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Interventional radiologic procedures in liver transplantation

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Abstract Postoperative biliary and vascular complications contribute significantly to morbidity and mortality in liver transplantation. Interventional radiologists are an integral part of the multidisciplinary team necessary for optimizing the management of these complications. During a 15-year period, 39 cadaveric and 25 living related liver transplantations were performed at the Chang Gung Memorial hospital, Taiwan. Of 64 liver transplant recipients, 9 (3 adult and 6 pediatric) underwent 13 interventional radiological procedures for the treatment of biliary sludge-casts ($n = 2$), bile duct occlusion or stenosis ($n = 2$), hepatic veins thrombosis ($n = 1$), hepatic veins stenosis ($n = 1$), portal vein stenosis with splenorenal shunting ($n = 1$), biloma ($n = 1$), and infected fluid collection or ascites ($n = 4$). Antegrade or retrograde interventional approach was used to successfully treat all biliary complications, and all percutaneous drainage procedures were effective in the control of intra-abdominal fluid collections. Portal vein stenosis was treated by balloon dilatation, and the associated splenorenal shunt was closed by metallic coil embolization via transhepatic catheterization of the portal vein. Hepatic vein stenosis was effectively treated by balloon dilatation and expandable metallic stent deployment via transfemoral and jugular venous approaches, respectively. Hepatic vein thrombosis was only partially lysed by transvenous streptokinase administration, and surgical thrombectomy was needed to achieve complete recanalization. The total success rate of the interventional procedures was 92% with no procedure-related complications. The overall survival rate in this series is 89%, and all patients who underwent living related liver transplantation maintain to date a 100% survival rate. We can conclude that interventional radiological procedures are very useful for managing biliary and vascular complications after liver transplantation. These techniques provide a cure in most situations, thus obviating the need for further surgical intervention or re-transplantation.

Keywords Liver transplantation · Postoperative complication · Bile duct · Hepatic vein · Hepatic artery · Portal vein

Introduction

Liver transplantation has become an important option in the management of end-stage liver disease. The combination of recent improvements in operative technique, immunosuppression, and organ utilization has contributed to better posttransplant outcomes. However, biliary and vascular complications are still significant causes of graft failure in liver transplantation, especially in pediatric cases. The incidence of hepatic artery thrombosis has been reported to be 4% in adults and 12% in pediatric cases. In children under 1 year of age, the rate rises up to 30% and is the most common indication for retransplantation in this age group [8, 16, 18]. Reduced-size liver transplants are associated with increased rates of biliary complications, and it has been suggested that most of these complications can be handled non-operatively [1, 11]. Interventional radiologists are an integral part of the multidisciplinary team necessary in the optimization of the management of these complications [1]. In this study we report our experience with posttransplant vascular and biliary complications and their treatment, applying interventional radiological procedures.

Materials and methods

From March 1984 to May 1999, 64 liver transplantations were performed at Chang Gung Memorial Hospital in Taiwan. These 39 cadaveric and 25 living related liver transplantations were carried out in 27 adult and 37 pediatric recipients. The underlying diseases in the adult patients were Wilson's disease ($n = 12$), hepatitis B cirrhosis ($n = 5$), hepatitis C cirrhosis ($n = 4$), hepatoma ($n = 2$), Budd-Chiari syndrome ($n = 1$), choledochal cyst ($n = 1$), autoimmune disease ($n = 1$) and primary biliary cirrhosis ($n = 1$). They underwent cadaveric whole liver transplantation ($n = 26$) and living related liver transplantation ($n = 1$). Among the 37 pediatric recipients, the indications for transplantation were biliary atresia ($n = 33$), glycogen storage disease ($n = 3$) and Wilson's disease ($n = 1$). The liver transplantation procedures performed were; living related ($n = 24$), full-sized cadaveric ($n = 5$), reduced-size ($n = 5$), and split ($n = 3$). All patients with biliary atresia had undergone at least one Kasai operation in their early infancy. A total of 9 (3 adult and 6 pediatric) of the 64 liver transplant recipients underwent 13 interventional radiological procedures for the treatment of biliary sludge cast or stone ($n = 2$), bile duct occlusion or stenosis ($n = 2$), hepatic vein thrombosis ($n = 1$), hepatic vein stenosis ($n = 1$), portal vein narrowing with splenorenal shunting ($n = 1$), biloma ($n = 1$), and infected fluid collection or ascites ($n = 4$).

