Review

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Novel classification of non-malignant portal vein thrombosis: A guide to surgical decision-making during liver transplantation

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Summary

Non-tumoral portal vein thrombosis (PVT) is present at liver transplantation in 5% to 26% of cirrhotic patients, and the prevalence of complex PVT as defined here (grade 4 Yerdel, and grade 3,4 Jamieson and Charco) has been reported in 0% to 2.2%. Adequate portal inflow is mandatory to ensure graft and patient survival after liver transplantation. With time, the proposed classifications of non-tumoral chronic PVT have evolved from being anatomy-based, to also incorporating functional parameters. However, none of the currently proposed classifications are directed towards decision-making, regarding the choice of inflow to the graft during transplantation and the outcomes thereof. The present scoping review i) addresses the limits of the currently available classifications in terms of surgical decisiveness, ii) clarifies the concept of physiological or non-physiological portal inflow reconstruction, and subsequently, iii) proposes a new classification of non-tumoral PVT in candidates for liver transplantation; to help tailor the surgical strategy to an individual patient, in order to provide portal inflow to the graft together with control of prehepatic portal hypertension whenever feasible.

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Key point

Prevalence of non-malignant PVT in cirrhotic patients ranges from 5% to 26% at the time of LT.

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Introduction

Adequate portal inflow is necessary to ensure graft and patient survival after liver transplantation (LT);[1] thus, coexisting portal vein thrombosis (PVT) was long considered an absolute contraindication for LT due to the high mortality associated with the procedure.[2] The first successful LT in a patient with PVT was reported in 1985,[3] where the portal vein trunk was resected *en bloc* with the thrombus, and porto-portal anastomosis was performed with an interposed cadaveric vein jump graft.

Though initial studies reported worse post-LT outcomes in patients with PVT compared to those without PVT, most studies published after the year 2000 have reported similar 1-year survival in both groups.[4,5] However, the vast majority of these studies did not detail post-LT results according to the extent/grade of PVT, which may influence the post-LT outcome to a large extent.[4,6,7] In a recent meta-analysis, Zanetto *et al.*[8] found that postoperative mortality was higher (27%) in patients with grade 4 (Yerdel) PVT in the 10 studies that reported on mortality by grade of PVT. One-year mortality was also higher in patients with complete (42%) compared to partial (22%) PVT in 3 studies. Meanwhile, previous studies have shown that even in higher grades of PVT, if it is possible to achieve a porto-portal anastomosis, there is no major impact on post-LT survival.[9,10]

With time, the proposed classifications of non-tumoral chronic PVT have evolved from being anatomy-based (site and extent), to also incorporating functional parameters (presence of symptomatic portal hypertension [PHT] or a portal cavernoma), which may aid in decision-making with regards to the medical management of these patients (role of transjugular intrahepatic portosystemic shunt [TIPS], variceal ligation, embolisation of spontaneous portosystemic shunts *etc.*).[11,12] None of the 9 currently proposed classifications[12–20] are directed towards decision-making, regarding the choice of inflow to the graft during LT. Though the functional classification proposed by Sarin *et al.*[12] has incorporated thrombus and patient characteristics, it does not allude to the pre-transplant approach towards ensuring portal vein patency for eventual porto-portal anastomoses in these patients.

Methods

This study is a scoping review of the English-language literature on the currently available classifications of PVT (their usefulness and limitations in defining surgical strategy during LT), and methods described for portal inflow to the graft during LT in the case of diffuse PVT (with their associated outcomes). Since the body of evidence on this topic is complex, and suffers from heterogeneity, a precise systematic review is not possible. Also, the surgical options, and an algorithmic approach to surgical management during LT in cases of "complex PVT", as defined here, have not been comprehensively reviewed before. This review tries to consolidate the current evidence available

on the management of diffuse PVT in the liver transplant setting, as well as mapping out the results achieved to date. We have also tried to clarify the concept of physiological *vs.* non-physiological inflow reconstruction, and proposed a new algorithm for the surgical strategy during transplant, which could provide portal inflow to the graft together with control of prehepatic PHT whenever feasible.

Current grading systems for non-tumoral PVT and a new proposed classification

Nine classification systems have been proposed to grade non-tumoral PVT[12–20] (Table S1). All but one[12] include 4 grades, and there is no one grade common to all classification systems. Some include grades pertaining to thrombosis of intrahepatic portal vein branches without portal trunk thrombosis. These grades have limited value, if any, in the setting of LT, because the native liver, together with the thrombosed portal vein branches, will be removed in its entirety during LT. So far, the Yerdel,[16] Jamieson,[17] and Charco[18] grading systems are best at describing a correlation between the extent of thrombosis and surgical management at the time of LT. In Yerdel's classification,[16] grade 4 PVT denotes complete splanchnic vein thrombosis, including thrombosis of the portal vein and proximal superior mesenteric vein (SMV) and splenic vein. The surgical decisiveness of this classification is limited because it does not consider the coexistence of large spontaneous or surgical shunts that could be used for portal inflow reconstruction. The Jamieson[17] and Charco[18] classification systems aim to define the complete or partial nature of thrombosis, denote the extent of thrombosis along the portal system, and account for the existence of large portosystemic collaterals. In both classification systems, grade 3 is defined as diffuse thrombosis of the splanchnic venous system with large accessible collaterals, whereas grade 4 includes extensive thrombosis of the splanchnic venous system with only fine collaterals. To define the surgical strategy for LT, group Yerdel grade 4 and Jamieson and Charco grades 3 and 4 PVT can be grouped together as "complex PVT" because the technical strategy for portal inflow reconstruction would be similar. In the same vein, we propose to classify less severe PVT (Yerdel grade 1-3 PVT) as "non-complex PVT". These patients have partial or complete thrombosis limited to the portal vein trunk and/or the very distal part of the splenic vein and/or the SMV. Due to technical improvements, this can be resolved during LT using surgical thrombectomy, with standard porto-portal reconstruction, or an interposition vein graft from the SMV to the graft portal vein. Optimal outcomes with these approaches have been reported extensively and will not be discussed here.[21–26]

