Management of Occluded Metallic Stents in Malignant Hilar Biliary Stricture

Masakuni Fujii[1], Hirofumi Kawamoto[2], Koichiro Tsutsumi[1], Hironari Kato[1], Ken Hirao[3], Naoko Kurihara[4], Osamu Mizuno[5], Etsuji Ishida[6], Tsuneyoshi Ogawa[3], Hirotoshi Fukatsu[7] and Kazuhide Yamamoto[1]

[1]Department of Gastroenterology and Hepatology, Okayama University Graduate School of Medicine,
Dentistry and Pharmaceutical Sciences, Okayama, Japan

[2]Department of General Internal Medicine 2, Kawasaki Medical School, Okayama, Japan

[3]Department of Internal Medicine, Hiroshima City Hospital, Hiroshima, Japan

[4]Kurashiki Medical Center, Okayama, Japan

[5]Mizuno Medical Clinic, Hyogo, Japan

[6]Department of Gastroenterology, Kurashiki Central Hospital, Okayama, Japan

[7]Department of Internal Medicine, Himeji Red Cross Hospital, Hyogo, Japan

Corresponding author: Masakuni Fujii, MD, Department of Gastroenterology and Hepatology,
Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, 2-5-1,

Abstract

Background/Aims: Little is known about the management of occluded multiple metallic stent (MS) deployed in malignant hilar biliary strictures (HBS). The purpose of this study was to evaluate the endoscopic management of occluded multiple MSs deployed in HBS. **Methodology:** 55 patients with unresectable biliary tract carcinoma had multiple MSs inserted due to HBS. The endoscopic intervention through the duodenal papilla was performed on 30 cases who had MS occlusion. The procedure success rate, the survival time after the procedure, and the number of endoscopic interventions before death were analyzed, retrospectively. **Results:** The causes of MS obstruction were tissue ingrowth (n=20), sludge (n=7), tumor overgrowth (n=2), and hemobilia (n=1). Endoscopic cleaning or deployment of plastic stents or MSs was performed on these patients and was successfully accomplished only via the transpapillary approach. The survival time after MS obstruction was 219 days. The median number of endoscopic interventions before death was 3. The median interval of endoscopic intervention after the first plastic stent occlusion was 84 days. **Conclusions:** Our long-term data regarding the endoscopic management of occluded MSs deployed in malignant hilar biliary strictures are acceptable although the patency time of plastic stents deployed after MS occlusion was relatively short.

KEY WORDS: Malignant hilar biliary stricture; Metallic stent; Obstruction; Management

ABBREVIATION: Metallic stents (MSs); Plastic stents (PSs); Hilar biliary strictures (HBS) Biliary tract carcinoma (BTC)

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INTRODUCTION

Since metallic stents (MSs) provide relatively longer patency time than plastic stents (PSs), they have been widely applied to patients with malignant biliary strictures who are not amenable to surgical treatment (1-6). Although the endoscopic deployment of multiple MSs in malignant hilar biliary strictures (HBS) is technically demanding, recent several articles have reported its satisfactory outcomes (7-13). Apart from the challenges involved in their deployment, the subsequent occlusion of MSs is not rare (3%–39.1%) (8), and its management depends on the case (10). Generally, percutaneous or transpapillary biliary decompression is chosen to ameliorate the morbidities associated with MS occlusion. To provide good outcomes to these patients, the management of occluded MSs is one of the greatest concerns, because insufficient decompression induces a worse prognosis (14). Due to the complicated structures at the confluence constructed with the MS deployed with a partial stent-in-stent procedure, the management of occluded MS would appear to be difficult (11). However, we demonstrated in our previous report that the management of occluded MS was feasible and safe (7), and the negotiation of interstices with hydrophilic guidewire was not as difficult as expected. We usually insert two or more PSs through the MS interstices at the confluence and place the distal end in the intrahepatic ducts. The merit of PSs is that they are exchangeable in the case of PS occlusion. However, the long-term outcomes of this procedure are limited. Furthermore, treatment other than endoscopic PS deployment may be necessary sometimes. In this study, we analyzed our transpapillary management of occluded MS deployed in HBS caused by unresectable biliary tract carcinoma (BTC) and evaluated the merits and drawbacks of this treatment for these patients.

METHODOLOGY

Patients

Between January 2004 and March 2009, we inserted multiple MSs in 55 consecutive patients with unresectable cholangiocarcinoma or gallbladder carcinoma. The patient demographic data are shown in the left column of **Table 1**. The diagnosis was made principally via imaging modalities. Histological or cytological confirmation of malignancy was obtained from all patients. Each patient had 2 or more JOSTENT SelfX units deployed via the endoscopic retrograde route using a partial stent-in-stent procedure. The technique of multiple MS deployment using a partial stent-in-stent procedure has been described elsewhere (7-13). The number of branches achieved after MS deployment depended on the case, but we made 2 or 3 or 4 branches using this technique. Written informed consent was obtained from all patients, and our ethical committee approved the protocol. After successful MS deployment, 42 patients received chemotherapy with either gemcitabine (n=34; 600 –1000 mg/m2/wk, weekly for 3 of every 4 weeks) or S-1 (an oral fluorouracil antitumor drug that combines 3 pharmacologic agents: tegafur, which is a prodrug of 5-fluorouracil; 5-chloro-2,4-dihydroxypyridine,which inhibits dihydropyrimidine dehydrogenase activity; and potassium oxonate, which reduces gastrointestinal toxicity; n=8; 80 mg/body/day, for 2 of every 3 weeks).

