Covered versus uncovered self-expandable nitinol stents in the palliative treatment of malignant distal biliary obstruction: results from a randomized, multicenter study

CME

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Background: Covered biliary metal stents have been developed to prevent tumor ingrowth. Previous comparative studies are limited and often include few patients.

Objective: To compare differences in stent patency, patient survival, and complication rates between covered and uncovered nitinol stents in patients with malignant biliary obstruction.

Design: Randomized, multicenter trial conducted between January 2006 and October 2008.

Setting: Ten sites serving a total catchment area of approximately 2.8 million inhabitants.

Patients: A total of 400 patients with unresectable distal malignant biliary obstruction.

Interventions: ERCP with insertion of covered or uncovered metal stent. Follow-up conducted monthly for symptoms indicating stent obstruction.

Main Outcome Measurements: Time to stent failure, survival time, and complication rate.

Results: The patient survival times were 116 days (interquartile range 242 days) and 174 days (interquartile range 284 days) in the covered and uncovered stent groups, respectively ($P = .320$). The first quartile stent patency time was 154 days in the covered stent group and 199 days in the uncovered stent group ($P = .326$). There was no difference in the incidence of pancreatitis or cholecystitis between the 2 groups. Stent migration occurred in 6 patients (3%) in the covered group and in no patients in the uncovered group ($P = .030$).

Limitations: Randomization was not blinded.

Conclusions: There were no significant differences in stent patency time, patient survival time, or complication rates between covered and uncovered nitinol metal stents in the palliative treatment of malignant distal biliary obstruction. However, covered stents migrated significantly more often compared with uncovered stents, and tumor ingrowth was more frequent in uncovered stents. (Clinical trial registration number: NCT00280709.) (Gastrointest Endosc 2010;72:915-23.)

Abbreviations: CONSORT, Consolidated Standards for Reporting Trials; cSEMS, covered metal self-expandable stent; PTC, percutaneous transhepatic cholangiography; SEMS, self-expandable metal stent; uSEMS, uncovered self-expandable metal stent.

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The vast majority of patients who present with obstructive jaundice caused by a malignant bile duct obstruction either have an advanced stage of the disease or are unfit for surgical resection for other medical reasons.[1,2] For many years, endoscopic stent placement has played a pivotal role in the palliative management of these patients.[3] Because stent patency virtually determines the success of this palliative strategy, self-expandable metal stents (SEMSs) are now used instead of traditional plastic stents.[4-9] Several clinical trials have demonstrated improved patency and cost-effectiveness with the use of SEMSs.[10-12] However, despite improvements in materials and stent design, problems remain, as exemplified by the 13% to 44% reintervention rate attributed to stent failure with SEMSs.[13-16] A number of factors have been suggested to explain this relatively high failure rate, including epithelial hyperplasia, tumor ingrowth and overgrowth, dislocation, debris formation, and clot accumulation.[1,17,18] To better counteract tumor ingrowth in uncovered SEMSs (uSEMSs), covered SEMSs (cSEMSs) were developed by placing a thin nonporous membrane on the inside of the metal mesh. Possible advantages of such a stent design have so far been addressed in relatively few small clinical studies, and the results have been partly conflicting.[19-21] The major objective of the current trial was to compare the stent patency of cSEMSs and uSEMSs in the palliative treatment of patients with a distal malignant bile duct obstruction. Secondary objectives were to compare patient survival time and complications, including the incidence of cholecystitis, pancreatitis, and stent migration.[20,22-24]

Take-home Message

- There are no significant differences in patient survival or stent patency time between covered and uncovered self-expandable metal stents in the palliative treatment of malignant distal biliary obstruction. Covered stents migrated significantly more often compared with uncovered stents, whereas an increase in tumor ingrowth was seen in uncovered stents. There does not seem to be an increased risk for cholecystitis or pancreatitis when using covered stents.

PATIENTS AND METHODS

Between January 2006 and October 2008, 400 patients fulfilled the criteria for inclusion in the study, and 200 patients were randomized to the cSEMS group and 200 to the uSEMS group. The study eligibility and exclusion criteria are shown in Table 1. A Consolidated Standards for Reporting Trials (CONSORT) flowchart, illustrating the progress of patients throughout the trial, is shown in Figure 1.

Design

The study was designed as a multicenter, randomized, controlled trial involving 10 Swedish hospitals serving a total catchment area of approximately 2.8 million inhabitants. A total of 21 endoscopists participated, and they had 4 to 25 years of experience performing ERCP. The trial compared a polycarbonate-polyurethane covered nitinol stent with an uncovered nitinol metal stent (Nitinella; ELLA-CS, Hradec Kralove, Czech Republic). The study protocol was approved by the Ethics Committee of Southeast Sweden. Informed consent was obtained from each patient enrolled in the study.

