To evaluate 792 patients with malignant biliary obstruction after inner-stents drainage procedure

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Abstract

Objective

To evaluate the clinical effects and values of stent placement for treating malignant biliary obstruction/MBO

Methods

792 patients with malignant biliary obstruction, in which 398 suffered from perihilar biliary obstruction, 394 suffered from middle and lower biliary obstruction. The treatment methods of “Single site, single stent placement”, “Dual sites, dual channels, double stent placement”, “Single site, single channel, double stents placement,” and “Single stent + PTCD were applied.

Results

There were significant differences in serum total bilirubin level between the pre-operation and post-operation (p<0.05) for 792 cases. The 6 months’ survival rate was 73% (573/792). The survival rate of over 6 months was 64% (505/792). The survival rate of 12 months or over 12 months was 45% (329/792).

Conclusion

1. The treatment methods of “Single site, single stent placement”, “Dual sites, dual channels, double stent placement”, “Single site, single channel, double stents placement,” and “Single stent + PTCD were effective ways to achieve entire internal drainage on hepatic-hilar-biliary obstruction. It had an evidently clinical value.

2. Stents combined with other anti-tumor treatment can increase the survival rate and decrease the rate of stent re-stenosis.

Key words

Jaundice; Biliary obstruction; Hepatic hilar; Inner-stents; Multiple

Multi-site, multi-segment extrahepatic, perihilar and hilar malignant biliary obstruction (MBO) refer to the blockage of any part of bile ducts caused by invasion or compression of primary cholangiocarcinoma located at hepatic ducts, common bile duct, and the confluence of left and right hepatic ducts or surrounding malignant tumors. The obstruction usually discovers at the advanced stage. The opportunities of surgical resection and palliative bypass surgery are impossible. If the biliary obstruction is not cleared immediately, progressive biliary obstruction, hepatic failure and mortality would be occurred. From March 1995 to December 2008, a total of 792 patients with MBO were admitted and treated with percutaneous transhepatic metal stent placement, facilitating internal biliary drainage and jaundice was reduced. We mainly focused on the clinical significance of stent placement technique and the combination of stent placement and anti-tumor therapy for treating multi-site, multi-segment perihilar biliary obstruction.

1 Materials and methods

1.1 Materials

476 male and 316 female, aged 28 to 93 years old, mean age (56.5 ± 11.8) years old were admitted. 398 cases were confirmed as perihilar biliary obstruction. In this group, 211 cases were confirmed as obstruction located at the common hepatic ducts (within the location of 1 cm surrounding the confluence of left and right hepatic ducts). 187 cases were multi-site, multi-segment hepatic obstructions at the hepatic hilar region. 115 cases were obstruction occurred simultaneously at the left and right hepatic ducts, confluence site and the upper common hepatic duct. 35 cases were multiple obstructions at left and right intra-hepatic duct. 37 cases were obstruction at left and right hepatic duct. A total of 394 cases were middle and lower biliary obstruction. In this group, 132
cases were located at hepatic and common bile ducts. 125 cases were located at middle and lower common bile duct. 137 cases were located at bottom of common bile duct. 197 cases were confirmed cholangiocarcinoma. 91 cases were gallbladder cancer. 151 cases were metastatic carcinoma. 109 cases were primary liver cancer. 106 cases were carcinoma of head of pancreas. 67 cases were ampullary carcinoma, and 71 cases were gastric cancer. Serum total bilirubin were between 162.7 – 960.2 μmol/L, average level 283.4 ± 175.4 μmol/L, featured with major increase of direct bilirubin. All cases were confirmed as inoperable and treated by using biliary stent placement.