Stent occlusion

These patients were observed until August 2010. During this period, 50 patients (90.9 %) died and 30 patients (54.5 %) experienced MS occlusion. These patients' demographic data are shown in the right column of **Table 1**. Stent occlusion was suspected in patients with laboratory parameters that indicated cholestasis, fever, and/or jaundice. The cause of stent occlusion was confirmed with endoscopic examination with IDUS. Usually, the occluded region in the MS lumen showed up as a radiopaque thread or defect with contrast material, where an echogenic soft-tissue density was observed with IDUS. We defined the cause as tissue ingrowth, when the occluded region remained in the same condition as the contrast materials after intraductal movement of the retrieval balloon. On the other hand, when it disappeared after this procedure, the cause was conceived as debris or sludge. In this case, debris or sludge appeared from the duodenal papilla.

Occasionally, the edge of the occlusion exceeded one or both ends of the MS even after the previous motion of the retrieval balloon. In this case, the cause was defined as tissue overgrowth whether the tissue ingrowth was accompanied or not. In addition, most cases with tissue ingrowth or overgrowth accompanied the sludge in the stent lumen. In this study, when the cause of MS occlusion was defined as sludge, the patients had neither tissue ingrowth nor tissue overgrowth.

Endoscopic intervention to occluded MS

For the treatment of a patient with suspected MS occlusion, transpapillary biliary decompression was chosen as an initial therapy. We usually inserted multiple 7-Fr plastic stents (Zimmon-type plastic stent; Wilson-Cook Medical Inc.) into 2, 3 or 4 lobes through the lumen of the previously deployed MS, because the confluence of multiple MSs was involved in all cases. The technique for the deployment of multiple plastic stents through the lumen of an occluded MS is as follows **(Figure 1)** (15). After the repetition of deep cannulation into the common bile duct, 2 guidewires were inserted into the target hepatic ducts. To negotiate the stricture and MS interstices, it is very important to choose an appropriate guidewire. Usually, we employed Revowave (Piolax Medical Devices, Yokohama, Japan), or Radifocus (Terumo, Tokyo, Japan). These guidewires have a flexible and hydrophilic tip with deep angle and excellent torque-conductivity. After the tip of the guidewire reached the target hepatic duct, the guidewire was exchanged for a 0.035-inch THSF (Wilson-Cook Medical Inc, Winston-Salem, NC) with the over-the-wire technique, because we needed stiffness to allow the tip of a plastic stent to pass through the stricture and interstices. In addition, when three plastic stents were inserted into the occluded three-branched MS, three THSFs were not placed at the same time, simply because three THSFs interfere with the movement of the scope and its elevator due to their excessive stiffness. Therefore, we recommend two-guidewire placement at one time. The third guidewire should be inserted into the remaining branch after the deployment of the

first plastic stent. When the cause of MS occlusion was sludge, we removed the sludge with a retrieval balloon catheter (Multi-3V Extraction Balloon, proximal injection type; Olympus). The sludge was removed via the pull-motion of the inflated balloon catheter or washed out via saline injection **(Figure 2)**. When the cause was tumor overgrowth to the papillary end, an additional MS was inserted to the papillary end. In one case, the MS edge at the papillary end made the common bile duct kinked, and sludge was formed in the MS lumen. To accommodate the axis of the MS to the common bile duct, we deployed another MS in the common bile duct with its distal end exposed in the duodenum **(Figure 3)**. When the obstruction was at the intrahepatic end, multiple PSs were deployed.
We evaluated the technical success and clinical success of our procedures. Technical success was defined as the successful deployment of plastic or metallic stents or the opacification of the stent lumen after the removal of sludge. Clinical success implies the discharge of the patient with clinical improvement after the procedures.

Statistical analysis

Statistical analyses of patient data and clinical parameters are shown in terms of median and range. Overall survival time and MS patency time of all patients and patients with MS occlusion, patient's survival after MS obstruction, and PS patency time were analyzed by the Kaplan-Meier method. Survival was defined as the time from MS obstruction to death or the date of last follow-up evaluation. Patency time was defined as the time from the stent deployment to the endoscopic intervention for the treatment of stent occlusion. All analyses were performed with Statistical Analysis System software, version 8 (SAS Institute, Inc., Cary, NC).