Randomization and stent insertion

All procedures were performed under fluoroscopic guidance, and biliary sphincterotomy was performed routinely in all patients. Prophylactic antibiotics were not used, and antibiotics were only administered if there were signs of cholangitis or other ongoing infections. The randomization process, in which opaque sealed envelopes with computer-generated random numbers in blocks of 20 (10:10) were used, was performed by the endoscopist when the patient was in the ERCP suite and after the guidewire had passed the stenosis. Stratification of disease groups was not done. The endoscopist decided which SEMS length to use, either 52 or 72 mm, depending on the anatomic circumstances and the length of the stenosis. Fully expanded, the stents reached an inner diameter of 10 mm. When in an adequate position, the stents should be visible from the duodenal lumen. The membrane of the covered stent was placed inside of the metal mesh, and only the distal 5 mm of the covered stent was uncovered. The delivery systems for the cSEMSs and uSEMSs were 8F and 7F, respectively.

Follow-up

We recorded all procedure-related complications according to current routine and consensus.[24,25] To confirm a successful drainage procedure, liver function tests were performed before and 2 to 5 days after stent insertion. The criteria for a successful stent insertion included radiological confirmation (at ERCP) that the stent was in an appropriate position and at least a 30% decrease in bilirubin level during the first 5 days after stent insertion. Clinical follow-up was performed once per month, starting at 1 month, and the endpoint was 12 months after randomization. Liver function tests were repeated at the 1-month follow-up. At the 2- to 12-month follow-ups, liver function tests were only performed if there had been any history or clinical signs of jaundice, cholangitis, or itching during the past month. Patients who were not able to visit the outpatient clinic were contacted (or, when necessary, their caregivers were contacted) by a trained study nurse using a standardized questionnaire with regard to symptoms indicating signs of stent dysfunction. When needed,

TABLE 1. Eligibility and exclusion criteria

Eligibility criteria
≥20 years of age
Information given and informed consent obtained
Clinical data in accordance with malignant bile duct obstruction
Bilirubin >50 μmol/L (normal <26 μmol/L)
US and/or CT performed before inclusion; findings in accordance with malignant common bile duct obstruction
Typical radiological appearance of malignant common bile duct stenosis at ERCP
Proximal margin of malignant bile duct stenosis ≥2 cm from the hepatic confluence
Patient considered not suitable for radical surgery; if in doubt, temporary stenting with a plastic stent possible if the patient is randomized and endoprosthesis replaced with a metal stent within 4 weeks
Exclusion criteria
Informed consent not obtained
Possible candidate for curative surgical resection
Active hepatitis or other hepatic diseases that may cause jaundice
Multiple hepatic metastases with significant blockage of one or more liver segments (if no segment blockage, metastasis is not an exclusion criteria)
Stenosis located within 2 cm from the hepatic confluence
Suspicion of nonmalignant bile duct obstruction
Severe coagulation disturbance (PK-INR >1.6, normal 0.9-1.2)
Previous Bismuth II or Roux-en-Y gastric resection or a significant duodenal obstruction making ERCP difficult
Previous inclusion in the study

PK-INR, Prothrombinkomplex international normalized ratio.

records from hospices and other primary care facilities were evaluated.

The study endpoints were uneventful follow-up for 12 months, death with a patent stent, and confirmed stent failure (ERCP or percutaneous transhepatic cholangiography [PTC]). However, in a few patients, radiological confirmation of stent failure was not possible, and these patients were considered clinically as stent failures based on symptoms and liver function test results.

Sample size and statistical analysis

To demonstrate an increase from 50% to 75% probability for uncensored stents to survive after 12 months using a log-rank test with an α of .05 and a power of 0.90, approximately 360 patients (180 in each group) were required. Patient survival was expected to be 10% after 12 months, and the probability for stent failure while the patient was still alive (observed stent failure) was estimated to be 22% and 10%, respectively. The power calculation was based on 10,000 simulations in which stent failure time and patient survival time had independently shifted exponential distributions starting at day 29, and a general censoring was planned after day 365 (end of follow-up).

Stent patency and patient survival time were estimated by the Kaplan-Meier method, and the log-rank test was used to assess differences between the groups on an intent-to-treat basis. Either the Fisher exact test or the χ^2 test was used for comparison of qualitative data, and continuous numerical data were compared using the Mann-Whitney U test. A P value <.05 was considered significant.

RESULTS

Patient characteristics

There were no significant differences in patient characteristics (Table 2) between the 2 groups, with 1 exception. In the cSEMS group, 90 patients (45%) had hepatic and/or other metastases (metastases in lymph nodes, peritoneum, and/or other organs) at the time of inclusion. The corresponding number for the uncovered group was 66 patients (33%) (P = .018). There was no significant difference in the cause of malignant biliary obstruction between the 2 groups. The most common cause of obstruction was pancreatic cancer, which occurred in 76% in the cSEMS group and 77% in the uSEMS group. Stratification of disease groups was not done.

Histological verification of malignant disease was obtained in 90 patients (45%) in the cSEMS group and 84 patients (42%) in the uSEMS group. In the remaining patients, the diagnoses of malignant disease were based solely on the results of US and/or CT findings, ERCP findings, and the clinical course. Twenty-five patients (13%) in the cSEMS group and 27 (14%) in the uSEMS group also underwent magnetic resonance imaging investigation.

