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Cost Efficacy of Metal Stents for Palliation of Extrahepatic Bile Duct Obstruction in a Randomized Controlled Trial

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See Covering the Cover synopsis on page 2; see editorial on page 20.

BACKGROUND & AIMS: Endoscopic stents are placed for palliation of extrahepatic bile duct obstruction. Although self-expandable metal stents (SEMS) remain patent longer than plastic stents, they are more expensive. We aimed to evaluate which type of stent (plastic, uncovered SEMS [uSEMS], or partially covered SEMS [pcSEMS]) is the most effective and we assessed costs. **METHODS:** We performed a multicenter randomized trial in 219 patients at 18 hospitals in The Netherlands from February 2008 through February 2013. Patients were assigned randomly for placement of a plastic stent (n = 73), uSEMS (n = 75), or pcSEMS (n = 71) during endoscopic retrograde cholangiopancreatography. Patients were followed up for up to 1 year. Researchers were not blinded to groups. The main study end points included functional stent time and costs. **RESULTS:** The mean functional stent times were 172 days for plastic stents, 288 days for uSEMS, and 299 days for pcSEMS ($P < .005$ for uSEMS and pcSEMS vs plastic). The initial placement of plastic stents (€1042 or $1106) cost significantly less than placement of SEMS (€1973 or $2094) ($P = .001$). However, the total cost per patient at the end of the follow-up period did not differ significantly between plastic stents (€7320 or $7770) and SEMS (€6932 or $7356) ($P = .61$). Furthermore, in patients with short survival times (≤3 mo) or metastatic disease, the total cost per patient did not differ between plastic stents and SEMS. No differences in costs were found between pcSEMS and uSEMS. **CONCLUSIONS:** Although placement of SEMS (uncovered or partially covered) for palliation of extrahepatic bile duct obstruction initially is more expensive than placement of plastic stents, SEMS have longer functional time. The total costs after 1 year do not differ significantly with stent type. Dutch Clinical Trial Registration no: NTR1361.

Keywords: ERCP; Pancreatic Cancer; Cost Comparison; Randomized Trial.

Extrahepatic bile duct obstruction is a common complication in patients with pancreatic adenocarcinoma, cholangiocarcinoma, or malignant lymphadenopathy. The majority of patients already have metastatic or locally advanced disease at the time of diagnosis and therefore only 10%–20% of patients are eligible for curative surgical resection.[1,2] For all other patients, treatment consists of palliative placement with a plastic or self-expandable metal stent (SEMS) to relieve symptoms of jaundice, pruritus, malabsorption, and cholangitis.[3–5]

Randomized controlled studies have shown that SEMS are superior to plastic stents in terms of recurrent biliary obstruction, number of reinterventions, and functional stent time.[6–11] Nonetheless, SEMS placement is not accepted

Abbreviations used in this paper: **CI, confidence interval; ERCP, endoscopic retrograde cholangiopancreatography; fcSEMS, fully covered self-expandable metal stent; HR, hazard ratio; IQR, interquartile range; PTC, percutaneous transhepatic cholangiography; pcSEMS, partially covered self-expandable metal stent; SAE, serious adverse event; SEMS, self-expandable metal stent; uSEMS, uncovered self-expandable metal stent.**

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universally as standard treatment. The high cost of SEMS and the uncertainty that these high costs might not be offset by a reduction in costs for reinterventions are the main reasons for reluctance, especially in patients with a short predicted survival time. Although several studies have investigated costs associated with plastic and SEMS placement, results of these studies have been inconclusive on the cost effectiveness of SEMS use, particularly in patients with an expected short survival time.[9–13] Most studies have suggested that SEMS are cost effective only in patients with a long survival time (ie, longer than 4–6 mo). Based on these results, the use of SEMS often is reserved for patients with a prolonged survival expectancy, whereas plastic stents are used in patients with a limited survival expectancy (<3 mo).[14–16] Besides tumor size and presence of (hepatic) metastasis, there are no criteria that can predict survival reliably.[9,10,15,17,18] Furthermore, all but one study compared plastic stents with uncovered SEMS (uSEMS)[11] while partially covered SEMS (pcSEMS) and fully covered SEMS increasingly are being used.[19] As a result, to date there are no strong recommendations regarding stent choice for the palliation of malignant extrahepatic bile duct obstruction.

The aim of this study was to evaluate which type of stent, either a plastic stent or SEMS, is superior for the palliation of malignant extrahepatic bile duct obstruction with regard to clinical effects and associated costs, both in patients with a short and long survival time. For this, we compared the 3 most commonly used stent types (plastic, uSEMS, and pcSEMS) in a multicenter randomized controlled trial, with a full cost comparison using detailed information on health care use.

Patients and Methods

We conducted a multicenter randomized trial between February 2008 and February 2013 in 3 tertiary referral centers and 15 general hospitals. The study protocol was reviewed and approved by the ethics committees of all participating centers and registered at the Dutch Trial Registration (NTR1361).

