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ORIGINAL PAPERS

Comparison of covered and uncovered self-expandable stents in the treatment of malignant biliary obstruction

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ABSTRACT

Background and objective: Drainage with metallic stents is the treatment of choice in malignant obstructive jaundice. Technical and clinical success with metallic stents is obtained in over 90% and 80% of cases, respectively. There are self-expandable metallic stents designed to increase permeability. The aim of this study was to describe the results obtained with totally covered self-expandable and uncovered self-expandable metallic stents in the palliative treatment of malignant biliary obstruction.

Patients and methods: Sixty eight patients with malignant obstructive jaundice secondary to pancreatobiliary or metastatic disease not amenable to surgery were retrospectively included. Two groups were created: group A (covered self-expandable metallic stents) (n = 22) and group B (uncovered self-expandable metallic stents) (n = 46).

Results: Serum total bilirubin, direct bilirubin, alkaline phosphatase and gamma glutamyl transferase levels decreased in both groups and no statistically significant difference was detected (p = 0.800, p = 0.190, p = 0.743, p = 0.521). Migration was greater with covered stents but it was not statistically significant either (p = 0.101). Obstruction was greater in the group with uncovered stents but it was not statistically significant either (p = 0.476).

Conclusion: There are no differences when using covered self-expandable stents or uncovered self-expandable stents in terms of technical and clinical success or complications in the palliative treatment of malignant obstructive jaundice.

Palabras clave: Self-expadable stents. Malignant biliary obstruction.

INTRODUCTION

Advanced stages of pancreatic, biliary and metastatic cancer are often complicated by obstructive jaundice. Drainage of the biliary tract with metallic stents is the treatment of choice if a life expectancy over one month is predicted (1). Technical and clinical success with self-expandable metallic stents (SEMS) is possible in over 90% and 80% of cases, respectively (1). Shah et al. proved that uncovered Z-stents and Wallstent SEMS are equal in terms of placement and permeability (2). However, in a randomized clinical trial, partially covered SEMS were occluded less often (14%) than uncovered stents (38%) (3). There are currently totally covered SEMS that further decrease obstruction resulting from tumor growth into the lumen, although the risk of migration is increased; nevertheless, in a study of totally covered SEMS in malignant biliary obstruction palliation, only one migration case was detected among 58 patients (4). The aim of this study was to describe our results with the use of totally covered SEMS and uncovered SEMS in the palliation of malignant biliary obstruction.

MATERIAL AND METHODS

We conducted a retrospective study between May 2012 and September 2014 that included patients above the age of 18 and of both genders, with malignant obstructive jaundice due to pancreatobiliary or metastatic disease who were not surgical candidates; their functional status according to Karnofsky's index was above 50, and during endoscopic retrograde cholangiography, type I stenosis (Bismuth-Corlette) of the biliary hilum or of the mid or distal common bile duct was observed. Patients with previous biliary tract derivation (surgical, endoscopic or percutaneous) as well as patients with massive liver infiltration were excluded from the study. Patients were divided into two groups: group A, those treated with totally covered SEMS, and group B, patients treated with uncovered SEMS. In all cases, stents were chosen according to the endoscopist's preference. Patients who died within the first 15 days after stent placement or lacking control laboratory work-up were not considered in the analysis. Technical success was defined as the placement of the stent

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at least 1 cm from the tumor borders and with adequate contrast drainage. Clinical success referred to a 30% or above decrease in total bilirubin serum values 15 days after stent placement. A complication referred to any event directly related to stent placement or to its design (perforation, migration, obstruction, hemorrhage, pancreatitis, cholecystitis). Stent obstruction was diagnosed if jaundice recurred or laboratory parameters were compatible with biliary tract obstruction. Complications were considered as "early" if they developed within 30 days and as "late" if they developed 30 days after stent placement. The following variables were studied: age, gender, tumor origin, total bilirubin (TB) serum values, direct bilirubin (DB), alkaline phosphatase (AP), gamma glutamyl transferase (GGT) and total leukocyte count before and after stent placement. The number of patients with a permeable stent until death was also evaluated.

Statistical analysis

Descriptive statistics of the recorded variables were performed according to the type of variable: nominal or ordinal variables are presented as proportions, and quantitative variables are presented as averages and standard deviations. Differences between both comparison groups were determined with the Chi^2 test for qualitative variables and Student's t-test for independent samples in the case of quantitative variables. Estimation of the difference in the proportion of complications (migration or obstruction) between the study groups was obtained with Fisher's exact test. Survival was established with the Kaplan-Meier method and between-group differences were calculated with the Log Rank test. A Cox proportional hazards model was obtained to identify the effect of the type of stent on overall survival as well as on permeability, adjusting for the use of chemo and/or radiotherapy. A p value < 0.05 was considered to be statistically significant. The analysis was conducted with SPSS v21 software.