RESULTS

The mean patency time of occluded MS was 139 days (range, 21-1590 days). Major findings of MS occlusion were increase of liver and biliary tract enzymes (n=30: 100%), fever (n=24: 79%), and bile duct dilation on medical imaging (n=22: 75%). The causes of MS occlusion and its relation with the endoscopic treatment are shown in **Table 2**. Tissue ingrowth was the main cause of MS occlusion (n=20: 66.7%). To treat the morbidities associated with MS occlusion, stent deployment was the major procedure (83.3%: 25/30). We deployed PS in 21 cases (70%) and MS in 4 cases (13.3%). Multiple PS deployment was performed in 20 patients, whose cause of MS occlusion was tissue ingrowth involving the confluence (n=19) and hemobilia (n=1). One patient had MS occlusion at the confluence. However, due to severe right hepatic atrophy with tumor involvement, one PS was adequate to resolve the jaundice. In three patients, a kink of the common bile duct at the papillary end of the MS caused sludge. Therefore, we corrected the form of the common bile duct with a PS (n=1) or MS (n=2) after the removal of sludge. In the latter cases, the distal end of the MS was placed in the duodenal lumen. In the remaining 2 cases with additional MS deployed, tissue ingrowth or overgrowth existed in the common bile duct. These procedures were successfully accomplished only via the transpapillary route. All patients became outpatients after these technically successful procedures addressing the first event of MS obstruction. The overall survival time after MS obstruction was 219 days **(Figure 4)**. The median number of endoscopic interventions during their survival was 3 (range 1–16; one time, n=6; two to three times, n=14; four or more, n=10). The median interval of the endoscopic intervention after the first PS occlusion was 84 days and its patency curve is shown in **Figure 5**. The correlation between the number of PS exchanges and the median interval of the PS exchange is shown in Table 3. As the number of PS exchanges increased, the interval tended to become shorter, but the difference was not significant (p=0.053).

DISCUSSION

Recent development of effective antitumor drugs, such as gemcitabine, and their combination therapy has contributed to longer survival of patients with BTC (16,17). Therefore, the management of HBS has become more important than ever before for patients with BTC, because inadequate biliary decompression jeopardizes their lives despite the anticipated longer life expectancy. For more than 6 years, we have deployed multiple MSs in cases with unresectable HBS caused by BTC, due to the long patency and acceptable complications of this therapy. Furthermore, we have demonstrated that multiple MS deployment is applicable even to patients who were receiving chemotherapy for this morbidity (7). Recently, several studies regarding the endoscopic management of HBS with deployment of multiple MSs have been conducted (10-13). Some of the studies have mentioned the technical feasibility of the endoscopic procedure after MS occlusion. However, the outcomes of patients with MS occlusion have not been sufficiently evaluated in the literature. In this retrospective study, we analyzed the outcomes of patients with MS occlusion and demonstrated that endoscopic management of the occluded multiple MSs achieved satisfactory technical and clinical outcomes. Furthermore, even after MS occlusion, a long survival was attained with this procedure although frequent endoscopic intervention was mandatory after MS occlusion due to the short patency of the plastic stents deployed.

Several conditions such as tumor invasion to MS, tissue hyperplasia, and sludge jeopardize the MS patency (18). When MS occlusion is suspected in patients with fair condition, we should conduct an appropriate treatment for them to live as long as possible. We usually perform an interventional endoscopic procedure on these patients via the transpapillary route. In this study, tissue ingrowth was the main cause of MS occlusion. Under such conditions, we employed multiple PSs because the site of MS occlusion usually includes the hilar portion. To avoid cholangitis in the undrained segment, we deployed as many PSs as possible. Furthermore, we could repeat this procedure in the case of PS occlusion, because the exchange of the occluded PS was feasible under the endoscopic procedure. It is true that this procedure is somewhat technically demanding, especially in negotiating the interstice at the hilar portion with guidewire and in making the tip of the PS pass through it afterward. However, recent advancements in devices and instruments have enabled us to overcome these technical difficulties. Incidentally, the proximal end of MS deployed in the intrahepatic duct became a guide to advancing the tip of the guidewire. Therefore, if only the MS is placed in the appropriate direction, we can provide favorable management of a patient with HBS even under MS occlusion. Furthermore, although the patency time of PSs deployed under MS occlusion was not particularly satisfactory, we would like to emphasize that all patients became outpatients without external catheterization after the first endoscopic procedure. It has been suggested that multiple PS deployment after MS occlusion is one of the choices for salvaging patients with HBS due to unresectable BTC. Park et al have reported a biliary diversion technique using EUS-guided hepaticogastrostomy for an occluded biliary metal stent after failed ERCP (19). We think this could become another salvage procedure if we fail in the transpapillary approach.

We must admit that there are several limitations to this study: it was retrospective in nature, with a small sample size and conducted in a single center. However, the number of patients with HBS due to BTC is generally small and the follow-up of patients after MS deployment can be difficult, because of the typically advanced age of the patient. Nevertheless, this study was conducted under uniform conditions regarding the type of MS deployed. Furthermore, the number of patients who were followed-up is acceptable. Therefore, our results may become a reference to compare the outcomes of management for patients with HBS due to BTC. However, the results may not be reproducible if the employed MS, PS, or the other devices are different. The MS we employed was an open-cell type, the results of which have not been described in many reports other than our own[7]. Closed-cell type MSs have smaller spaces in their interstices compared with the open-cell type. Overall, our results seemed excellent given the technical difficulties of the procedure. The management of occluded MS of the open-cell type deployed in malignant HBS may be easier than that of the closed-cell type.

In conclusion, our long-term data regarding the endoscopic management of occluded MSs deployed in malignant HBS are acceptable despite the relatively short patency time of PSs deployed after MS occlusion.

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FIGURE LEGENDS

FIGURE 1. A 52-year-old male patient with gallbladder carcinoma had MS occlusion 445 days after 3-branched multiple MS deployment. After the negotiation of the strictures and MS interstices, two guidewires were inserted into the MS lumens of the left hepatic duct and the posterior branch of the right hepatic duct **(A)**. The first PS was deployed in the left hepatic duct and the remaining MS, deployed in the anterior branch of the right lobe, was sought with a guidewire. Then two more PSs were deployed in the other lumens **(B)**.