1.2 Methods

1.2.1 All patients were inoperable and treated by placing stents. Under DSA monitoring, PTCD and stent placement were achieved via right mid-axillary line. 1.2.2. For extrahepatic biliary obstruction, 394 patients were placed with stents via route of right hepatic duct – common bile duct at the right mid-axillary line. 6 methods of stent placement were used for perihilar biliary obstruction. ① stents were placed in 211 patients with obstructions at the upper common hepatic duct 1cm surrounding the confluence of left and right hepatic ducts via route of right hepatic duct – common bile duct at the right mid-axillary line. ② 58 patients with obstruction at both left and right hepatic ducts and upper bile duct were punctured at left and right hepatic ducts at right mid-axillary line and xyphoid. 2 stents were introduced through 2 guide wires in common bile duct in Y-shaped configuration, dilating the obstructed segments at the site before the right and left hepatic ducts connection and at the upper common hepatic duct. ④ Double stents, single channel placement: For 43 patients with simultaneous obstruction at left and right hepatic ducts and upper common hepatic duct, the internal drainage channel by placing stent between the left and right hepatic ducts was firstly established, followed by that between right hepatic duct and common bile duct or between left hepatic duct and common bile duct, achieving the adequate biliary drainage through left hepatic duct - right hepatic duct – common bile duct or right hepatic duct - left hepatic duct – common bile duct. The two stents were placed in form of “F” or “η” configuration, i.e., double stents and single channel technique. ⑤ 14 patients were confirmed with simultaneous obstruction at left and right hepatic ducts and upper common hepatic duct. It was impossible to place the stent from right hepatic duct to left hepatic duct or left hepatic duct to common hepatic duct. As a result, the drainage were established by puncturing the right hepatic duct of the same level via left hepatic duct, achieving full biliary drainage via route of left hepatic duct - right hepatic duct – common bile duct. ⑥ 35 patients with multiple hepatic duct obstruction in right hepatic duct: the stent was placed between hepatic ducts in right liver with easier drainage as so to realize bile flow between intra-hepatic duct and bile ducts. Another stent was placed between right hepatic duct and common hepatic duct. ⑦ 23 patients with left and right hepatic duct obstruction, stent were placed in right hepatic duct and external drainage catheter (PTCD) was placed in left hepatic duct. ⑧ 14 patients with right hepatic duct obstruction where stent channel cannot be established between right hepatic duct and common bile duct, the stent channel between left hepatic duct and common bile duct was created by puncturing under xyphoid and multi-site external drainage catheter was placed at right hepatic duct.

1.2.3 792 MBO patients were given anti-tumor therapy within 7-15 days after the stent placement, of which interventional intra-arterial infusion and embolotherapy 3-4 times, n=187; stereotactic radiotherapy n=143; one patient with cholangiocarcinoma was not given anti-cancer therapy. Commonly used drugs included hydroxy camptothecin 30mg, epirubicin 50mg, embolization agent ethiodized oil 10-20ml + cisplatin 80mg, perfusion plus embolotherapy were implemented for the target vessel with abundant blood supply. The interval of interventional treatment was 30-40 days, with an average of 2-3 times. The simulation under CT scan was conducted 2-3 weeks after the stent placement, with a radiation source from the linear accelerator.

2 Results

2.1 398 cases of perihilar biliary obstruction at porta hepatitis n=398, multi-site, multi-segment perihilar biliary obstruction at porta hepatitis n=187, middle and lower extrahepatic MBO n=394. Individualized stents with different configuration were selected or designed according to the results of medical imaging and the physiological characteristics of hepatic duct and bile duct anatomy. Stents were introduced by 6 methods. (1) 412 pieces of memory nickel-titanium alloy stents (secondary stent placement due to re-obstruction n=62) and 44
pieces of imported self-expanding stents were placed for 394 patients with middle and lower extrahepatic MBO, total 456 pieces. (2) 238 pieces of memory nickel-titanium alloy stents were placed at common hepatic duct and common bile duct for 211 patients with obstruction at upper common hepatic duct (secondary stent placement due to re-obstruction n=27). (3) For 187 patients with multi-site, multi-segment hepatic duct obstruction, each of the patients was placed two stents, whereby 286 pieces of memory nickel-titanium alloy stents and 28 pieces of imported self-expanding stents, total 314 pieces.

2.2 For all the patients, the serum total bilirubin were decreased from the preoperative level of 162.7 ~ 960.2 μmol / L (mean 283.4 ± 175.4 μmol / L) to the postoperative value of 36.3 ~ 267.3μmol / L (mean 63.2 ± 11.8 μmol / L), showing significant reduction (P <0.05), which were mainly due to the decrease of bilirubin. For multi-site, multi-segment hepatic duct obstruction, only 13 cases got jaundice reductions, which were not a satisfied result after internal drainage by multiple stent placement, including 11 cases with multi-vessel intra-hepatic biliary obstruction caused by multiple intra-hepatic tumors, 2 cases with diffuse intra-hepatic metastasis caused by primary liver cancer and more extensive intra-biliary cancer embolus and cancer embolus of portal vein. Among 13 patients, 2 were died within 30 days after the stent placement, and 11 were died within 2 to 3 months.

2.3 Until the end of the study, the period of follow-up after stent placement was 28 months. The survival rates of 792 patients measured as the duration of 1~3 months, 6 months, >6 months and ≥1 year were 1.6%(13/792), 73%(578/792),64%(505/792) and 45%(329/792), respectively. The number of patients, who had intervention therapy by using intra-arterial infusion and embolotherapy 3-4 times, with the survival period of one year or more, was 187. The number for those who had stereotactic radiotherapy was 141. One patient with cholangiocarcinoma was not given anti-cancer therapy.

