

Research progress on biliary stents

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Highlights

- Plastic stents are more suitable for diseases such as benign bile duct stenosis.
- Metal-uncoated biliary stents are available for patients with malignant biliary obstruction.
- Degradability of biliary stents is a major research direction at present.

Abstract

Bile duct stenosis is a common condition in gastroenterology and hepatobiliary surgery and can be divided into benign stenosis and malignant stenosis according to different etiologies. The implantation of a gall stent into the site of the stenosis or obstruction is currently an important means of treating the bile duct stenosis. Biliary stents encompass two main types: plastic stents and metal stents. In recent years, biodegradable biliary stents and drug-eluting stents have also emerged. The material and structure of biliary stents have an important influence on their performance. In this paper, the research progress on biliary stent implantation technology in the treatment of biliary stenosis is reviewed. Besides, the advantages and disadvantages of biliary stents made from different materials and structures, along with their respective indications are summarized, and the development trend of degradable biliary stents is prospected.

Keywords: Bile duct stenosis, biliary stents, structural design, biodegradable biliary stents

Introduction

The bile system of the human body primarily consists of the gall bladder, the common liver canal, and the common bile duct. The common bile duct is a small tubular structure (average 7.5–11 cm long and 6–8 mm wide) that transports bile stored in the gallbladder to the duodenum [1]. Due to complex clinical pathologies, the lumen of the bile duct may be narrowed or structured, resulting in obstruction of normal bile flow [1]. Bile duct stenosis can be benign or malignant. Biliary stricture, without appropriate clinical intervention, can lead to impaired liver function, secondary biliary cirrhosis, and even death.

Li et al. reported that endoscopic retrograde cholangiopancreatography (ERCP) and percutaneous transhepatic biliary drainage are effective

means for the treatment of biliary stricture and biliary obstruction [2]. ERCP is less aggressive with fewer complications than surgery, so endoscopic therapy is the preferred treatment for benign strictures [3]. In 1979, Soehendra et al. performed endoscopic biliary stenting for the first time using plastic stents (PSs), performing palliative drainage in patients with malignant biliary stenosis [4]. In patients with malignant biliary strictures such as distal or hilar stenosis, less than 20% of patients can undergo radical resection due to local spread and distant metastasis. Among these patients, 70% to 90% have biliary obstruction, resulting in jaundice, cholangitis, pruritus, malabsorption, coagulopathy, and hepatocellular dysfunction [3]. Due to the higher safety profile, ERCP is currently considered the optimal option for palliative care in patients with malignant distal biliary obstruction that cannot be resected or inoperable [5].

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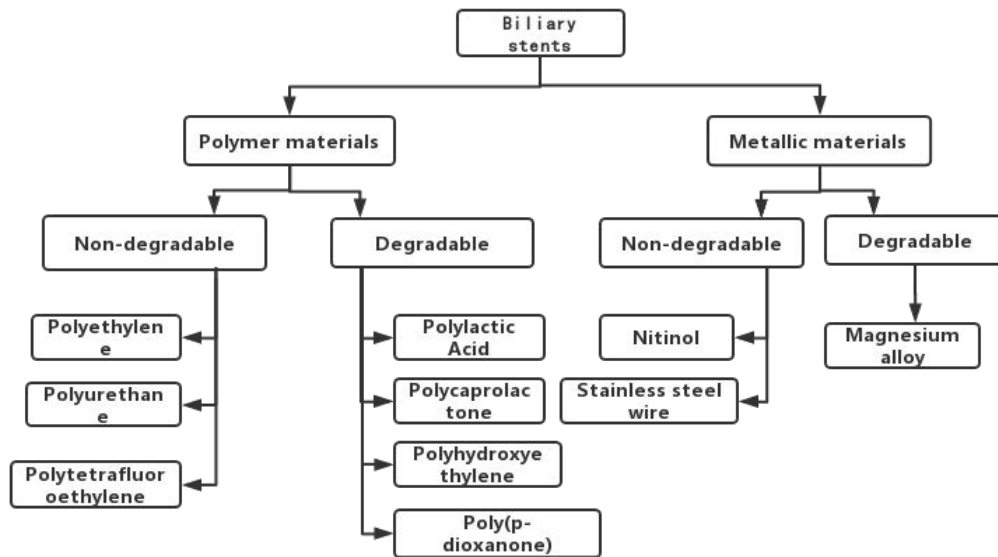


Figure 1. Classification of common biliary stents.

Biliary stents are tubular medical devices. According to the different stent materials, they are categorized into PSs and self-expanding metal stents (SEMSs). The plastic scaffold is mainly composed of polymer materials, including non-degradable polymer and degradable polymer. Metal scaffolds are also composed of non-degradable and degradable metals (Figure 1). Endoscopic stenting is the most commonly used method for the treatment of biliary stenosis, and there are two ways to insert biliary stents through the ERCP route: Endoscopic Retrograde Biliary Drainage and Endoscopic Metal Biliary Endoprosthesis. Of them, the PSs (Figure 2A) inserted through Endoscopic Retrograde Biliary Drainage is much cheaper than the metal stents, but it is prone to frequent occlusion in about three to six months after stenting and needs to be replaced in time. Metal stents (Figure 2B) can be divided into bare metal stents, partially coated stents, and fully coated stents [6, 7]. Bare metal stents should be considered when the expected survival period exceeds 6 months. Due to its large diameter and high resilience, it is often used in cases of malignant biliary stricture.

