CLINICAL STUDY

Comparative Study of Percutaneous Transhepatic Biliary Stent Placement with or without Iodine-125 Seeds for Treating Patients with Malignant Biliary Obstruction

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ABSTRACT

Purpose: To prospectively evaluate safety and efficacy of biliary stent placement with iodine-125 (^{125}I) seeds in patients with malignant obstructive jaundice (MOJ).

Materials and Methods: From July 2011 to June 2014, 55 patients were enrolled (group A, 11 men and 17 women, mean age 70.93 y ± 8.58; group B, 14 men and 13 women, mean age 70.26 y ± 9.71). All patients were randomly assigned to placement of a biliary stent with ^{125}I seeds (group A) or biliary stent only (group B). After stent placement, outcomes were measured regarding relief of MOJ. Clinical success rate, survival time, and safety were recorded. $P < .05$ was considered to indicate significant difference.

Results: Stents were successfully placed in all 55 patients. MOJ was relieved in all patients, and there were no significant differences in complications related to stent insertion between the 2 groups. Mean and median stent patency were 191 days ± 19.8 (95% confidence interval [CI], 152–230 d) and 179 days ± 191.4 (95% CI, 87–267 d) in group A and 88.3 days ± 16.3 (95% CI, 61–114 d) and 77 days ± 88.2 (95% CI, 65–86 d) in group B ($P < .001$, log-rank test). Mean and median survival time were 222.6 days ± 21.0 (95% CI, 181–263 d) and 241 days ± 18.2 (95% CI, 179–270 d) in group A and 139.1 days ± 14.5 (95% CI, 110–167 d) and 142 days ± 16.3 (95% CI, 83–177 d) in group B ($P < .001$, log-rank test).

Conclusions: ^{125}I seeds combined with biliary stent placement could significantly improve stent patency. The procedure seems to be safe and to extend survival compared with self-expandable biliary stent placement.

ABBREVIATIONS

CI = confidence interval, ^{125}I = iodine-125, MOJ = malignant obstructive jaundice

Malignant obstructive jaundice (MOJ) is the most common outcome caused by various adenocarcinomas, including cholangiocarcinoma, gallbladder cancer, pancreatic cancer, and cancer metastasis. Because the clinical process is usually silent and insidious, MOJ accounts for only 10%–20% of patients who are eligible for surgery. Despite improvements in treatment in recent decades, the 3-year survival rate after resection is < 50%; this is partially due to the higher probability of tumor recurrence and liver failure (1–4). Although chemotherapy can rapidly improve local drug concentration in the tumor microenvironment and reduce the toxicity (5), it is still limited by the elevated bilirubin level with suboptimal clinical effects (6).

For patients with unresectable malignant biliary obstruction or for patients who are unwilling to undergo surgery, biliary stent placement can effectively relieve symptoms and improve patients' quality of life (7), and it has become the first choice of palliative treatment (8–10). Studies suggest that biliary stent placement should be done before any chemotherapy (11). However, the

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biliary stent itself has no therapeutic effect on tumors, which could easily grow into the lumen through the stent mesh, resulting in new obstruction and affecting treatment efficacy (12). Iodine-125 (^{125}I) seeds as a sustained radiation source can inhibit the replication of tumor cells via direct damage of DNA double-strand helix and induce tumor cell apoptosis (13). Furthermore, implantation of ^{125}I leads to $CD3^+$ and $CD4^+$ cell activation, producing antitumor immune responses (14).

Luo et al (15) reported that endovascular placement of ^{125}I seed strand and stent combined with chemoembolization was safe and feasible to treat hepatocellular carcinoma with tumor thrombus in the main portal vein. Preliminary clinical results have also shown that biliary stent placement combined with brachytherapy is a safe and tolerable procedure for patients with MOJ. However, it is unknown whether biliary stent placement combined with brachytherapy extends patient survival (16). This prospective clinical study was performed to evaluate the safety and efficacy of ^{125}I seeds combined with biliary stent placement in patients with MOJ and to report their survival.

