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Percutaneous transhepatic self-expanding metal stents for palliation of malignant biliary obstruction

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Background. Malignant biliary obstruction is often inoperable at presentation and has a poor prognosis. Percutaneously placed self-expanding metal stents (SEMS) have been widely used for palliation of malignant biliary obstruction as an alternative to major bypass surgery or when endoscopic drainage is not technically feasible. The success rate, procedural complications and outcomes in patients who underwent placement of SEMS in a tertiary referral centre are presented.

Methods. All patients who had percutaneous transhepatic cholangiography (PTC) and SEMS for palliation of malignant biliary obstruction between May 2008 and July 2010 at Groote Schuur Hospital, Cape Town, were reviewed. A retrospective chart review was undertaken using multidisciplinary case notes of all patients. The data analysed included demographic information, diagnosis, level of biliary obstruction, number and type of procedures, efficacy and complications of SEMS insertion. Boston Scientific 69 mm by 10 mm Wallstent SEMS were used in all patients.

Results. Fifty patients (28 men, 22 women, mean age 61 years, range 48 - 80 years) underwent percutaneous SEMS placement. Twenty-one patients had biliary obstruction at the level of the hilum involving the hepatic duct bifurcation, 5 in the mid-common bile duct and 24 in the low common bile duct. In 20 patients (40%) SEMS were placed at the time of initial biliary drainage (one-stage procedure), while the remaining 30 patients underwent stent placement within 2 - 23 days of biliary drainage as a two-stage procedure because of difficult access through the lesion during the initial procedure. Five patients (10%) required bilateral SEMS insertion. Stent placement was successful in all patients and biliary obstruction was relieved in all.

The mean serum bilirubin level decreased by a mean of 56% from 294 μmol/l to 129 μmol/l measured 5 days after stent insertion. Mean hospital stay after stent insertion was 4.1 days. The average length of hospital stay for patients who underwent a one-stage procedure was 3.2 days (range 1 - 11 days), and for patients who underwent a two-stage procedure 7.6 days (range 3 - 23 days).

Nine patients (18%) developed a procedure-related complication, which included cholangitis after stent insertion (*n*=4), cholangitic liver abscesses (*n*=1), subphrenic liver collection (*n*=1), bile leakage (*n*=1) and cholecystitis (*n*=2). Three patients (6%) developed complications unrelated to SEMS insertion, which included myocardial ischaemia (*n*=2) and pneumonia (*n*=1).

Stent occlusion occurred in 4 patients (8%) within a week as result of stent migration (*n*=3) or presumed biliary sludge (*n*=1); 2 (4%) stents occluded between 7 days and 1 month. Four patients (8%) died during hospital admission due to pre-existing biliary sepsis (*n*=3) and pneumonia (*n*=1). Nine patients developed duodenal obstruction due to disease progression and required endoscopic duodenal stenting. Four patients (8%) survived less than 1 month, 12 (24%) between 1 month and 3 months, 11 (22%) between 3 and 6 months, and 10 (20%) beyond 6 months. Follow-up was not possible for 9 patients (18%) from distant referral sites.

Conclusion. These results demonstrate that percutaneously placed SEMS achieved satisfactory palliation with a low complication rate in a high-risk patient group with advanced malignant biliary obstruction.

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Cancers of the pancreas, gallbladder and bile ducts are the commonest causes of malignant biliary obstruction. Surgery is the only curative treatment, but fewer than 20% of biliary malignancies are resectable.[1] Untreated patients who have irresectable malignant biliary obstruction and symptomatic jaundice have a poor quality of life and a dismal prognosis. Unresolved biliary obstruction predisposes patients to life-threatening complications, which include cholangitis and progressive renal and hepatic failure. Early relief of the biliary obstruction may prevent these complications and offers symptomatic relief of severe pruritus. Palliative surgical biliary

drainage is also effective and has the advantage of allowing the addition of a gastrojejunostomy if duodenal obstruction is present or imminent.[2] However, morbidity after palliative surgery in elderly, frail, jaundiced patients is substantial and hospital mortality rates of up to 20% have been recorded in this high-risk group of patients.[1]