This article reviews the current progress on biliary stent implantation for the treatment of biliary strictures, compares the stent patency after the implantation of stents made from different materials and structures, and outlines the necessity for re-intervention and the incidence of stent dysfunction. In addition, this review summarizes the advantages and disadvantages

of biliary stents made from different materials and structures, along with their respective indications, and finally prospects the development trend of degradable biliary stents.

PSs

Non-degradable PSs

The first literature on PSs was reported in 1979. Soehendra et al. successfully unobstructed the biliary system through percutaneous transhepatic bile duct implantation of a PS and achieved palliative bile drainage in patients with malignant biliary stenosis [4]. At that time, surgery such as biliary anastomosis was still the primary palliative means of reducing jaundice, while PSs, on the other hand, have a limited patency period and seem to be more suitable for preoperative or temporary internal drainage of benign diseases. Since 1979, researchers have continued to improve the function of plastic biliary stents. The advantages of PSs are low cost and easy to remove [8]. Commonly used non-degradable polymer materials are polyethylene (PE), polyurethane (PU), and polytetrafluoroethylene. Due to the limitation of endoscopic attachment access, the diameter of a stent is usually 3 - 5 mm, and therefore the stents tend to clog 3 to 6 months after placement [1, 6]. According to the characteristics of PSs, they are generally used in patients with malignant obstructive jaundice with an estimated survival of less than 3 months, or for patients with benign bile duct obstruction, who have an expected

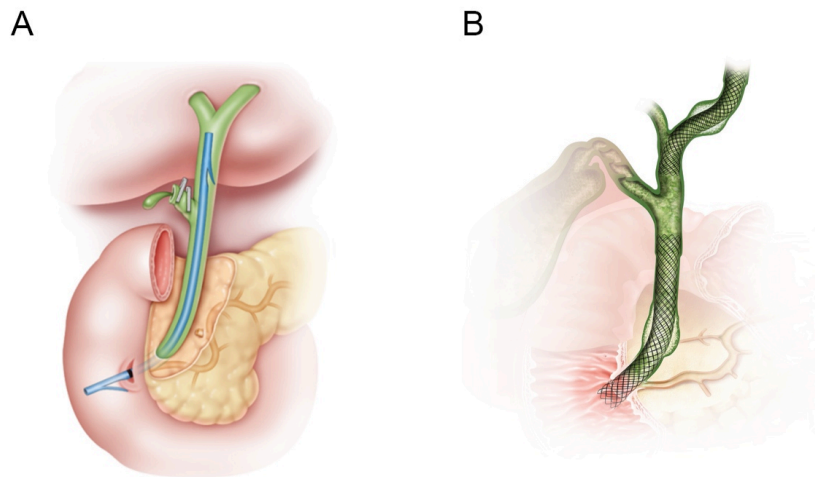


Figure 2. Schematic diagram of insertion of stents in biliary duct. (A) plastic stents; (B) metal stents. This figure is cited from [7].

life of over 3 months, for temporarily drainage along with surgical treatment [9, 10].

In terms of PS structure, depending on the degree of stricture, the length of non-degradable plastic biliary stent is about 5-20 cm and the diameter is about 3-5 mm. Although the PS can be bent, its diameter cannot be changed, so the type of stent needs to be determined according to intraoperative angiography. Notably, due to the limitation of the duodenoscopic channel, the maximum stent can only pass through 14F catheter at present. In 1982, Huibregtse et al. first placed a large-bore (10F) PS endoscopically into the bile duct, and the stent used single or double flaps instead of braids to prevent displacement [11]. Although this bracket has a unique flap design to eliminate the side holes, its performance was still not significantly different from that of traditional brackets. In 1988, Speer et al. demonstrated that the 10F stent had a much greater flow capacity than physiological bile flow due to its large diameter, so it was recommended to use a stent with a diameter of at least 10F to alleviate biliary obstruction caused by malignant tumors [12].

In terms of materials used in PSs, the first material widely used for stents in clinical treatment of biliary stenosis was PE in 1979. PE stents have been shown to have better plasticity and are easier to adapt to the shape of the biliary tract. However, due to the limitation of the diameter, PSs are prone to blockage. Vaishnavi et al. systematically characterized the complex chemical biofilm formed on the surface of the stent and clarified that smaller stent diameter, longer residence time (more than 6 months), and the presence of cholangitis at the time of implantation, could all lead to an increased risk of biofilm formation [13]. Easy displacement is

also a major problem of PSs that needs to be improved. Johanson et al. retrospectively analyzed 322 cases of biliary stenting and found a distal displacement rate of 5.9% and a proximal displacement rate of 4.9% [14]. Cheon et al. compared a new PU rack (Cotton-Leung SOF-Flex bracket; Cook Endoscopy, Winston-Salem, NC, USA) and a standard 10F PE stent (Cook Endoscopy) [15]. The two types of scaffolds were found to have similar structures but different fabrication materials. Their results showed that there was no difference in patency between the two, but the total mobility and distal mobility of the PU rack were significantly lower than those of the PE stent (4.5% versus 29%, $P=0.032$ and 4.5% vs. 26.1%, $P=0.049$, respectively). Overall, PU stents are made of medical-grade PU, which has excellent biocompatibility, is not easy to scab, prevents against both distal and proximal stent migration, and has a smooth surface for easy placement and extraction.