FIGURE 2. A 68-year-old male patient received MS cleaning with a retrieval balloon **(A)**. After the pull-motion of the retrieval balloon, debris appeared through the duodenal papilla **(B)**.

FIGURE 3. A 60-year-old woman received four-branched multiple MS deployment due to HBS caused by bile duct carcinoma. The stiffness of the papillary end of the MS caused a kink in the bile duct **(A: arrow)**, and sludge was removed by cleaning with a retrieval balloon **(B)**. We inserted another MS into the common bile duct with its distal end exposed in the duodenum **(C)**.

FIGURE 4. Survival after MS occlusion

FIGURE 5. Plastic stent patency

TABLE 1. Demographic data of patients with unresectable biliary tract carcinoma who underwent multiple MS deployment

	All (n=55)	**Patients with MS obstruction (n=30)**
Age, y, mean (range)	69 (52-88)	67 (52-87)
Gender M/F	32/23	20/10
Disease		
Cholangiocarcinoma	42	23
Gallbladder carcinoma	13	7
Bismuth classification		
Ⅱ/Ⅲa/Ⅳ	9/8/38	4/5/21
Treatment		
Gemcitabine/S-1/BSC	34/8/13	18/5/7
Mean patency time (days)	229	139
Median overall survival period (days)	251	460
Follow-up period (days), mean (range)	232 (30-1741)	427 (75-1741)

MS: metallic stent; BSC: best supportive care

TABLE 2. Cause of first MS obstruction, endoscopic treatment, and outcome

Cause	n	Treatment			Outcome	
		PS	Cleaning	MS	Technical success (%)	Clinical success (%)
Ingrowth	20	19	0	1	20 (100)	20 (100)
Sludge	7	0	5	2	7 (100)	7 (100)
Overgrowth	2	1	0	1	2 (100)	2 (100)
Hemobilia	1	1	0	0	1 (100)	1 (100)

TABLE 3. Times and median interval of PS exchange after MS obstruction

The number of PS exchange	n (%)	The median interval of PS exchange (days)
0	6 (24)	
1	4 (16)	108
2	6 (24)	73
3	5 (20)	56
more than 4	4 (16)	46