Patients

Patients were included if they presented with an increased serum bilirubin level (≥30 mmol/L) and/or clinical symptoms of obstructive jaundice resulting from an inoperable obstructive malignancy at the level of the extrahepatic common bile duct. A patient was considered to be inoperable if the tumor was locally irresectable, distant metastases were present, or when the patient was in poor medical condition. Exclusion criteria included a malignancy involving the intrahepatic bile ducts or duodenum, a known history of cholecystitis (unless cholecystectomy had been performed), a history of surgery to the bile duct, and a World Health Organization performance score of 4 (100% of time in bed). Written informed consent was obtained before randomization.

Randomization

Patients were randomized for endoscopic placement of a plastic stent, uSEMS, or pcSEMS during endoscopic retrograde cholangiopancreatography (ERCP). The randomization process was conducted before the start of the ERCP using a web-based randomization program with stratification for center of inclusion and for primary stent placement or stent placement for a first episode of stent dysfunction (ie, a second stent). Patients included for primary stent placement could be included again in the study in case of a first period of stent dysfunction. No blinding was performed.

Stent Placement Procedure

All endoscopic procedures were performed in patients under conscious sedation with midazolam or propofol (with or without fentanyl). After successful bile duct cannulation and guidewire placement across the stricture, retrograde cholangiography was performed to visualize the stricture. If no stricture was visualized or intrahepatic involvement was seen, the patient was excluded. If the stricture comprised an extrahepatic stricture without hilar involvement, the assigned type of stent was placed. For plastic stents this included a 10F polyurethane stent (Boston Scientific Corporation, Natick, MA) or a 10F polyethylene stent (Cook, Inc, Winston-Salem, NC) in lengths of 5–10 cm. For both types of SEMS, a 10-mm Wallstent RX (Boston Scientific Corporation), either uncovered or with a partial permalume cover in lengths of 4, 6, or 8 cm, was used. Stent types were randomized in a 1:1:1 fashion. Stent length was chosen according to the stricture location and length. Sphincterotomy was performed at the discretion of the endoscopist. In case of failed stent placement, stent insertion was conducted during an additional attempt, either with ERCP, percutaneous transhepatic cholangiography (PTC), or using a combined approach (rendezvous).

Follow-Up Evaluation and End Points

Study end points included functional stent time, proportion of patients with stent dysfunction, cause of stent dysfunction, patient survival, serious adverse events (SAEs), and costs. Functional stent time was defined as the time from stent placement to stent dysfunction, patient death, or 1 year of follow-up evaluation if no stent dysfunction occurred. Stent dysfunction was defined as the presence of symptoms of obstructive jaundice or cholangitis in combination with confirmation of stent obstruction or migration during ERCP. SAEs were divided into short-term (<7 days) and long-term (≥7 days) events. Cost evaluation included costs for initial stent placement (including secondary procedures in case of initial failure), costs for total initial treatment (initial stent placement and hospitalization), follow-up evaluation costs (diagnostics, treatment, and hospitalization for stent dysfunction and complications), and endoscopic costs (costs for initial stent placement and costs for additional endoscopic procedures during follow-up evaluation).

Patients were followed up prospectively by home visits or telephone calls by study personnel at 14 days, 1 month, and then monthly until 6 months, and then bimonthly thereafter until a maximum of 1 year after treatment. Patients received a diary in which symptoms of obstructive jaundice were scored every day for 1 month and every week thereafter. In case of symptoms of obstructive jaundice, patients were evaluated in the hospital and ERCP was performed, if permitted by the patients' clinical condition. Further treatment was at the discretion of the treating physician and included stent replacement,

additional stent placement, or stent cleaning. Patients with a first episode of stent dysfunction were eligible to be re-included in the study in the stent dysfunction stratum. The volume of health care use, including all diagnostic and therapeutic procedures and hospital admissions, was listed in standardized case record forms during all follow-up moments and hospital visits.

Sample Size and Statistical Analysis

For the sample size, we calculated that 80 patients were required in each stent group if the hazard ratio for stent dysfunction was at least 0.5 for the comparison of the 2 treatment groups (plastic vs uSEMS and plastic vs pcSEMS) with an α value of .05 and a β value of .8, considering a stent failure rate of 30%–50% for plastic stents, 15%–35% for uSEMS, and 10%–20% for pcSEMS.[7–11,20]

Comparison between the groups was performed with the Student t test or the Mann–Whitney test for continuous variables and with the χ^2 test or the Fisher exact test for categoric variables. Functional stent time and survival were calculated according to the Kaplan–Meier method and the 3 groups were compared by the log-rank test and Cox regression analysis. No P value adjustment was performed for multiple comparisons.

