin data before and after stent placement. A P value of less than 0.05 was accepted as statistically significant.

Results

Five of the eight (62.5%) patients were female, and three of the eight (37.5%) were male. Patients were between 48 and 65 years old (mean 57.5±5.70). The etiology of the malignant biliary obstructions in the study population was as follows: cholangiocarcinoma in three patients (37.5%), metastasis in three patients (37.5%), one patient with a gall bladder carcinoma (12.5%) and one with a pancreatic cancer (12.5%). One of the patients (12.5%) had a hepaticojejunostomy operation due to previous pancreatic carcinoma (Fig. 1).

Percutaneous transhepatic cholangiography showed effective or impending isolation of the right anterior, right posterior and left hepatic ducts in all patients (Figs. 2 and 3). In two patients (25%), there was trifurcation of the bile ducts (Fig. 4). One patient (12.5%) experienced a transient self-limited hemorrhage, and another patient (12.5%) experienced a self-limited bile leak from the right side entrance tract.

Pruritus and cholangitis in the patients improved within the first week. There was a significant decrease in the serum bilirubin levels (pre-interventional mean total bilirubin level was 15.83±4.41; 15th-day post-interventional mean total bilirubin was 3.00±0.75; 3rd-month post-interventional mean total bilirubin was 2.82±1.43; $P < 0.05$), resulting in levels that were very near to normal limits (Table). Two patients died: one died in the fourth month and the other in the eighth month. In one of them, recurrent cholangitis developed and the patient died before any intervention could be performed. The other patient died because of a heart attack. The mean patency rate was 179±18.81 (97 to 245) days. There was no procedure-related or 30-day mortality in the study group.

Discussion

Percutaneous biliary interventions in the setting of malignant biliary obstructions are safe and effective techniques to relieve obstructive symptoms in the case of unresectable tumors (1–9). The percutaneous approach is the preferred method, especially for high-level obstructions, or for low-level obstructions in which previous endoscopic approaches have failed. External drainage, external-internal drainage and metallic stenting are choices for palliation in the percutaneous approach. In a previous prospective, multicenter, observational cohort study, metallic stenting was found to be superior to plastic stenting for hilar malignant biliary obstructions with respect to short-term results (18). In a study by Wagner et al. (19), success and patency rates were found to be better for metallic stents than for plastic stents in patients with hilar malignant biliary obstructions. Metallic stenting has the advantages of reestablishing the patency of a previously obstructed duct and maintaining physiological drainage. Patients will not have an uncomfortable external catheter and the associated risk of infection. Metallic stenting can be achieved by the percutaneous approach, the endoscopic approach or by a combination of both (2, 3, 5).

One of the issues concerning metallic stenting is the question of how many stents might be required for the lesions at hilar or suprahilar malignant biliary obstructions to achieve palliation of the obstructive symptoms. In these types of tumors, isolations may extend to the subsegmental level. It was reported that 30% of normally functioning hepatic parenchyma drainage was sufficient to relieve pruritus or to normalize serum bilirubin levels in patients without liver dysfunction or chemotherapy-

