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# Progress in the Application of Interventional Technique in Malignant Obstructive Jaundice

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**Abstract:** Malignant obstructive jaundice (MOJ) is usually due to the terminal stages of tumor, so there is no time for curative surgery. Hyperbilirubinemia caused by MOJ can cause damage to systems throughout the body and affect the survival prognosis. Symptomatic treatment is needed even in the advanced stage of the disease. Interventional therapy and surgery are the main means to relieve biliary obstruction, but patients have poor tolerance to surgery at this time, and the risk of surgery is high. At this time, the focus of treatment is to remove the obstruction of the biliary tract as early as possible to avoid the further aggravation of jaundice, progressive deterioration of liver function and other serious complications. Biliary interventional therapy has the special advantage of minimally invasive, and is an effective treatment for patients with advanced MOJ. Currently, bile duct interventional therapy mainly includes bile duct interventional drainage, biliary stent implantation, iodine-125 ($^{125}$I) seed strand implantation, biliary radiofrequency ablation（RFA）and Intraluminal brachytherapy (ILBT), etc. Each of which has its own advantages and disadvantages in clinical application. With the progress of medical technology and the improvement and perfection of hardware equipment, the combination of multiple clinical departments and multiple operation methods will become a new trend of MOJ interventional therapy.

**Keywords:** MOJ, Interventional Therapy, Bile Duct Interventional Drainage, Biliary Stenting

## 1. Introduction

MOJ is caused by malignant tumor invading the intrahepatic and extrahepatic biliary system, that resulting in cholestasis, elevated bilirubin, and jaundice [1]. If the obstruction is not removed in time, it often leads to biliary infection, endotoxin into the blood, damage to multiple systems of the whole body. In severe cases, multiple organ dysfunction or even failure may occur. Common malignant tumors that cause MOJ include pancreatic cancer, cholangiocarcinoma, liver cancer. Gastric cancer that presses on the biliary tract, or lymph node metastasis that press on the biliary system can also lead to MOJ. Due to the occult onset of MOJ, most cases of MOJ were already in the late stage of the disease at the time of diagnosis, and can only be treated by palliative care instead of curative surgical treatment, with poor clinical prognosis. Even in this case, relief of the patient's biliary obstruction is required to relieve jaundice and cholangitis manifestations, or in some cases to prepare for subsequent chemotherapy or radiotherapy. At present, the clinical treatment of advanced MOJ patients mainly adopts interventional methods, including bile duct interventional drainage, biliary stenting, $^{125}$I seed strand implantation, RFA and ILBT therapy, etc. Different studies have differed on the efficacy of different procedures. A recent study showed that in clinical practice, it is recommended to select the treatment plan with multiple operations according to the site of obstruction, the purpose of drainage (as preoperative operation or palliative care) and the experience level of interventional therapy in each treatment center [2]. In such cases, the presence of a multidisciplinary team of surgeons, interventional radiologists, and oncologists is critical [3]. The progress of interventional treatment and combined treatment of malignant obstructive jaundice in recent years were studied.

## 2. Bile Duct Interventional Drainage

### *2.1. Percutaneous Transhepatic Biliary Drainage (PTBD)*

PTBD is an image-guided surgery that can be performed under fluorosc opy or a combination of ultrasound and fluoroscopy. The indications for it are varied, including both obstructive and non-obstructive etiologies. For example: cholangitis, pruritus, pain relief, access to the biliary system for further palliative interventions (such as stenting for cholangiocarcinoma or intrahepatic brachytherapy). Clinical assessment of the need for PTBD therapy in patients with MOJ is based on the location of the obstruction. MOJ of high position is mainly caused by liver metastasis of gallbladder carcinoma, cholangiocarcinoma and other primary tumors, and is mostly suitable for PTBD to treatment. Endoscopic biliary drainage (ENBD) is often used to treat MOJ of low position caused by pancreatic head and neck carcinoma and Vater ampullary carcinoma. Clinical common hilar cholangiocarcinoma often involves the left and right bile ducts. According to Bismuth-Corlette classification, there are four types: type I located below the hilar confluence; type II accumulative hilar confluence; type III extends to one side of the secondary bile duct; type IV extends to bilateral secondary bile ducts. If obstruction of the confluence is involved, at least 1/6 of the bile in the liver parenchymal should be drained by PTBD. At the same time, there should be no atrophy of the target liver lobe or involvement of the portal vein, as liver function does not improve with the release of biliary obstruction even after bile drainage [4].