Fig.1A

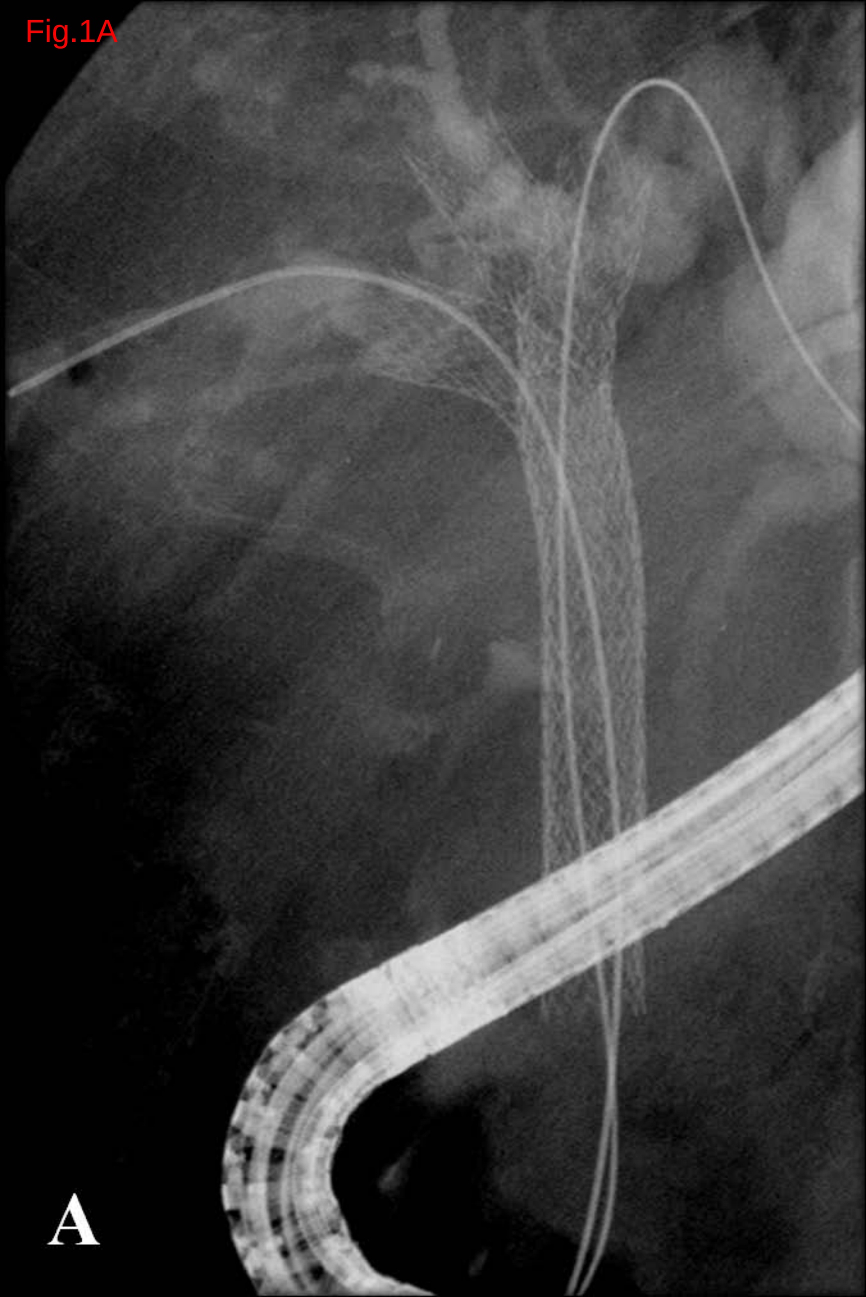


Fig.1B

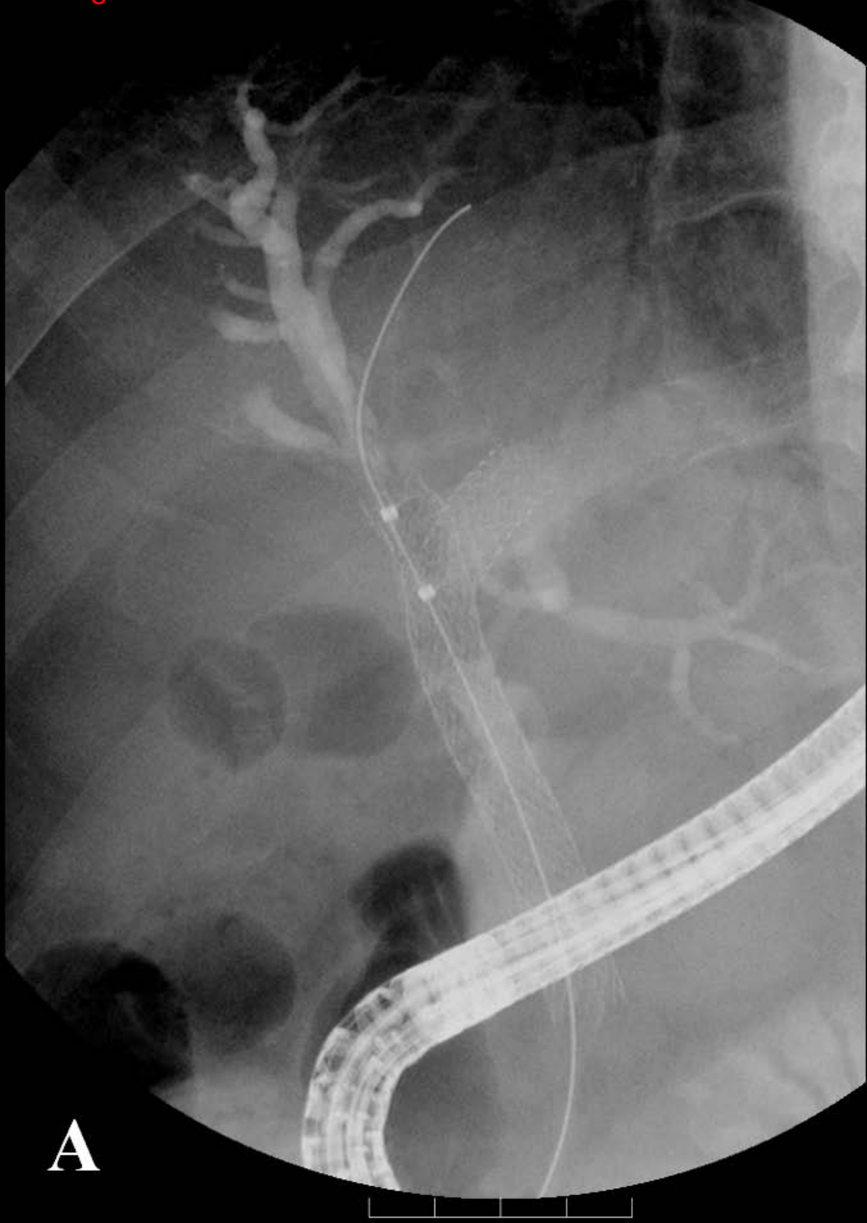


