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REVIEW

From portal to splanchnic venous thrombosis: What surgeons should bear in mind

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Abstract

The present study aims to review the evolution of surgical management of portal (PVT) and splanchnic venous thrombosis (SVT) in the context of liver transplantation over the last 5 decades. PVT is more commonly managed by endovenous thrombectomy, while SVT requires more complex technical expedients. Several surgical techniques have been proposed, such as extensive eversion thrombectomy, anastomosis to collateral veins, reno-portal anastomosis, cavo-portal hemi-transposition, portal arterialization and combined liver-intestinal transplantation. In order to achieve satisfactory outcomes, careful planning of the surgical strategy is mandatory. The excellent results that are obtained nowadays confirm that, even extended, splanchnic thrombosis is no longer an absolute contraindication for liver transplantation. Patients with advanced portal thrombosis may preferentially be referred to specialized centres, in which complex vascular approaches and even multivisceral transplantation are performed.

Key words: Liver transplantation; Portal vein thrombosis; Splanchnic vein thrombosis; Thrombectomy; Vascular graft; Spleno-renal shunt; Cavo-portal hemi-transposition; Portal vein arterialization; Intestinal transplantation; Multi-visceral transplant

Core tip: The present study aims to review the evolution of surgical management of portal and splanchnic venous thrombosis in the context of liver transplantation.

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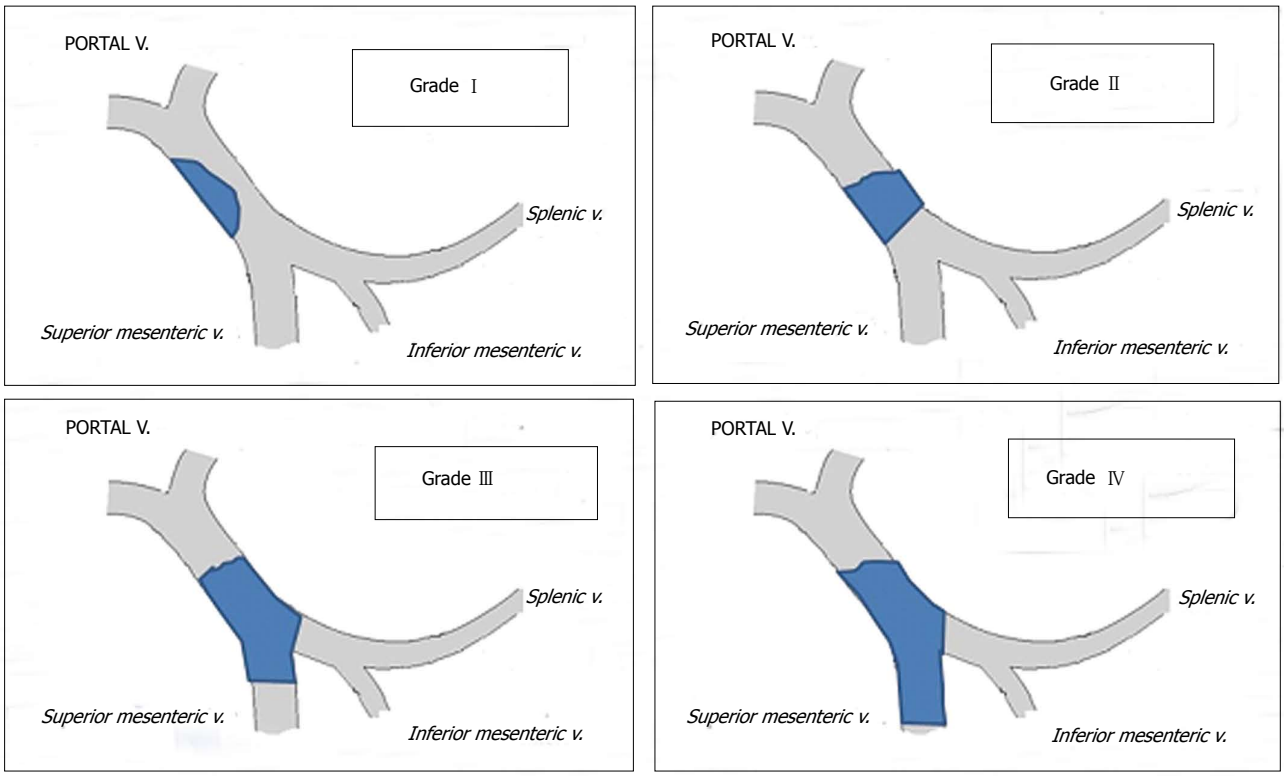
INTRODUCTION