In summary, the affordability of non-degradable PSs makes it widely used in clinical practice, although there are still shortcomings such as short patency time and easy displacement. There are also clinical reports of new non-degradable PSs. Researchers have modified the material to reduce the friction coefficient of the inner surface, improve the anti-bacterial adhesion performance, and increase the diameter of the stent, thereby prolonging the patency time of the PSs and reducing the occurrence of stent displacement.

Biodegradable PSs

Biodegradable biliary stent (BDBS), as a novel type of stent, is safe and effective and does not need to be replaced, with great applica-

Table 1. Comparison of stents made of different polymer materials

Polymer	Degradation time	Advantages	Deficiencies
PLA	About two years	Less bile drains and drains can be removed earlier; Easy deployment; Good immediate self-deployment	The radial support force is much lower than that of the metal stents [23].
PDX	In 3 months	8 mm self-expanding PDX stents with radial force up to 90% of normal metal stents [24]; Better flexibility, slower hydrolysis rate, and longer retention of mechanical properties in bile [25].	Cholangitis is prone to occur after surgery.
PDO	In 3-6 months	Superior flexibility and elasticity; Longer retention of mechanical properties.	Mild cholangitis

Note: PLA, polylactide; PDX/PDO, polydioxanone.



Figure 3. ARCHIMEDES biliary stent. This figure is cited from [21].

tion prospects. At present, the materials used in degradable plastic biliary stents include polylactide (PLA), polycaprolactone (PCL), polydioxanone (PDX or PDO), polyglycolic and their copolymers, etc. Since 2003, Ginsberg et al. reported the first in vivo experiment on BDBS. They successfully implanted PLA stents in the normal bile ducts of pigs without obvious stent complications, and the stents were still unblocked after six months [16]. In 2007, Laukkarinen et al. explored the therapeutic role of BDBS after cholecystectomy in minipigs, showing that compared with PSs, the PLA stent resulted in less bile drainage and earlier drainage tube extubation [17]. In 2010, Petry et al. pioneered the use of biodegradable stents in human bile ducts and successfully placed the PDX stent using percutaneous hepatic puncture cholangiogram in two patients with biliary anastomotic stenosis [18]. Cholangitis occurred after surgery, but no recurrence of stenosis during 2-year follow-up. Mauri et al. reported a study of PDO biodegradable biliary stents in 107 patients in 2013 and 2016, respectively [19]. They concluded that percutaneous placement of biodegradable biliary stents is a viable and safe strategy for the treatment of benign biliary strictures. PDO stents are superior in

flexibility and can degrade within 3-6 months, and they can maintain their mechanical properties longer than most polymers such as PLA [20]. A degradable plastic biliary stent, ARCHIMEDES™ (Figure 3), has obtained Conformité Européenne certification in February 2019, which is a biliary and pancreatic drainage device made of degradable PDX. ARCHIMEDES is available in three different degradation rates to address different indications, offering products in sizes ranging from 2-3.4 mm in diameter and 40-225 mm in length [21]. The stent degrades rapidly within a few weeks of implantation and loses its mechanical strength, but its safety and efficacy still need to be further demonstrated in large-scale clinical trials. PLA typically takes an average of 2 years to fully degrade in the body, but the advantage of absorbable polymers is that the degradation rate can be adjusted to some extent by copolymerizing the appropriate polymer [1]. For example, PLA, polycaprolactone (PCA) and PGA, i.e., synthetic copolymers (lactide-co-glycolide-co-caprolactone)/PLGCL are completely absorbed within six months [22]. **Table 1** compares the degradation rates and advantages and disadvantages of PLA, PDX and PDO. However, at present, there is relatively little research on polycaprolactone stents, which means that there is still a lot of room for exploration in the future.

Metal biliary stents

Non-biodegradable metal stents

At the end of 1980s, SEMSs were introduced, and Nam et al. proved its superior patency than PSs [26]. With the development of minimally invasive technology, interventional therapies tend to be primary palliative treatment for

Table 2. Bismuth classification of hilar cholangiocarcinoma

Type	Feature
1	The tumor is located in the common hepatic duct and does not invade the confluence.
2	The tumor invades the common hepatic duct and the confluence of the left and right hepatic ducts.
3a	The tumor invades the common hepatic duct, the confluence of the left and right hepatic ducts, and the right hepatic duct.
3b	The tumor invades the common hepatic duct, the confluence of the left and right hepatic ducts, and the left hepatic duct.
4	The tumor invades the common hepatic duct, the confluence of the left and right hepatic ducts, and simultaneously invades the left and right hepatic ducts.

malignant bile duct obstruction in the hepatic portal [26]. There are two ways that metal stents unfold in the body: self-expanding and balloon-expanding. SEMSs can be divided into uncoated stents, partially coated stents, and fully coated stents, with metal uncoated stents being the first to be applied in practice, which are not easy to shift, but have the disadvantage of being difficult to take out due to tissue ingrowth. The fully coated metal stents have a non-porous membrane coating designed to reduce occlusion rates and are easy to remove, but with a higher risk of stent displacement [27]. Metal stents are often metal mesh cylinders, designed primarily by laser cutting, and some by knitting or braiding [1]. Metal stents have an inner diameter of up to 8-12 mm and a common length 4-12 cm [28]. When being implanted into the body, the metal stent is completely expanded to its full diameter. Therefore, the patency time of metal brackets is longer than that of PSs, usually 10 months.