For each patient, real medical costs were calculated by multiplying volume of care (units of health care utilization reported in the case record forms) with their corresponding unit prices. For the most important cost item, stent placement during ERCP, the unit price was determined using the microcosting method, which is based on a detailed inventory and measuring of all the resources used.[21] All other unit prices were determined using proxy charges of real costs, based on Dutch consumer price indices and the Dutch Health Authority.[22,23] Reference prices are listed in Supplementary Appendix. Because costs per patient typically are highly skewed, we used nonparametric bootstrapping techniques to calculate the mean costs per patient and to derive a P value for the differences in cost distributions.[24] Discounting was not relevant because of the limited time horizon per patient. All statistical analyses were performed using an intention-to-treat approach and with SPSS software version 20 (SPSS, Inc, Chicago, IL).

All co-authors had full access to the study data and reviewed and approved the final manuscript.

Table 1. Patient Characteristics of 219 Patients With Malignant Extrahepatic Bile Duct Obstruction

	Primary stent placement (N = 171)	Second stent placement (N = 48)	P value
Male sex, n (%)	80 (47)	28 (58)	.16
Mean age (SD), *y*	73 (13)	71 (10)	.07
Tumor cause, n (%)			.004
Pancreas	148 (87)	33 (69)	
Other	23 (13)	15 (31)	
Metastatic disease, n (%)			.14
Yes	83 (49)	31 (65)	
No	87 (51)	17 (35)	
Median bilirubin level (IQR), *μmol/L*[a]	187 (122–254)	56 (52–97)	<.001
Reason for inoperability, n (%)			.37
Local irresectable	80 (47)	22 (46)	
Poor clinical condition	32 (18)	6 (12)	
Metastatic disease	49 (29)	14 (30)	
Combination	10 (6)	6 (12)	
Mean WHO score (SD)	1.4 (0.9)	1.3 (0.9)	.36
Histologic diagnosis, n (%)			.11
Yes	39 (23)	18 (38)	
No	132 (77)	30 (62)	

WHO, World Health Organization.
[a]Normal value < 21 μmol/L.

Results

A total of 240 patients were enrolled in the study, 188 patients with a first stent placement and 52 patients with a stent placement after a first episode of stent dysfunction. Eight patients were included in both strata. Twenty-one patients were excluded after the ERCP procedure (involvement of intrahepatic ducts, n = 7; no stenosis, n = 4; withdrawal of informed consent, n = 4; duodenal involvement, n = 2; benign stricture, n = 2; surgical candidate, n = 1; and previous surgery of bile duct, n = 1), resulting in a final inclusion of 219 patients (Figure 1). Patient characteristics per stratum

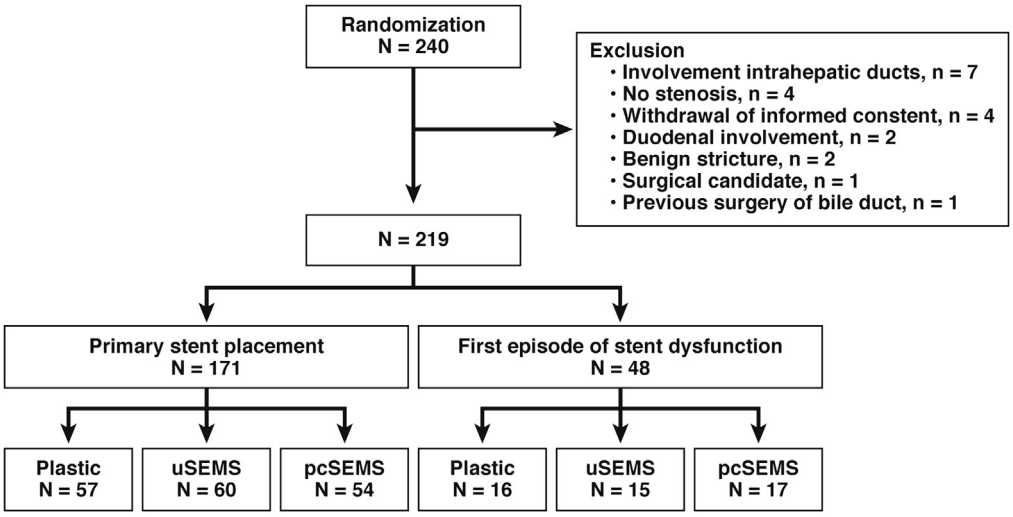

Figure 1. Flow chart showing the patients' course during the study.

are listed in Table 1. Pancreatic cancer was the most common stricture cause in both strata. However, in patients with primary stent placement this proportion was significantly higher compared with patients with a second stent placement (87% vs 67%; $P = .004$). Furthermore, the mean bilirubin level was significantly higher in patients with a primary stent placement (187 vs 56 mmol/L; $P < .005$). No difference was observed between the 3 different stent groups in both strata.

Stent Placement

Stent placement during the first ERCP was successful in 174 of 219 patients (79%). Stent placement was unsuccessful in 44 of 171 patients (26%) with a primary stent placement, and in 1 of 48 patients (2%) with a first episode of stent dysfunction. The main reason for failure was inability to cannulate the common bile duct (31 of 45 patients; 69%). There was no difference in the initial failure rate between the different stent groups (plastic, 25%; vs uSEMS, 19%; vs pcSEMS, 18%; $P = .57$). The failure rate was higher in general hospitals (23%) compared with tertiary referral centers (14%), although this difference was not significant ($P = .12$).