Patient survival

The median patient survival time (Fig. 2) was 116 days in the cSEMS stent group and 174 days in the uSEMS stent group, a nonsignificant difference (P = .320). The corresponding interquartile ranges (middle 50), as measures of dispersion, were 242 and 284 days, respectively. There was no difference between intent-to-treat and per-protocol analyses.

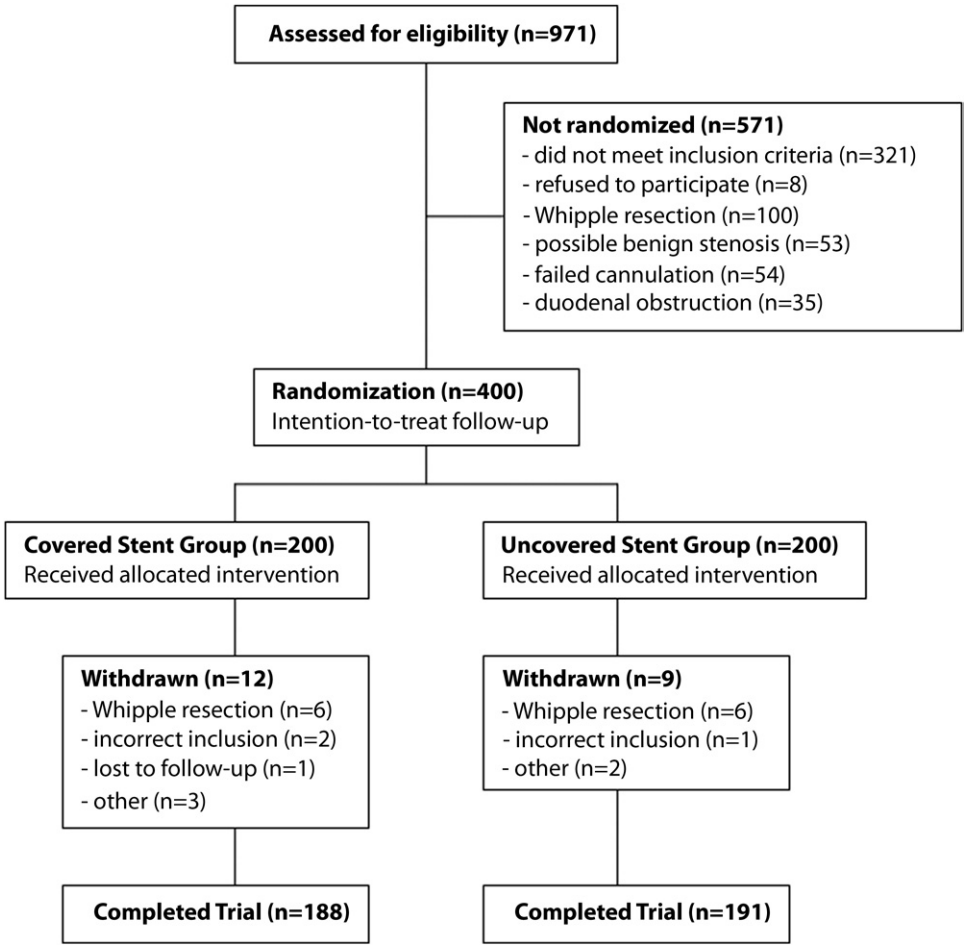

Figure 1. CONSORT flowchart illustrating the progress of patients throughout the randomized controlled trial.

Stent patency

Stent patency revealed no significant difference between the 2 groups (Fig. 3). The first quartile stent patency time, ie, the day when 25% of the stents had occluded, was 154 days in the cSEMS group and 199 days in the uSEMS group ($P = .326$). Stent patency at 1, 3, 6, and 12 months was 95%, 83%, 74%, and 50% in the cSEMS group, and 97%, 87%, 78%, and 56% in the uSEMS group. There was no difference between intent-to-treat and per-protocol analyses. Stratified log-rank tests regarding stent patency related to the group of patients with pancreatic cancer versus the other groups reached a P value of .348. Without stratification the difference in patency between cSEMSs and uSEMSs had a P value of .326. Because the other groups are proportionately small compared with the group of patients with pancreatic cancer, stratification of disease groups was not performed in the statistical analysis.

As seen in Table 3, the majority of patients in both groups died within 12 months with a patent stent, and 10% of the patients in the cSEMS group and 15% in the uSEMS group were alive at 12 months with a patent stent. Thus, observed stent occlusion during follow-up in the cSEMS and uSEMS groups occurred in 47 (24%) and 45 patients (23%), respectively. The causes of stent obstruction and the measures taken are summarized in Table 4. The findings of tumor overgrowth (above and/or below the stent), tumor ingrowth (through the mesh of the stent), and stent impaction because of sludge formation were mainly based on the operator's endoscopic and cholangiographic findings at reintervention. Most of these patients (72%) also underwent US or CT before reintervention. Stent migration occurred in 6 patients (3%) in the cSEMS stent group and in no patients in the uSEMS group ($P = .030$).

Complications

There was no procedure-related mortality. The overall complication rates (Table 5) in the cSEMS and the uSEMS groups were 7% and 10% ($P = .370$), respectively. Hemorrhage necessitating transfusion with 2 units of blood occurred in 1 patient. Retroperitoneal leakage of contrast medium was observed in 2 patients, 1 in each group. Both were successfully treated conservatively without further intervention.

