CLINICAL STUDY

The application and efficacy of stent place for Budd-Chiari syndrome

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ABSTRACT

Objective To evaluate the application value and efficacy on stent place for Budd-Chiari syndrome (BCS).

Methods From January 1990 to May 2017, 2228 patients with BCS were admitted to our institution. The mean age was 43.3 years. Stents were placed in inferior vena cava (IVC), hepatic vein (HV), or both after balloon dilation. During follow-up period, the patency of stent was evaluated by ultrasound regularly and the clinic sign was surveyed by letter, telephone or clinic visit. The restenosis of stent were treated with balloon dilatation and thrombolysis to restore the its function.

Results IVC type was diagnosed in 1492 cases, HV type in 510 cases, and mixed type in 226 cases. Eighteen patients aborted treatment because of economic reasons, advanced liver cancer, severe scoliosis, or both bilateral iliac veins and total IVC occlusion. Among the other 2210 cases who underwent endovascular therapy, stents were implanted into IVC in 339 cases, HV in 97 cases, mixed type in 64 cases. The rate of restenosis in IVC stent was 11.50% (39/339). After repeat angioplasty, the long-term patency rate reached to 98.12%. The incidence of HV occlusion caused by IVC stent was 12.09% (n = 41). Restenosis occurred in 47 cases (48.45%) after HV stent placement. However, the 5-year patency rate was 91.75% (89/97) after repeat dilatation and stent re-implantation. The incidence of IVC obstruction caused by HV was 3.33% (3 cases).

Conclusion IVC stent placement appears to be an effective treatment for the cases of IVC segmental occlusion, and at the same time, the stent has the dual role of compression and fixation of thrombus and support of lumen. The HV and accessory hepatic vein obstruction could happen when the IVC stent crossed these veins ostium. The incidence of the stent restenosis in the HV was higher than that in the IVC.

Keywords: angioplasty, Budd-Chiari syndrome, restenosis, stent.

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INTRODUCTION

Because of widespread application of ultrasound, computed tomography (CT), magnetic resonance image (MRI), and digital subtraction angiography (DSA), Budd-Chiari syndrome is not a rare disease found in China (1). In the past three decades, 2228

patients who come from 31 provinces were admitted to our hospital. These patients underwent interventional therapy and received remarkable outcomes.

Here, we conducted a retrospective study to evaluate the application value and efficacy of the inferior vena cava (IVC) and hepatic vein (HV) stents for BCS.

PATIENTS AND METHODS

From January 1990 to May 2017, 2228 patients with BCS were diagnosed by ultrasound, CT or MR at our institution. Of the patients included in the study, 1237 were male and 991 were female. The mean age was 43.3 years (range 2–79 years). Eighteen patients aborted treatment due to economic reasons, advanced liver cancer, severe scoliosis, or both bilateral iliac veins and IVC occlusion. The other 2210 cases were confirmed by angiography. Of them, 2201 patients underwent percutaneous transluminal angioplasty (PTA) in IVC and/or hepatic vein (HV), while 9 patients underwent transjugular intrahepatic portosystemic stent shunt (TIPS).

Stents were placed in the IVC after balloon dilation. The IVC stent was implanted through femoral vein or jugular vein routine. And the HV stent was implanted only through jugular vein. It was delivered under fluoroscopy and checked with accurate location. This was the key procedure. During follow-up period the patency of stent was evaluated by ultrasound regularly. Once restenosis was confirmed, angioplasty with balloon and thrombolytic therapy were tried to restore the stent function. If the effect of expansion was not acceptable, other stent would be placed again.

According to the data of this study, especially the results of long-term patency and complications of stents, we propose the indications and contraindications of the stent implantation as follow.

Indications for IVC

1. The segment of inferior vena cava occlusion, pressure of IVC-atrium cavity after balloon dilatation > regular;
2. IVC obstruction with attachable thrombus. After thrombolysis it still hinder the blood flow;
3. Repeat restenosis after angioplasty with balloon dilatation for the treatment of membranous and segmental occlusion of IVC;
4. Restenosis after IVC stent implantation which not response to repeat balloon expansion;
5. Thrombus filling within IVC, which has contraindication of thrombolysis and requires stent to oppress and fix thrombus;
6. Rupture of IVC and its communicating branches after balloon dilatation (covered stent).

