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Percutaneous Placement of Self-Expandable Metallic Stents in Patients with Obstructive Jaundice Secondary to Metastatic Gastric Cancer after Gastrectomy

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Objective: To evaluate the outcomes of patients undergoing percutaneous placements of a biliary stent for obstructive jaundice secondary to metastatic gastric cancer after gastrectomy.

Materials and Methods: Fifty patients (mean age, 62.4 years; range, 27-86 years) who underwent percutaneous placements of a biliary stent for obstructive jaundice secondary to metastatic gastric cancer after gastrectomy were included. The technical success rate, clinical success rate, complication rate, stent patency, patient survival and factors associated with stent patency were being evaluated.

Results: The median interval between the gastrectomy and stent placement was 23.1 months (range, 3.9-94.6 months). The 50 patients received a total of 65 stents without any major procedure-related complications. Technical success was achieved in all patients. The mean total serum bilirubin level, which had been 7.19 mg/dL \pm 6.8 before stent insertion, decreased to 4.58 mg/dL \pm 5.4 during the first week of follow-up ($p < 0.001$). Clinical success was achieved in 42 patients (84%). Percutaneous transhepatic biliary drainage catheters were removed from 45 patients (90%). Infectious complications were noted in two patients (4%), and stent malfunction occurred in seven patients (14%). The median stent patency was 233 \pm 99 days, and the median patient survival was 179 \pm 83 days. Total serum bilirubin level after stenting was an independent factor for stent patency ($p = 0.009$).

Conclusion: Percutaneous transhepatic placement of a biliary stent for obstructive jaundice secondary to metastatic gastric cancer after gastrectomy is a technically feasible and clinically effective palliative procedure.

Index terms: Biliary tract, malignant obstruction; Biliary tract, interventional procedures; Prosthesis, stent; Gastric carcinoma

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INTRODUCTION

Gastric cancer is the second leading cause of cancer-related deaths in the world and the increasing incidence of gastric cancers is being observed in association with the increasing life-span of the general population (1). Obstructive jaundice is an uncommon manifestation of metastases from gastric cancer and its incidence is reported to be 1.3-2.3% (2-4). Chemotherapy, surgical

decompression, interventional decompression, and radiation treatment are usually recommended with palliative intent (5). Although the main treatment for gastric cancer metastases is chemotherapy, jaundice is one of the contraindications for chemotherapy, and the prognosis for these patients is generally poor (6). Therefore, biliary drainage is needed to relieve jaundice, prevent complications, start chemotherapy and improve prognosis.

Percutaneous or endoscopic self-expandable metallic stent insertion is a well-established method for palliating a patient with an inoperable malignant biliary obstruction due to hepatic, pancreatic, and gallbladder carcinoma and metastatic lymphadenopathy (7-11). Although there have been many studies on the outcomes after palliative stenting for unresectable tumors, less is known about the outcomes after stenting for obstructive jaundice secondary to gastric cancer after resection. As endoscopic stenting is usually difficult in patients with Billroth-II reconstruction or Roux-en-Y esophagojejunostomy, the endoscopic approach is not usually used in these patients. To our knowledge, there have been few studies on the outcomes of percutaneous stents placement for obstructive jaundice secondary to metastatic gastric cancer and these studies included inoperable gastric cancers (6, 12, 13). A large study is required to determine the role of percutaneous stenting as a palliative treatment in patients who were treated with gastrectomy. Therefore, the purpose of this study is to evaluate the outcomes of percutaneous stents placement for obstructive jaundice secondary to metastatic gastric cancers after gastrectomy.

MATERIALS AND METHODS

Patient Population

We collected data from three referral hospitals. This retrospective study was approved by the institutional review boards of the three participating hospitals and the requirement for individual patient consent was waived for this study. We searched the patients who had percutaneous stenting and gastrectomy from medical record or database. Patients with obstructive jaundice secondary to afferent loop syndromes or patients with extensive liver metastasis causing liver failures were excluded. Patients whose primary tumor was treated by endoscopy were also excluded. From January 2003 to March 2010, 50 patients who had obstructive jaundice secondary to metastatic gastric cancer after gastrectomy underwent percutaneous placement of a self-expandable metallic stent via a percutaneous

transhepatic biliary drainage (PTBD) tract. The patients included 31 men and 19 women (mean age: 62.4 years, age range: 27-86 years). All gastric tumors were histologically confirmed as malignant advanced gastric cancers. All diagnoses of cancer metastasis and obstructive jaundice were based on clinical findings in addition to computed tomography (CT), cholangiogram findings and serum bilirubin levels (14, 15).