Results

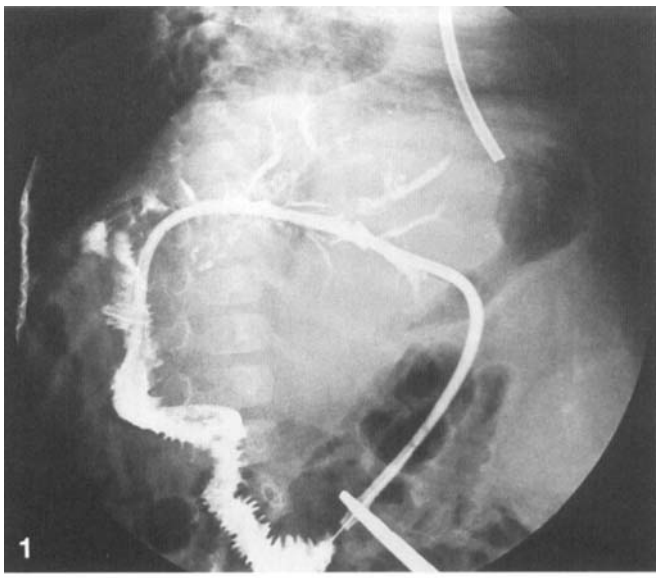
Results per case are summarized in Table 1.

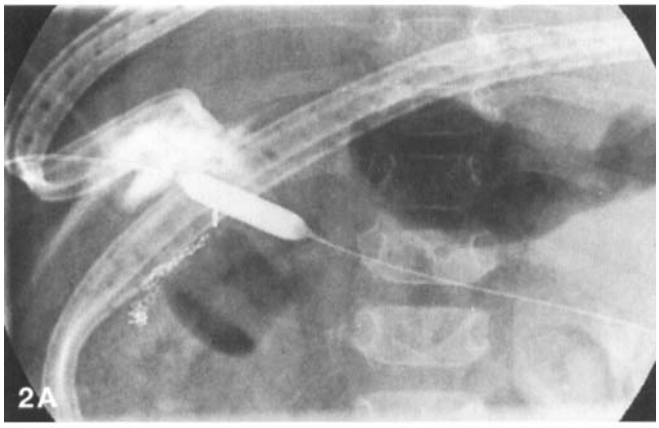
Biliary complications and intra-abdominal fluid collections

All the biliary complications were detected by Doppler ultrasound, while the exact location of the lesions was confirmed by computed tomography and cholangiogra-

Table 1 Interventional procedures in treatment of post-transplantation complications. *LT* Liver transplantation, *LRLT* living related liver transplantation, *OLT* orthotopic liver transplantation, *RSLT* reduced-size liver transplantation, *SLT* split liver transplantation, *M* male, *F* female, *PTBD* percutaneous transhepatic biliary drainage, *y* year, *m* month

No. of patient	Complications	Sex /Age	Indication of LT	Type of LT	Interventional radiologic procedures	Outcome
1	Biliary sludge cast	F/18y	Wilson's	OLT	Extraction of biliary sludge-casts through T tube	Survived 3 years Died of traffic accident
2	Common bile duct stone	F/24y	Wilson's	OLT	Extraction of common bile duct stone through T tube	Alive
3	Multiple biliary stenosis	F/1y2m	Biliary atresia	LRLT	PTBD, dilatation external-internal drainage	Alive
4	1. Bile duct occlusion 2. Biloma	F/1y4m	Biliary atresia	LRLT	1. PTBD, dilatation 2. Percutaneous biloma drainage	Alive
5	Intestinal perforation with infected fluid collection	M/2y5m	Biliary atresia	LRLT	Percutaneous drainage	Alive
6	Intestinal perforation with infected fluid collection	M/2y7m	Biliary atresia	RSLT	Percutaneous drainage	Died of B cell lymphoma
7	1. Hepatic vein thrombosis 2. Intestinal perforation with infected fluid collection	M/3y8m	Biliary atresia	RSLT	1. Thrombolytic therapy 2. Percutaneous drainage	Died of sepsis
8	1. Portal vein narrowing 2. Splenorenal shunt	M/2y11m	Biliary atresia	SLT	1. Portal vein dilatation 2. Metallic coil embolization	Died of multiple organ failure
9	1. Hepatic veins stenosis 2. Massive ascites	M/17y	Wilson's	LRLT	1. Dilatation & metallic stent deployment 2. Percutaneous drainage	Alive