Finally, successful stent placement was achieved in 204 of 219 patients (91%) during ERCP (n = 179), PTC (n = 14), or rendez-vous (n = 11). Fifteen patients (9%) were not treated with a stent, but were treated conservatively (n = 9), with a PTC drain (n = 4), or underwent palliative gastrojejunostomy (n = 2).

The overall median length of hospital stay after stent placement was 4 days (interquartile range [IQR], 2–6 days), with a significant difference between patients with successful stent placement (median, 3 days; IQR, 2–6 days) and patients with initial stent failure (median, 8 days; IQR, 5–12 days; $P < .05$).

Patient Survival

After 1 year of follow-up evaluation, 182 of 219 patients died (83%), 30 patients (14%) were still alive, and 7 patients (3%) were lost to follow-up evaluation. The overall median survival time was 109 days (95% confidence interval [CI], 85–133), with no difference in survival time between the different stent types (Figure 2*A*). Survival was significantly shorter for patients with metastatic disease compared with patients without metastasis (80 days; 95% CI, 62–98; vs 172 days; 95% CI, 105–239 days; $P = .001$) (Figure 2*B*). The median survival time in patients with placement of a second stent was significantly longer (171 days; 95% CI, 118–224 days) compared with patients with primary stent placement (89 days; 95% CI, 66–112 days; $P = .031$) (Figure 2*C*). At 3 months, 47% of patients with primary stent placement were still alive compared with 77% in the group of patients with a second stent ($P < .001$).

Stent Dysfunction and Functional Stent Time

During a mean follow-up period of 131 days (IQR, 34–209 days), stent dysfunction was observed in 42 of 171 patients (25%) with primary stent placement; 23 in the plastic stent group (40%), 10 in the uSEMS group (17%), and 9 in the pcSEMS group (17%) ($P = .003$). The mean functional stent time was 172 days (95% CI, 126–219), 268 days (95% CI, 219–317), and 286 days (95% CI, 240–332), respectively ($P = .001$) (Figure 3*A*). Patients with SEMS had a significantly lower hazard (uSEMS: hazard ratio [HR], 0.33; 95% CI, 0.16–0.69; pcSEMS: HR, 0.32; 95% CI, 0.15–0.69)

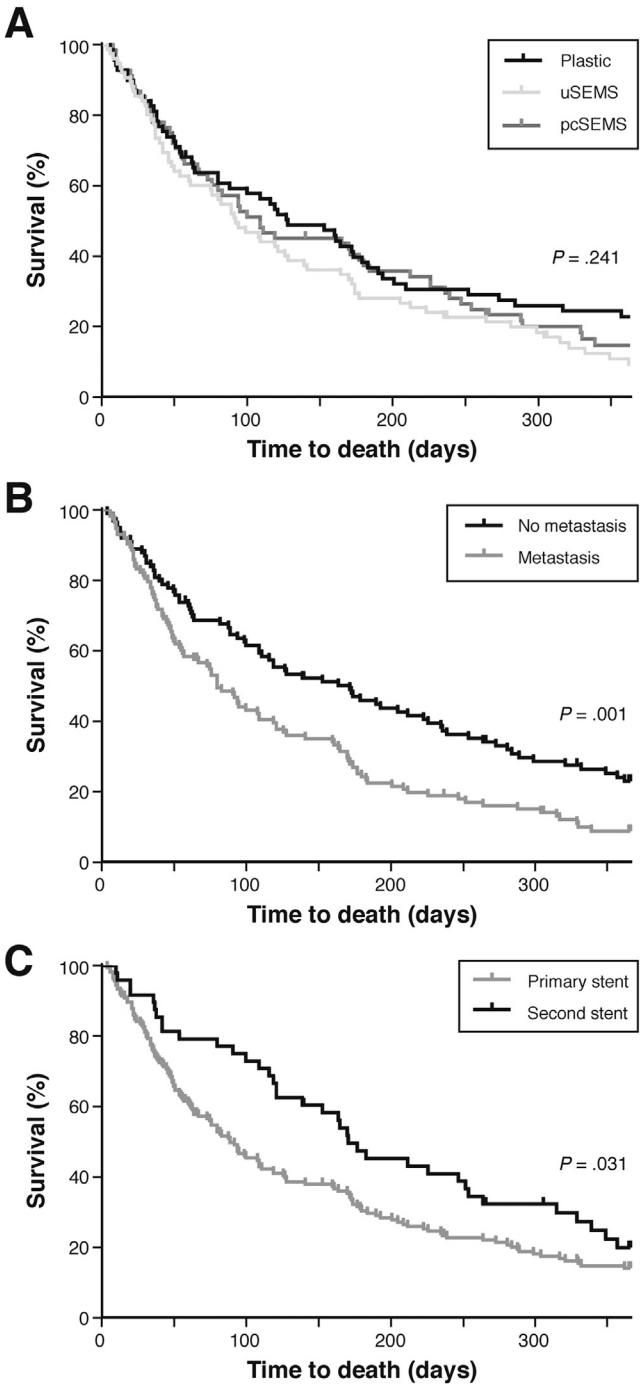

Figure 2. Patient survival after stent placement for palliation of malignant extrahepatic bile duct obstruction using the Kaplan–Meier method by (*A*) stent type, (*B*) presence of metastasis, and (*C*) primary or second stent placement.