PTBD, Stent Placement and Follow-up

Percutaneous transhepatic biliary drainage procedures were performed to treat obstructive jaundice and provide access for the placement of a biliary stent. Broad spectrum antibiotics were given intravenously 24 hours before each PTBD procedure and for at least 48 hours afterwards (16). Procedures were performed with the patient under local anesthesia with 2% lidocaine hydrochloride and intravenous conscious sedation. Under the guidance of ultrasonography and fluoroscopy, unilateral PTBD was performed in 45 patients (right, n = 29; left, n = 16) and bilateral PTBD was performed in 5 patients.

All placement of a biliary stent was performed 2-42 days (mean, 14.35 days) after PTBD for decompressions of the bile duct, improvements of cholangitis, and restorations of liver function. Before placement of the biliary stents, cholangiograms were obtained by injecting iodine contrast media through a previously inserted PTBD catheter to assess the decompression, stenosis site and exact anatomy of the bile duct. After inserting the 0.035-inch guide wire, the PTBD catheter was removed and a 5 Fr catheter was advanced through the PTBD tract. The guide wire and catheter were advanced across the stenosis to the duodenum. The stenosis was opacified with injections of contrast media through the catheter and the length was measured. Balloon dilation of the stenosis before stent placement was not routinely performed unless the stenosis was tight. Balloon dilation was performed before stent placement in five patients. The stent was placed to lie across the stenosis. Stents were 3-4 cm longer than the stricture to cover it completely including the proximal and distal adjacent portions. Stent diameters ranged from 8 mm to 10 mm and the average stent length was 6.6 cm (range: 4 to 10 cm).

Fifty patients received a total of 65 metallic stents. We used various kinds of self-expanding metallic stents in this study including Hercules DH biliary stents (S&G Biotech, Seongnam, Korea) (n = 26), BONA stents (Standard Sci-Tech

Inc., Seoul, Korea) (n = 19), Hanaro stents (MI Tech, Seoul, Korea) (n = 8), Wallstents (Boston Scientific, Natick, MA, USA) (n = 4), GD stents (TaeWoong Medical, Gimpo, Korea) (n = 3), Sentinel stents (Boston Scientific) (n = 3), and Zilver stents (Cook, Bloomington, IN, USA) (n = 2). The GD stent is a partially covered stent and other stents are uncovered stents.

Unilateral stenting was performed in forty patients (80%) with the placement of one or two stents. In five patients, separate stents were placed in the hepatic hilum to achieve a Y-configuration. A T-configuration was achieved in five patients using BONA stents with a mesh through technique (17, 18). At the time of the initial stent placement, the 50 enrolled patients received a total of 62 stents. An additional 3 stents were inserted to treat tumor ingrowths in three patients.

After the stents placement, an 8.5 Fr drainage catheter (Cook, Bloomington, IN or Sungwon medical, Cheongju, Korea) was placed in the duct proximal to the stent and cholangiograms were obtained to check the immediate stent patency. After 2-3 days of waiting for spontaneous stent expansions, follow-up cholangiograms were obtained. Symptoms of biliary obstruction such as fever, pain, bile leakage, and serum bilirubin level were also checked before follow-up cholangiograms from medical records. If stent function was appropriate with spontaneous passages of contrast media to the duodenum, dilatation of the bile ducts was improved on the follow-up cholangiogram and there was no symptom of biliary obstruction, thus, the drainage catheter was removed after PTBD catheter clamping for one day. In cases with symptoms of biliary obstruction, the PTBD drainage was maintained.