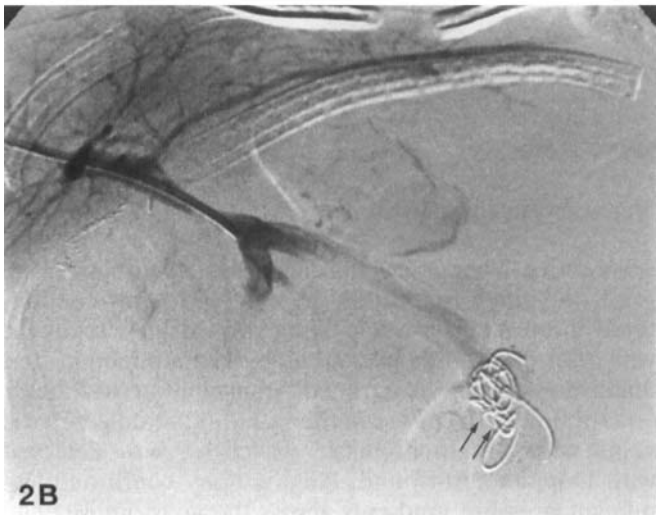


Fig. 1 Multiple intrahepatic biliary strictures were found in a living related liver transplant. An external-internal drainage tube improved her condition and prevented further complication

Fig. 2 A, B Case of portal vein stenosis with splenorenal shunt. **A** Percutaneous transhepatic balloon catheter across the stenosis and inflated to dilate anastomotic strictures of the portal vein. **B** The associated splenorenal shunt was embolized by multiple metallic coils (arrows)

phy. Biliary sludge cast and stone formation were found in our first two transplants, which happened 6 weeks and 4 years after transplantation, respectively. Retrograde extraction of biliary cast and stones through the T-tube tract was successfully performed. Multiple intrahepatic biliary stenoses were found 7 weeks after transplantation in a biliary atresia recipient who presented with an abnormal liver function test and sepsis. Diffuse biliary tree dilatation with multiple stenosis was detected by ultrasound and computed tomography. The septic condition resolved after percutaneous transhepatic biliary drainage, and an external-internal drainage catheter was kept in the graft for 2 years (Figure 1). An isolated segment 2 bile duct dilatation with biloma on the cut edge of the graft was detected 2 weeks after transplantation in a 1.3 year-old living related liver recipient. Percutaneous transhepatic biliary tract and extrahepatic biloma drainage were performed. Subsequent reoperation for anastomosis of the segment 2 bile duct to a Roux-en-Y limb of jejunum confirmed a missed biliary radicle in this case. However, restenosis of the new anastomosis occurred, and further dilatation and stenting of a postoperative stricture through the initial drainage tract were performed successfully. All percutaneous procedures were effective in the drainage of intra-abdominal fluid collections, including infected fluid collection due to intestinal perforation ($n = 3$), and prolonged ascites due to portal vein stenosis ($n = 1$).

Portal vein complications

Portal vein stenosis with splenorenal shunting was found in one pediatric split liver transplant patient presenting with massive ascites and metabolic acidosis 1 month after undergoing transplantation. An inadequate portal flow < 7 ml/min per kg was detected by Doppler ultrasound. Angiography demonstrated portal vein stenosis with splenorenal shunting. Percutaneous transhepatic portography confirmed a significant pressure gradient of 12 mm Hg across the stenosis. A low-profile angioplasty balloon catheter (5-mm balloon) was inserted coaxially across the stenosis and inflated to dilate the anastomotic stricture of the portal vein. After dilatation, the pressure gradient dropped to 2 mm Hg. The associated splenorenal shunt was closed with