With good expansion, better drainage effect, and larger lumen than PSs, metal biliary stents are commonly used in malignant biliary stenosis. Malignant bile duct stenosis is mainly caused by cholangiocarcinoma, periampullary cancer, pancreatic head cancer, tumor metastasis, or lymph node compression of the bile duct. Among the many types of cholangiocarcinoma, there is a unique type - high-lying cholangiocarcinoma (hilar cholangiocarcinoma of the liver). Liang et al. classified hilar cholangiocarcinoma into type 1, 2, 3, and 4 by Bismuth classification method (as shown in **Table 2**), of which type 3 can be divided into type 3a and 3b [29]. Patients with type 1 cholangiocarcinoma should be treated with ERCP for drainage or internal stent therapy, and patients with type 2 should be treated with double stenting.

Wagner et al. noted that in hilar tumors of the liver, metal stents improved patency and reduced the incidence of cholangitis compared to PSs [30]. The study of Chang et al. pointed out that double-branch drainage significantly reduced the occurrence of sepsis, decreased the mortality, and prolonged survival compared

with single-branch drainage [31]. However, due to the difficulty of bilateral stent implantation and high operational technical requirements in clinical practice, it has not been popularized. The Y-shaped metal biliary stent, on the one hand, combines the advantages of metal stent and double branch drainage, and on the other hand is less difficult to implant than previous parallel double stents. Y-shaped metal biliary stent, characterized by a more open wire-woven mesh in the central section to facilitate the placement of the contralateral stent through the central section. Kim et al. retrospectively investigated the technical approach and clinical efficacy of implanting a new self-expanding biliary stent with nitinol material in the treatment of malignant hilar occlusion, which is a transverse stent with Y-shaped structure that combined of spiral stent and Z-shaped stent, called Y-shaped stent (NITI-S biliary Y stent, MI Tech, Heol, Korea) [32].

Bilateral stenting in patients with hilar cholangiocarcinoma requires multiple intubations with many instruments such as catheters, guidewires, dilators, and stents. Firstly, the first stent should be placed on the more curved side of the bile duct for successful access to the contralateral side. Secondly, the newly designed Y-shaped stent has a longer central mesh segment, and the braided part of the main stent is about 10-25 mm, allowing for better placement of the central part of the stent in the hilar bifurcation. The desired catheter can be deflected from the lateral wall of the common hepatic duct or common bile duct to the desired catheter through the middle and distal openings of the three-lumen catheter or the distal guidewire of the rotatable ERCP cannula. Finally, a slimmer open-hole stent can be used as the second scaffold to help the second scaffold pass more easily through the tight central mesh of the first stent. Tex et al. performed Y-shaped metal biliary stenting on 8 patients with hilar cholangiocarcinoma, 4 cases by external cardiopulmonary resuscitation, 3 cases by percutaneous transhepatic cholangio drainage, and 1 case by combining the two, of which 7 cases achieved good treatment results [33]. Kim et al. per-

formed Y-shaped metal biliary stenting on 12 patients with hepatic hilar cholangiocarcinoma, and the success rate of the operation reached 83.3% (10/12) [34]. In China, Y-shaped metal biliary stenting for the treatment of hilar malignant bile duct obstruction started late, and the patient data in the study of Li et al. showed that after Y-shaped metal biliary stent drainage, jaundice subsided rapidly and obviously, and there were no early complications such as cholangitis and bleeding [35].

Mukai et al. showed that uncoated metal stents, with a wire mesh structure, did not block the para-bile duct branches near the liver portal lesion, and the patency was better than that of the PSs [36, 37]. Srinivasan et al. pointed out that after the stent implantation, epithelial hyperplasia embedded in the tissue wall and blocked the stent, making it easier for the tumor to grow inward between the stent reticular filaments and overgrow proximal or distal to the stent as the main mechanism of SEMS obstruction [38, 39]. The inability to change or remove the stent after implantation is a major disadvantage of uncoated metal stents. Studies are underway to overcome these limitations to extend stent patency time. The Bonastent M-Hilar scaffold (Standard Sci Tech, Seoul, Korea) has a mesh structure with a smaller mesh size (1.6 mm * 1.6 mm) in the 25 mm central section, which Kwon et al. noted that could reduce tumor ingrowth [40]. At present, the commonly used materials for metal biliary stents are platinum (platinum core and nitinol sleeve), stainless steel, and nitinol. The study of Park et al. showed that compared with uncoated metal stents, coating silver nanoparticles in nitinol stents and then implanting them into extrahepatic bile ducts in rabbits significantly reduced submucosal fibrosis and inflammation, which can improve silt accumulation and epithelial hyperplasia [41]. But at present, related research is only limited to in vitro experiments and animal experiments. Emerging partial coverage (PCSEMS) and full-coverage self-expanding metal scaffolds (FCSEMS) are covered with a thin polymer membrane that prevents tumor growth inward and is easy to remove [42]. At present, commonly used polymer coating materials include degradable or non-degradable materials such as polytetrafluoroethylene, PU, and silicone. Metal-covered stents are commonly used for malignant hilar biliary obstruction. Naitoh et al. reported a significant advantage of CSEMS, which was their removability during reintervention, they also found that FCSEMS was easier to remove than PCSEMS during reintervention [8]. FCSEMS was easily removed in all re-intervention cases, while PCSEMS could