The patients were followed-up as outpatients during the follow-up period. Serum bilirubin levels were checked to determine whether biliary drainage was impeded. If patients had obvious jaundice or a higher bilirubin level than before stent placements, the stent was assumed to be obstructed. In cases of recurrent jaundice or increased bilirubin levels, patients were evaluated with CT. CT scans showed dilation of the intrahepatic duct and the enhancement of inside the stent which is interpreted as tissue growths (19). Stent occlusion was diagnosed according to clinical, laboratory, and radiologic findings. In the case of stent occlusion, we performed decompressions of the bile duct by secondary percutaneous interventional procedures depending on the condition of the patients (20).

Definitions and Study Endpoints

Technical success was defined as placement of the stents by providing continuous drainage of bile without any major procedure-related complications. Clinical success was defined as a > 30% decrease in the serum bilirubin level relative to the baseline value (i.e., before stent insertion) within the first week after stent insertions (21). In cases where serum bilirubin level was normalized after PTBD, clinical success was defined as maintenance of the serum bilirubin level within the normal range after stent placements.

Procedural complications were classified either as major or minor according to the reporting standards of the Society of Interventional Radiology (22). Major complications result in admissions to a hospital for therapy, an unexpected increase in the level of care, prolonged hospitalization, permanent adverse sequelae, or death. Minor complications resulting in no sequelae may require a short hospital stay for observation.

Cholangitis was defined as recurrent episodes of inexplicable fever. Stent patency was defined as the time interval between initial stent placement and recurrence of obstruction. At the time of death, a stent was assumed to be patent if the patient had normal or only mildly elevated serum bilirubin levels (< 3 mg/dL). If the patients had obvious jaundice or higher serum bilirubin levels as compared to before the stent placement at the time of death, then the stent was assumed to have been obstructed.

We evaluated the characteristics of primary gastric cancers and malignant biliary obstructions. Also, we evaluated the technical success rates, clinical success rates, complication rates, stents patency and patient survivals. The serum bilirubin levels before and during the follow-up period were statistically analyzed using the Paired-sample *t* test with PASW Statistics software (version 17.0; SPSS Inc., Chicago, IL, USA). The stent patency and patient survival with 95% confidence intervals (CIs) were calculated using the Kaplan-Meier survival (life-table) analysis. The following variables were analyzed: gender, histology of previous gastrectomy, serosal invasion, lymph node metastasis of primary gastric cancer, hepatic metastasis after gastrectomy, level of biliary stenosis, stent configuration, total serum bilirubin after stenting, chemotherapy after stenting. We used univariate log rank analysis and Cox's proportional hazard model to find significant variables.

RESULTS

Thirty-five patients (70%) had undergone subtotal gastrectomy and Billroth type II procedures while fifteen patients (30%) underwent total gastrectomy and Roux-en-Y procedures. In 33 patients (66%), the primary carcinomas were located either in the pylorus or in the antrum with or without involvements of the stomach. In 17 patients (34%), the primary carcinomas were located either in the body or in the fundus (Table 1).

The mean interval from surgery to PTBD was 27.5 months (range, 3.9-94.6 months). The mean total serum bilirubin level before PTBD was 15.24 mg/dL. All patients had node metastases. CT showed bile duct dilation and lymph nodes in the hepatoduodenal ligament and retropancreatic portion. Eleven patients (22%) had hepatic metastasis. Stenoses were diagnosed on CT and cholangiogram after PTBD and before biliary stent placement. Main level of stenoses were located at the common hepatic duct in 23 patients (46%), proximal common bile duct in 16 patients (32%) and the distal common bile duct in 11 patients (22%) on cholangiogram. Among 23 patients who had stenosis in the common hepatic duct, 10 patients also had stenosis at the hilum (Table 2).

Technical success was achieved in all 50 patients. The mean total serum bilirubin level, which was 7.19 mg/dL \pm 6.8 before stent insertion, decreased to 4.58 mg/dL \pm 5.4 during the first week of follow-up, and this difference was statistically significant ($p < 0.001$). Clinical success was achieved in 42 of 50 patients (84%). Among the eight patients, who didn't achieve clinical success, total serum bilirubin was increased after stent insertions in 5 patients and total serum bilirubin was mild decreased in 3 patients. In thirty patients (60%), total serum bilirubin level decreased \leq 2 mg/dL after stenting. Forty-five patients (90%) showed a decrease in total serum bilirubin levels within the first week after stent placement. The PTBD catheter could be removed in these 45 patients because the stents were patented on cholangiogram acquired 2-3 day after stent insertions and there were no symptoms of biliary obstruction (Fig. 1). One patient wanted the drain catheter to be removed despite clinical failures and died 30 days later due to disease progressions. In other four patients, the PTBD catheter could not be removed due to clinical failures. PTBD catheter was kept and changed to prevent cholangitis.