Portal vein thrombosis (PVT) has been described as a multi-factorial condition resulting from the combination of both inherited and acquired factors[1]. Cirrhosis represents the most common etiologic factor, accounting for up to 24%-32% of cases[2]. Other common causes include cancer, infection, inflammation and thrombophilic disorders.

The incidence of PVT also correlates with the severity of cirrhosis[3], thus being a common problem during liver transplantation (LT). PVT usually arises within the liver and extends downwards into the extra-hepatic portion of the portal vein (PV). In some cases the thrombosis further extends to the mesenteric branches resulting in



Venous involvement	Grade 1	Grade 2	Grade 3	Grade 4
PV	< 50%	> 50%	Complete	Complete
"Proximal" SMV	± Minimal	± Minimal	Complete	Complete
"Distal" SMV	None	None	None	Complete

Figure 1 Portal vein thrombosis classification according to Yerdel *et al*[3]. PV: Portal vein; SMV: Superior mesenteric vein.

a splanchnic venous thrombosis (SVT).

Until the late 1980's, PVT and SVT were considered contra-indications for LT due to concerns about compromised portal allograft inflow.

The first successful LT in a patient with PVT was reported by the Pittsburgh group in 1985 using a free iliac vein allograft[4]. Two years later, the same group presented the first large series of LT in patients with PVT (n = 22), representing a landmark paper in this field[5]. Since that seminal experience, several new techniques have been proposed to overcome this problem. The present study reviews the surgical evolution in this field of LT over the last five decades.

DIAGNOSIS AND CLASSIFICATION

Despite progress in preoperative and cross-sectional imaging, a substantial number of cases of PVT or SVT are still discovered at the time of LT[6,7]. Doppler-ultrasound examination remains the most common initial diagnostic tool. However, it has limitations in detecting thrombosis due to (spontaneous or medical) recanalization and because of thrombus extension to the mesenteric veins, which cannot always be visualised clearly. Therefore, computed tomography and magnetic resonance angiography have an important role in diagnosing this condition[8]. The presence of arterial enhancement in contrast-enhanced ultrasound may help differentiate between malignant and benign thromboses[9].

The sensitivity in detecting complete venous thrombosis ranges from 92% to 100%, decreasing to 14%-50% in partial thrombosis[10]. The preoperative identification of PVT enables surgical planning and the exclusion of patients with malignant thrombosis from listing for LT. Several classifications have been proposed so far; the Yerdel classification gained the greatest acceptance and widespread clinical application[3] (Figure 1). Grade I and II PVT can almost always be managed by portal vein resection with or without thrombectomy; grade III and IV PVT require a more complex technique (Figure 2).

Management of grade I-II PVT

The initial strategy for grades I-II PVT is the removal of the thrombus. This is best done by removing it together with the innermost layer of the vessel (thromboendovenectomy)[3]. If the thrombosis involves a short segment of the PV, this can be resected; the residual part of the thrombus can also be fixed to the vessel wall[3]. The thrombus is separated from the PV wall using an endarterectomy spatula and the thrombus is freed under direct vision whilst everting the vessel wall[11-13]. Thrombi extending up to the mesenteric vein can be extracted successfully with this technique. Blind extraction using