### *2.2. ENBD and Endoscopic Ultrasonic-Guided Biliary Drainage*

In the clinical work of MOJ, ENBD is carried out more frequently than PTBD due to its advantages of small trauma, rapid recovery and high safety. However, there is no clear data showing that the effect of ENBD is better than that of PTBD. Duan Feng [2] showed that the incidence of cholangitis and pancreatitis after ENBD was higher than that after PTBD. There may be two reasons for the high infection rate after ENBD. First, bile drainage may be incomplete. Especially in patients with severe obstruction, it is difficult to ensure complete drainage of each bile duct. Bacterial growth in cholestasis after incomplete drainage leads to secondary infection. Secondly, ENBD operation sometimes open the duodenal papilla, which destroys the regular structure of the duodenal papilla. Since this structure prevents intestinal bacteria from retrograde entry into the bile or pancreatic ducts, this is the most important route of infection caused by bile drainage. Endoscopic ultrasonic-guided biliary drainage (EUS-BD) has been recently adopted and is rapidly being accepted. This technology is mainly used after the failure of ENBD, and currently it has been used as a first-line option in pilot trials [5]. The accurate visualization of intrahepatic and extrahepatic bile ducts, and the ability to easily access these anatomical structures, opens a new chapter in the field of endoscopic biliary drainage. Although there are no established guidelines for EUS-BD, a literature review conducted by experts suggests that EUS-BD should be considered by an experienced endoscopist when ENBD is not feasible for the common bile duct. EUS-BD can be performed in four ways. The first type is a common bile duct duodenostomy, in which a stent is placed to connect the extrahepatic bile duct to the duodenum. The second type of liver gastrostomy use a stent to connect the liver and intrahepatic catheter to the stomach. The third type is anterograde stenting, in which stents pass through the stomach (intrahepatic biliary access) or duodenal bulb (extrahepatic biliary access) to bypass the bile duct stricture and drain through Vater's ampulpit. The fourth type is a conjunctive pathway, in which the guide wire enters the duodenal papilla through the intrahepatic or extrahepatic bile ducts (through the stomach or the duodenal bulb, respectively). The guide wire can then be used as a way to place the stent [6].

## 3. Biliary Stenting

### *3.1. Biliary Stent Selection*

Biliary stenting, as a non-operative palliative care, also has specific applications. The number and location of stents required during the procedure depends on the degree of biliary obstruction. Type I, II by left hepatic duct into the road to place a single bracket, type III can place double stents via the left and right hepatic duct into the road, type IV due to involve hepatic duct confluence jams, should be placed on both sides stents, stents via the left hepatic duct, hepatic portal vein, posterior lobe of liver is placed into the road, bracket two via right anterior lobe, common bile duct, liver duodenum is placed into the road. Among them, "Y-type" and "T-type" stents can be selected for hilar hepatis due to different angles at the confluence of left and right hepatic ducts [7]. Biliary stents can be plastic or metal, depending on the cause of biliary obstruction (benign or malignant), life expectancy, and affordability. In the case of palliative care, such as unresectable malignant tumors, self-expanding metallic stents (SEMS) with full coverage are more suitable for permanent stent implantation than plastic stents due to their better patencies.