not be removed in all cases. Kullman et al. proposed and explained that the biggest problem with coated stents compared to non-coated stents is that the covering material can block the opening of the cystic and pancreatic ducts, resulting in cholecystitis and pancreatitis, which in turn can lead to cell epithelial hyperplasia around FCSEMS [43, 44].

In the case of choosing a metal stent, there is still some controversy over whether to choose a coated stent or an uncoated stent. The development of metal-coated stents overcame the problem of luminal stenosis caused by intratumor growth after bare stent implantation. Isayama et al. have confirmed that although covered stents reduce stent occlusion caused by intratumor growth and are relatively easier to replace and remove, they also increase the possibility of stent displacement. In addition, there are cases of re-blockage after implanting covered stents, mainly due to external growth of tumors, bile sludge formation, and stent displacement [45]. The main evaluation indicators of biliary stents include stent patency and patient survival. The results of Almadi et al. showed that there were no differences in stent patency and survival at 6 and 12 months after implantation between patients with the two stents [46]. It was suggested that coated stents had lower occlusion rates than bare stents, and there were no significant differences in survival and adverse events [47]. Therefore, without considering economic factors, Isayama et al. believe that choosing a coated stent is more likely to be beneficial [45].

Drug-eluting stents

At present, the drug-eluting stent is still in its infancy. Chun et al. showed that for malignant biliary obstruction, drug-eluting stents coated with antitumor agents could inhibit tumor ingrowth, thereby improving stent patency [48]. Paclitaxel has shown apoptotic, antiproliferative, and angiogenic activities in a variety of tumor-related chemotherapy. In basic studies, paclitaxel demonstrated dose-dependent inhibition against the proliferation of gallbladder epithelial cells, fibroblasts, and pancreatic cancer cells. In a canine ureteral model, Shin et al. concluded that paclitaxel - eluting stents exhibited inhibitory effects on proliferative tissue [49]. Shi et al. of Xi'an Jiaotong University developed paclitaxel-coated PLA stents and applied it in pig biliary anastomosis model. Their results showed that compared with stent-free and simple BDDBS, paclitaxel-coated BDDBS significantly reduced biliary anastomotic tissue hyperplasia, showing that paclitaxel-coated BDDBS



Figure 4. Unity-B magnesium alloy degradable biliary stent. This figure is cited from [55].

can reduce anastomosis granulation formation and excessive proliferation of extracellular matrix, thereby preventing biliary-intestinal anastomosis stenosis [50]. Lee et al. also showed that after implanting drug-eluting stents in the bile ducts of pigs, only local inflammatory reactions were manifested, and there were no complications such as perforation and necrosis [51]. However, the study using paclitaxel-eluting CSEMS by Song et al. did not show clear advantages in stent patency and patient survival [52]. In the study by Jang et al., they mainly analyzed the effects of drug concentration, stent membrane type, and shape on the effect of stent use [53, 54]. They concluded that the novel paclitaxel-eluting scaffold containing 10% Pluronic F-127 was safe and provided enhanced topical drug delivery.

In drug loading methods using polymer materials as drug carriers, the adverse consequences of limited drug loading, uneven distribution, and increased wall thickness of the stent due to the use of polymer materials have been demonstrated. The maintenance and efficacy of the drug-eluting stents in long term are still not clear, and there are few corresponding studies in this field. By summarizing the relevant studies of drug-eluting vascular stents, it is shown that directly coating the drug on the stent cannot produce obvious anti-restenosis effect due to the “storm effect” released in the early stage. The first problem is that the polymer drug-loaded coating is unfirmly combined with the stent, and the poor adhesion can easily lead to coating falling off, and the drug coating may be damaged when the stent is stretched. The second is whether the biocompatibility of the scaffold can be maintained for a long time. Third, for biodegradable polymer drug-loaded

scaffolds, the degradation rate of scaffolds in the generation of new cells is also a problem that needs to be explored. So, a great deal of work needs to be done in the research and application of drug-eluting scaffolds, but there is no doubt that combining drug elution characteristics with absorbability to have coordination advantages will be a major development direction of biliary stents in the future.

Biodegradable metal stents

Mg, Fe, Zn and their alloys are the most favorable metals in the research of degradable medical implants, including stents. The Unity-B magnesium alloy degradable biliary stent has obtained Conformité Européenne certification in June 2021 (Figure 4) [55]. According to different degradation rates, it is divided into three types: (1) rapid degradation stent (1-3 months), (2) moderate degradation stent (3-6 months), and (3) slow degradation stent (more than 6 months). The stent diameter ranges from 5-10 mm (1 mm apart) and the length ranges from 17-77 mm. The radial retraction of the stent is 2.8-4.1%. This type of stent can be implanted via three routes, namely ERCP, percutaneous intervention, and hepatic, biliary and pancreatic surgical placement. The degradable metal stent avoids secondary surgical removal, greatly reducing the incidence of complications and alleviating the burden on patients.