Acute cholecystitis occurred in 4 patients, 2 (1.1%) in each group. Two of these (cSEMS group) underwent cholecystectomy, and the other 2 were successfully treated

TABLE 2. Patient characteristics at inclusion

Characteristic	Covered (n = 200)	Uncovered (n = 200)	*P* value
Sex (male/female), no.	88/112	91/109	>.50
Age, y, median (range)	79 (39-100)	76 (51-95)	.050
WHO classification (0,1,2,3,4)	47,47,77,27,2	42,48,74,30,6	>.50
Previous cholecystectomy, no. (%)	23 (12)	22 (11)	>.50
Plastic stent before inclusion, no. (%)	29 (15)	30 (15)	>.50
Days with plastic stent, median	14	14	
Antibiotic treatment or prophylaxis, no. (%)	20 (10)	29 (15)	.222
Sphincterotomy performed, no.	200	200	
Precut performed, no. (%)	58 (29)	57 (29)	>.50
Length of stent, mm, no. (%)			
52	93 (47)	90 (45)	>.50
72	107 (53)	110 (55)	>.50
Tumor etiology, no. (%)			
Pancreatic cancer	152 (76)	155 (77)	>.50
Cholangiocarcinoma	12 (6)	10 (5)	>.50
Gallbladder cancer	8 (4)	3 (2)	>.220
Ampullary cancer	8 (4)	9 (4)	>.50
Metastatic nodes	16 (8)	18 (9)	>.50
Unknown	4 (2)	5 (3)	>.50
Hepatic or other metastasis, no. (%)	90 (45)	66 (33)	.018
Ingrowth in large vessels, no. (%)	63 (32)	57 (29)	>.50
Portal vein thrombosis, no. (%)	11 (6)	10 (5)	>.50

WHO, World Health Organization.

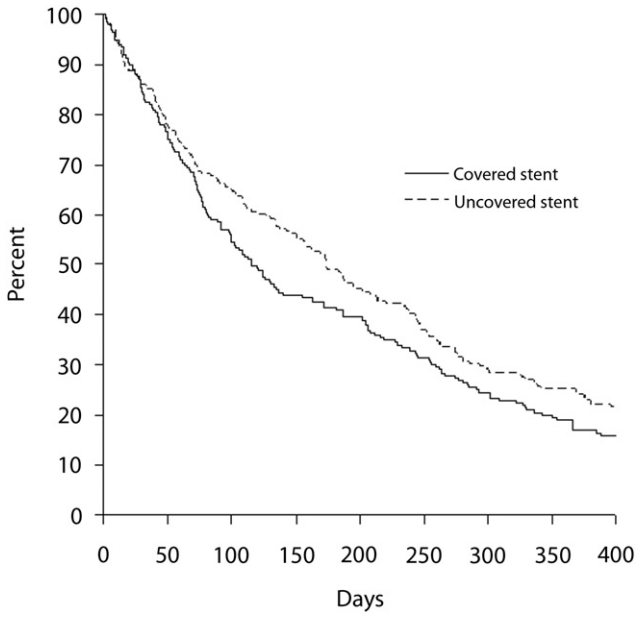

Figure 2. Kaplan-Meier graph showing patient survival time (intent-to-treat analysis). No significant difference was observed between the cSEMS and uSEMS groups (log-rank test; $P = .320$).

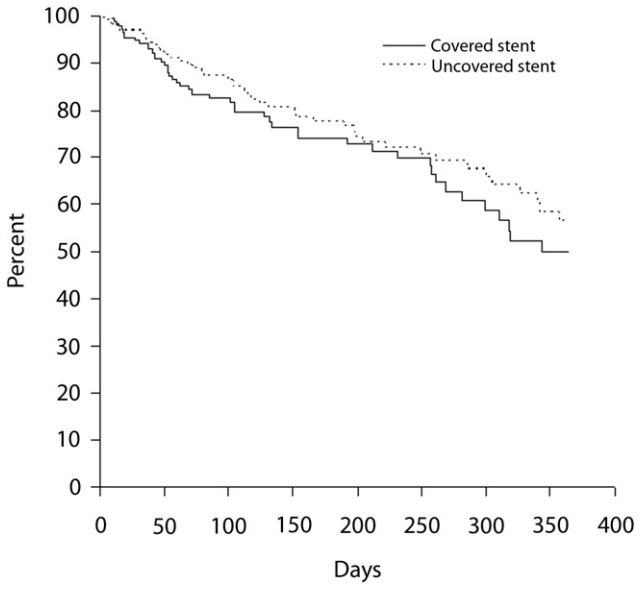

Figure 3. Kaplan-Meier graph showing stent patency time (intent-to-treat analysis). No significant difference was observed between the cSEMS and uSEMS groups (log-rank test; $P = .326$).

with percutaneous drainage and lavage of the gallbladder. No patient had a gallbladder stent inserted. Post-ERCP pancreatitis developed in 3 patients (1.5%) in the cSEMS group and 4 (2.0%) in the uSEMS group. Four of these, 2 in each group, were classified as mild pancreatitis. The remaining 3 patients, 1 in the cSEMS group and 2 in the uSEMS group, had severe pancreatitis. All patients recovered within 2 weeks.