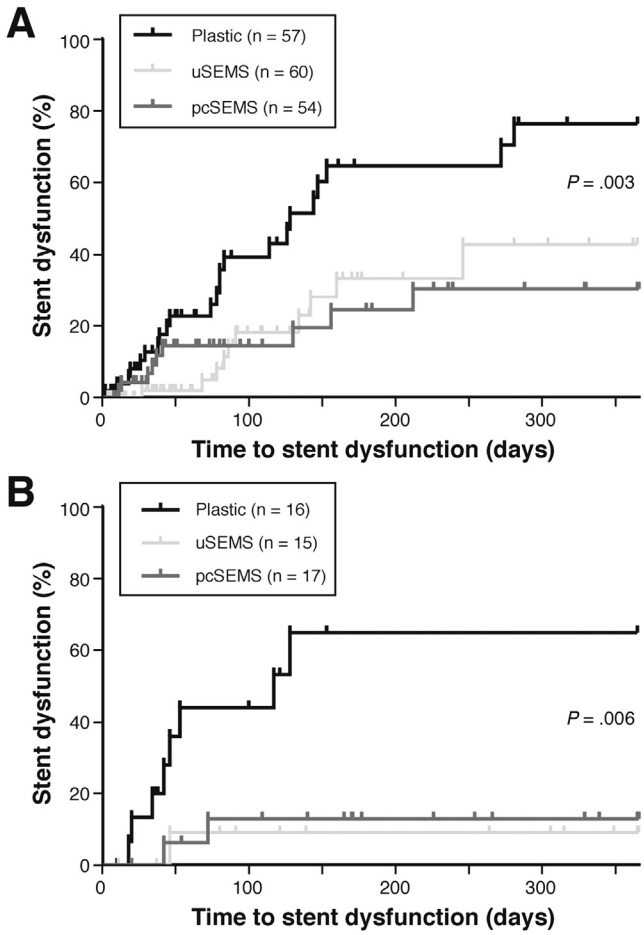

Figure 3. Functional stent time after stent placement for palliation of malignant extrahepatic bile duct obstruction using the Kaplan–Meier method for (*A*) patients with primary stent placement and (*B*) patients with a second stent.

for developing stent dysfunction before death or the end of the study compared with patients with a plastic stent. The mean number of reinterventions was 0.65 for patients in the plastic stent group, 0.28 in the uSEMS group, and 0.27 in the pcSEMS group ($P = .002$).

Eleven of 48 patients (23%) with stent placement after a first episode of stent dysfunction developed another stent dysfunction: 8 in the plastic stent group (50%), 1 in the uSEMS group (7%), and 2 in the pcSEMS group (12%) ($P = .006$) during a mean follow-up time of 193 days (IQR, 93–325 days). The mean functional stent time was 170 days (95% CI, 85–255), 367 days (95% CI, 282–391), and 326 days (95% CI, 274–378), respectively ($P = .002$) (Figure 3*B*). In the subgroup of patients with a second stent, patients, patients with SEMS also had a significantly lower hazard, uSEMS (HR, 0.10; 95% CI, 0.01–0.082) and pcSEMS (HR, 0.15; 95% CI, 0.03–0.70), for developing stent dysfunction compared with patients with a plastic stent. The mean number of reinterventions was 0.69 for patients in the plastic stent group, 0.07 for patients in the uSEMS group, and 0.10 for patients in the pcSEMS group ($P = .003$).

In both strata no significant differences were found in functional stent time and risk of stent dysfunction between

Table 2. Mechanism of Stent Dysfunction per Stent Type

	Plastic (N = 73)	uSEMS (N = 75)	pcSEMS (N = 71)
Debris	24	3	5
Migration	5	1	0
Ingrowth	0	6	0
Overgrowth	0	1	2
Other/unknown	2[a]	0	4[b]
Total	31 (42%)	11 (15%)	11 (15%)

[a]Combination of debris and migration (n = 2).
[b]No ERCP was performed because of the poor clinical condition of the patient (n = 2), hemobilia (n = 1), failed ERCP as a result of duodenal stenosis (n = 1).

uSEMS and pcSEMS. One quarter of patients with stent dysfunction presented with cholangitis (13 of 53 patients); 5 in the plastic stent group, 5 in the uSEMS group, and 3 in the pcSEMS group ($P = .147$). Mechanisms of stent dysfunction are shown in Table 2.