SEMS range from 4-12 cm in length and 6-10 mm in diameter. Allowable delivery systems range from 6.5 Fr to 8.5 Fr. French (Fr) is a unit of measurement for the external diameter of a bile duct stent equal to one-third of a millimeter. The stent placement is completed by the outer protective sleeve, and the protective sleeve is removed after the stent placement, so that the stent can expand naturally. SEMS come in different designs: hook and cross shaped, hand woven, laser cut, etc., and some have recycling rings to aid in repositioning or recycling brackets after placement. The surface of SEMS is coated with coverings, which can make the stent easier to place and remove. Meanwhile, the coated stent can inhibit the growth of tumor and the proliferation of surrounding tissues to a certain extent, and avoid stent blockage, but the disadvantage is that it is prone to displacement and prolapse. Generally, SEMS are more expensive than plastic stents, and therefore, plastic stents are preferred for patients with a life expectancy of less than 4 months. However, despite their high initial cost, SEMS have a statistically significant lower incidence of occlusion, less treatment failure, and thus less need for reintervention, less length of hospital stay, and lower incidence of cholangitis [8]. As a result, SEMS can reduce the use of medical resources and reduce overall medical costs.

Plastic biliary stents vary in length from 1 to 25 cm, but standard models range in length from 5 to 18 cm and in diameter from 3 to 11.5 Fr, with standard outer diameters of 7.0, 8.5, 10.0 and 11.5 Fr. Plastic supports can be straight, curved, wedge-shaped, angled, winged, with a single or double tail fiber (rarely used). While the wedge-shaped brackets have no valves, the other brackets have valves that can be either external or internal, with single, two or four valves to prevent dislocation. The supports are made from polyethylene (most common), polyurethane, a polyethylene/polyurethane mixture, teflon, or a soft polymer mixture. Some types of brackets are made from a perfluorinated inner layer, a stainless steel intermediate layer, and a polyamide elastomer outer layer. The European Society of Gastrointestinal Endoscopy (ESGE) recommends against the use of teflon stents as they are not as flexible as polyethylene stents [6].

### *3.2. Biliary Stent Placement Technique*

Materials required for plastic stent insertion include radiopaque guide wire, stent placement system, and expander. The guide wire has a stiffer shaft and a hydrophilic tip, while a balloon catheter or probe can also dilate the narrow section, making it easier to pass through the narrow biliary duct. The guide wire has an anti-slip mechanism to prevent the guide wire from sliding during replacement. The stenting system allows the catheter to be removed while the guide wire remains in the biliary tract, so the insertion of multiple plastic stents will be feasible. The stent placement system consists of a plastic guide tube (marked with impermeable rays), a stent, and a push-tube. Stent length was assessed on the basis of cholangiography and should be the shortest possible length to allow drainage. One end of the stent should extend 1-2 cm beyond the proximal biliary stenosis and the other end should enter the duodenum 1 cm. If the endoduodenal portion of the stent is longer, perforation or bleeding ulcers may occur. During the operation, flush the guide tube and the support with salt water, and load the support onto the guide tube. The stent placement system introduces the duodenoscope operation channel. After narrowing, the guide tube is disconnected from the push tube and gradually inserted into the bracket. Rotate the instrument and pull the endoscope to more easily insert the stent. Throughout the procedure, the endoscope must be close to the nipple to avoid winding the catheter over the duodenal disc. When the support is in place, pull out the guide wire and guide tube and bring the push tube into contact with the support to prevent dislocation. Finally, the stent position and drainage patency were determined by fluoroscopy [9].

## 4. Research Progress of Double Interventional Therapy

### *4.1. Biliary Stent Combined with $^{125}$ I Seed Chain Implantation*

Occlusion after biliary stent implantation is the most common complication. In recent years, coated stents and drug-eluting stents have become the focus of research on the prevention of restenosis after stent implantation [10, 11]. Coated stents are prone to displacement, which increases the incidence of cholecystitis and pancreatitis. Neither method has achieved satisfactory clinical results. The $^{125}$ I seed is a new type of low dose rate particle source developed in recent years. The effective radiation radius is 15-20 mm, the half-life is 59.43 d, the X-ray energy is 27.4 keV, and the R-ray energy is 35.5 keV. Through continuous illumination result in higher targets within the dose, damage the double-stranded DNA of tumor cells and reduce its proliferation ability, so as to achieve the targeted tumor cells to produce strong killing effect on the surrounding normal tissues did not significantly influence, at the same time can help to reduce support both ends caused by tumor proliferation and granulation tissue hyperplasia problem such as stent occlusion [12]. Wang Huiwen [13] found that extending the coverage of the $^{125}$ I seed chain to both ends of the biliary stent could prevent re-obstruction at both ends. Due to these advantages, $^{125}$ I particle implantation has achieved good results in the treatment of various solid malignancies in recent years [14].