During follow-up, 20 patients, 8 in the cSEMS group and 12 in the uSEMS group, had suspected clinical symptoms of cholangitis. These patients responded to antibiotic treatment (orally or intravenously), and liver values returned to normal. Repeat ERCP to exclude stent dysfunction was not necessary, and they were not considered stent failures.

DISCUSSION

Decompression of malignant biliary obstruction by endoscopic stent insertion is a well-established treatment strategy, and there are numerous studies showing that

TABLE 3. Mortality without stent failure and observed stent failures during follow-up

	Covered (n = 200)	Uncovered (n = 200)	*P* value
Withdrawn, no. (%)	12 (6)	9 (5)	>.50
Death within 12 mo with patent stent, no. (%)	122 (61)	116 (58)	>.50
Alive at 12 mo with patent stent, no. (%)	19 (10)	30 (15)	>.127
Observed stent failure, no. (%)	47 (24)	45 (23)	>.50

TABLE 4. Etiology and measures taken in patients with observed stent failures

	Covered (n = 47)	Uncovered (n = 45)	*P* value
Etiology, no. (%)			
Stent migration	6 (3)	0	.030
Encrustration (sludge)	12 (6)	4 (2)	.071
Tumor over- and/or ingrowth	27 (13)	31 (15)	>.50
Proximal overgrowth	11	3	.053
Distal overgrowth	3	2	>.50
Proximal and distal overgrowth	4	5	>.50
Ingrowth	9	21	.035
Unknown	2 (1)	10 (5)	.036
Measures taken at stent failure, no. (%)			
ERCP	41	33	
PTC	5	4	
None	1	8	

PTC, percutaneous transhepatic cholangiography.

TABLE 5. Complications

	Covered (n = 200)	Uncovered (n = 200)	*P* value
Hemorrhage, no. (%)	—	1 (0.5)	>.50
Cholecystitis, no. (%)	2 (1.1)	2 (1.1)	>.50
Pancreatitis, no. (%)	3 (1.5)	4 (2.0)	>.50
Retroperitoneal perforation, no. (%)	1 (0.5)	1 (0.5)	>.50
Cholangitis (medical therapy), no. (%)	8 (4.0)	12 (6.0)	.492
Total	14 (7.0)	20 (10.0)	.370

SEMSs are superior to plastic stents in maintaining biliary drainage by reducing the need for subsequent interventions for stent failure.[5,9,26,27] The question as to whether cSEMSs offer a more durable biliary drainage compared with uSEMSs has been widely discussed, but comparative studies are limited and often include few patients.[18-23,28,29] Although the multicenter trial presented here is thus far the largest comparative study conducted in this field, we were unable to demonstrate a significant difference between uSEMSs and cSEMSs concerning the primary objective of the study, ie, stent patency.

As could be expected, we observed no significant difference regarding median patient survival time, which was 116 days (interquartile range 242 days) in the cSEMS group and 174 days (interquartile range 284 days) in the uSEMS groups. This is also in accordance with results reported by others.[18,19,21-23,30,31] Differences in patient survival time between studies are mainly explained by differences in the selection of patients and in the duration of follow-up.

The frequency of observed stent failure occurred in the expected range, 24% and 23% for cSEMSs and uSEMSs, respectively. This also corresponds well to previous smaller series reporting an observed stent occlusion rate for both cSEMSs and uSEMSs between 20% and 38%.[19,20,22,28,30,32] Previous published studies comparing cSEMSs and uSEMSs in malignant distal biliary obstruction are summarized in Table 6.[18-20,33-36] Because the study design, selection of patients, duration of follow-up, and the statistical methods are not uniform, it is difficult to compare the results from these studies with each other. However, 2 aspects seem to be a general feature in these studies; namely, that cSEMSs migrated significantly more often compared with uSEMSs, and stents made of stainless steel migrated more often than those made of nitinol.

An explanation for the paucity of reported reasons for stent failure is that information is usually based solely on ERCP findings, sometimes making it difficult to delineate detailed information about all underlying causes of stent failures. We also noted an increased prevalence of unknown causes for stent failure in the uSEMS stent group compared with the cSEMS group (10 and 2 patients, respectively). This is probably random and can be explained by the fact that fewer patients in the uSEMS group were subjected to reintervention when clinical signs of stent occlusion occurred, but of course we cannot exclude bias because the study was not double blinded.