Among forty-two patients who achieved clinical successes, twenty-two patients (53%) were treated by chemotherapy

Table 1. Characteristics of Primary Gastric Cancer

Variable	n	%
Location of primary tumor		
Upper 1/2	17	34
Lower 1/2	33	66
Macroscopic type		
Borrmann type 1	2	4
Borrmann type 2	7	14
Borrmann type 3	36	72
Borrmann type 4	5	10
Histologic type		
Differentiated	45	90
Signet ring cell	5	10
Serosal invasion		
No	20	40
Yes	30	60
Lymph node metastasis		
No	4	8
Yes	46	92
Previous gastrectomy		
Total gastrectomy	15	30
Subtotal gastrectomy	35	70

Table 2. Characteristics of Malignant Biliary Obstruction

Variables	n	%
Main level of obstruction		
Common hepatic duct, hilum	23	46
Proximal common bile duct	16	32
Distal common bile duct	11	22
Hepatic metastasis	11	22

after stent insertions. Other twenty patients didn't receive chemotherapy due to disease progressions, poor conditions or denials for further treatment. Forty-seven patients (94%) were discharged from hospital after stent placement. Three patients died during hospitalization (mean: 18 days, range: 3-32 days): two died due to disease progressions, and one secondary to pneumonia.

There were no major procedure-related complications. In one patient who underwent a subtotal gastrectomy and Billroth type II procedure, a sludge material was noted in the CBD on the follow-up cholangiogram; however, this patient was managed conservatively and the catheter was being removed. Complications were noted in nine patients (18%) during the follow-up period. Infectious complications including cholecystitis and hepatic abscess was noted in two patients (4%) (mean: 151 days, range: 38-264 days), who were treated with percutaneous cholecystostomy and percutaneous hepatic abscess drainage. Two hundred sixty-