MATERIALS AND METHODS

This prospective study was approved by the ethical committee of our hospital and was registered as a Chinese clinical trial (registration no. ChiCTR-TRC-11001456), for which each patient provided written informed consent.

Inclusion and Exclusion Criteria

Inclusion criteria were as follows: biliary obstruction caused by previous surgical procedures or by any adenocarcinoma with histologic confirmation, unresectability, or patient refusal to be surgically treated; Bismuth-Corlette type I or II bile duct obstruction; Karnofsky performance scale score > 40; and estimated life expectancy > 3 months. Patients with the following conditions were excluded: brain metastases, Bismuth-Corlette classification type III or IV bile duct obstruction, prior malignant history (exceptions included biopsy or resection of in situ cervical cancer, nonmetastatic basal or squamous cell skin cancer, and cancer diagnosis with > 5-y survival), and uncontrolled infections; patients who were uncooperative or could not provide authorization and signature and patients who were pregnant or breast-feeding were also excluded.

Previous studies reported that the bare biliary stent patency duration for treatment of unresectable malignant biliary obstruction was approximately 5.4–6.7 months, whereas patency when stent placement was combined with radiation therapy could be extended to 9.8 months; we estimated that the median survival time of patients in the irradiation stent group was approximately 8.5 months. In this study, with an α level of .05 (1-sided test) and a β error of .20, we estimated about 5% of patients lost to follow-up, and the analysis was planned for 29 cases in each group.

Patient Data

From July 2011 to June 2014, 55 patients were enrolled in the study. The Consolidated Standards of Reporting Trials flow diagram shows the randomization and flow of patients throughout the trial (Fig 1). There were 11 men and 17 women with a mean age of 70.93 y ± 8.58 (range, 50–84 y) in group A and 14 men and 13 women with a mean age of 70.26 y ± 9.71 (range, 47–84 y) in group B. Randomization was conducted using block randomization (block size 4) to balance stent assignment by using a random number generator. Except for the interventional radiologists, all patients, the nurses caring for the patients, and the statistician performing the analyses in the study were masked to the type of stent used.

Table 1 summarizes the baseline characteristics of the patients included in the analysis distributed according to randomization. As shown, both groups were identical or nearly identical ($P > .05$).

Stents and ^{125}I Seeds

A nitinol self-expandable stent (S.M.A.R.T.; Cordis Corporation, Miami Lakes, Florida) with 6- to 8-mm diameter and 60- to 80-mm length was used in this study. ^{125}I seeds (Beijing Atom Hi-Tech Co., Ltd., Beijing, China) with diameter of 0.8 mm and length of 4.5 mm ± 0.5 were used. The radioactivity of each ^{125}I seed is 0.9 mCi with a half-life of 59.43 days. The principal photon emissions are 27.4 keV for x-rays, 31.4 keV for χ-rays, and 35.5 keV for γ-rays, with a 20-mm effective range.

Placement of ^{125}I Seeds

Before stent placement, cholangiography was performed to document the site and length of the lesion. To determine how many ^{125}I seeds to implant (N), the following formula was used: N = length of the obstructive segment of bile duct (mm)/4.5 + 4. In group A, to prevent the ^{125}I seeds from dislodging, the seeds were arranged linearly and sealed into a transparent 4-F catheter (PBN MEDICALS Denmark A/S, Stenlose, Denmark) using heat to seal both ends (Fig 2). A 0.035-inch, 260-cm-long stiff wire (Terumo Corporation, Tokyo, Japan) was inserted into the diseased bile duct. An 8-F guiding catheter (Cordis Corporation) was introduced into the obstructed bile duct over the wire, and the wire was removed. Two 0.035-inch, 260-cm-long stiff wires were inserted through the guiding catheter, and the guiding catheter was then removed. A guiding catheter was inserted through 1 of the wires for the delivery of the ^{125}I seed strand, and the wire was withdrawn. The other wire was prepared for stent insertion (Fig 3). A self-expandable stent of appropriate