Conclusion

Since its first clinical application in 1979, biliary stenting has made great progress. Biliary stents have also evolved from the early days of using only PSs without any customization, to patient-specific self-expanding metal and absorbable stents. The cumulative patency of metal stents generally exceeds that of PSs. Although new PSs continue to be introduced, there have been no reports found that the cumulative patency of PSs exceeds that of metal stents, and there is no significant difference in cumulative survival between the two. In terms of the incidence of complications and adverse events, there is no significant difference in the early adverse events between the plastic and metal stents, while PSs are associated with higher late adverse event and total adverse events, and the main differences were reflected in sepsis, cholangitis, obstruction caused by bile sludge and reintervention caused by various causes. The advantages of PSs are low cost, simple operation, and easy removal and replacement in the event of blockage. However, its disadvantages are also obvious, including high incidence of re-obstruction in about 3

months and easy to cause cholangitis. For the above reasons, PSs are more suitable for benign bile duct stenosis, sclerosing cholangitis, and biliary fistula, which can be used after endoscopic dilation, and their cost is much lower than that of metal stents. The advantages of metal stents are long stent patency time and low incidence of re-obstruction, but they are expensive and difficult to remove after implantation. The leading causes of restenosis after bare metal stent implantation include intratumoral growth, cholestasis, and granulation tissue hyperplasia. Management of restenosis after stent implantation include (1) re-implantation of the stent, (2) changing the structure of the scaffold, such as inserting metal-coated stents, drug-eluting stents, double-layer stents, and biodegradable coated stents (still under study), (3) combination therapy, such as combined radiotherapy, combined radiofrequency ablation, combined photodynamic therapy, and combined percutaneous perfusion chemotherapy. Although USEMS metaloid stent implantation has obvious advantages over PSs in terms of surgical safety, long-term patency rate, and total medical cost during survival, its disadvantage is that it is difficult to remove after implantation, and permanent metal stent implantation should be contraindicated for those who cannot identify benign and malignant lesions and who intend to undergo surgery. Where economic permits, fully coated metal stents are also indicated for patients with benign biliary stenosis or whose nature is pending. Moreover, non-degradable PSs and metal stents have a common disadvantage, that is, secondary occlusion when the stent is placed for a long time, so the degradability of biliary stents is a major research direction at present.

Prospect

With the continuous update of biliary stent design and materials, various types of SEMS, such as anti-migration, anti-reflux, drug elution, radioactivity, 3D printed scaffolds, and bioresorbable scaffolds, have been introduced. Although many emerging stents are still in the research stage, it is certain that the performance of stents will be further optimized, and more high-performance and targeted stents will be developed to benefit patients. It is foreseeable that more research on drug-eluting stents and drug-eluting degradable stents will be conducted in the future to play their synergistic advantages, reduce the risk of secondary stenosis, and reduce the cost of coated stents. Besides, we also look forward to the development of 3D and 4D printing micro-size stent technology.

References

- [1] Choudhury S, Asthana S, Homer-Vanniasinkam S, et al. Emerging trends in biliary stents: a materials and manufacturing perspective. *Biomater Sci* 2022;10(14):3716-3729.
- [2] ERCP Group, Chinese Society of Digestive Endoscopy; Biliopancreatic Group, Chinese Association of Gastroenterologist and Hepatologist; National Clinical Research Center for Digestive Diseases. Guidelines for ERCP in China (2018 edition). *Chin J Dige Endoscopy*. 2018;35(11):777-813.
- [3] Davids PH, Tanka AK, Rauws EA, et al. Benign biliary strictures. Surgery or endoscopy? *Ann Surg* 1993;217(3):237-243.
- [4] Soehendra N, Reynders-Frederix V. Palliative biliary duct drainage. A new method for endoscopic introduction of a new drain. *Dtsch Med Wochenschr* 1979;104(6):206-207.
- [5] Cabral JGG, Taglieri E, Pelosof A, et al. Comparative Study between Plastic and Metallic Stents for Biliary Decompression in Patients with Distal Biliary Obstruction. *Gastroenterol Res Pract* 2017;2017:7621821.
- [6] Isayama H, Nakai Y, Kogure H, et al. Biliary self-expandable metallic stent for unresectable malignant distal biliary obstruction: which is better: covered or uncovered? *Dig Endosc* 2013;25 Suppl 2:71-74.
- [7] Boston Scientific. Advanix™ Biliary Stent with NaviFlex™ RX Delivery System. Available at: <https://www.bostonscientific.com/en-US/products/stents--gastrointestinal/advanix-biliary-stent-with-naviflex-rx-delivery-system.html>
- [8] Naitoh I, Inoue T. Optimal endoscopic drainage strategy for unresectable malignant hilar biliary obstruction. *Clin Endosc* 2023;56(2):135-142.
- [9] Sawas T, Al Halabi S, Parsi MA, et al. Self-expandable metal stents versus PSs for malignant biliary obstruction: a meta-analysis. *Gastrointest Endosc* 2015;82(2):256-67.e7.
- [10] Almadi MA, Barkun A, Martel M. Plastic vs. Self-Expandable Metal Stents for Palliation in Malignant Biliary Obstruction: A Series of Meta-Analyses. *Am J Gastroenterol* 2017;112(2):260-273.
- [11] Huibregtse K, Tytgat G. Palliative treatment of obstructive jaundice by transpapillary introduction of large bore bile duct endoprosthesis. *Gut* 1982;23(5):371-375.
- [12] Speer AG, Cotton PB, MacRae KD. Endoscopic management of malignant biliary obstruction: stents of 10 French gauge are preferable to stents of 8 French gauge. *Gastrointest Endosc* 1988;34(5):412-417.