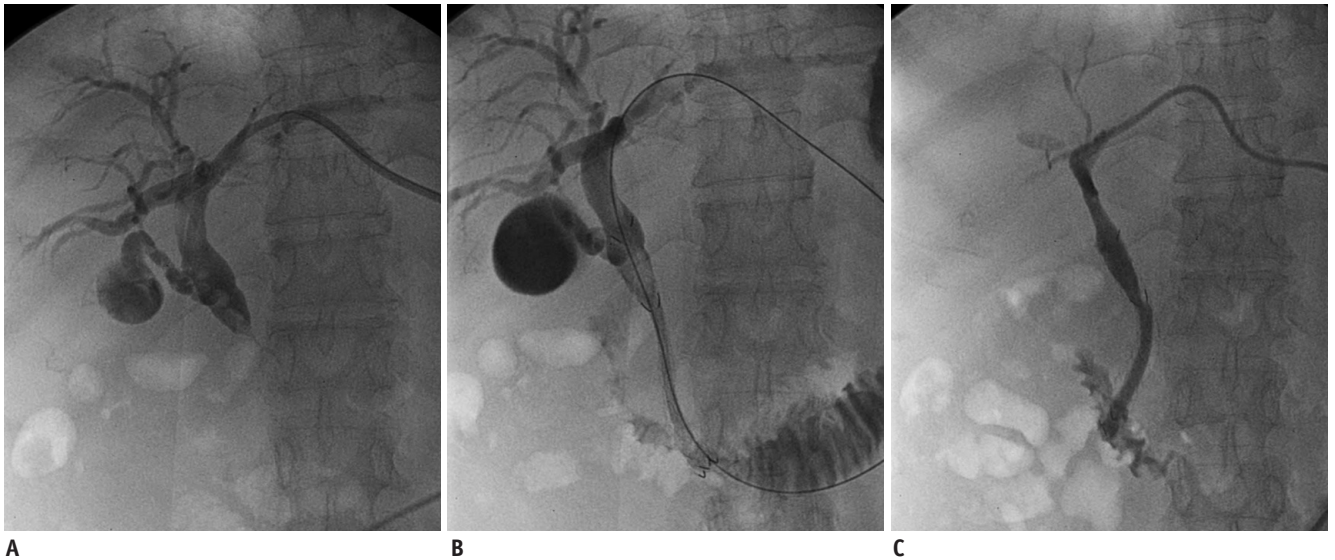


Fig. 1. Sixty four-year-old female with obstructive jaundice resulting from gastric cancer after gastrectomy.
A. Cholangiogram via left PTBD tract shows severe stricture at distal common bile duct. **B.** Guide wire was passed into duodenum and partially covered stent was inserted into common bile duct. **C.** Cholangiogram obtained three days after stent placement demonstrating further expansion of stent and good passage of contrast media. PTBD = percutaneous transhepatic biliary drainage

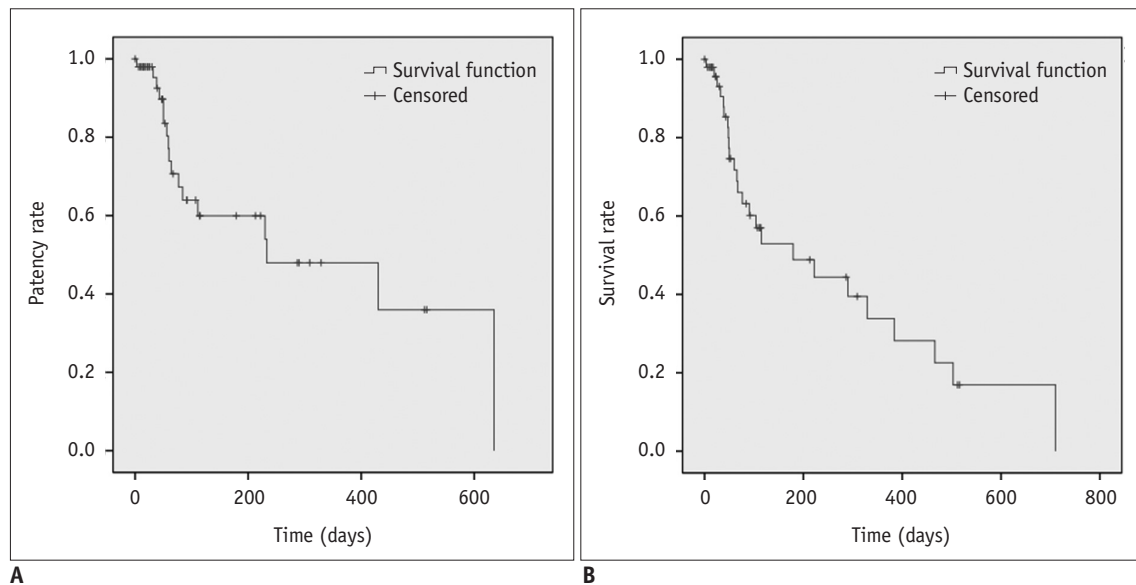


Fig. 2. Kaplan-Meier analysis of stent patency and patient survival.
A. Kaplan-Meier analysis of primary stent patency. Median stent patency time was 233 ± 99 days (95% CI, 38-427 days). **B.** Kaplan-Meier analysis of patient survival. Median patient survival time was 179 ± 83 days (95% CI, 16-342 days). CI = confidence interval

four days after the stent placements, about 3 cm sized, left lateral segmental hepatic abscess developed in one patient who placed the stent through right PTBD tract. Recurrent jaundice was noted in seven patients (14%) after a mean of 243.9 days (range: 56-635 days); all showed increased total serum bilirubin levels, intrahepatic ductal dilation, and enhancements inside the stent on CT scans. These seven patients were treated by PTBD, and second biliary stent was placed in three patients.