Indications of HV

1. HV segmental occlusion;
2. Membranous occlusion of HV/accessory HV, the pressure difference of HV-IVC after balloon dilatation > regular;
3. Restenosis after balloon expansion of HV and accessory HV;
4. Repeat restenosis after HV stent implantation.

Contraindications

1. The diameter below IVC membranous was greater than the caliber of stent;
2. Mesh stent and covered stent was forbidden to use if IVC stent should span the HV and accessory HV ostium;
3. “Z” type stent cannot be used when the distance between the proximal IVC membranous occlusion and right atrium was less than 1 cm;
4. Be caution to use binodal “Z” type stent in the IVC membranous occlusion;
5. Be caution to use stent with length greater in the membranous occlusion of HV/accessory HV.

Treatment and follow-up protocol after stent placement

The patients with stent placement were given warfarin orally to anticoagulation for more than 1 year. Patients with IVC attachable thrombus were given warfarin at least for 3 years. Coagulation function was monitored during warfarin taking regularity. Ultrasound was performed every 6 months within 3 years post procedure, then annually. At the same time, complete blood count, liver function, and α-fetoprotein were measured.

RESULTS

According to the classification of Budd-Chiari syndrome identified by the Chinese interventional radiology group, Budd-Chiari syndrome was divided into hepatic vein obstruction type, inferior vena cava obstruction type and mixed type. The number and

Table 1 Incidence of different types (N = 2228).

Type	Cases	%
Hepatic vein obstruction	510	22.89
Inferior vena cava obstruction	1492	66.97
Mixed obstruction	226	10.14
Totality	2228	100

Table 2 Number of placed stent (N = 2210).

Type of obstruction	Cases	Number of placed stent	%
Hepatic vein	497	97+9 (TIPS)	21.33
Inferior vena cava	1487	339	22.79
Mixed	226	64 (48+16*)	28.32
Total	2210	509	100

Note: * The hepatic vein and inferior vena cava were also placed.

Table 3 The complication after stent placement.

Complication	HV stent	IVC stent
Migrate in right atrium		1
IVC stent block the hepatic vein		41
HV stent block the IVC	2	
Fracture (Z type)	2	6

Table 4 The effect of balloon dilation and stent in hepatic vein.

Treatment	Patency	Restenosis	χ^2	*P*
Balloon dilation	262	99	4.945	0.026 > 0.05
Stent	65	41		

Note: There was no statistically significant difference between the two treatment methods. There was no difference in the incidence rate of restenosis.

Table 5 The effect of balloon dilation and stent in inferior vena cava.

Treatment	Patency	Restenosis	χ^2	*P*
Balloon dilation	972	162	1.713	0.191 > 0.05
Stent	300	39		

Note: There was no statistically significant between the two treatment methods. There is no difference in the rate of restenosis.

Table 6 The effect of balloon dilation between hepatic vein and inferior vena cava.

Treatment	Patency	Restenosis	χ^2	*P*
IVC	972	162	32.800	0.000 < 0.01
HV	262	99		

Note: There was the statistically significant between two groups. Restenosis of hepatic vein is more than inferior vena cava.

Table 7 The effect of stent between hepatic vein and inferior vena cava.

Treatment	Patency	Restenosis	χ^2	*P*
IVC	300	39	40.440	0.000 < 0.01
HV	65	41		

Note: There was the statistically significant between two groups. Restenosis of hepatic vein stent is more than inferior vena cava.

Table 8 Compare the time of the stent restenosis in different parts.

Site	Cases	Average months of the restenosis occurs
HV stent	41	23.65±2.60
IVC stent	39	40.54±4.65

percentage of each type are shown in Table 1. In this group, 509 patients were placed with 525 stents in hepatic vein, inferior vena cava or both respectively (see Table 2). The complications of stent implantation can occur in the process of implantation, while more complications are long-term complications which included the IVC stent block the hepatic vein. The HV stent block inferior vena cava and fracture (see Table 3). Our follow-up results showed a higher incidence of restenosis after implantation of the hepatic venous stent, with no statistically difference compared with the long-term patency rate of pure balloon dilatation (see Table 4).