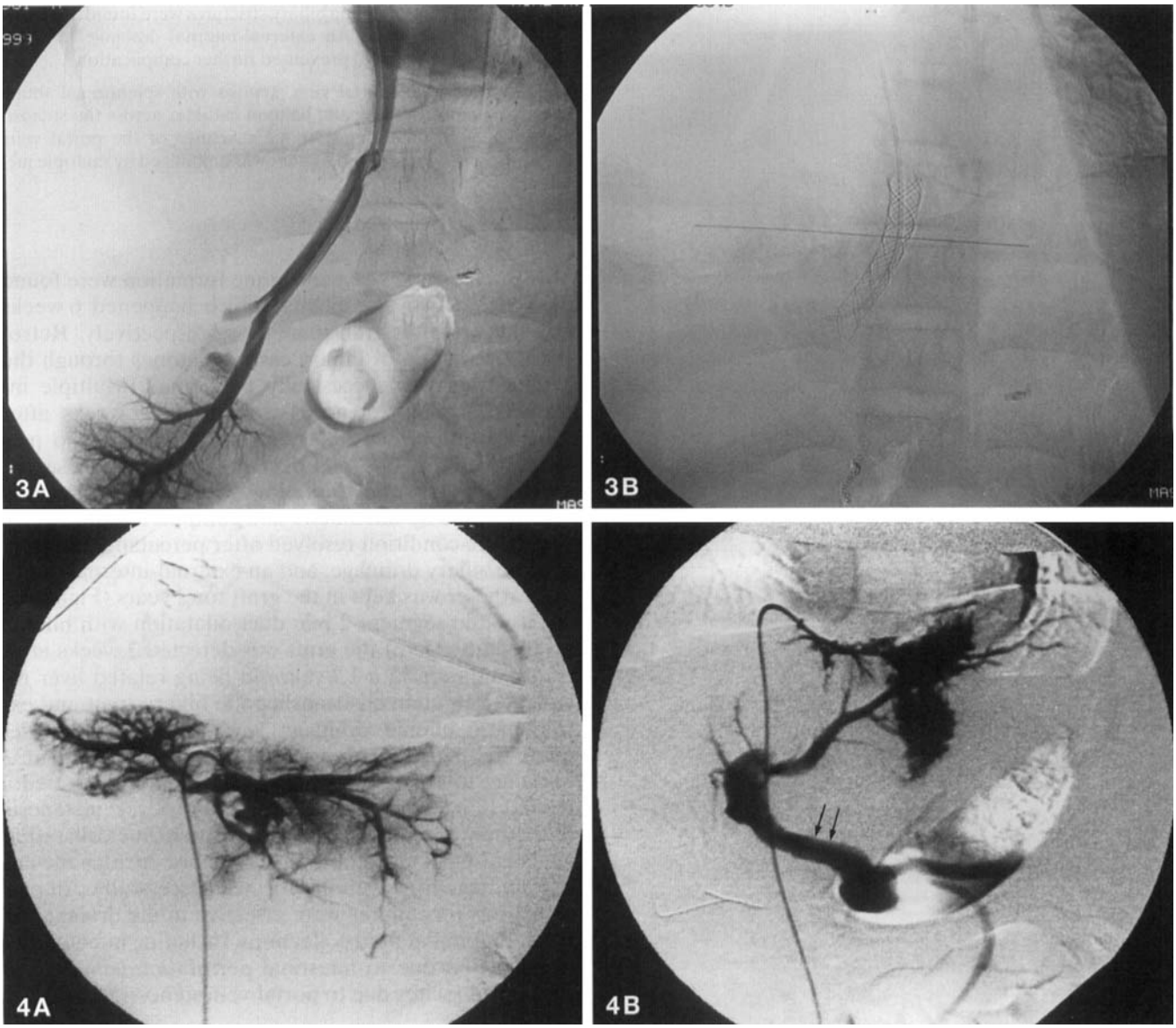


Fig. 3 A, B Case of hepatic vein stenosis. **A** Hepatic venography showed stenosis of the middle hepatic vein. **B** An expandable metallic stent was inserted across the anastomotic site via transjugular approach. Reduction of the venous pressure gradient was obtained

Fig. 4 A, B Case of hepatic vein thrombosis. **A** Hepatic venography demonstrated an extensive venous thrombus in the left and middle hepatic veins with hepatofugal flow (*arrows*). **B** The hepatic vein thrombus was partially lysed by direct intrathrombotic administration of streptokinase

multiple metallic coils (5 × 5mm) (Figure 2A & 2B). At the end of the procedure, the intraparenchymal tract was occluded with gelatin sponge pledgets. Improvement of the metabolic acidosis and ascites were noted after the procedure.