Serious Adverse Events

Short-term SAEs were seen in 5 patients in the plastic stent group (7%), in 5 patients in the uSEMS group (7%), and in 3 patients in the pcSEMS group (3%) ($P = .76$) (Table 3). In all 3 groups 10 long-term SAEs occurred ($P = .99$). Cholecystitis was reported in 2 patients: in 1 patient with a plastic stent and in 1 patient with a pcSEMS. Pancreatitis was reported in only 1 patient with a plastic stent. Gastric outlet obstruction requiring surgery or stent placement was the most common long-term complication (n = 9; 30%).

Table 3. Serious Adverse Events After Stent Placement for Malignant Extrahepatic Bile Duct Obstruction

	Plastic (N = 73)	uSEMS (N = 75)	pcSEMS (N = 71)
Short-term SAE	5 (7%)	5 (7%)	3 (4%)
Postprocedural fever	3	1	2
Post-ERCP pancreatitis	-	1	-
Other[a]	2	3	1
Long-term SAE	10 (14%)	10 (13%)	10 (14%)
Cholecystitis	1	-	1
Pancreatitis	1	-	-
Gastric outlet obstruction	3	3	3
Other[b]	5	7	6

[a]Included the following: pneumonia (2), pulmonary embolism (2), cardiac arrest (1), and urosepsis (1).
[b]Included hospital admissions for dehydration (3), pneumonia (2), portal vein thrombosis (2), unknown fever (1), spontaneous bacterial peritonitis(1), leakage of PTC drain (1), retroperitoneal bleeding after celiac plexus neurolysis (1), collum fracture (1), cardiac arrest (1), rectal blood loss (1), hematemesis (1), deep vein thrombosis (1), pulmonary embolism (1), and severe ascites (1).

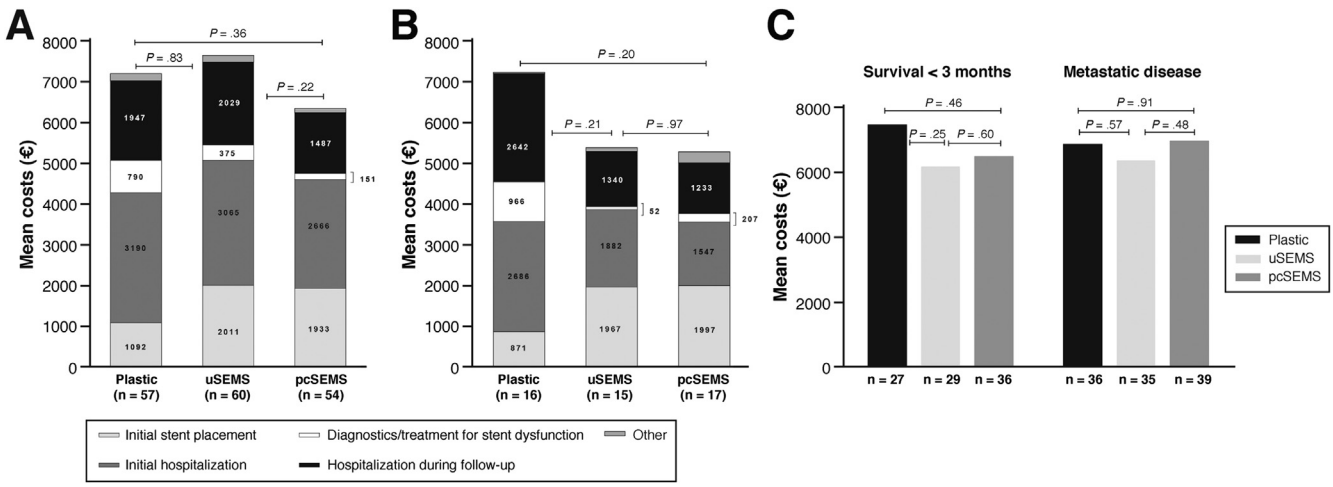

Figure 4. Mean costs during the follow-up period (per patient in euros) for palliation of malignant extrahepatic bile duct obstruction. (*A*) Primary stent placement. (*B*) Second stent placement. (*C*) Short survival time (<3 mo) and metastatic disease.

Costs

Costs for the initial stent placement were significantly higher for both SEMS types compared with plastic stents in both patients with primary stent placement (€2011 and €1933 vs €1092; $P = .001$) (Figure 4*A*) and patients with stent placement for a first episode of stent failure (€1967 and €1997 vs €871; $P = .001$) (Figure 4*B*). Costs for the whole initial treatment were not statistically significant different between patients with a plastic stent, uSEMS, and pcSEMS in patients with primary stent placement (€4282 vs €5076 vs €4599; $P = .44$) (Figure 4*A*), as well as in patients with secondary stent placement (€3556 vs €3545 vs €3849; $P = .88$) (Figure 4*B*).