The median and mean overall stent patency period was 233 ± 99 days (95% CI, 38-427 days) and 286 ± 49 days (95% CI, 190-382 days), respectively. Univariate log rank analysis showed that total serum bilirubin level after stenting ($p < 0.001$) and chemotherapy after stenting ($p = 0.002$) were significantly associated with stent patency. Multiple Cox's proportional hazard regression analysis showed total serum bilirubin level after stenting ($p = 0.009$) was independent predictor of stent patency. Median

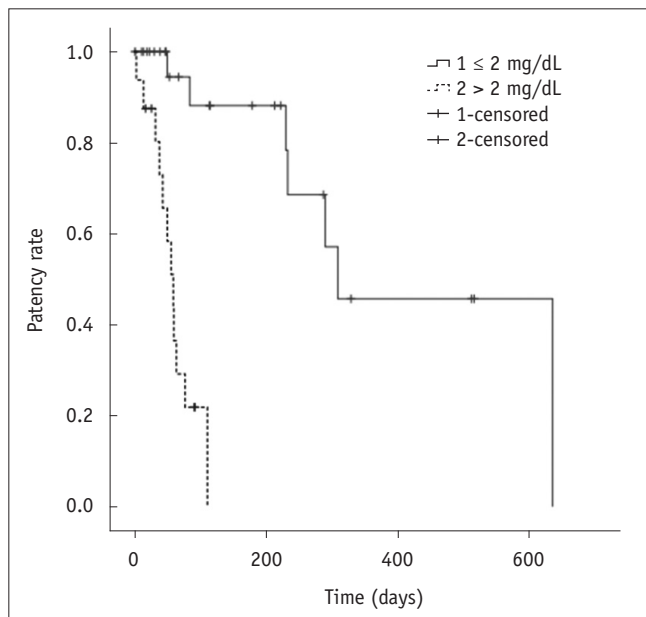


Fig. 3. Multiple Cox's regression analysis of stent patency.

Kaplan-Meier curves showing stent patency according to total serum bilirubin after stenting.

stent patency period was significantly longer in patients with total serum bilirubin level ≤ 2 mg/dL (309 days; 95% CI, 119-498 days) compared to in > 2 mg/dL (59 days; 95% CI, 43-75 days) after stenting. During the follow-up period, 25 patients died 3-710 days after stent placements. Among these 25 patients, 12 patients had normal or mildly elevated serum bilirubin levels (< 3 mg/dL). The median and mean of overall patient survival period was 179 ± 83 days (95% CI, 16-342 days) and 274 ± 47 days (95% CI, 181-367 days), respectively (Figs. 2, 3).

DISCUSSION

Although malignant biliary obstruction is an uncommon complication of gastric cancer, metastatic gastric cancer is the most frequent cause of metastatic obstructive jaundice (50%), followed by colon cancer (20%), breast cancer and melanoma (6, 23). Metastatic lymphadenopathy along the hepatoduodenal ligament is one of the main causes of biliary obstruction of gastric cancer, and its most common site is around the cystic duct. Standard D2 lymph node dissection does not remove lymph nodes along the hepatoduodenal ligament. Two-thirds of such node metastases causing malignant biliary obstructions derived from gastric cancer in the antrum are located closely to the hepatoduodenal ligament. Direct invasion of recurrent gastric cancer also causes obstructive jaundice. During

balloon dilation or stent insertion, eccentric smooth round or oval-shaped defects on the right lateral wall of the bile duct were commonly noted and this finding was due to extrinsic compressions from enlarged lymph nodes (15). In our study, 66% of patients had gastric cancer located in the lower 1/2 of the stomach, while bile duct stenoses were located at the common hepatic duct and proximal common bile duct in 78% of patients.

The surgical approach to malignant biliary obstruction is less applicable to biliary obstruction caused by metastatic tumors to the porta hepatis with extrinsic obstruction. Palliative bypass can prolong patient survival if properly performed. Two studies have shown that surgical treatment is associated with higher postoperative mortality, morbidity and a longer hospital stay than non-surgical drainages (24, 25). Endoscopic retrograde cholangiography (ERCP) is usually difficult in these patients because of a distorted bowel loop due to the Billroth II reconstruction or Roux-en-Y esophagojejunostomy (26, 27). Afferent loop perforation is a specific complication of ERCP in these patients and these patients have a mortality rate varying from 0.7-5% (27). Therefore, we use PTBD as an initial treatment for patients with malignant biliary obstruction caused by metastatic gastric cancers. Although PTBD is expected to improve obstructive jaundice and drain the infected bile, it could also be associated with catheter-related complications and lead to a deteriorating quality of life due to difficulties maintaining an external catheter and the need for regular catheter changes. Frequently encountered complications of PTBD are catheter dislodgement, cholangitis, and bile leakage (3, 28). Self-expandable metallic stents provide more comfort than PTBD. Although there have been many studies of percutaneous stent placement for malignant biliary obstruction, studies of stent placement for obstructive jaundice caused by gastric cancer after limited gastrectomy (6, 12).