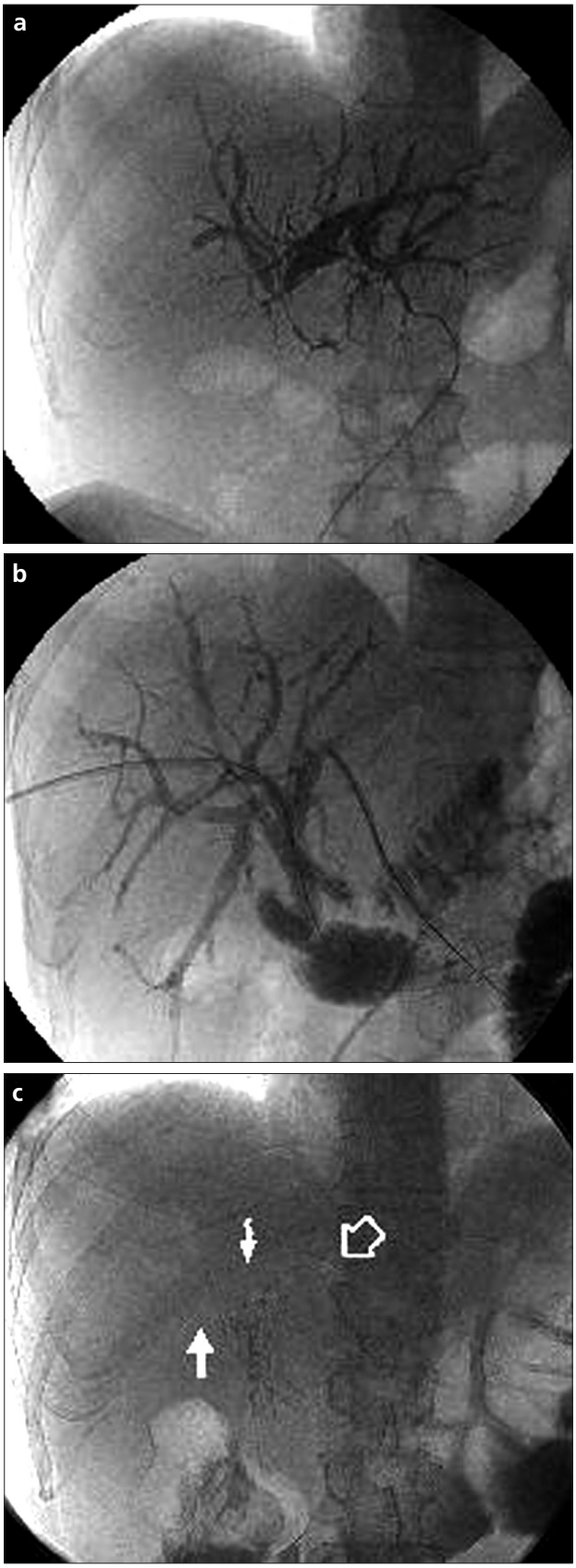

Figure 1. a–c. External drainage in a patient with hepaticojejunostomy **(a)**. Triple stenting of each of the main ducts **(b)**. Abdominal radiograph shows air densities in the bile ducts **(c)** which are signs of functioning stents *(arrows)*.