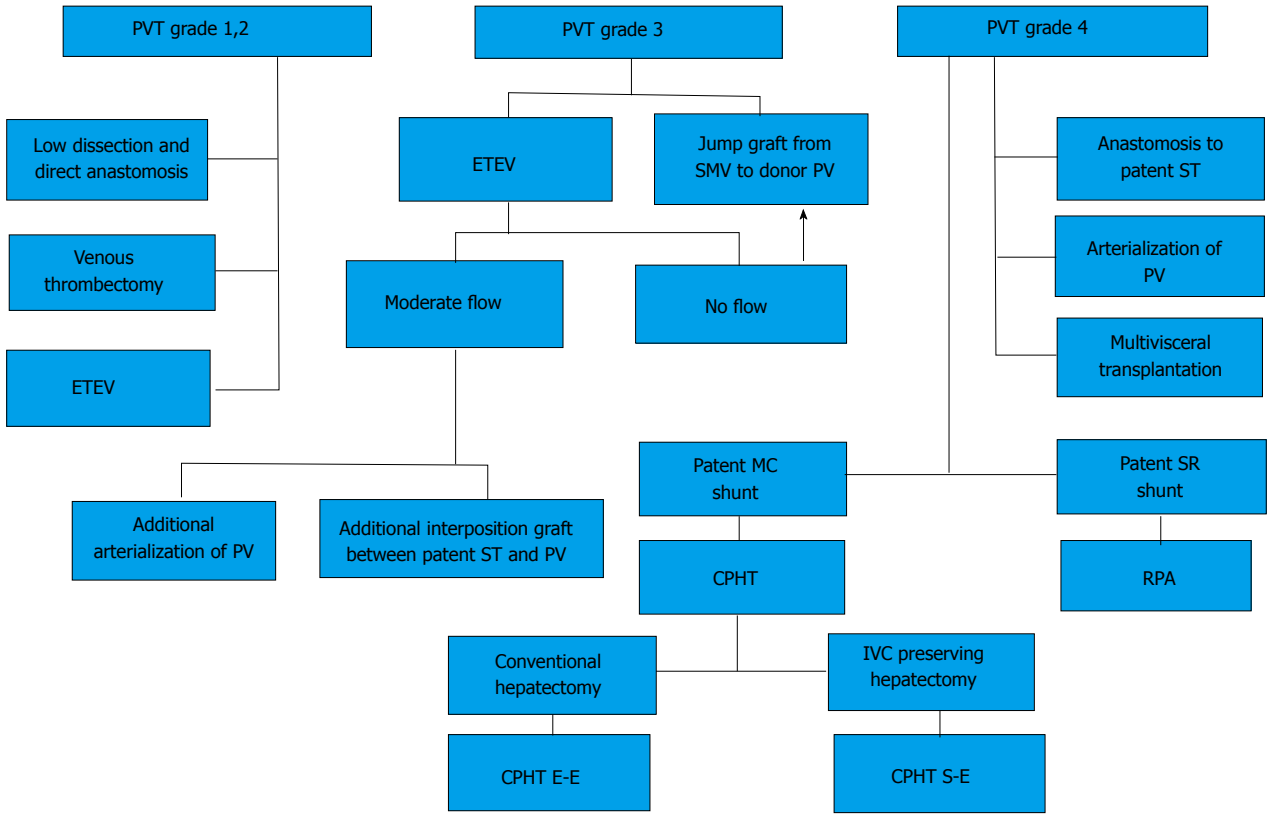


Figure 2 Algorithm for the management of portal and splanchnic vein thrombosis during liver transplantation. CPHT: Cavo-portal hemitransposition; CPHT E-E: End-to-end cavo-portal hemitransposition; CPHT S-E: Side-to-end cavo-portal hemitransposition; ETEV: Eversion thromboendovenectomy; IVC: Inferior vena cava; MC: Mesocaval shunt (spontaneous or surgical); PV: Portal vein; PVT: Portal vein thrombosis; RPA: Reno-portal anastomosis; SMV: Superior mesenteric vein; SR: Splenorenal shunt (spontaneous or surgical); ST: Splanchnic tributary (coronary, gastroepiploic vein). From Paskonis *et al*[43], with modifications.

vascular clamps should be avoided as it can rip the vessel, which may result in uncontrollable bleeding, especially at the level of the pancreatic head. The completeness of the thrombectomy can be verified by restoration of an adequate portal blood flow (Figure 3).