2.4 Complications: The operation-related complications included biliary-cardiac reflex, biliary tract hemorrhage, bile peritonitis, biliary tree infection induced by the stent via duodenal papilla. These complications could be controlled by homeostasis and anti-infection treatment. In order to reduce the complication, attention should be paid when puncturing blood vessels. Long-term complication was mainly the jaundice caused by the stent re-stenosis. During follow-up period, 87 patients needed to place the second stent due to stent re-stenosis. After the reduction of jaundice, standardized anti-cancer therapy was performed.

3 Discussion
Malignant biliary obstruction refer to the blockage caused by invasion or compression of primary cholangiocarcinoma located at common hepatic duct, common bile duct, the confluence of right and left hepatic ducts or by the surrounding malignant tumor, such as liver cancer, carcinoma of head of pancreas, ampullary carcinoma and metastatic tumor. These patients were at advanced stage. The success rate by surgical resection was only 10.4%. The success rate by using palliative shunt bypass surgery was only 19%. The post-operative mortality rate was 13% [1-2] with high complication rate. Percutaneous transhepatic biliary stent placement could achieve a completely internal biliary drainage. This method created favorable conditions for anti-tumor therapy, which was significantly extending survival time and improving quality of life [3-4].

3.1 The significance of complete internal biliary drainage in enhancing jaundice reduction: Obstructive jaundice may be caused by the obstruction at any part of bile duct due to fact that tumors grew in size and migrated into the bile duct or compressed the duct. The complete internal drainage for the extrahepatic bile duct obstruction could be achieved easily and successfully by using percutaneous stent placement. For 792 patients with malignant biliary obstruction, the stents were placed using conventional methods through the route of right mid-axillary line - right hepatic duct – common bile duct. It completely eliminated jaundice. But for the patients with multiple MBO at porta hepatis, tumor leaded to the obstruction at the region of left and right hepatic ducts, the confluence segment of hepatic ducts and common hepatic duct [5]. The previous interventional treatment advocated only the single stent drainage at bile duct with favorable conditions. However, it may cause the infection of obstructive bile duct at the non-drainage region, incomplete jaundice regression, slow down hepatic function recovery and affect further anti-tumor treatment schedule. Therefore, single stent placement was only applicable for partial drainage of half liver, while multi-stent placement could increase the drainage area and thus the adequate internal biliary drainage could be achieved. It significantly improved the jaundice.
3.2 Improvement and significance of multiple stent placement technique for multiple perihilar biliary obstruction:

3.2.1 Biliary system is in dendritic distribution and malignant tumors may invade bile duct at any level. For the multiple MBO at porta hepatitis, since tumors grow at this anatomical location of porta hepatitis, it is difficult to conduct surgery, which features low resection rate, easy relapse and high mortality. It is a difficult topic and worth to discuss how to achieve full and adequate internal biliary drainage by intervention techniques on complex multiple biliary obstruction.

3.2.2 Among 187 patients with multi-site, multi-segment, perihilar-biliary obstruction, single stent via the route of right hepatic duct – common bile duct and external drainage catheters in left hepatic duct were placed for 12 patients, multi-site external drainage catheters were placed for 2 patients, double stents were placed using three more complex techniques for 126 patients. All achieved the aim of full biliary drainage of several obstructed hepatic ducts. “Single channel and double stents” technique was performed for 7 patients, where drainage pathways of left hepatic duct-right hepatic duct and right hepatic duct-common bile duct, achieving full biliary drainage through left hepatic duct-right hepatic duct-common bile duct. The two stents were in “γ-shaped” configuration, i.e., “single channel and double stents” technique. A feasibility trial of “single channel, double stents” shall be made before the treatment in order to decrease the complications of puncture injury and hemorrhage [3,6]. However, most operations failed were due to the serious obstruction or the acute angle of anatomy was too small. Figure (5-8).

3.2.3 For 37 cases, stents in “Y-shaped” configuration were placed by puncturing the right mid-axillary line and xyphoid, respectively. The obstructive segment was dilated before left and right hepatic ducts connecting to common hepatic duct and the stenosis region of upper common hepatic duct. During stent placement, attention should be paid on the positioning relationship between two stents and tried to release them synchronized. It could avoid the chance of occurrence for the first released stent affecting or oppressing the release and expansion of the second one as the space is limited. The proximal part of left hepatic duct stent should be located in the left hepatic duct. For the three patients with multiple hepatic duct obstruction in right liver, we placed stent between hepatic ducts to facilitate drainage and another stent was then placed between right hepatic duct and common hepatic duct. For the multi-site, multi-segment perihilar-biliary obstruction, three operational techniques were used for the stent placement, i.e., “dual site, dual channel, double stents placement”; “single site, single channel, double stents placement” and “single stent plus external drainage catheter”. Except unsatisfied jaundice regression in six cases due to extensive intra-hepatic metastasis of tumor, full internal biliary drainage were achieved in 90% patients, gaining satisfied jaundice regression and good liver function recovery. Due to the complete internal drainage, biliary infection was well under control, laying good foundation for anti-cancer treatment. Figure (9-10).