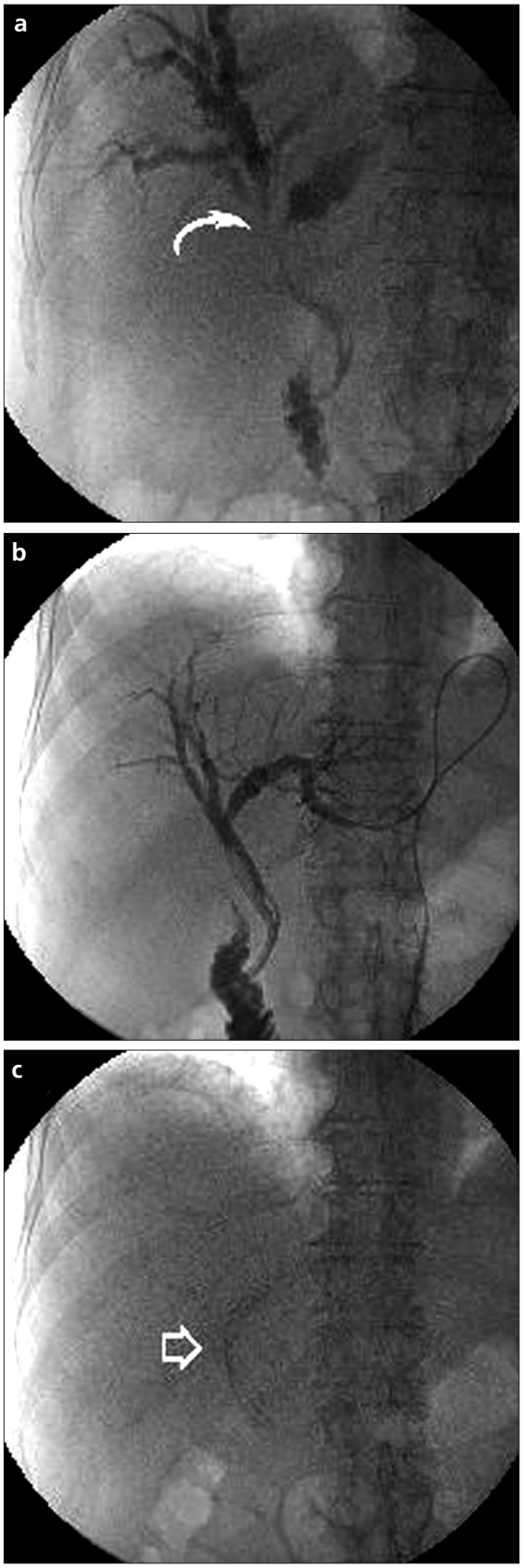

Figure 2. a–c. Effective and impending isolation in the right anterior, right posterior and left hepatic bile ducts **(a**, *curved arrow***)**. Control cholangiography **(b)** after stents were placed. Abdominal radiograph **(c)** of the stents *(open arrow)*. There are no air densities in the ducts because in this case the sphincter of Oddi was preserved.

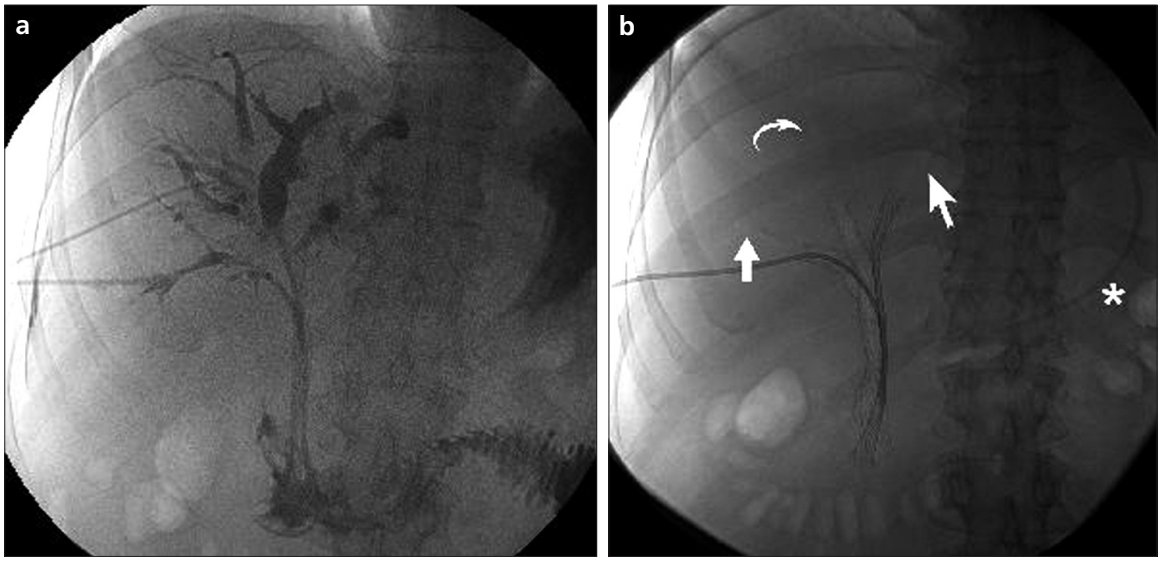

Figure 3. a, b. Effective isolation of the main ducts **(a)**. Abdominal radiograph **(b)** of the stents. In this case the stent in the left hepatic duct was placed with the endoscopic approach. Air densities *(arrows)* show that the stents were functioning. White asterisk shows the displaced plastic stent.