Eversion thromboendovenectomy (ETEV) is another surgical technique applicable to type Ⅰ-Ⅲ thromboses. Type Ⅳ thrombosis can only be occasionally treated with this technique, but typically requires more complex procedures. With ETEV, the clot is progressively and circumferentially freed with the aid of a tonsil clamp by everting the venous wall, and clamping the free edge of the clot with a tonsil. Some authors consider ETEV a risky technique, as a piece of diseased venous wall with thrombogenic potential is left in place[14].

Pan *et al*[15] described a modification of ETEV, called improved eversion thrombectomy, in which 1 cm of the anterior wall of the PV is cut, with the final removal of the smooth wall of PT after clot removal. This technique was reported in 23 type Ⅰ-Ⅲ cases, with no PVT recurrences or post-operative deaths.

Several single-centre series have been reported in relation to the treatment of grade Ⅰ-Ⅱ PVT[14-19]. A large review of 1957 LT recipients with PVT[10] showed that thrombectomy and/or thromboendovenectomy with end-to-end portal anastomosis was the most frequently used technique (75% of cases) with a very low risk of PVT recurrence and complications.

Management of grade Ⅲ PVT

In the case of type Ⅲ PVT, ETEV alone can be insufficient, due to involvement of the distal portion of the SMV[15]. If portal flow is insufficient, different options can be considered in order to establish an adequate portal flow (> 600 mL/min). Porto-systemic shunt collaterals can be suture-ligated; in the case of spontaneous or surgical spleno-renal shunt, the left renal vein can be divided[20]. Sometimes a reno-portal anastomosis using a free iliac vein graft between the left renal vein and the PV (end-to-side or end-to-end anastomosis) can provide adequate portal inflow[21]. Another technique in grade Ⅲ PVT may consist of anastomosing (eventually with a venous graft) the PV to recipient collaterals (coronary or choledochal veins). All these techniques can be considered when the PV is found to be a small fibrotic vessel.

A jump graft can be used in cases in which a low dissection of the retro-pancreatic PV or distal SMV part is required. This method avoids hazardous dissection with potential fatal bleeding and risk of pancreatitis[5,22].

Rodríguez-Castro *et al*[10], adopted venous interposition grafting between donor and recipient PV in 158 cases (8.4%), which represents the second most commonly used surgical technique after thrombectomy/thromboendovenectomy.