Fig.2A

Fig.2B

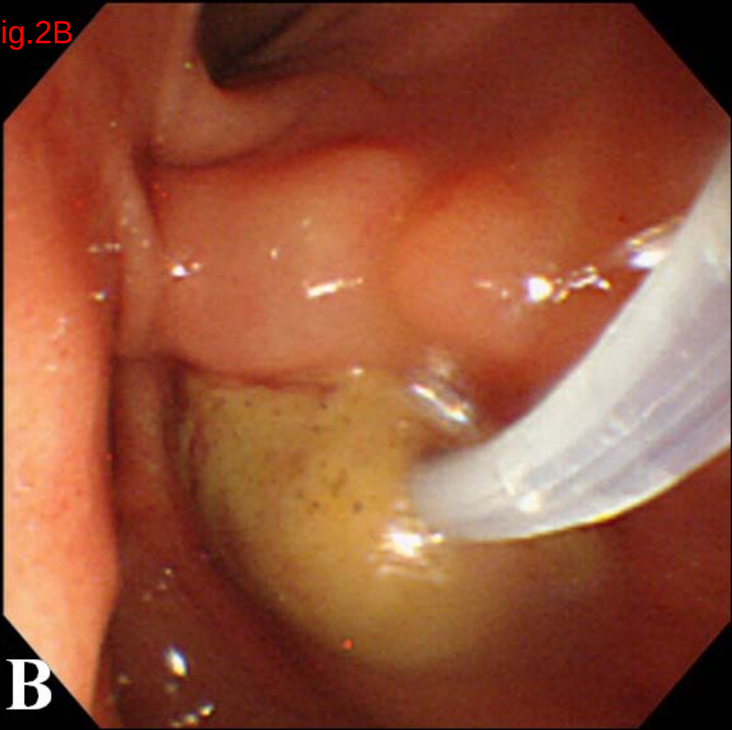
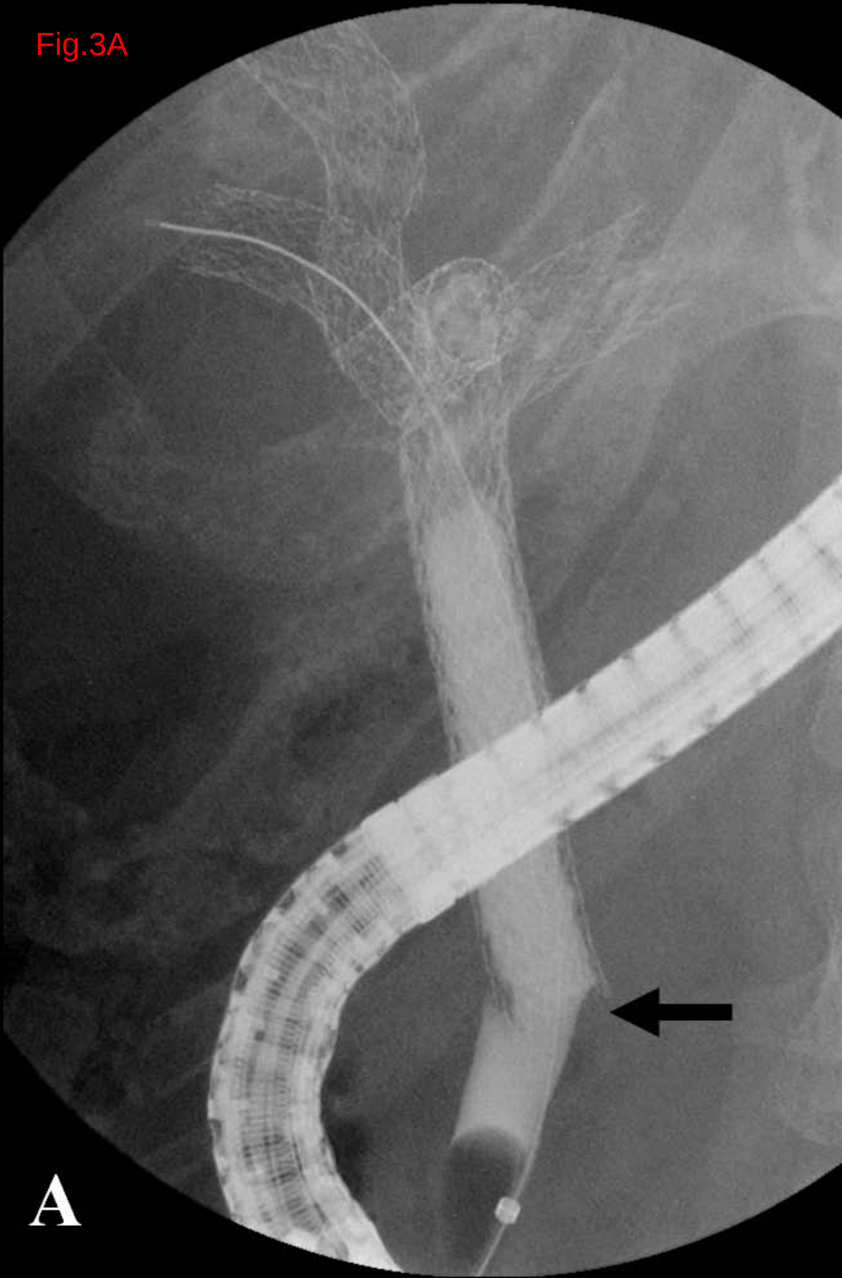