Non-surgical palliative options include endoscopic or transhepatic biliary stenting using plastic or metal stents. Percutaneous transhepatic biliary drainage is used when endoscopic drainage is not possible due to tumour infiltration of the duodenum or ampulla or if the tumour involves the hepatic duct bifurcation. In patients with short life expectancy, symptoms of jaundice can be palliated effectively by percutaneous placement of a biliary endoprosthesis with a low rate of recurrence and a complication rate no higher than that associated with endoscopic biliary drainage. While both fixed-calibre plastic stents and self-expanding metallic stents (SEMS) are currently available,[3] metal stents have been shown to be superior to plastic stents with longer patency rates, better symptom-free survival and improved quality of life, as well as fewer complications and overall lower costs.[4,5]

The aim of this study was to evaluate the safety and efficacy of percutaneously placed transhepatic SEMS for relief of malignant biliary obstruction in patients treated between May 2008 and July 2010 at a tertiary referral centre in Cape Town.

Patients and methods

Inclusion criteria

A retrospective chart review was performed using the multidisciplinary case notes of all patients who had obstructive jaundice due to irresectable malignant tumour and were referred for percutaneous biliary stenting. Patients with jaundice due to irresectable hilar cholangiocarcinoma underwent percutaneous transhepatic cholangiography (PTC) and biliary stenting as the initial procedure, while those with bile duct obstruction below the hilum had endoscopic retrograde cholangiopancreatography (ERCP) and stenting as the initial procedure. If endoscopic biliary stenting was unsuccessful, transhepatic stenting was used.

Technique of transhepatic biliary stent placement

Routine PTC was performed on patients referred for transhepatic biliary stent placement. The decision to access the biliary system via either the right- or left-side ducts was determined by information based on computed tomographic and magnetic resonance imaging findings. Each patient's coagulation profile, including the International Normalised Ratio and platelets, and renal function was reviewed and corrected if necessary. Signed informed consent was obtained from all patients. Empiric intravenous antibiotic therapy was administered before commencing the PTC.

Access to the biliary system was facilitated using ultrasound and fluoroscopic guidance. Once the site and level of the stricture were identified, a guidewire was passed through the stricture and an attempt was made to insert a SEMS. This pliable, self-expanding metal mesh prosthesis is woven from surgical grade stainless steel alloy filaments and braided into a flexible tube in the longitudinal axis (Wallstent; Boston Scientific, Switzerland). The unexpanded stent is mounted on a 100 cm delivery system and constrained and elongated by a membrane.[3] The constrained outer diameter measures 6 Fr.[6] The delivery system with the constrained stent is inserted over a 0.035 mm guidewire. The radio-opaque stent and markers on the delivery catheter allow fluoroscopic control of stent release after positioning across the stricture. After progressive withdrawal of the membrane, the prosthesis expands to 8 - 10 mm diameter (30 Fr) and shortens from 10 cm to 6.9 cm. An external biliary drainage catheter is left in place to allow post-procedural cholangiography.

Technique of endoscopic duodenal stent placement

All procedures were performed under conscious sedation in the endoscopy suite using fluoroscopic guidance. SEMS were placed under direct vision with a side-viewing duodenoscope (Olympus TJF-260; Olympus, Tokyo, Japan) with a 4.2 mm working channel using a 'through-the-scope' technique. The duodenal stricture was first traversed with a guidewire (JagwireTM SuperStiff; Boston Scientific, Natick, Mass., USA). A guiding catheter (Wilson-Cook Medical, Winston-Salem, NC, USA) was then advanced over the guidewire and the guidewire removed. Contrast was injected through the guiding catheter to ensure that the catheter was in the bowel lumen and there was no obstruction beyond the stricture. The length and distal extent of the stricture were estimated. The guidewire was reintroduced through the guiding catheter, which was then removed. A 6 or 9 cm uncovered Boston WallflexTM enteral duodenal stent (Boston Scientific) with an internal diameter of 2.2 cm was advanced over the guidewire through the working channel of the duodenoscope into position across the stricture. The distal-release stent was then deployed and positioned across the stricture under fluoroscopic guidance. Oral intake was started when the patient had recovered from the sedation. A plain abdominal radiograph was taken 24 hours after placement to assess and confirm stent expansion and position. Patients were discharged from hospital when they were able to eat and drink without requiring parenteral fluid support.