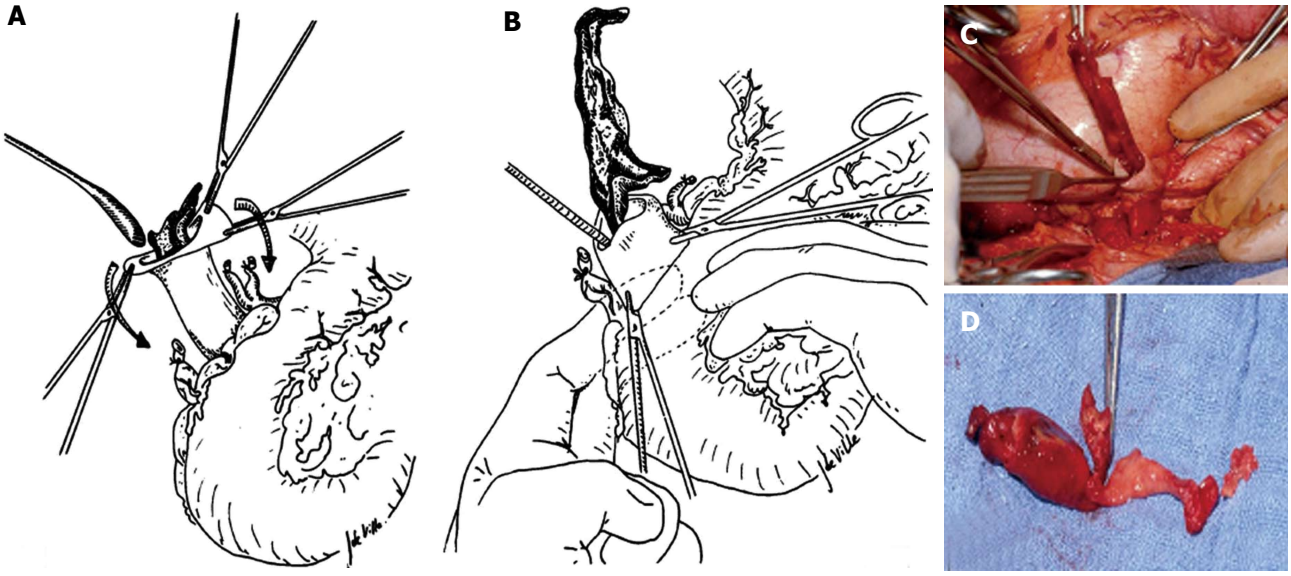


Figure 3 Eversion venous thrombectomy technique. A and B: Schematic representation of the manoeuvre; C: Intraoperative image of thrombectomy procedure; D: The thrombus removed from the portal vein. Modified from Lerut *et al*[13]. Figures from the experience of Prof. Jan Lerut.

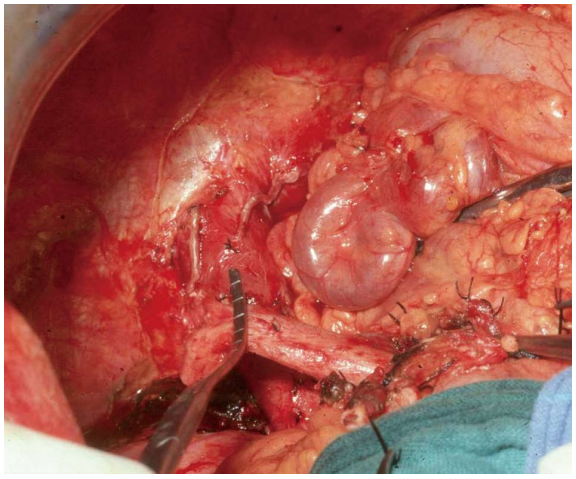


Figure 4 Intraoperative image of a large coronary vein and a thrombosed portal vein. Figure from the experience of Prof. Jan Lerut.

Kim reported 50 cases of living donor LT with PVT: in one case (2.4%) of partial PVT, the PV was reconstructed using a cryopreserved interposition graft after resection of a thrombosed segment; in 3/7 cases of total PVT, the distal SMV or coronary vein were used for the inflow using a jump graft; two patients with SVT, both needed jump grafts[17].

Management of grade IV PVT

Up to 15 years ago, patients with diffuse SVT were not considered for LT. More recently, 5 different surgical techniques to restore portal inflow have been suggested: (1) anastomosis to a patent splanchnic tributary (APST); (2) PV arterialization (PVA); (3) reno-portal anastomosis (RPA); (4) cavo-portal hemitransposition (CPHT); (5) hepato-intestinal or (6) multi-visceral transplantation (MVT).

APST represents, when feasible, the preferred approach in the case of SVT as it is the "easiest" to perform. This technique was initially described by Lerut *et al*[5] and Hiatt *et al*[23]. In the review by Rodríguez-Castro *et al*[10], 49 (2.4%) cases of APST were described; the reported series rarely contain more than 5 cases[3,24]. Virtually any large collateral (2 cm of diameter or more) can suffice to supply the graft; these are mostly a bile duct varix or a middle colic or coronary (left gastric) veins (Figure 4). The venous flow must be tested before implanting the graft to ensure adequate inflow. An interposition graft is sometimes necessary[25]. Particular care must be taken when suturing these variceal structures to the donor portal vein.

PVA is a simple method to restore the portal blood flow into the graft, anastomosing the PV of the graft to the hepatic or gastro-duodenal artery or aorta using an iliac interposition graft. This revascularisation procedure is well documented in surgery for portal hypertension[26] and post-LT arterial thrombosis[27] or, more commonly in the setting of PVT during LT[28-35]. It is occasionally used to deal with early PVT complicating LT. Here, PVA is usually associated with PV thrombectomy. PVA has been reported once in a case of auxiliary heterotopic LT[36].