Important mechanisms causing stent occlusion are tumor overgrowth and ingrowth, which in this series occurred in 27 patients (13%) in the cSEMS group and in 31 patients (15%) in the uSEMS group. This corresponds well

TABLE 6. Previous studies comparing covered and uncovered metal stents in malignant distal biliary obstruction

	Study													
	Krokidis et al,[33] 2010		Yoon et al, [20] 2006		Isayama et al, [18] 2004		Park et al,[19] 2006		Telford et al,[34] 2007 (abstract)		Gonzalez-Huiz et al,[35] 2008 (abstract)		Cho et al,[36] 2009 (abstract)	
	Covered	Uncovered	Covered	Uncovered	Covered	Uncovered	Covered	Uncovered	Covered	Uncovered	Covered	Uncovered	Covered	Uncovered
Study design	RCT (PTC)		Retrospective		RCT (ERCP or PTC)		Retrospective		RCT		RCT		RCT	
No. of patients	40	40	36	41	57	55	98	108	50	50	61	53	39	38
Stent material	Nitinol		Stainless steel		Nitinol		Stainless steel		Stainless steel		Stainless steel		Stainless steel/nitinol	
Stent migration, no. (%)	3 (7.5)	1 (2.5)	2 (5.6)	1 (2.4)	1 (1.8)	0	6 (6.1)	0	4 (8.0)	0	7 (11.5)	0	N/A	N/A
Survival, d	247 (N/A)*	203 (N/A)*	392 ± 60†	308 ± 4†	255 (N/A)*	237 (N/A)*	209 (2-667)*	207 (2-917)*	N/A	N/A	N/A	N/A	N/A	N/A
Cholecystitis, no. (% of gallbladder in situ)	0	0	1 (3)	0	2 (4.8)	0	5 (6.1)	1 (1)	2 (N/A)	2 (N/A)	2 (N/A)	0	N/A	N/A
Pancreatitis, no. (%)	0	0	0	0	5 (8.8)	1 (1.8)	6 (6.1)	2 (1.9)	N/A	N/A	1 (1.6)	0	N/A	N/A
Stent patency time, %	— 97.5 92.5 87.6	— 77.5 69.8 69.8	83‡ 78‡ 67‡ 54‡	83‡ 66‡ 54‡ 36‡	— 100 91 74	— 81 68 55	92 72 56 47	92 77 54 37	217§	236§	N/A	N/A	227§	195§
Patency: *P* value	.007		.73		.007		.53		.67		.5		>.05	

N/A, Not available; *PTC*, percutaneous transhepatic cholangiography; *RCT*, randomized, controlled trial.
*Median (interquartile range) or mean (range).
†Mean ± standard deviation.
‡At 1, 3, 6, or 12 months or 100, 200, 300, or 400 days.
§Median patency time.

to the results of most other studies, although occasional authors have reported no tumor ingrowth with cSEMSs. However, these series often include few patients and frequently have a relatively high prevalence of tumor overgrowth or sludge formation as a cause of stent failure.[17-23,28,30,32]

In this study, we found a significant difference in the frequency of ingrowth between cSEMSs in 9 patients (5%) and uSEMSs in 21 patients (11%). Accordingly, even with a significant difference in this respect, stent design alone is not the only crucial factor causing stent occlusion. Although ingrowth of neoplastic and/or regenerative tissue is of particular concern, the differences can also be explained by classification bias.[17,20] As already discussed, it is notoriously difficult in some cases to distinguish between overgrowth, ingrowth, and encrustation. In our study, as well as in previous reports, the mechanisms of stent dysfunction are mainly based on cholangiographic findings.

Stent obstruction by sludge formation and encrustation remains a problem with SEMSs. Although this was not found to be a significant difference, it occurred more often with cSEMSs (6% vs 2%), which is in agreement with findings by others who have reported sludge formation, with or without food impaction, to be the most common cause of stent occlusion in cSEMSs.[9,19,22,23] Interestingly, studies analyzing extracted dysfunctional covered stents all contained sludge.[18,20,37] Whether the mechanisms causing sludge formation are primarily dislocation and/or overgrowth or de novo formation of sludge similar to the biofilm formation in plastic stents has so far not been elucidated.

Although not proven in clinical studies, it has been claimed that cSEMSs might increase the prevalence of cholecystitis and pancreatitis by blocking the cystic duct and the pancreatic duct orifice.[18,21,23,38,39] Another objective of this study was therefore to assess the risk of these complications. We found cholecystitis in 2 patients (1%) in each group, which should be compared with the 1% to 7% prevalence reported by others.[9,19-22,28,32,40]

Post-ERCP pancreatitis in this study developed in 3 patients (1.5%) in the cSEMS group and in 4 patients (2%) in the uSEMS group. Some authors have reported a prevalence of pancreatitis of 0 with cSEMSs.[9,20] However, postprocedural pancreatitis in our study seems to be of the same magnitude as that reported in the majority of previous studies, ie, a 2% to 6% prevalence of pancreatitis with cSEMSs, and no significant difference between cSEMSs and uSEMSs.[19,22,23,28,32]

A potential clinical advantage of cSEMS is that, if necessary, this stent can more easily be removed.[16,19,37,41] However, a possible advantage of cSEMS in this regard is of limited value in most patients in whom the indica-

tion for stent insertion is palliative treatment. A disadvantage of cSEMSs is related to the limitation confining the use of these stents to close to or through the hepatic confluence.