There was no statistically difference between the two treatment methods. There was no difference in the incidence rate of restenosis. The incidence of restenosis after stent implantation was lower than that of pure balloon dilation, but there was no statistical difference (see Table 5). There was no statistically significant between the two treatment methods. There is no difference in the rate of restenosis.

In our patients the long-term patency rate of balloon dilation of inferior vena cava was higher than that of hepatic vein. The incidence of restenosis after hepatic venous balloon dilatation was higher than that of inferior vena cava (see Table 6). There was the statistically significant between two groups. Restenosis of hepatic vein is more than inferior vena cava. Our follow-up results showed that the long-term patency rate of the inferior vena cava was higher than that of the hepatic venous stent, and the restenosis rate of the hepatic venous stent was higher than that of the inferior vena cava (see Table 7). There was the statistically significant between two groups. Restenosis of hepatic vein stent is more than inferior vena cava. We found that the occurrence time of restenosis after stent implantation was different between hepatic vein and inferior vena cava, and the occurrence time of hepatic venous stent restenosis was significantly earlier than that of inferior vena cava (see Table 8).

DISCUSSION

Since 1974, Eguchi et al. had reported the use of percutaneous balloon dilatation for the treatment of inferior vena cava occlusion (2). The interventional therapy for BCS was widely used. In 1990, Furui et al. reported that IVC obstruction was treated with Gianturco expandable metallic stent (3). Behind Fujimoto et al. reported percutaneous place stent in HV in 1991 (4). In China, Wang et al. reported that using stent to treat IVC occlusion in 1993 (5). We placed to treat the patients with HV occlusion, IVC occlusion and IVC occlusion with attachable thrombus from 1994 (6-8). After long-term follow up period of the patients with BCS post stent placement, we found that clinical application of stents has both advantages and disadvantages.

Due to the large differences among the position, extent, number and thrombus of hepatic vein and inferior vena cava obstruction, it is constantly lack experts of results from large groups of cases and consensus whether it was necessary to implant stent after hepatic vein and inferior vena cava balloon dilatation. In the circumstance where minimally invasive treatment is gradually replacing surgery which is huge traumatic and interventional therapy has become the preferred treatment of BCS, we organize a panel of experts from the interventional radiology, pathology, diagnostic radiology, ultrasonic, and vascular surgery departments to define the membrane and segment occlusion of IVC and HV (9), on the basis of results from more than two thousand cases undergoing interventional therapy. We also presented the subtype of the BCS based on imaging manifestations (10). This new subtype classification can further clarify indications, contraindications, prevention of complications, and it can guide the choice of interventional therapy.

The operation of the stent placement is relatively easy However, once stent released, it was unable to take out or adjust. Thus, it is necessary to control the indications strictly and precise localization. The indications for stent implantation included diameter of local lumen after balloon dilatation and transmembrane pressure difference. Therefore, we use the pressure difference of IVC-right atrium or HV-IVC as the preferred index of stent implantation.

In addition, it was reported that the incidence rate of IVC obstruction with thrombus was 10%–12% (11,12). While our patients the rates of thrombosis were 16.96% (253/1492) in the IVC obstruction type and 11.36% (253/2228) in the whole cohort respectively, which were consistent with the literature. However, the incidence of HV occlusion with thrombosis was 8.04% (41/510) in the HV occlusion type and only 1.84% (41/2228) in the whole patients respectively, which were significantly lower than that abroad, (13,14).

The treatment of thrombosis associated with inferior vena cava and hepatic vein obstruction was once a problem. The problem has been solved. Fresh thrombosis can be solved by thrombolysis, while solid and large thrombosis hinders blood flow cab be solved by stent, this moment the stent plays a dual role in supporting the lumen and pressing the thrombus (15).

It was frustrating that not only restenosis occurred after balloon dilation of HV and IVC, but also occurred post stent place, even more disturbing was the recurrence of restenosis up to 7 times in 3 patients who had received a hepatic venous stent. Nevertheless, stent implantation is still necessary in patients with restenosis after two balloon dilations. Stent implantation is a complement and refinement therapy of balloon dilatation, although restenosis might happen after that.