The PV can be directly anastomosed to the recipient hepatic artery[28,29,32,33], or anastomosed to the supra- or infra-renal aorta with an interposition graft from a segment of donor iliac artery[28-31]. In one case, PV was anastomosed to the accessory right hepatic artery originating from the superior mesenteric artery[34]. However, this is associated with significant mortality due to haemorrhage, right heart failure, acute[28,32] and secondary PVT[28,30-34]. Some patients developed graft fibrosis due to modified hepatic microcirculation[28,32], right-sided heart decompensation[29] as well as persistent portal hypertension due to "over-arterialization"[28,32]. Experimental syngenic rat

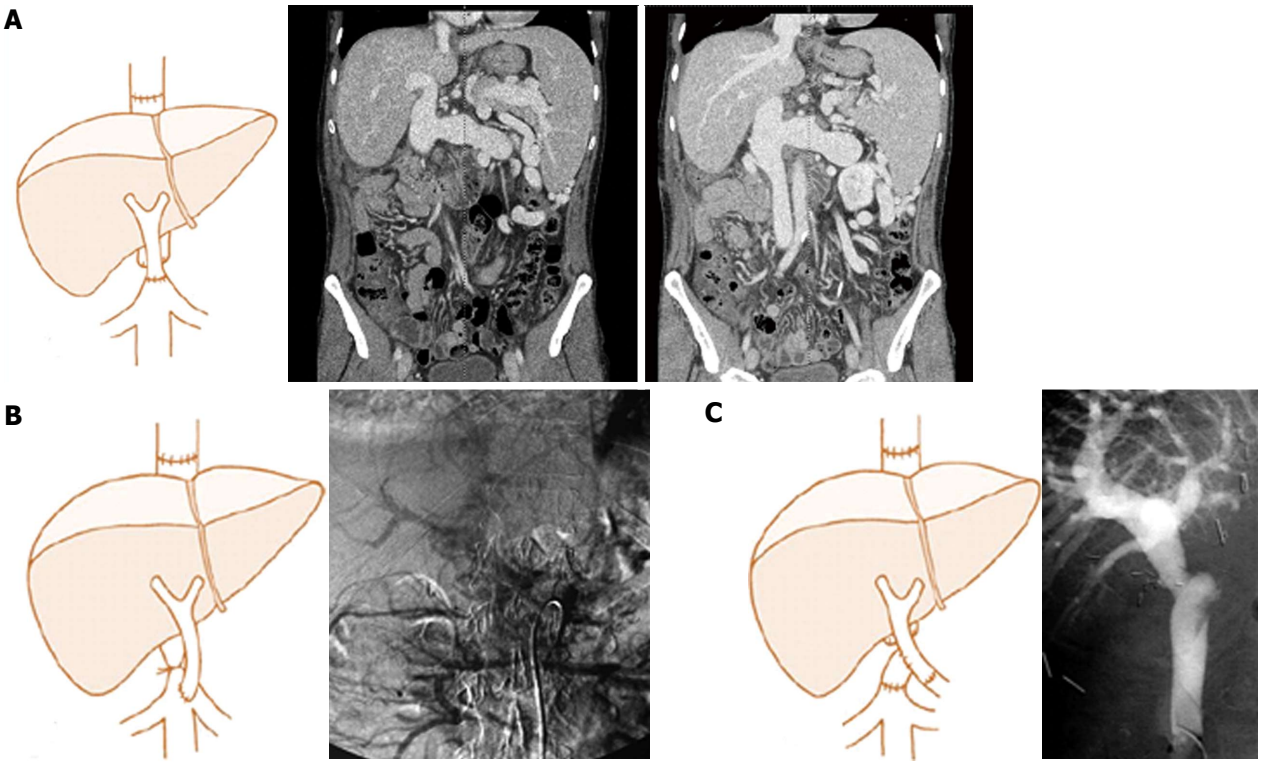


Figure 5 Examples of different techniques of portal flow reconstruction during cavo-portal hemitransposition. A: End-to-end cavoportal anastomosis; B: Side-to-end cavoportal anastomosis with retro-hepatic caval vein constriction; C: End-to-side cavoportal anastomosis using vein interposition graft distal to the conventional portal vein anastomosis. Modified from Paskonis *et al*[43]. Figures from the experience of Prof. Jan Lerut.

models confirmed that PV "over-arterialization" during LT can lead to liver fibrogenesis[37]. A possible solution for this problem is the surgical modulation of the arterialized portal inflow. There is, however, no agreement regarding the "ideal" flow to aim at in this setting; some authors propose 0.6-0.8 L/min[33], others 1 L/min[30] or even 1.5-1.8 L/min[32]. The calibration of arterio-portal anastomosis can also be done either surgically or radiologically using coil embolization of the artery anastomosed to the PV[29,36]. In the 3 cases in which calibration of PVA was performed either surgically or radiologically favourable outcome were observed, with a follow-up up to 36 mo[29,36]. However, the progressive aneurysmal dilatation of intrahepatic portal branches and the possible risk of liver fibrosis suggest that PVA should be used only exceptionally.