RESULTS

A total of 132 SEMS were placed during the study period and 73 were included in the study. The rest were excluded because patients continued their follow-up and treatment elsewhere. Of the 25 patients in group A (covered SEMS), 3 were not included in the analysis: 2 died, 10 and 11 days after stent placement respectively, and a third patient died 32 days after stent placement but did not undergo follow-up studies. Among the 22 remaining cases (Table I), 8 were male and 14 were female, with an average age of 58 (range, 34-79). The etiological diagnoses were pancreatic cancer (n = 11), ampulloma (n = 1), cholangiocarcinoma (n = 5), gallbladder cancer (n = 3) and ovarian metastases (n = 2). Technical success and clinical success in the 22 patients were 100% and 95.4% (21/22), respectively. Eleven (50%) were treated with chemoradiotherapy: 4 before, 6 after and 1 before and after stent placement. Fifteen WallFlex® (BostonScientific) (68.2%), 5 (22.7%) WallStent® (Boston Scientific) and 2 (9.1%) Niti-S® (Taewoong Medical) stents were placed. Mean total bilirubin (TB) and direct bilirubin (DB) at the time of stent placement were 17.4 ± 9.7 mg/dl and 9.4 ± 6 mg/dl, respectively. Mean TB and DB 15 days after placing the stent were 5.07 ± 3.9 mg/dL and 2.4 ± 2.1 mg/dL, respectively (Table II). AP, GGT and serum total leukocytes also decreased. Among complications, there were 2 (9,1%) cases of late migration on day 45 and day 125, and in both cases they were Niti-S stents. There was one (4.5%) case of obstruction due to tumor growth on day 127. Fourteen (63.63%) patients died with a permeable stent during the first 90 days of follow-up. Between days 91 and 180, 18.18% (n = 4) died and only 18.18% (n = 4) survived more than 180 days.

Table I. Clinical and demographic characteristics

Parameter	*TCBS n = 22*	*UCBS n = 46*	*p*
Gender			0.453
Male	8 (36.4%)	19 (41.3%)	
Female	14 (63.6%)	27 (58.7%)	
Age	58 (34-79)	57.2 (39-80)	
Etiology			0.773
Ampulloma	1 (4.5%)	6 (13%)	
Pancreatic cancer	11 (50%)	24 (52.5%)	
Cholangiocarcinoma	5 (22.7%)	9 (19.6%)	
BT cancer	3 (13.6%)	5 (10.9%)	
Metastases	1 (9.1%)	2 (4.3%)	
Karnofsky			0.374
60%	1 (4.5%)	4 (8.7%)	
70%	3 (13.6%)	12 (26.1%)	
80%	12 (54.5%)	24 (52.2%)	
90%	6 (27.3%)	6 (13%)	
Chemo-radiotherapy	11 (50%)	24 (52.2%)	0.778
Before	4 (18.2%)	8 (17.4%)	
After	6 (27.3%)	9 (19.6%)	
Before and after	1 (4.5%)	5 (10.9%)	
Technical success	22 (100%)	46 (100%)	
Clinical success	21 (95.4)%	40 (86.9%)	
Migration	2 (9.1%)	0	0.101
Obstruction	1 (4.5%)	4 (8.6%)	0.476

Group B (uncovered SEMS) included 48 patients. Two patients were not included in the analysis because they died 26 and 41 days, respectively, after stent placement, one as a result of pneumonia and the other, due to upper gastrointestinal bleeding and he had no follow-up laboratory results. Among the 46 remaining patients (Table I), there were 21 males and 27 females with an average age of 57.2 (range, 39-80). The etiological diagnoses were cancer of the pancreas (n = 24), ampulloma (n = 6), cholangiocarcinoma (n = 9), cancer of the gallbladder (n = 5) and breast cancer metastases (n = 2). In these patients, technical success and clinical success were 100% and 86.9% (40/46), respectively. Twenty-four (52.2%) were treated with chemoradiotherapy: 8 before, 9 after, and 5 before and

Table II. Success indicators after stent placement

		SEMS-Covered Mean (SD)	*SEMS-Uncovered Mean (SD)*	*p*
Parameter	Total bilirubin	5.07 (± 3.94)	4.7 (± 5.78)	0.080
	Direct bilirubin	2.40 (± 2.13)	2.41 (± 3.11)	0.190
	Alkaline phosphatase	370 (± 239.39)	398.48 (± 249.00)	0.743
	GGT	200.22 (± 181.15)	189.04 (± 189.04)	0.521
	Leukocytes	10,177 (± 4,963.67)	8,656.52 (± 4,339.97)	0.300

after stent placement. Thirty-five (76%) Wall Flex® (Boston Scientific), 10 (21,7%) WallStent® (Boston Scientific) and 1 (2.1%) Zilver® (Wilson Cook) stents were placed.

In this group, initial TB and DB were 12.2 ± 8.1 mg/dL and 7.5 ± 5.2 mg/dl, respectively. Mean TB and DB 15 days after the procedure were 4.7 ± 5.7 mg/dl and 2.4 ± 3.1 mg/dL, respectively (Table II). AP, GGT and total serum leukocytes also decreased. Among complications, there were 4 (8.7%) cases of obstruction: one was due to biliary sludge on day 10, and 3 were the result of tumor ingrowth on days 125, 171 and 195. During the first 90 days of follow-up, 50% (n = 23) of patients died with no signs of stent obstruction. Between days 91 and 180, 23.9% (n = 11) of patients died and only 26.1% (n = 12) survived over 180 days.