Fig.3A



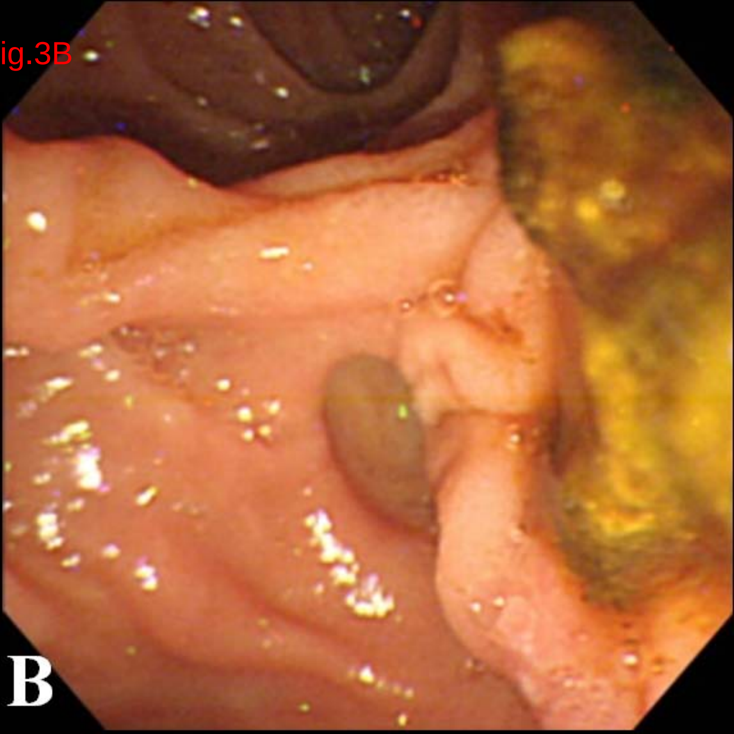


Fig.3B

Fig.3C

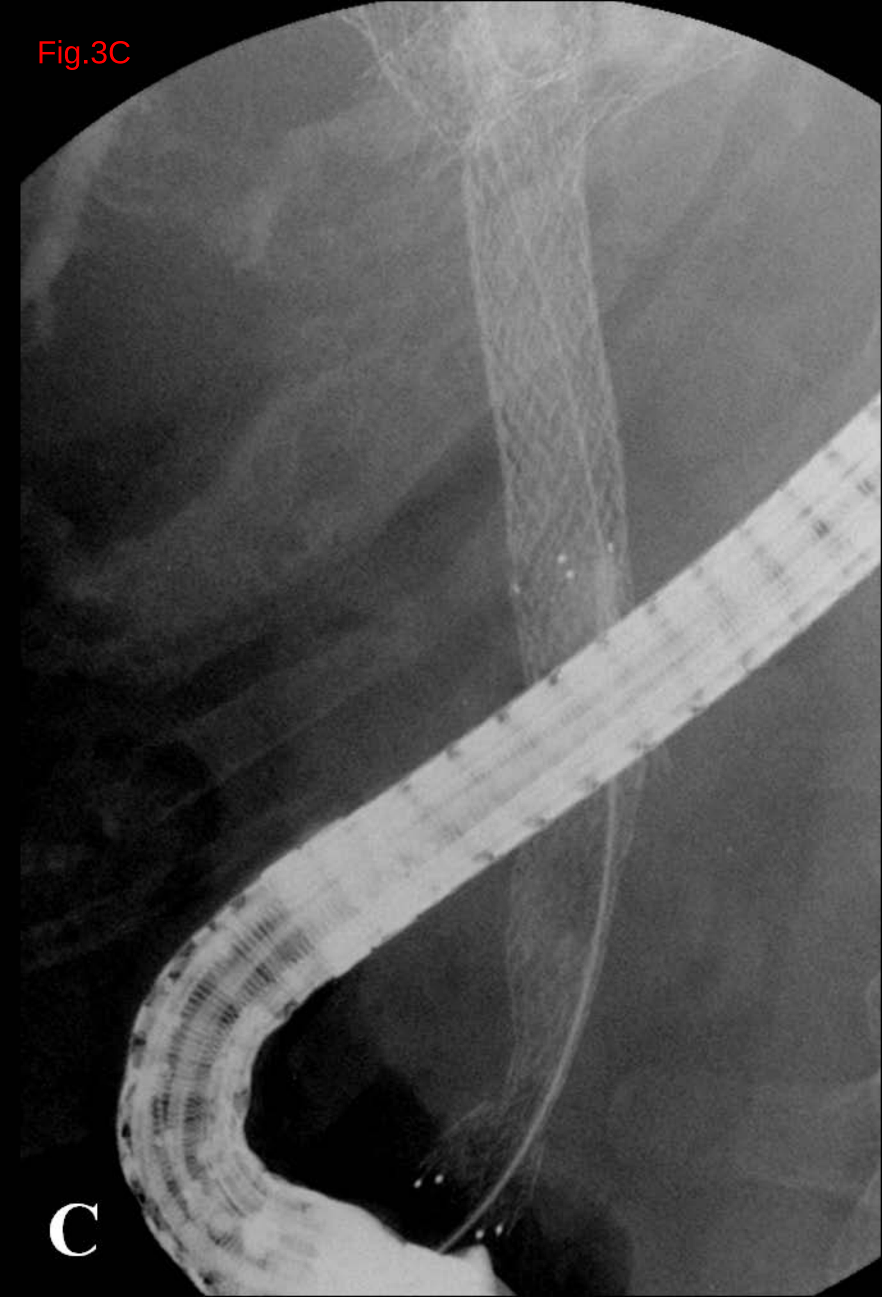
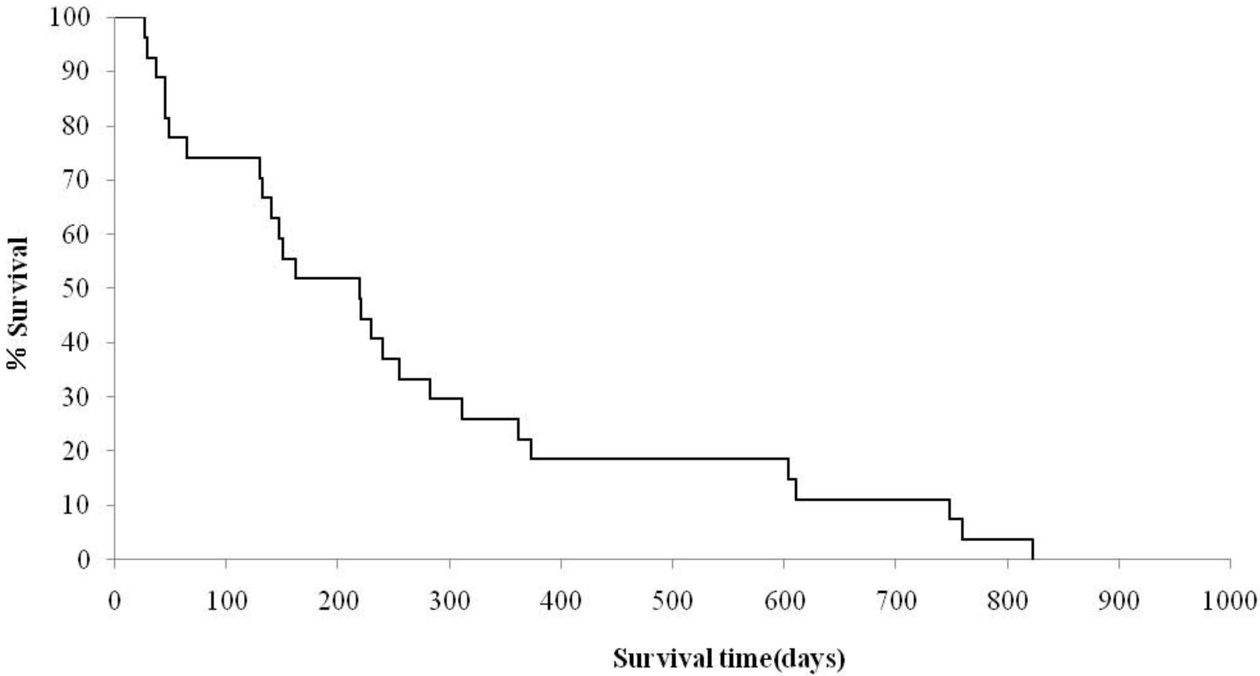