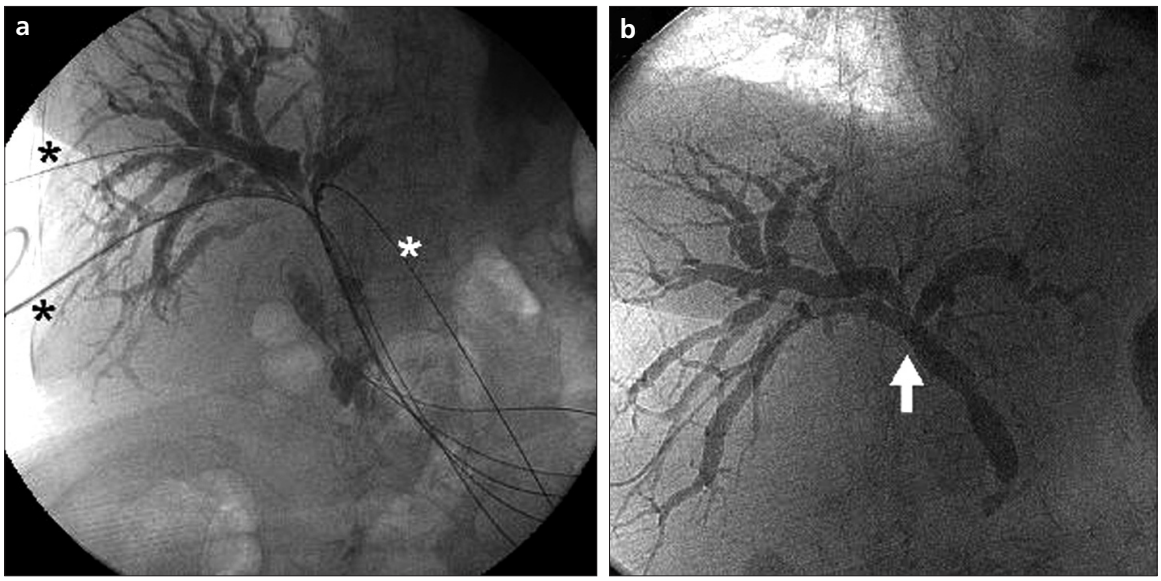

Figure 4. a, b. Trifurcation of the bile ducts **(a)** and effective-impending isolations. Asterisks show the percutaneously placed guidewires that enabled stent placement. Stents **(b**, *arrow***)** after placement.

Table. Summary of findings before and after triple stenting

		Pre-intervention			Post-intervention (15th day)			Post-intervention (3rd month)			
Patients	Histopathology	Pruritus[a]	TB (mg/dL)	Cholangitis	Pruritus[a]	TB (mg/dL)	Cholangitis	Pruritus[a]	TB (mg/dL)	Cholangitis	Primary stent patency (day)
1	GBC	2	12.4	+	0	2.05	-	0	1.89	-	189
2	MET	4	20.0	+	0	3.77	-	0	2.35	-	163
3	CHO	1	14.1	+	0	3.33	-	2	6.14	+	120 (ex)
4	PAN	3	22.0	+	0	4.12	-	0	3.52	-	97
5	CHO	2	15.0	-	0	2.10	-	0	2.0	-	215
6	MET	1	8.6	+	0	3.0	-	0	2.5	-	168
7	MET	3	15.2	+	0	2.5	-	0	1.92	-	238 (ex)
8	CHO	2	19.4	+	0	3.2	-	0	2.25	-	245

GBC, gall bladder cancer; MET, metastasis; CHO, cholangiocarcinoma; PAN, pancreas cancer; TB, total bilirubin; ex, exitus
[a]Pruritus scaling (ASA): 0, none; 1, mild scratching when undistracted; 2, active scratching without abrasion; 3, abrasion; 4, cutaneous mutilation with bleeding and scarring

associated steatohepatitis (3, 5). Inal et al. (8) reported no significant difference in clinical response to treatment or stent patency rate with unilobar versus bilobar drainage, even in Bismuth Type 2 and Type 3 hilar obstructions. In a study by Maybody et al. (10), patency of a single stent placed for a high bile duct obstruction was longer than that of multiple stents placed for a similar obstruction (201 days versus 261 days). In that article, it was stated that the percutaneous stenting of multiple bile ducts was an effective palliative method when indicated. Also, according to van Delden et al. (2), when tumor progression causes recurrent jaundice, prior unilobar drainage makes a repeat procedure for the contralateral lobe difficult. In these patients, repeat procedures may be needed after several months. Because of this, stenting both the right and left lobes is preferred in grades III and IV hilar lesions, as it leaves the option to choose the most appropriate lobe for drainage when a repeat procedure is necessary (2).