During the follow-up evaluation, in patients with primary stent placement the mean costs for diagnostic procedures and therapy for stent dysfunction were significantly higher in patients with a plastic stent (€790) compared with patients with uSEMS (€375; $P = .04$) and pcSEMS (€151; $P = .002$). In patients with a second stent placement costs for stent dysfunction were also significantly higher in the plastic stent group (€966) compared with uSEMS (€52; $P = .03$) and pcSEMS (€207; $P = .007$). Costs for hospitalization during the follow-up evaluation were not statistically different between the stent groups in both strata (Figure 4*A* and *B*).

The mean total costs per patient for the total treatment were not significantly different between the 3 different stent types in both patients with primary stent placement and patients with a second stent.

Costs in Patients With a Successful Initial Stent Placement

The costs for initial stent placement were not different from the costs of one ERCP, as shown in Supplementary Appendix. The costs for hospitalization also were not significantly different between groups ($P = .26$). The costs for the whole initial treatment were higher in the SEMS group (€2614) compared with the plastic stent group (€2225), although this difference was not significantly different ($P = .06$). There was no significant difference between uSEMS and pcSEMS. The mean total costs, including follow-up evaluation, were not significantly different between the 3 different stent types (€6906 for plastic stents, €7039 for uSEMS, and €5801 for pcSEMS; $P = .28$).

Costs in Short-Term Survivors

For patients with a short survival time (≤3 mo) and patients with metastatic disease, we found no difference in the total costs between plastic stents and SEMS (Figure 4*C*). In patients with successful initial stent placement, total costs also were not different between plastic stents and SEMS in patients with a short survival time (€6555 vs €5719; $P = .4$) or metastatic disease (€6593 vs €6179; $P = .69$). In all subgroups there were also no differences in costs between pcSEMS and uSEMS placement.

Endoscopic Costs

The mean costs per patient for the endoscopy department (ie, only ERCP-related costs) were not different in the overall study population. In patients with a primary stent placement, the mean costs were €1724 for plastic stents, €2081 for uSEMS, and €2021 for pcSEMS ($P = .20$). The mean costs in patients with a second stent were €1733, €2205, and €2019 ($P = .19$), respectively.

However, costs for the endoscopy department were significantly higher for SEMS compared with plastic stents in patients with a short survival time (<3 mo) (€1255 vs €1796; $P = .006$), patients with metastatic disease (€1542 vs €1987; $P = .012$), and patients with successful initial stent placement (€1769 vs €2201; $P = .018$). There were no differences in costs between uSEMS and pcSEMS placement.

Discussion

This multicenter randomized study compared 3 different stent types for the palliation of malignant extrahepatic bile duct obstruction. We found that total medical costs are not

different between patients treated with a plastic stent or with SEMS, even in patients with a survival shorter than 3 months. In addition, we confirmed previous findings showing that SEMS are superior to plastic stents with regard to functional stent time and stent dysfunction.

Since the introduction of SEMS for the palliation of malignant biliary obstruction in 1989, the costs of SEMS have been a subject of debate.[25,26] Placement of SEMS, approximately 10 times the price of a plastic stent, will be cost effective only when the high initial costs are offset by a reduction in costs during follow-up evaluation. There is convincing evidence that for patients with a relatively long survival time after stent placement (ie, longer than 4–6 mo), total health care costs of SEMS placement compare favorably with plastic stent placement.[7–12,27,28] For patients with an expected survival time of only 3–4 months or for patients with metastatic disease, plastic stents generally are recommended as the most economic option. However, this recommendation is based largely on decision-analysis studies and is supported by only 2 randomized clinical studies.[9,10,12,13] In our study, the total treatment costs for patients with a short survival time and for patients with metastatic disease were not different between plastic stents and SEMS. In fact, we found that the cost differences for initial stent placement already were outweighed when costs of hospitalization after stent placement were included in the initial treatment costs.

The median duration of hospital stay after stent placement in our study was 4 days, and costs for hospitalization comprised 60% of the total costs of the initial treatment. Interestingly, only 2 other studies included costs for hospital stay after stent placement in their cost analysis.[6,9] Lammer et al[6] reported a relatively long hospital stay after stent placement, with a mean of 10 and 21 days for SEMS and plastic stents, respectively. It is not surprising that these investigators concluded that hospital stay was the main cost driver of the initial treatment. However, stent placement in this study was performed using a percutaneous approach and therefore cannot be compared directly with the endoscopic setting. Prat et al[9] included a fixed duration of 2 days of hospital admission for all patients in their cost calculation, irrespective of the actual duration of admission. The use of such a standard price for the initial treatment actually has been used in all previously performed randomized studies.[7–11] As a result, none of these previously published studies have taken into account costs associated with failure of stent placement and hospital stay and therefore unlikely reflect real health care costs. We included all health care costs associated with the treatment and found that stent costs are only a minor contributor to the total health care costs. This may hold even more strongly in countries where costs for hospital stay are higher than in our study, such as the United States.