- [13] Vaishnavi C, Samanta J, Kochhar R. Characterization of biofilms in biliary stents and potential factors involved in occlusion. *World J Gastroenterol* 2018;24(1):112-123.
- [14] Johanson JF, Schmalz MJ, Geenen JE. Incidence and risk factors for biliary and pancreatic stent migration. *Gastrointest Endosc* 1992;38(3):341-346.
- [15] Cheon YK, Oh HC, Cho YD, et al. New 10F soft and pliable polyurethane stents decrease the migration rate compared with conventional 10F polyethylene stents in hilar biliary obstruction: results of a pilot study. *Gastrointest Endosc* 2012;75(4):790-797.
- [16] Ginsberg G, Cope C, Shah J, et al. In vivo evaluation of a new bioabsorbable self-expanding biliary stent. *Gastrointest Endosc* 2003;58(5):777-784.
- [17] Laukkanen J, Sand J, Leppiniemi J, et al. A novel technique for hepaticojejunostomy for nondilated bile ducts: a purse-string anastomosis with an intra-anastomotic biodegradable biliary stent. *Am J Surg* 2010;200(1):124-130.
- [18] Petrtýl J, Brůha R, Horák L, et al. Management of benign intrahepatic bile duct strictures: initial experience with polydioxanone biodegradable stents. *Endoscopy* 2010;42 Suppl 2:E89-90.
- [19] Mauri G, Michelozzi C, Melchiorre F, et al. Benign biliary strictures refractory to standard bilioplasty treated using polydioxanone biodegradable biliary stents: retrospective multicentric data analysis on 107 patients. *Eur Radiol* 2016;26(11):4057-4063.
- [20] Siiki A, Rinta-Kiikka I, Sand J, et al. A pilot study of endoscopically inserted biodegradable biliary stents in the treatment of benign biliary strictures and cystic duct leaks. *Gastrointest Endosc* 2018;87(4):1132-1137.
- [21] Medtronic C. ARCHIMEDES™* Biodegradable Biliary and Pancreatic Stent. Available at: <https://www.medtronic.com/covidien/en-gb/products/therapeutic-endoscopy/archimedes-biliary-and-pancreatic-stent.html#>
- [22] Boland EL, Shine R, Kelly N, et al. A Review of Material Degradation Modelling for the Analysis and Design of Bioabsorbable Stents. *Ann Biomed Eng* 2016;44:341-356.
- [23] Ginsberg G, Cope C, Shah J, et al. In vivo evaluation of a new bioabsorbable self-expanding biliary stent. *Gastrointest Endosc* 2003;58(5):777-784.
- [24] Grolich T, Crha M, Novotný L, et al. Self-expandable biodegradable biliary stents in porcine model. *J Surg Res* 2015;193(2):606-612.
- [25] Sabino MA, González S, Marquez L, et al. Study of the hydrolytic degradation of polydioxanone PPDx. *Polym Degrad Stab* 2000;69(2):209-216.
- [26] De Palma GD, Pezzullo A, Rega M, et al. Unilateral placement of metallic stents for malignant hilar obstruction: a prospective study. *Gastrointest Endosc* 2003;58(1):50-53.
- [27] Isayama H, Komatsu Y, Tsujino T, et al. A prospective randomised study of "covered" versus "uncovered" diamond stents for the management of distal malignant biliary obstruction. *Gut* 2004;53(5):729-734.
- [28] Pfau PR, Pleskow DK, Banerjee S, et al. Pancreatic and biliary stents. *Gastrointest Endosc* 2013;77(3):319-327.
- [29] Liang DB, Dai J, Hu BD. Research progress of endoscopic treatment of malignant bile duct stenosis. *J Minimally Invasive Med* 2021;16(02):157-161.
- [30] Wagner HJ, Knyrim K, Vakil N, et al. Plastic endoprotheses versus metal stents in the palliative treatment of malignant hilar biliary obstruction. A prospective and randomized trial. *Endoscopy* 1993;25(3):213-218.
- [31] Chang WH, Kortan P, Haber GB. Outcome in patients with bifurcation tumors who undergo unilateral versus bilateral hepatic duct drainage. *Gastrointest Endosc* 1998;47(5):354-362.
- [32] Kim DU, Kang DH, Kim GH, et al. Bilateral biliary drainage for malignant hilar obstruction using the 'stent-in-stent' method with a Y-stent: efficacy and complications. *Eur J Gastroenterol Hepatol* 2013;25(1):99-106.
- [33] Tex S, Hahn E, Hochberger J. Endoscopic retrograde implantation of Y-configured metal stents in the hilus-an effective drainage for malignant hilar stenosis. *Gastrointest Endosc* 2000;51(4):181.
- [34] Kim JH, Yoo BM, Choi JH, et al. Y-Shaped Endoscopic Bilateral Stenting with New Wider-Mesh Biliary Stent in Malignant Hilar Obstruction: Long-Term Results. *Gastrointest Endosc* 2005;61(5):193.
- [35] Li ZS, Cao J. Y-shaped metal stent drainage in the treatment of malignant bile duct obstruction in the hilar part of the liver. *Chin J Dig Endoscopy* 2006;23(1):2.
- [36] Mukai T, Yasuda I, Nakashima M, et al. Metallic stents are more efficacious than PSs in unresectable malignant hilar biliary strictures: a randomized controlled trial. *J Hepatobiliary Pancreat Sci* 2013;20(2):214-222.
- [37] Sangchan A, Kongkasame W, Pugkhem A, et al. Efficacy of metal and PSs in unresectable complex hilar cholangiocarcinoma: a randomized controlled trial. *Gastrointest Endosc* 2012;76(1):93-99.
- [38] Srinivasan I, Kahaleh M. Biliary stents in the millennium. *Adv Ther* 2011;28(11):960-972.