The term "isolation" becomes an important factor when considering multiple stents for high bile duct obstruction. Covey and Brown (3, 5) described three types of isolation. In complete ductal isolation, cholangiography shows no opacification of the isolated system(s). Opacified ducts do not drain in effective isolation, and in impending isolation, ducts are both opacified and drained. However, in impending isolation, there is a central narrowing that will cause effective or complete isolation in the near future. Effective and impending isolations have a high risk of cholangitis because of ineffective drainage and colonization. In patients with high bile duct obstruction and contralateral complete isolation, it may be advisable to use a primary stent if there has not been a previous endoscopic intervention or bilioenteric bypass. If the decrease in the serum bilirubin level is not sufficient, or if cholangitis develops, it may be necessary to achieve complete drainage or even triple stenting. Also, if there is ongoing cholangitis, a nonfunctional part of the liver (secondary to portal vein thrombosis and atrophy) may need to be drained. When metallic stenting is considered in patients with cholangitis, all of the infected ducts must be drained. In our study, all of the patients except one (87.5%) presented with acute cholangitis, and there were impending or effective isolations in all patients.

Endoscopic multiple stent-in-stent deployment of metallic stents in high-grade malignant biliary strictures was described previously by Kawamoto et al. (13, 14). A 150-day mean patency was found, and the technique was declared to be effective and safe even in patients receiving chemotherapy (13). High success rate, low incidence of morbidity and good recovery after obstruction were observed by the authors, although some early obstructions were reported. In this study, primary patency of up to 16.4 months was also reported (14). The stent-in-stent technique was not used in this study as a triple stenting treatment. Side branch stents advanced into the main stent through the mesh may cause dense struts in the common hepatic duct or choledochus and may imitate the behavior of a covered stent and thereby risk covering a cystic duct. Covered stents were found to have a high incidence of acute cholecystitis in a previous study by Bezzi et al. (20). Also, Kawamoto et al. reported one case of cholecystitis as a short term complication in a patient after endoscopic three-branched stent-in-stent deployment (14).

In patients with advanced biliary hilar malignancies, a percutaneous, transhepatic, criss-cross configured, dual stent placement for trisectoral drainage was described by Bae et al. (15). They found a primary patency rate of 187 days and a median patient survival time of 247 days, with no major complications related to the procedure. In this study, two stents were used to maximize hepatic drainage in patients with advanced biliary hilar malignancy and drainage from three sectors was achieved. Although it is feasible, safe and effective, the replacement style of the stents in this technique leads to some anatomical reorientation of the bile ducts. In the technique that we used, anatomic orientations of the bile ducts were preserved, with one disadvantage being of using one more percutaneous access tract and stent. Also, an obstruction in the stent that is placed into the common bile duct or choledocus in the criss-cross stent technique may have the potential to impair the function of the other stent. However, there was no difference when considering the primary patency rates. In our study, when one of the three stents occluded, all stents were assumed to be occluded.

The factors that cause stent occlusion are tumor ingrowth, distal and proximal overgrowth, sludge formation, food debris, clot formation and bacterial overgrowth (10, 12). We found a mean primary stent patency rate of 179±18.81 days (between 97 and 245 days). In the sixth month, the cumulative patency rate was 50%. Overall, mean primary patency rates in different series were between 141 and 231 days (8–15). In the study by Maybody et al. (10), an overall mean primary patency rate of 227.7 days was found in patients with multiple noncoaxial stents.

In our patient population, there were two deaths: one in the fourth month and the other in the eighth month. These deaths were unrelated to the percutaneous interventions. The cumulative patency rate in the sixth month in our study was acceptable for evaluating patency success for palliative stenting for malignant disease (1).

In the two patients in whom we performed triple stenting, there were trifurcation anomalies. Malignant biliary obstruction in patients with a trifurcation anomaly in the hilar region may necessitate triple stenting.

One limitation of this study is the small number of patients. We performed triple stenting in patients in whom cholangitis and isolations (impending-effective) were existent concomitantly. This restricted the number of patients treated with triple stenting.

We achieved early success in improving the patients' clinical and biochemical conditions. The bilirubin levels of all patients dropped to acceptable limits within 15 days. Pruritus and cholangitis were all controlled within the first week. In previous studies, procedure-related mortality and 30-day mortality were reported as 0–13% and 0–39% (2). We observed no procedure-related mortality or 30-day mortality.

In conclusion, malignant biliary obstruction could be palliated with metallic stenting. Triple metallic stenting did not improve primary patency rates significantly in patients with Bismuth-Corlette Type 3A obstructions or in the patients with a trifurcation anomaly and malignant hilar obstruction. In select patients, the beneficial effects of triple stenting include rapidly improv-

ing clinical and biochemical findings. Also, triple stenting will be beneficial in preventing isolation, which can cause cholangitis.

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