Restenosis is still existing problem after stent placement. Our results show that the time of restenosis in HV was average 23.6 months and in IVC was 40.5 months, The patency time of HV stent was obviously shorter than that IVC stent group.

The stent of IVC and HV play an active role in resolving lumen retraction and maintaining patency after balloon dilatation, but long-term complications such as restenosis, obstruction of adjacent vessels ostium and rupture after place should be highly valued.

Despite the presence of 11.5% restenosis of the inferior vena cava stent, the immediate effect of implanting the stent after segmental occlusion of the inferior vena cava is encouraging. Fortunately, restenosis of the inferior vena cava stent can be resolved by balloon dilation and thrombolysis In this study, 39 cases of inferior vena cava stent restenosis were treated by balloon dilation and thrombolysis in 35 cases, and 4 cases were not successfully treated because of the long stent and the hard thrombus. In total, the over 5 years patency rate of the IVC stent could reach 98.82% in our center.

It is worth noting that the inferior vena cava stent can block the opening of hepatic vein, leading to iatrogenic hepatic vein obstruction. It is difficult to open and open the obstructed hepatic vein through the

inferior vena cava stent, but it can be achieved. However, it is extremely difficult to open the hepatic vein through the mesh vena cava stent. Iatrogenic hepatic vein obstruction was 8.04% in our patients, therefore, we emphasize that the placement of the inferior vena cava stent across the opening of the hepatic vein should be cautious.

Another event of concern is the "anterior jump" of the z-type stent upon release, which is one of the reasons for the stent to enter the right atrium or lower membrane.

Hepatic vein occlusion of interventional therapy is much more difficult than the inferior vena cava. When the obstruction of inferior vena cava from the jugular vein and femoral vein two-way into catheterize to determine the position of the obstruction and length, it is easy to confirm the position of puncture the membrane, however hepatic vein has 2–3 opens, it is difficult to determine the position of the hepatic vein openings under the fluoroscopy. The anatomical structure of hepatic vein is from fine to thick, while the diameters of both ends of the existing stent are equal. The proximal end of the stent meets the requirements of the diameter of the opening of hepatic vein, while the distal end of the stent is over larger than the diameter of blood vessel, the distal expansion of the stent can lead to local endothelial hyperplasia and restenosis.

The study by Xia et al. had turned out that restenosis would occur in the distal of the stent that is straight tubular within three months after delivery into HV of dogs, in contrast, it did not occur after conical type stent (16). In our patients the incidence of restenosis after HV stent implantation was 48.45% (47/97), which was higher than the results from Zhang et al. (17). We thought it depended on the long term follow-up period. Of 509 cases in this study, 301 patients were followed regularly for more than 5 years, some of them were followed over 23 years. In a word, the incidence rate of restenosis of the HV stent was significantly higher than that of the IVC stent.

The preferred treatment for the restenosis of the distal end of HV stent is balloon dilatation, for thrombosis within stent is thrombolysis. However, it's extremely difficult to remove the hard thrombus within stent.

It was rare that HV stent cause IVC obstruction due to overlong in IVC, three cases in our patients were treated with balloon dilatation.

The rupture of proximal part of IVC or HV could lead to death of patient (18,19). In this situation, the effective measure is covered stent implantation. In our patients five patients including four cases of IVC rupture and one case of HV rupture, were rescued by place covered stent. Four cases were alive and one patient died.

Besides, the rare complication also included stent dislocation into right atrium (2 cases) and fracture (8 cases) (20). The fractured stent can move into the right ventricular and the branches of pulmonary artery. If the patients no symptom, closely observation and follow-up could also be taken.

In western countries, the causes of BCS were mainly related to coagulation dysfunction and thrombosis. Anticoagulation, angioplasty and TIPS were preferred (21,22). However, the etiology of BCS in China was unclear. And the pathological changes were membranous, segmental obstruction and secondary thrombosis, so angioplasty with balloon/stent was the first choice in our center, The patients with secondary thrombosis were given balloon dilatation and stent implantation after thrombolytic therapy,

Our clinical practices based on a large group of 2200 cases, showed that the interventional therapy can replace traumatic surgical membrane resection, bypass, and shunt.

In conclusion, interventional therapy has become the first-line treatment of BCS in China (23), of among which stent implantation plays an important role.

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