RPA was originally reported by Sheil *et al*[38], and subsequently modified with a venous interposition graft by Bhangui *et al*[39] and Kato *et al*[40]. This approach represents a good option in grade IV PVT when engorged collateral vessels are unavailable or when their blood flow is inadequate. However, the liver pathophysiological consequences of this reconstruction are not yet clearly elucidated[41,42]. This method, when possible to adopt, is safe[43]. Until now, RPA has been reported in about 50 cases worldwide; however, only a handful of series contain more than five cases[39,40].

After identification and control of the renal vein, a free iliac vein can be anastomosed either end-to-end or side-to-end to the renal vein. Next, the renal vein itself or the interposition graft will be anastomosed to the donor PV. Kocherisation of the duodenum can be useful when the renal vein has a lower location.

This technique also has some complications such as ascites, renal dysfunction, GI-bleeding, deep venous thrombosis and oedema of lower limbs. These events are all due to a persistent portal hypertension that is resolved only partially by this technique[44].

CPHT represents an exceptional technique to overpass an extensive splanchnic venous thrombosis. The inflow from IVC is used to perfuse the PV of the allograft. CPHT was developed in animal models for the treatment of some metabolic diseases[45-47]. The first human series were performed by Starzl *et al*[48] and Riddell *et al*[49] for glycogen storage disease. In 1998, Tzakis *et al*[50] reported a series of nine cases of CPHT performed during LT due to diffuse PVT. To date, 107 cases have been reported worldwide (Table 1) with the largest series described by Tzakis (n = 23)[14,15,24,50-80].

CPHT can be performed either as an end-to-end or an end-to-side anastomosis between IVC and PV; with the latter carried out in the case of IVC sparing hepatectomy (Figure 5). Both connections may require the use of an interposition graft. In the end-to-side anastomosis, the IVC is best ligated in order to redirect the systemic venous blood flow to the allograft. This procedure carries a high mortality [36 (33.6%) patients] mainly due to sepsis and multiple organ failure. The longest reported survival is 139 mo.

Postoperative complications are mainly related to

Table 1 Cavoportal hemitransposition: Experiences worldwide

Ref.	Year	Country	Pts	Post-LT			Mortality	Survival (mo)[1]
				Variceal bleeding	Cavo-portal thrombosis	Severe renal failure		
Weeks *et al*[52]	2000	United States	1	0	1	0	0	20
Varma *et al*[53]	2000	United States	1	0	0	0	0	12
Olausson *et al*[55]	2001	Sweden	6 (1[2])	1	2	2	1	13
Santaniello *et al*[56]	2001	Italy	1	1	0	1	0	9
Bakthavatsalam *et al*[58]	2001	United States	1[2]	0	0	0	0	12
Urbani *et al*[59]	2002	Italy	6 (2[2])	1	1	1	1	23
Gerunda *et al*[60]	2002	Italy	2	2	0	2	1	12
Azoulay *et al*[61]	2002	France	8	2	0	1	3	37
Shrotri *et al*[62]	2003	United Kingdom	1	0	1	0	0	12
Kumar *et al*[63]	2003	United Kingdom	1	0	0	0	0	24
Verran *et al*[64]	2004	Australia	1[2]	0	0	0	0	6
Bertelli *et al*[66]	2005	Italy	1	1	0	0	0	84
Wang *et al*[67]	2005	China	1	0	0	0	0	6
Ozden *et al*[68]	2006	Turkey	1[2]	0	0	0	0	13
Lipshutz *et al*[69]	2006	United States	7 (1[2])	0	0	0	2	96
Egawa *et al*[70]	2006	Japan	1	0	0	1	1	0
Lladó *et al*[24]	2007	Spain	1	0	0	0	1	1
Selvaggi *et al*[71]	2007	United States	23	7	6	3	13	112
Li *et al*[72]	2008	China	1	0	1	0	0	18
Yan *et al*[73]	2008	China	3	1	0	0	1	48
Pan *et al*[15]	2009	China	1	0	0	0	1	-
Tao *et al*[16]	2009	China	2	0	1	0	0	-
Gao *et al*[74]	2009	China	2	1	0	0	2	6
Campsen *et al*[75]	2010	United States	10	0	0	0	0	-
Suarez *et al*[76]	2010	Spain	4	-	-	-	2	-
Ravaioli *et al*[77]	2011	Italy	6	0	0	0	1	-
Shi *et al*[78]	2011	China	1	0	0	0	0	-
Lai *et al*[79]	2012	Belgium	8	3	4	2	5	139
Chmurowicz *et al*[80]	2013	Poland	1[2]	0	0	0	0	-
Total			103 (7[2])	20	17	13	35	