Migration of covered GI stents is a well-known clinical problem.[42-45] This is usually associated with stent dysfunction, and to decrease this risk with cSEMSs, these stents often have a semicovered design with an uncovered portion in the distal and/or proximal end of the stent. Migration of covered biliary stents has been reported to occur in 6% to 12% of cases.[19,22,23,28,32] It seems that this happens more frequently in stents made of stainless steel than in those made with nitinol. In our total series of 400 patients, migration of cSEMSs occurred in 6 of 200 patients (3%) compared with none in the uSEMS group. Although of clinical importance, this did not affect the statistical significance of total stent patency between the 2 groups.

In conclusion, there are no significant differences in patient survival or stent patency time between cSEMSs and uSEMSs in the palliative treatment of malignant distal biliary obstruction. CSEMSs significantly more often migrated compared with uSEMSs, whereas an increase in tumor ingrowth was seen in uSEMSs. There does not seem to be an increased risk of cholecystitis or pancreatitis when using cSEMSs.

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REFERENCES

1. Stern N, Sturgess R. Endoscopic therapy in the management of malignant biliary obstruction. Eur J Surg Oncol 2008;34:313-7.
2. Shah JN, Muthusamy VR. Endoscopic palliation of pancreaticobiliary malignancies. Gastrointest Endosc Clin N Am 2005;15:513-31.
3. Ballinger AB, McHugh M, Catnach SM, et al. Symptom relief and quality of life after stenting for malignant bile duct obstruction. Gut 1994;35:467-70.
4. Davids PH, Groen AK, Rauws EA, et al. Randomised trial of self-expanding metal stents versus polyethylene stents for distal malignant biliary obstruction. Lancet 1992;340:1488-92.
5. Moss AC, Morris E, Leyden J, et al. Do the benefits of metal stents justify the costs? A systematic review and meta-analysis of trials comparing endoscopic stents for malignant biliary obstruction. Eur J Gastroenterol Hepatol 2007;19:1119-24.
6. Kaassis M, Boyer J, Dumas R, et al. Plastic or metal stents for malignant stricture of the common bile duct? Results of a randomized prospective study. Gastrointest Endosc 2003;57:178-82.
7. Knyrim K, Wagner HJ, Pausch J, et al. A prospective, randomized, controlled trial of metal stents for malignant obstruction of the common bile duct. Endoscopy 1993;25:207-12.
8. Maire F, Hammel P, Ponsot P, et al. Long-term outcome of biliary and duodenal stents in palliative treatment of patients with unresectable adenocarcinoma of the head of pancreas. Am J Gastroenterol 2006;101:735-42.
9. Soderlund C, Linder S. Covered metal versus plastic stents for malignant common bile duct stenosis: a prospective, randomized, controlled trial. Gastrointest Endosc 2006;63:986-95.
10. Arguedas MR, Heudebert GH, Stinnett AA, et al. Biliary stents in malignant obstructive jaundice due to pancreatic carcinoma: a cost-effectiveness analysis. Am J Gastroenterol 2002;97:898-904.
11. Weber A, Mittermeyer T, Wagenpfeil S, et al. Self-expanding metal stents versus polyethylene stents for palliative treatment in patients with advanced pancreatic cancer. Pancreas 2009;38:7-12.
12. Shah RJ, Howell DA, Desilets DJ, et al. Multicenter randomized trial of the spiral Z-stent compared with the Wallstent for malignant biliary obstruction. Gastrointest Endosc 2003;57:830-6.
13. Ahmad J, Siqueira E, Martin J, et al. Effectiveness of the Ultraflex Diamond stent for the palliation of malignant biliary obstruction. Endoscopy 2002;34:793-6.
14. Dumonceau JM, Cremer M, Auroux J, et al. A comparison of Ultraflex Diamond stents and Wallstents for palliation of distal malignant biliary strictures. Am J Gastroenterol 2000;95:670-6.
15. Ferlitsch A, Oesterreicher C, Dumonceau JM, et al. Diamond stents for palliation of malignant bile duct obstruction: a prospective multicenter evaluation. Endoscopy 2001;33:645-50.
16. Petersen BT. SEMS removal: salvage technique or new paradigms. Gastrointest Endosc 2005;62:911-3.
17. Loew BJ, Howell DA, Sanders MK, et al. Comparative performance of uncoated, self-expanding metal biliary stents of different designs in 2 diameters: final results of an international multicenter, randomized, controlled trial. Gastrointest Endosc 2009;70:445-53.
18. Isayama H, Komatsu Y, Tsujino T, et al. A prospective randomised study of covered versus uncovered diamond stents for the management of distal malignant biliary obstruction. Gut 2004;53:729-34.
19. Park do H, Kim MH, Choi JS, et al. Covered versus uncovered Wallstent for malignant extrahepatic biliary obstruction: a cohort comparative analysis. Clin Gastroenterol Hepatol 2006;4:790-6.
20. Yoon WJ, Lee JK, Lee KH, et al. A comparison of covered and uncovered Wallstents for the management of distal malignant biliary obstruction. Gastrointest Endosc 2006;63:996-1000.
21. Fumex F, Coumaros D, Napoleon B, et al. Similar performance but higher cholecystitis rate with covered biliary stents: results from a prospective multicenter evaluation. Endoscopy 2006;38:787-92.
22. Ornellas LC, Stefanidis G, Chuttani R, et al. Covered Wallstents for palliation of malignant biliary obstruction: primary stent placement versus reintervention. Gastrointest Endosc 2009;70:676-83.
23. Nakai Y, Isayama H, Komatsu Y, et al. Efficacy and safety of the covered Wallstent in patients with distal malignant biliary obstruction. Gastrointest Endosc 2005;65:742-8.
24. Freeman ML. Adverse outcomes of endoscopic retrograde cholangiopancreatography: avoidance and management. Gastrointest Endosc Clin N Am 2003;13:775-98.
25. Cotton PB, Lehman G, Vennes J, et al. Endoscopic sphincterotomy complications and their management: an attempt at consensus. Gastrointest Endosc 1991;37:383-93.