Follow-up and definition of endpoints

Follow up data were obtained from information recorded at clinic visits and by contacting patients or relatives telephonically. Both primary and secondary endpoints were evaluated. Primary endpoints were the technical success of stent placement, therapeutic success rate (measured by a decline in the bilirubin level), duration of stent patency (defined as recurrence of jaundice or cholangitis with a dilated bile duct requiring intervention), occlusion rate, cause of occlusion, stent migration, duration of hospital stay after stent insertion, and survival after discharge. Secondary endpoints included complications related to the procedure, including cholangitis, cholecystitis and pancreatitis, and any untoward event, even if unrelated to the procedure. Kaplan-Meier survival analysis was used to determine the actual survival time.

Results

Between May 2008 and July 2010, 50 consecutive patients (28 men, 22 women, median age 61 years, range 48 - 80 years) with malignant biliary obstruction underwent SEMS placement. The most common malignancy in this study was pancreatic adenocarcinoma (n=24), followed by cholangiocarcinoma (n=11), gallbladder carcinoma (n=4), biliary compression by

malignant nodes in the porta hepatis (*n*=4), and gastric (*n*=3), duodenal (*n*=2) and ampullary carcinoma (*n*=2). Twenty-one patients had obstruction at the level of the hepatic hilum, 5 in the mid-common bile duct and 24 in the distal common bile duct. Stent insertion was technically successful in all patients. A SEMS was placed as a one-stage procedure in 20 patients (40%) at the initial PTC. Thirty patients (60%) in whom one-stage stenting was not feasible returned for a second or third procedure which entailed conversion of either an existing external drain or an internal/external drain to SEMS stenting. All stent insertions were ultimately successful. Five patients (10%) required bilateral SEMS insertion, of whom 2 had hilar cholangiocarcinoma, 2 gallbladder carcinoma and 1 extensive metastatic hilar nodal compression secondary to gastric carcinoma. In 3 patients biliary sepsis occurred in the undrained opposite side after initial stent placement, and in 2 patients jaundice did not resolve, necessitating stenting on the opposite side.

Twenty-one patients (42%) developed complications while in hospital. Nine patients (18%) had procedure-related complications, which included cholangitis after stent insertion (*n*=4), cholangitic liver abscess (*n*=1), subphrenic abscess (*n*=1), bile leak (*n*=1) and cholecystitis (*n*=2). All procedure-related complications resolved on treatment with antibiotics, other than a subphrenic abscess that was drained percutaneously. Twelve patients (24%) developed complications unrelated to SEMS insertion, which included gastric outlet obstruction requiring endoscopic metal stenting (*n*=9), myocardial ischaemia (*n*=2) and pneumonia (*n*=1).

Early stent occlusion occurred in 4 patients (8%) within a week of placement as result of stent migration (*n*=3) or presumed biliary sludge or clot (*n*=1). Three of these patients required a second SEMS, while the last patient had an endoscopic plastic stent placed. Two stents (4%) occluded between 7 days and 1 month. The stent occlusion at 7 days was due to a combination of sludge and stent migration, while that at 1 month was due to tumour ingrowth. Both these patients subsequently underwent successful endoscopic plastic stent insertion.

Intervention was technically successful in all 50 patients. The mean serum bilirubin level decreased from 294 μmol/l to 129 μmol/l (56% reduction) measured 5 days after stent insertion. Mean hospital stay after stent insertion was 4.1 days. After a median follow-up of 2.5 months (range 1 - 14 months), biliary obstruction recurred in 6 patients (12%).

Four patients (8%) died in hospital, 3 due to pre-existing biliary sepsis and 1 from lobar pneumonia. Two patients developed cholangitis after initial endoscopic stenting, while the 3rd patient developed cholangitis after transhepatic SEMS insertion. Four patients (8%) died within 30 days of stenting. These patients had all been discharged home after stenting. Twelve patients (24%) survived between 1 month and 3 months, 11 (22%) between 3 and 6 months, and 10 (20%) longer than 6 months. The mean survival time by Kaplan-Meier survival analysis was 91 days.

Discussion

The fundamental objectives of palliative transhepatic biliary drainage are to improve quality of life by relieving jaundice and pruritus, prevent cholangitis, and avert liver failure caused by progressive biliary obstruction.[7] In this study of 50 patients with symptomatic jaundice due to advanced irresectable malignancy in whom a surgical bypass or endoscopic stenting was not possible, percutaneous biliary transhepatic self-expanding metal stent insertion was technically successful in all cases. The advantages of metal endoprostheses include placement through small-calibre percutaneous transhepatic tracts while providing a 30 Fr internal lumen when fully expanded in the bile duct. This large internal biliary lumen reduces the risk of occlusion due to bile encrustation[8,9] by 34% compared with endoscopic plastic endoprostheses and also facilitates biliary access if subsequent endoscopic intervention is required.[1] Once deployed, metal stents are theoretically permanent as the metal interstices gradually become embedded in the bile duct wall; this reduces the chance of migration, although they may sometimes be retrieved within the first 48 hours.