### *4.2. Biliary Stent Combined with RFA*

Currently, PTBD and biliary stents are commonly used in the diagnosis and treatment of the disease, and the novel bipolar RFA is an excellent tool for the treatment of biliary stricture. The use of SEMS is an effective method to treat MOJ. However, SEMS can be occlusivewith tumor overgrowth, tumor growth inwards, epithelial hyperplasia, biofilm deposition and bile sludge formation, and the average biliary stent patentability is about 120 days [15]. Current treatment methods for occluding SEMS include mechanical cleaning and insertion of a second stent through endoscope, which are risky and costly. Clinically, an effective method is needed to reopen biliary stents. RFA has been widely used to treat malignant solid tumors and has even become the standard treatment for some inoperable tumors, such as liver and lung cancer. Its safety and effectiveness are well recognized. Recently, many clinical reports have demonstrated the safety and effectiveness of RFA in endoscopic palliative care [16]. Novel bipolar RFA can delay tumor growth and keep SEMS unobstructed for a long time. In turn, successful drainage can prolong patient survival. Khorsandi [17] performed extensive preclinical in vivo testing of EndoHPB radiofrequent catheter for novel bipolar RFA. Preliminary studies using pig models have shown that the catheter can be safely deployed in SEMS environments. In particular, intra-catheter radio-frequency therapy using such a catheter results in solidified combustion of the tissue within the catheter, but the heat associated with such combustion does not damage the surrounding tissue. In addition, in cases where previously deployed metal stent obstruction cannot be removed, this in-catheter RF approach can remove the obstruction and restore biliary flow without the need to insert a new stent into the blocked stent, thus saving the cost of a second stent. This study demonstrates the potential clinical value of the novel bipolar RFA technique in the treatment of biliary stricture, and demonstrates the efficacy and safety of the bipolar RFA technique in the treatment of MOJ and in-stent restenosis.

### *4.3. Biliary Stent Combined with ILBT*

The role of radiotherapy in the treatment of MOJ has long been a subject of debate. Many published studies have demonstrated that radiotherapy can significantly slow the growth of biliary malignancies and increase patient survival. The effective radiation range of ILBT is 0.5-2 cm, and the rapid radiation at the tumor site minimizes the impact on adjacent normal tissues. At the same time, because the treatment can be completed in a short time, the influence of organ movement on the treatment process can be reduced, and the shortcomings of conventional extracorpical radiotherapy caused by respiratory movement can be avoided. The use of biliary stents has further facilitated the wider application of ILBT in the treatment of MOJ. In the study of Jain [18], 12 inoperable MOJ patients who had undergone PTBD and biliary stent implantation were treated with high-dose intracavity brachytherapy, and the average duration of stent patencies in all patients was observed to be 9.8 months, which was significantly longer than the average duration of biliary stent patencies of 4 months [15]. This suggests that high-dose intramural brachytherapy following PTCD+ biliary stenting in MOJ patients is feasible and highly effective in preventing stent occlusion.

## 5. Conclusion

To sum up, with the progress of medical technology and the improvement and perfection of hardware equipment, the morbidity and mortality of MOJ show a downward trend. However, the long-term prognosis of MOJ remains poor due to the continued progression of the primary tumor. Nevertheless, in the current context, interventional care remains the recommended standard of palliative care for MOJ because it improves quality of life and has a clear immediate survival benefit. New scaffolds that need further research include bioabsorbable scaffolds and magnetic scaffolds. Magnetic stents have been studied and tested in animals, where the stents can be removed using magnets fixed from outside the body, thus avoiding the need for a second ERCP to remove the stents. The downside is that the bracket may move closer. At present, the combination of multiple departments and treatment methods has become a new trend of MOJ treatment. It is believed that with the continuous progress of medical technology, the MOJ treatment system will be more perfect and the quality of life of MOJ patients will be further improved.

## Conflicts of Interest

There are no conflicts of interest.

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