3.3 Effects of stent placement combined with anti-tumor therapy on survival time:

In this group, 98% of the patients after placement, the serum total bilirubin decreased from the preoperative average level of 283.4±175.4μmol/l to the postoperative minimal value of 36.3 ~ 267.3μmol / L, mean 63.2 ± 11.8 μmol / L. A complete and full internal biliary drainage was realized after stent placement for MBO. After the jaundice regression and liver function recovery gained, the anti-tumor therapy became the main clinical task. The anti-tumor therapy shall be chosen according to the causes of biliary obstruction. 329 cases with ≥1 year survival time, 187 patients received 3-4 times interventional intra-arterial infusion and embolotherapy. 141 patients were given stereotactic radiation therapy. Survival time of patients received anti-tumor therapy was extended significantly, indicating that anti-tumor therapy after stent placement for MBO has an important clinical significance in improving survival rate.

3.4 Clinical significance of anti-tumor therapy in reducing stent re-obstruction

Although full internal biliary drainage and significant jaundice elimination could be achieved after stent placement for MBO patients, the effect of keeping ducts unblocked over a long period was not achieved. No matter the stent was placed or not, the tumor was still growing rapidly. The metal stent would be blocked by invasive growth or vertical invasion of tumor tissue through mesh [3,7]. In addition, the stent re-obstruction could be caused by hyperplasia of inner membrane of bile duct due to the stimulation of the metal stent. All these became
an important factors affecting long-term efficacy, which still need to be solved by the clinicians. Active and effective anti-tumor therapy could make tumor reduce in size or delay tumor growth, thus reducing the chance of stent re-obstruction and increasing the long-term effects. During follow-up period, 37 patients were placed the second stent due to stent occlusion. After the re-regression of jaundice, standardized anti-cancer therapy was performed. Regular intra-arterial infusion plus embolotherapy were implemented for the tumors with abundant blood supply (indicated by vasography) and intra-arterial infusion plus stereotactic radiotherapy for tumors with insufficient blood supply. No stent stricture and stent occlusion occurred during follow-up. Therefore, stent placement combined with anti-tumor therapy could prevent or delay the tumor growth, reduce stricture and occlusion, which has important clinical significance.
Figure 1: Massive liver cancer at right liver lobe, lipiodol embolotherapy implemented ([1]), obstruction at confluence of left, right and common hepatic ducts ([1]), and obvious atrophy of right liver, left hepatic compensatory increase ([1]).

Figure 2: Two stents were placed in “Y-shaped” configuration by puncturing right mid-axillary line and under the xiphoid, dilating left and right hepatic ducts.

Figure 3: Malignant obstruction was found at the confluence of left, right and common hepatic ducts and at upper common hepatic duct ([1]).

Figure 4: Two stents were placed in “Y-shaped” configuration by puncturing the right mid-axillary line and under the xiphoid.

Figure 5: Malignant obstruction was found at the confluence of left, right and common hepatic ducts; guide wires were accessed left hepatic duct and common bile duct via right hepatic duct.

Figure 6: Adequate biliary drainage of the left hepatic duct - right hepatic duct - common bile duct was achieved by two stents placed at right hepatic duct - left hepatic duct and right hepatic duct - common bile duct in "Y-shaped" configuration, i.e., double stents and single channel technique.
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Figure 7: Left hepatic duct imaging under xyphoid puncture; malignant obstruction at the confluence of left, right and common hepatic duct, multiple obstruction at right hepatic duct.

Figure 8: Adequate biliary drainage of the right hepatic duct - left hepatic duct - common bile duct was achieved by two stents placed at left hepatic duct - right hepatic duct and left hepatic duct-common bile duct in "Y-shaped" configuration, i.e., double stents and single channel technique.

Figure 9: Puncture imaging through the right mid-axillary line and under the xyphoid showed the left, right and common hepatic ducts dilation, including strip shaped filling defects (↑).

Figure 10: The tissues taken by the biopsy forceps for proving to be cancer embolus. Two stents were placed through double ducts expanding respectively the obstructive segments before left and right hepatic ducts connecting to common hepatic duct and the obstructive segment at upper common hepatic duct. These two stents were in "Y-shaped" configuration.
References