When comparing the results in both groups 15 days after stent placement, serum values of TB, DB, AP and GGT all decreased. However, there was no statistically significant difference (p = 0.800, p = 0.190, p = 0.743, p = 0.521). Migration was more frequent with covered SEMS but it was not statistically significant (p = 0.101). Obstruction occurred more frequently in the group with uncovered SEMS but, again, the difference was not statistically significant (p = 0.476). Chemotherapy and radiotherapy did not seem to alter stents' permeability (p = 0.143). The group treated with uncovered SEMS had a greater survival rate although the difference was not statistically significant either (p = 0.875).

DISCUSSION

Stent placement is the palliative treatment of choice in most cases of malignant biliary stenosis (5-7). SEMS are used to relieve obstruction of the distal biliary tract when the expected survival is greater than one month (1). In our study, technical success was 100% in both groups and no differences were observed with previous communications in the literature (> 90%) (1). Unlike plastic stents, SEMS have a greater diameter and hence, more lasting permeability (8,9). In a multicenter, randomized study, Shah et al. showed that uncovered Z-stent and Wallstent stents are equal in terms of placement, percentage of occlusions and overall permeability (2). In that study, the mean time period until reintervention was 152 and 154 days for the Z-stent and Wallstent, respectively (p = 0.90) (2). These results and findings are similar to those reported in a study by Weston et al., which suggested there was no difference in results when uncovered SEMS were used regardless of their design (10). However, if used, the risk of obstruction remains, either as a result of tumor growth or due to granulation tissue in the stent or the formation of biliary sludge plugs. As a result, a randomized clinical trial was conducted to compare partially covered Diamond SEMS *versus* uncovered SEMS in the management of obstruction of the distal biliary tract; partially covered SEMS appeared to become occluded less frequently. Partially covered SEMS became occluded in 14% of cases, after a mean follow-up of 304 days compared to 38% of the uncovered SEMS, after a mean follow-up of 166 days (p = 0.0032) (3). Furthermore, Telford et al. reported a 12% migration rate with the use of partially covered SEMS, a percentage similar to that obtained with the use of plastic stents (5-10%) (1,11). This number is acceptable if, in return, permeability is prolonged.

Clinical success has been reported at 80%. This result depends on several circumstances since partially covered SEMS can also become occluded as a result of tumor growth or granulation tissue through the spaces in the stent's ends in 12% to 14% of cases (3,11,12). In our groups, clinical success according to the protocol of covered and uncovered SEMS was 95.5% and 87%, respectively, and there was no statistically significant difference in terms of biochemical parameter decreases. In our study, obstruction also developed in 4.5% of covered SEMS and in 8.7% of uncovered SEMS. It is important to consider that obstruction resolution depends on the stent remaining in place, which depends on the type of stent used. Totally covered SEMS appear to migrate more frequently (3%-12%) compared to uncovered SEMS (< 1%) (11-14). In our series, migration occurred in 9.1% (n = 2) of those with covered SEMS, although this was not statistically significant (p = 0.101). Cholecystitis has been described as a complication in 0-12% of cases when using covered SEMS (15) but did not develop in either of our 2 groups.

Covered SEMS were developed to provide prolonged permeability, but this has not been completely proven. Two clinical trials did not detect a difference when comparing

totally covered SEMS with uncovered SEMS (11,16). This is perhaps due to the fact that most patients with pancreatobiliary tumors are first evaluated in advanced stages of the disease and die within the first 6 months of palliation without evidence of stent dysfunction; it is, thus, difficult to establish a difference when comparing both types of stents. A meta-analysis found no difference in the development of stent dysfunction when comparing covered and uncovered SEMS. However, accumulated permeability is greater (61 days) and there is a tendency for a longer mean time to reobstruction with covered SEMS (17).

We understand that our study results are subject to biases, such as its retrospective nature, lack of randomization and the use of several types of stents. Nevertheless, they suggest there is no difference between using covered or uncovered SEMS in terms of technical success, clinical success and complication development when compared in the short-term (< 90 days) and medium-term (91-180 days). This seems logical if we take into account the fact that most patients died within 180 days of palliation. Hence, the long-term benefit of using fully covered SEMS is applicable in only a small number of patients. Regardless, their use may be beneficial to patients that are candidates to neoadyuvant treatment and surgery with curative intentions, if we take into account that neoadjuvant therapy has a mean duration of 104 days (18); besides, they do not need to be withdrawn before surgery and in many patients this will be the final treatment modality.

To conclude, the observed results suggest that there is no difference between using totally covered SEMS or uncovered SEMS in the palliative treatment of malignant biliary obstruction, in terms of technical and clinical success and development of complications in the short and medium-term. Randomized clinical trials comparing covered SEMS and uncovered SEMS are necessary to establish without a doubt whether or not there any significant differences and what they are.

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