Hepatic vein complications

Stenosis of 2 hepatic veins in an extended right lobe graft (including the middle hepatic vein) was encountered in an adult-to-adult living related liver recipient who presented with persistent hypoalbuminemia and massive ascites in the early posttransplant period. Inadequate flow < 10 cm/sec in the right and middle hepatic veins with flat monophasic waveform was detected with Doppler ultrasound. Angiography confirmed significant pressure gradients across the anastomose. The stenosis of the right hepatic vein was treated with sequential balloon dilatation, resulting in an increase in velocity from 7 cm/s to 16 cm/s and a conversion from monophasic to biphasic waveform. On the other hand, dilatation of the middle hepatic vein led to unsatisfacto-

ry results without any reduction of the pressure gradient. Since the stenosis was most likely due to torsion, deployment of a metallic prosthesis was opted for. An expandable metallic stent was inserted across the anastomotic site via transjugular approach. Reduction of the venous pressure gradient across the stenosis to almost zero and normal Doppler waveform and velocity were achieved. (Figure 3A & B) The ascites gradually decreased and serum albumin normalized. No further dilatation was required.

Intraluminal thrombosis of the left and middle hepatic veins occurred in a pediatric reduced-size livertransplant patient (Figure 4A). Doppler ultrasound revealed absence of blood flow inside the hepatic veins. Transfemoral inferior vena cavography and selective hepatic venography demonstrated complete thrombosis of the left and middle hepatic veins. There was total outflow occlusion with consequent hepatofugal portal flow. The hepatic vein thrombus was only partially lysed by direct intrathrombotic administration of streptokinase (Figure 4B) via an angiocatheter, and surgical thrombectomy was eventually required to achieve complete recanalization.

The overall success rate of the interventional procedures was 92%, and long-term success was achieved in 7 cases. There were no procedure-related complications; 3 patients died of other medical complications. The overall survival rate of liver transplantation in our program is 89%. To date, all living related liver transplant recipients reported herein are alive with functioning grafts.

Discussion

Biliary complications are frequent events in liver transplantation, especially in pediatric cases [11]. Clinical and biological manifestations are often non-specific and usually present as biliary obstruction. Imaging studies are therefore necessary in the diagnosis and management of these complications. The development of biliary tract complications is multifactorial but most often related to vascular, technical or immunologic events [17]. There is a big difference in severity and prognosis between complications secondary to hepatic artery thrombosis and isolated biliary complications [11, 17]. In all our cases, biliary lesions were demonstrated by sonography and computed tomography and confirmed by cholangiography. The complications of biliary sludge and common bile duct stone formation happened in our early experience with the first two liver transplants. Prolonged cold ischemia time with extensive necrosis of the epithelium and subepithelial connective tissue of the biliary tree was thought to be the cause (17). The stones were successfully extracted through the T-tube tract. The other two biliary complications requiring percutaneous drainage were classified as a missed biliary radicle and multiple intrahepatic bile duct strictures of unknown etiology. Missed biliary radicle has seldom been mentioned as a complication of the donor or recipient operation in living related liver transplantation [14]. In our experience, unusual routes of intrahepatic bile duct ramification complicated the surgical procedures in living related graft retrieval and bilio-enteric reconstruction in the recipient [3, 4]. Despite detection of all anatomical variations of the biliary tree by 3-dimensional computed tomographic cholangiography and confirmation by intraoperative cholangiography, a biliary radicle was still missed in this particular case. In the case of multiple biliary strictures, an external-internal drainage relieved the clinical symptoms, but the structural destruction of the intrahepatic bile ducts cannot be repaired, only re-transplantation can provide for a definitive cure. The patient has had the drain for 2 years. It is replaced every 2 months, and the patient simply opens it to a drainage bag whenever she feels abdominal discomfort, thus preventing repeat episodes of overt cholangitis. Since her liver function has remained good with mild enzyme elevation, growth rates are normal, and she performs well at school, retransplantation is not considered necessary at present.

Vascular complications are only second to biliary problems and represent a major cause of morbidity and mortality after liver transplantation, especially in pediatric cases. Hepatic artery thrombosis is the most common and major complication that frequently results in early graft failure, usually necessitating retransplantation [8, 16, 18]. In our series, all hepatic artery anastomoses for both full-sized and partial grafts were done using microsurgical technique since case 18, and no complication occurred [6]. This technical approach has been widely used in living related liver transplantation since it was introduced by Mori and colleagues [10] Complications involving the hepatic vein and portal vein are less common, compared to those arising from the hepatic artery [9]. The routine use of intraoperative Doppler ultrasound has greatly facilitated the early detection of vascular problems that could be remedied in the course of the same operation. We nevertheless encountered some postoperative venous complications in our series, all of them arising from partial liver grafts. Portal vein stenosis with splenorenal shunting occurred in a 2-year-11-month-old boy with biliary atresia who had the predisposing risk factor of portal vein hypoplasia (3-mm in diameter) and insufficient portal inflow with thrombosis that required an intra-operative repair of the anastomosis. Percutaneous transhepatic portal vein angioplasty obviated the need for surgical re-intervention, and metallic coil embolization effectively obliterated the shunt.