Fig.4


% Survival
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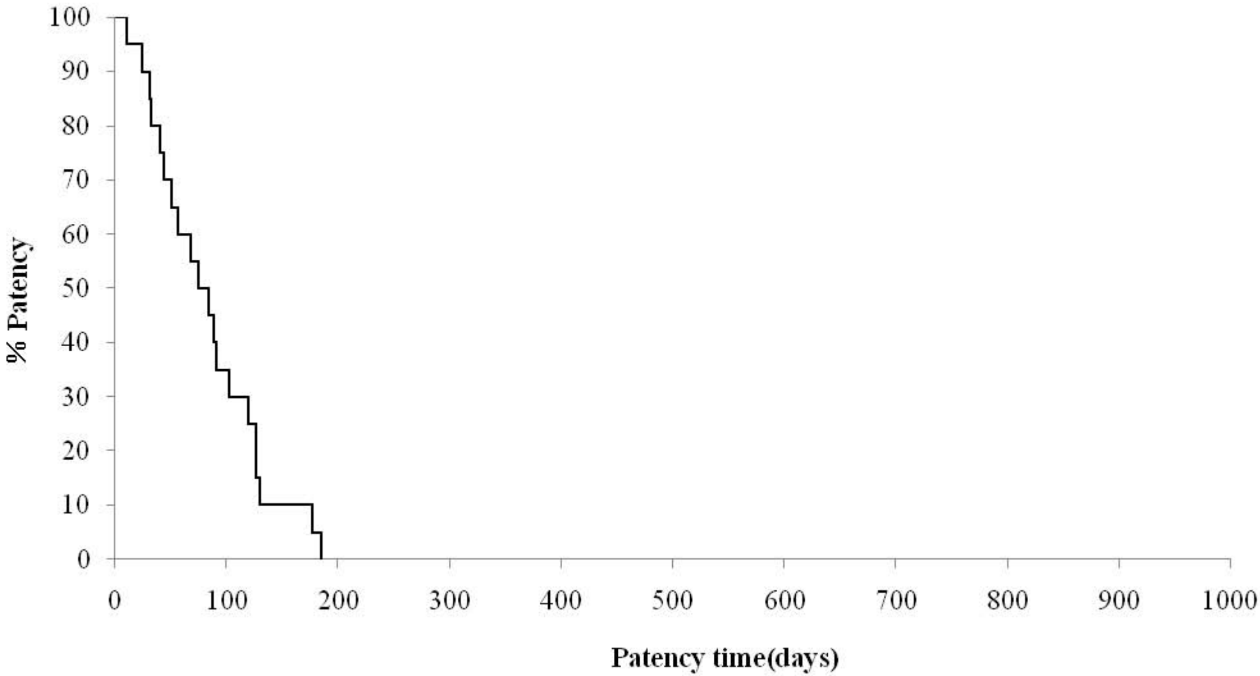
1000
Survival time(days)

Fig.5



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