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CLINICAL—BILIARY

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

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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,