SEMS placement is generally safe and effective when performed by an experienced radiologist.[10] No patients died during stent insertion in this study, despite having advanced malignancy, jaundice and substantial co-morbidity. Although the overall complication rate for percutaneous stent insertion was 42%, more than half of the complications were unrelated to the procedure and reflect the high incidence of co-morbidity in this high-risk group of hospitalised patients. As in other series, procedure-related complications were all managed conservatively.[10,11]

Nine patients in this study subsequently developed gastric outlet obstruction and required endoscopic stenting using SEMS. Duodenal obstruction occurs in up to 20% of biliopancreatic malignancies. In the past this required a palliative surgical gastrojejunal bypass,[12] but the newer non-invasive alternative is endoscopic placement of a SEMS in the duodenum. A meta-analysis of available studies comparing endoscopically placed duodenal SEMS and surgical gastroenterostomy shows that SEMS is associated with higher clinical success rates, a shorter time from procedure to starting oral intake, a lower incidence of delayed gastric emptying, and shorter hospital stay than surgical bypass.[13,14]

The reported incidence rate of recurrent jaundice requiring re-intervention after percutaneous transhepatic biliary drainage ranges between 10% and 30%.[11] Six patients in this study developed recurrent jaundice due to tumour ingrowth, stent migration or sludge. The most common causes of occlusion of uncovered metal stents are sludge formation, proximal and distal tumour overgrowth, tumour ingrowth[15] through the metal interstices, and stone formation. Early stent dysfunction caused by sludge or tumour ingrowth is uncommon, but may occur in patients who have mucin-producing tumours or gross haemobilia and clots after a traumatic intervention.[16] Rare complications include intrahepatic haematoma, hepatic abscess, bilio-venous/portal vein fistula and cholecystoduodenal fistula.[16] Late complications include stent occlusion secondary to tumour ingrowth or overgrowth, obstruction caused by biliary sludge aggregation and epithelial hyperplasia. Techniques for managing stent occlusion include placement of a second metal or plastic stent within the initial metal stent, as was done in this study. Failure to drain opacified segments can lead to a significantly poorer outcome with resultant recurrent cholangitis, which supports the practice of careful imaging prior to PTC with targeted drainage of specific lobes or segments.

Single or bilateral biliary stents were inserted, depending on the extent of the malignant occlusion. Single stents are adequate for obstructions of the main bile duct below the hepatic duct

confluence. However, for hilar lesions at the confluence there is controversy regarding whether single or double stents should be inserted. Given that only about 25% of liver volume needs biliary drainage for adequate palliation of icterus and pruritus, a single stent draining two segments of liver should suffice in the absence of biliary tract sepsis. Previous studies have compared unilateral and bilateral biliary drainage in hilar cholangiocarcinoma.[17] A prospective randomised control trial comparing unilateral with bilateral stents found that unilateral stents achieved higher insertion success rates (89% v. 77%) as well as improved drainage (81% v. 73%), together with lower early complication rates (19% v. 27%).[18] There was no difference in procedure-related mortality, late complications or survival, suggesting that unilateral stenting is likely to be effective in most cases. Advocates[19,20] of unilateral drainage quote lower complication rates, but warn that filling undrained intrahepatic ducts with contrast medium should be avoided to decrease the risk of subsequent cholangitis.

Biliary stenting is now established as a cornerstone in the management of most patients who develop malignant biliary obstruction. The use of SEMS with a larger outer diameter has increased owing to fewer long-term complications than occur with smaller internal diameter plastic stents, particularly early stent occlusion.[10] While covered metal stents[5,11,21] are now available, stent migration and occlusion of side ducts causing cholangitis, acalculous cholecystitis or pancreatitis are complications that may ultimately limit their use.[22]

The results of our study confirm that percutaneous insertion of self-expanding metal biliary endoprostheses has an important role in the management of patients with advanced malignant biliary obstruction and offers a safe and effective method of palliation with improved quality of life in those patients who are unsuitable for surgical or endoscopic intervention.

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