Due to the size discrepancy of the portal vein between an adult donor and pediatric recipient, Doppler sonography is often useful in detecting narrowing with turbulent flow at the portal anastomotic site in pediatric

liver transplantation. This is not usually the case with adult-to-adult transplants [12]. Measurement of pressure gradient across the stenosis is a reliable diagnostic tool, but the required angiographic procedure is an invasive one [13]. An alternative way of detecting flow abnormalities is by portal flow volume measurement using Doppler ultrasound. It has been demonstrated that the portal venous size and flow velocity correlated directly with the portal flow volume. In our experience, the mean velocity of the portal flow was 38.63 ± 8.31 cm/s and the portal blood flow volume per body weight was 22.54 ± 8.27 ml/min per kg in non-complicated vascular patients, with 9 ml/min per kg being defined as the lowest limit of acceptable portal flow volume during and after transplantation [5, 15]. In cases where low portal inflow is associated with suspected portal hypertension syndrome, angiographic hemodynamic confirmation or indirect pressure gradient measurement (hepatic wedge and splenic direct pulp pressure) is indicated [13].

Stenosis of the hepatic venous outflow anastomosis is rare [9]. Graft function impairment occurs only in severely compromised conditions. The diagnosis is suggested by low velocity and monophasic Doppler waveform [5] and confirmed by demonstration of a significant pressure gradient across the anastomosis by angiography. Management is usually by balloon dilatation through a transvenous (transjugular or transfemoral) or direct transhepatic approach, which can lead to satisfactory results [7]. Hepatic venous outflow narrowing was detected in an adult-to-adult living related liver transplant in this series. This patient had a complicated anatomy of donor hepatic veins, including double right hepatic veins, double right inferior hepatic veins, and double middle hepatic veins, which required multiple backtable venoplasties and triple venous anastomose. The structural anastomotic stenosis of the right hepatic vein was effectively managed by balloon dilatation, demonstrating a disappearance of the waisting over the balloon catheter after dilatation. However, outflow twisting with resultant narrowing about the middle hepatic venous anastomosis cannot be treated by simple balloon dilatation. The absence of waisting during balloon dilatation signified no fixed stricture point on the anastomotic site. Finally, insertion of an expandable metallic stent reduced the venous pressure gradient across the stenosis to almost zero. It is different from the structural surgical anastomotic stricture in which traditional balloon angioplastic dilatation alone is sufficient [7]. This demonstrated that the actual size of the middle hepatic venous opening was acceptable, but straightening and strengthening of the venous wall around the anastomosis was necessary to maintain an adequate vascular lumen that could sustain a good flow. It proved that vascular stenting using metallic prosthesis is feasible and therapeutic for hepatic venous outflow twisting caused by the improper positioning of corresponding veins during anastomosis. This therapy is useful for selected cases and can save the patient from having to undergo a further operation or retransplantation.

Hepatic venous thrombosis is another dreaded vascular complication often associated with a poor prognosis. Thrombolytic therapy or surgery in an attempt to cure such complication show unsatisfactory results [2]. In our case, the extensive intraluminal thrombus in multiple branches of the hepatic veins were not amenable to multiple catheterization for thrombolysis, and the total hepatic outflow occlusion led to a hepatofugal flow in the liver. Although thrombolytic infusion was administered at the proximal hepatic vein via the venographic catheter, the opposite direction of the hepatic blood flow directed the streptokinase into the portal vein. Insufficient contact between the thrombolytic agent with the thrombus decreased the effectivity of this method of treatment, and surgery had to be resorted to.

With the increasing number of liver transplantations, the number of biliary and vascular complications is likely to increase. Interventional procedures have a significant place in the postoperative management of these cases. Early diagnosis and close monitoring using Doppler ultrasound can lead to early intervention and provide a cure in most situations, thus avoiding further surgical interventions or retransplantation.

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