26. Moparty B, Carr-Locke DL. Metal or plastic stent for malignant biliary obstruction: what's got the most bang for your buck? Eur J Gastroenterol Hepatol 2007;19:1041-2.
27. Yoon WJ, Ryu JK, Yang KY, et al. A comparison of metal and plastic stents for the relief of jaundice in unresectable malignant biliary obstruction in Korea: an emphasis on cost-effectiveness in a country with a low ERCP cost. Gastrointest Endosc 2009;70:284-9.
28. Kahaleh M, Tokar J, Conaway MR, et al. Efficacy and complications of covered Wallstents in malignant distal biliary obstruction. Gastrointest Endosc 2005;61:528-33.
29. Paik WH, Park YS, Hwang JH, et al. Palliative treatment with self-expandable metallic stents in patients with advanced type III or IV hilar cholangiocarcinoma: a percutaneous versus endoscopic approach. Gastrointest Endosc 2009;69:55-62.
30. Yang KY, Ryu JK, Seo JK, et al. A comparison of the Niti-D biliary uncovered stent and the uncovered Wallstent in malignant biliary obstruction. Gastrointest Endosc 2009;70:45-51.
31. Togawa O, Kawabe T, Isayama H, et al. Management of occluded uncovered metallic stents in patients with malignant distal biliary obstructions using covered metallic stents. J Clin Gastroenterol 2008;42:546-9.
32. Kubota Y, Mukai H, Nakaizumi A, et al. Covered Wallstent for palliation of malignant common bile duct stricture: prospective multicenter evaluation. Dig Endosc 2005;17:218-23.
33. Krokidis M, Fanelli F, Orgera G, et al. Percutaneous palliation of pancreatic head cancer: randomized comparison of ePTEE/EEP covered versus uncovered nitinol biliary stents. Cardiovasc Intervent Radiol Epub 2010 May 14.
34. Telford JJ, Carr-Locke DL, Poneros JM, et al. A randomized trial comparing the covered and uncovered Wallstent in the palliation of malignant distal biliary obstruction: interim analysis [abstract]. Gastrointest Endosc 2007;65:AB123.
35. Gonzalez-Huix F, Huertas C, Figa M, et al. A randomized controlled trial comparing the covered (cSEMS) versus uncovered self-expandable metal stents (uSEMS) for the palliation of malignant distal biliary obstruction: interim analysis [abstract]. Gastrointest Endosc 2008;67: AB166.
36. Cho YD, Cheon YK, Yoo KS, et al. Uncovered versus covered self-expanding metal stents for inoperable malignant distal biliary obstruction: a prospective randomized multicenter study [abstract]. Gastrointest Endosc 2009;69:AB137.
37. Kahaleh M, Tokar J, Le T, et al. Removal of self-expandable metallic Wallstents. Gastrointest Endosc 2004;60:640-4.
38. Isayama H, Nakai Y, Togawa O, et al. Covered metallic stents in the management of malignant and benign pancreatobiliary strictures. J Hepatobiliary Pancreat Surg 2009;16:624-7.
39. Suk KT, Kim H. Risk factors for cholecystitis after metal stent placement in malignant biliary obstruction. Gastrointest Endosc Clin N Am 2006; 64:522-9.
40. Bezzi M, Zolovkins A, Cantisani V, et al. New ePTFE/FEP-covered stent in the palliative treatment of malignant biliary obstruction. J Vasc Interv Radiol 2002;13:581-9.
41. Familiari P, Bulajic M, Mutignani M, et al. Endoscopic removal of malfunctioning biliary self-expandable metallic stents. Gastrointest Endosc 2005;62:903-10.
42. Park KB, Do YS, Kang WK, et al. Malignant obstruction of gastric outlet and duodenum: palliation with flexible covered metallic stents. Radiology 2001;219:679-83.
43. Jung GS, Song HY, Kang SG, et al. Malignant gastroduodenal obstructions: treatment by means of a covered expandable metallic stent—initial experience. Radiology 2000;216:758-63.
44. Kim ID, Kang DH, Choi CW, et al. Prevention of covered enteral stent migration in patients with malignant gastric outlet obstruction: a pilot study of anchoring with endoscopic clips. Scand J Gastroenterol 2009; 45:100-5.
45. Schembre DB. Recent advances in the use of stents for esophageal disease. Gastrointest Endosc Clin N Am 2010;20:103-21.