We only achieved successful stent placement during the first ERCP in 78% of patients, compared with technical success rates of 88%–100% in other studies.[6–11,29] However, in all those studies patients were included in the study only if successful cannulation of the common bile duct was established. If we would have included patients only after successful cannulation of the common bile duct, as was performed in other studies, our technical success rate also would have been 93%.

To provide a detailed and complete overview of all costs associated with stent placement for palliation of malignant extrahepatic bile duct obstruction, we included the costs of all intramural health care use in our calculation. However, local reimbursement policies ultimately determine which costs have the highest impact. For example, in The Netherlands, the costs for the type of stent used are most important for the Endoscopy Department because these costs put the main pressure on the budget. We therefore also performed a subanalysis with only the costs for the Endoscopy Department. We found no cost differences between plastic stents and SEMS in the overall study population. However, subgroup analysis showed that costs for the endoscopy department were significantly higher for SEMS in patients with a short survival, metastatic disease, and in patients with successful initial stent placement. Beside differences in reimbursement policies, prices of unit costs also may vary considerably between countries. In an attempt to make a more generalizable cost analysis, decision analysis studies using cost ratios rather than unit costs were conducted.[11–13,15] Based on these decision models, it has been concluded that SEMS placement is cost effective when SEMS costs are less than half the costs of an ERCP.[12] In our setting, the costs of SEMS comprised 48% of the costs of the ERCP and indeed we found that SEMS are a cost-effective option. Nonetheless, in a study by Yoon et al,[27] it was shown that SEMS placement also can be cost effective when SEMS are 4 times the price of an ERCP.

When we started this study, pcSEMS were being used increasingly as an alternative for uSEMS to prevent recurrent biliary obstruction owing to tissue ingrowth through the stent meshes. Although we indeed found no cases of tissue ingrowth through the mesh of pcSEMS in our study, in other studies tissue ingrowth through the uncovered stent ends has been reported as a cause of stent failure.[30,31] To completely overcome the problem of tissue ingrowth, fully covered SEMS (fcSEMS) have been developed. These stents became available only during the course of this study. A recent meta-analysis, however, has not shown a clear benefit for either type of stent (ie, uSEMS, pcSEMS, or fcSEMS) in terms of functional stent time or survival. However, the most common causes of stent dysfunction differ considerably between these stent types, with tissue ingrowth being the predominant cause of stent dysfunction for uSEMS and migration for fcSEMS.[19,20,30–33] In an attempt to further reduce stent dysfunction and prolong stent patency, modifications of the SEMS design continuously are being developed, such as a fcSEMS with antimigration features.[34] If the efficacy of SEMS indeed will be increased further, this will strengthen the recommendation even more of using the more expensive SEMS for palliation of extrahepatic bile duct obstruction with SEMS.

The median survival of 109 days in our study is in the lower range compared with the median survival of 108–149 days in other studies comparing plastic stents and SEMS.[6,7,9–11] This probably can be explained by the high

percentage of patients with metastatic disease in our study (52%) compared with other studies (27%–39%).[6,10,11] Metastatic disease is known to have an adverse effect on survival, which also was observed in our study. Interestingly, we also found a significant difference in survival between patients with primary stent placement and those receiving a second stent (142 vs 199 days). It is remarkable that the latter group had a longer survival because these patients already had a prior period of stent placement. The significantly lower bilirubin level at baseline could implicate less-aggressive disease in this group of patients. However, it possibly also could be explained by less diagnostic delay in these patients.

The strength of this study was the randomized controlled study design with a comparison of 3 commonly used stents. Only one previous study compared plastic stents with covered SEMS and in none of the other studies were plastic stents compared with both uSEMS and pcSEMS. Furthermore, this was a large study in which plastic and metal stents for the treatment of malignant extrahepatic bile duct strictures were compared. Regarding the cost analysis, we thoroughly collected all items that contribute to the use of health care starting at the time of treatment but also during the follow-up evaluation. Because this was a multicenter study involving 18 centers, comprising approximately 20% of all Dutch hospitals, the results of this study likely reflect the quality of endoscopic palliative care of patients with extrahepatic bile duct obstruction in the entire country and not just from 1 center. A limitation of the study was that the power calculation was based on clinical outcome of stent placement and not on cost differences. Furthermore, as is true for all cost studies and discussed earlier, it was to some extent difficult to translate these results to countries with other costs and reimbursement systems.

In conclusion, this study showed that placement of SEMS is cost effective for the palliation of malignant extrahepatic bile duct obstruction. The clinical outcome of SEMS placement is superior compared with plastic stent placement, and although initial costs for stent placement are higher for SEMS, total costs are not different between both stent types. Furthermore, in patients with a short survival time, the total treatment costs also are not higher for SEMS. Because the clinical outcome with SEMS is favorable and the total costs are not different, we recommend SEMS placement for palliation of extrahepatic bile duct obstruction in all patients.

Supplementary Material

Note: To access the supplementary material accompanying this article, visit the online version of *Gastroenterology* at www.gastrojournal.org, and at http://dx.doi.org/10.1053/j.gastro.2015.03.012.

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