[1]Maximum survival in the series; [2]Retransplantation. LT: Liver transplantation.

anastomotic thrombosis or stenosis, congestion of the inferior vena cava (IVC) and incompletely resolved portal hypertension. Complications related to IVC congestion are mild to severe oedema of the lower torso and limbs and renal dysfunction. Mild renal dysfunction, observed in almost all patients, usually resolves spontaneously without the need for haemodialysis; haemodialysis was required in 13 (12.1%) patients. Within the second group of complications, the most commonly observed were ascites and (early or delayed) variceal bleeding. In 21 (19.6%) patients, bleeding occurred post-operatively due to persistent portal hypertension. Varma reported a case in which a venous graft was interposed between a retroperitoneal varix and the PV in order to improve the drainage of the portal venous system[53]. The majority of variceal bleedings were controlled with sclerotherapy, splenic artery embolization or splenectomy with or without gastric devascularization[79].

Thrombosis at the level of the anastomosis was seen in 17 (15.9%) patients. Such complication can sometimes be treated by endovascular stenting.

Hepato-intestinal or MVT represents the very last surgical option in grade Ⅳ PVT, allowing replacement of the entire splanchnic venous system of the recipient[81]. Such a radical expedient still represents a major technical and immunological challenge, and carries a high risk of rejection, infection and surgical complications. In recent years, surgical technique and peri-operative management have evolved substantially, achieving one- and three-year survival rates up to 80% and 70%[65,82,83]. Particular attention should be given to the graft procurement and to ensure a low cold ischemia time (≤ 6 h) in order to avoid irreversible intestinal mucosal injury[84,85]. The MVT surgical technique consists of complete replacement of the abdominal viscera after exenteration[86]. Arterial inflow is established with a unique anastomosis between the donor aortic patch encompassing the coeliac trunk and superior mesenteric artery and recipient aorta. Venous anastomosis is routinely performed with a piggy-back technique. A terminal ileostomy is created in order to allow endoscopic monitoring of the bowel graft. The decision to opt for a MVT may be undertaken during the transplant procedure. If adequate portal flow can be restored, the Indiana group led by Vianna proposed that only the liver should be implanted and the multivisceral graft split on the back table; the remaining organs are next directed towards a backup recipient needing an isolated intestinal transplantation. If portal flow cannot be established, then a MVT is required[87].

SVT used to represent a common indication for MVT in adults. The Pittsburgh experience consisting of five hundred transplants included MVT for SVT in 10% of

cases[88]. The Indiana group obtained excellent one- and three-year survival rates of 80% and 72%. However, the procedure carried a complication rate of 56% with half the patients requiring a surgical re-exploration[83]. Nowadays, MVT is less frequently offered in cases of SVT due to the introduction of more sophisticated surgical techniques when dealing with extended SVT.

CONCLUSION

PVT and SVT are no longer a contraindication for LT. However, in order to achieve satisfactory outcomes, the surgical strategy needs to be carefully planned before the transplant procedure. Patients with extended splanchnic thrombosis may need complex vascular interventions; others may even require a multivisceral transplantation.

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