- [39] Nam HS, Kang DH. Current Status of Biliary Metal Stents. *Clin Endosc* 2016;49(2):124-130.
- [40] Kwon C, Jeong S. Choice of stents for distal biliary obstruction. *Clin Endosc* 2013;46(46):295-302.
- [41] Park W, Kim KY, Kang JM, et al. Metallic stent mesh coated with silver nanoparticles suppresses stent-induced tissue hyperplasia and biliary sludge in the rabbit extrahepatic bile duct. *Pharmaceutics* 2020;12(6):563.
- [42] Hair CD, Sejal DV. Future developments in biliary stenting. *Clin Exp Gastroenterol* 2013;6:91-99.
- [43] Kullman E, Frozanpor F, Söderlund C, et al. Covered versus uncovered self-expandable nitinol stents in the palliative treatment of malignant distal biliary obstruction: results from a randomized, multicenter study. *Gastrointest Endosc* 2010;72(5):915-923.
- [44] Telford JJ, Carr-Locke DL, Baron TH, et al. A randomized trial comparing uncovered and partially covered self-expandable metal stents in the palliation of distal malignant biliary obstruction. *Gastrointest Endosc* 2010;72(5):907-914.
- [45] Isayama H, Nakai Y, Toyokawa Y, et al. Measurement of radial and axial forces of biliary self-expandable metallic stents. *Gastrointest Endosc* 2009;70(1):37-44.
- [46] Almadi MA, Barkun AN, Martel M. No benefit of covered vs uncovered self-expandable metal stents in patients with malignant distal biliary obstruction: a meta-analysis. *Clin Gastroenterol Hepatol* 2013;11(1):27-37.e1.
- [47] Moole H, Bechtold ML, Cashman M, et al. Covered versus uncovered self-expandable metal stents for malignant biliary strictures: A meta-analysis and systematic review. *Indian J Gastroenterol* 2016;35(5):323-330.
- [48] Chun HJ, Kim ES, Hyun JJ, et al. Gastrointestinal and biliary stents. *J Gastroenterol Hepatol* 2010;25(2):234-243.
- [49] Shin JH, Song HY, Choi CG, et al. Tissue hyperplasia: influence of a paclitaxel-eluting covered stent—preliminary study in a canine urethral model. *Radiology* 2005;234(2):438-444.
- [50] Shi J, Lv Y, Yu L, et al. Interest of a new biodegradable stent coated with paclitaxel on anastomotic wound healing after biliary reconstruction. *Eur J Gastroenterol Hepatol* 2013;25(12):1415-1423.
- [51] Lee DK, Kim HS, Kim KS, et al. The effect on porcine bile duct of a metallic stent covered with a paclitaxel-incorporated membrane. *Gastrointest Endosc* 2005;61(2):296-301.
- [52] Song TJ, Lee SS, Yun SC, et al. Paclitaxel-eluting covered metal stents versus covered metal stents for distal malignant biliary obstruction: a prospective comparative pilot study. *Gastrointest Endosc* 2011;73(4):727-733.
- [53] Jang SI, Kim JH, Kim M, et al. Porcine feasibility and safety study of a new paclitaxel-eluting biliary stent with a Pluronic-containing membrane. *Endoscopy* 2012;44(9):825-831.
- [54] Chung MJ, Kim H, Kim KS, et al. Safety evaluation of self-expanding metallic biliary stents eluting gemcitabine in a porcine model. *Journal of Gastroenterology Hepatol.* 2012;27(2):261-267.
- [55] Medical_Device_News M. UNITY-B Percutaneous Balloon Expandable Biodegradable Biliary Stent Receives European CE Mark. Available at: <https://infomeddnews.com/unity-b-percutaneous-balloon-expandable-biodegradable-biliary-stent/>