The clinical success in our study is comparable to that in previous studies that focused on PTBD efficacy for palliative treatment (4, 12). Migita et al. (12) reported significant serum bilirubin decreases in 76% of the patients after PTBD. After the intervention, performance status improved in 68% of patients; however, 45% of patients could not be discharged from the hospital after the intervention for progressions of the underlying malignancy or jaundice. In our study, 90% of PTBD catheters could be removed and 94% of our patients were discharged from the hospital after stent insertions. These results reveal that percutaneous

stent placement for obstructive jaundice resulting from gastric cancer after gastrectomy is an effective palliative treatment. Gwon et al. (13) reported their experience of palliative treatment in 117 patients with malignant biliary obstruction caused by metastatic gastric cancer. In patients who had previously undergone gastrectomy for primary gastric cancer, the median interval between previous gastrectomy and onset of biliary obstruction was 26 months. Clinical success was 91% of 54 patients who underwent stent placements. Median stent patency time was 351 days. Among 54 patients who underwent stenting, there were patients who did not undergo gastrectomy. They didn't find significant factors associated with stent patency. Our study only included patients who underwent gastrectomy. Percutaneous stenting was an effective palliative treatment and total serum bilirubin level after stenting was an independent predictor of stent patency.

The purpose of percutaneous stenting for the treatment of obstructive jaundice is not only to improve jaundice, but also to give the patients an opportunity to receive palliative treatments such as systemic chemotherapy. Many systemic chemotherapy drugs require intact mechanisms of bile excretion to prevent toxicity. Twenty-two of the fifty patients (44%) who had a significant decrease in serum bilirubin level after stent placement received chemotherapy. Previous studies suggested that the use of chemotherapy after PTBD or stenting might prolong the survival of patients with obstructive jaundices caused by the local recurrence of gastric cancers (4, 12, 13).

There were no major procedure-related complications in our study. During the follow-up period, complications were noted in nine patients (18%). Cholecystitis and hepatic abscess were noted in two patients (4%). Recurrent jaundices and stent malfunctions were noted in seven patients (14%). These seven patients were treated by PTBD and a second biliary stent was placed in three patients. Previous studies reported that 7-30% of patients who underwent biliary stenting for palliation had complications and 14-25% of patients had recurrent symptoms of jaundice during the follow-up periods (29-31). Our results are comparable to those described in the studies.

The stent patency and patient survival period in our study were better than those of previous studies on cholangiocarcinoma, gallbladder carcinoma, and pancreatic carcinoma (32, 33). However, making comparisons to previous studies is difficult because patients were treated at a different stage, and each tumor had a different

histological type and biological behavior. Yet, the response to chemotherapy in our patients may have improved the survival period. Thirty-nine patients (78%) had stenoses at the common hepatic duct and proximal common bile duct mainly due to extrinsic compressions by malignant lymphadenopathy. These extrinsic compressive lesions may have responded better to biliary stent placements, and thus, may have improved stent patency. A larger study is needed to identify independent factors associated with stent patency and patient survival rates.

There are several limitations to our study. First, this was a retrospective study. Second, this was a multicenter study with uncovered or partially covered types of stents used, which may have influenced stent patency. Third, gastric cancer recurrence was not confirmed histologically because reoperation or endoscopic biopsy for nodes in the hepatoduodenal ligament portion was very difficult. Jaundice was diagnosed during follow-up after gastrectomy due to the cancer, and mean interval from surgery to PTBD was 27.5 months. Imaging findings, clinical symptoms and laboratory findings were compatible with gastric cancer metastasis.

In conclusion, percutaneous transhepatic placement of a biliary stent for obstructive jaundice caused by metastatic gastric cancer after a gastrectomy is a technically feasible, safe, and clinically effective palliative procedure. Total serum bilirubin level after stenting was an independent factor for stent patency.

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