Prevalence of complex PVT in patients with cirrhosis at the time of LT

Published studies (1998–2017, over 2 decades) reporting on the initial diagnosis of PVT, prevalence, and grade of PVT at the time of LT (single centre series only) were reviewed. A total of 28 studies reported on a total of 19,325 cirrhotic patients (Table S2).[9,16,27–49] The prevalence of non-tumoral PVT at LT was 5% to 26%, and the prevalence of complex PVT, as defined here, would range from 0% (9/27 analysable series) to 2.2%. The prevalence of non-tumoral PVT at LT may be falsely low because, up until the last decade, many LT teams around the world considered it a contraindication for LT, and hence LT in these patients was refused. In a systematic review of PVT in the transplant population, Rodríguez-Castro *et al.*[50] analysed 41 studies published from 1986 to 2012 (25,753 patients) and found a 14.6% incidence of Yerdel grade 4 PVT (104/713 PVT cases), representing 2.8% of all LTs. The presence of large usable portosystemic shunts (spontaneous or surgical) was not analysed in either study. Similarly, 2 reviews based on the Organ Procurement and Transplant Network waitlist and first LT found that the prevalence of PVT at LT was between 6.8% and 8.7%.[4,51] The grade of PVT and the presence of shunts were not detailed in either review.

Key point

"Complex PVT" has been defined in the proposed novel classification as grade 4 (Yerdel), and Grades 3 and 4 (Jamieson and Charco's classifications).

Definition of physiological *vs.* non-physiological portal flow reconstruction revisited

In an audit of 174 cases of non-tumoral PVT at LT, Hibi *et al.*[47] defined portal inflow reconstruction as non-physiological when porto-portal anastomosis could not be performed. According to that definition, inflow achieved by renoportal anastomosis (RPA), cavoportal hemitransposition, or portal vein arterialisation (see below) would all be types of non-physiological portal flow reconstruction. They also defined the terms anatomical and non-anatomical to denote the use of interposed grafts for portal inflow reconstruction.

From a functional standpoint, we propose defining reconstruction of portal flow as physiological when the splanchnic venous blood (all or part of it) can be redirected to the liver graft. Hence, in addition to porto-portal anastomoses, reconstruction of physiological portal inflow is also possible by redirecting the blood flow from a large portosystemic shunt (spontaneous or surgical) to the graft, either by anastomosis of the shunt to the graft portal vein, or anastomosis of the tributary of the inferior vena cava (IVC), which drains this shunt, to the graft portal vein. This dichotomy is important because physiological portal flow reconstruction, as defined by us, should solve the problem of pre-existing prehepatic PHT due to PVT, either immediately or in the short/mid-term after LT. This is contrary to non-physiological portal flow reconstruction in which PHT persists, or even worsens following LT. Fur-

Key point

In complex PVT, portal reconstruction can be considered "physiological" when the splanchnic blood is somehow redirected to the graft, thus resolving the pre-existing PHT.

thermore, it could be better to clearly specify whether the reconstruction requires an interposed biological or synthetic graft, rather than using the misleading terms anatomical and non-anatomical to denote this.

Subsequently, we can consider that portal inflow reconstruction for non-complex PVT (as defined above) is always physiological. For patients with complex PVT, the available options for portal inflow reconstructions are dichotomised into physiological or non-physiological as follows.

Key point

Diligent management of PHT before, and after LT is key.

Physiological reconstructions

The prevalence of large spontaneous portosystemic shunts in patients with end-stage liver disease undergoing LT ranges from 20% to 40%.[52,53] However, the available literature does not clarify the prevalence of large spontaneous portosystemic shunts in patients with complex PVT, which could be used for portal inflow reconstruction.

Similarly, large collaterals (varices) that could be used for portal inflow in patients with cirrhosis and PHT include gastric (left gastric vein [LGV]), pericholedochal, and rarely dilated right superior colic, ileocolic, gastroepiploic, or the middle colic veins. The prevalence of gastric and pericholedochal varices in cirrhotic patients with significant PHT has been variably reported as 2–70%,[54] and 23–94%,[55] respectively. However, what percentage of these varices are large enough to serve as an inflow, and their prevalence in patients with complex PVT is not known.

Key points

Portal reconstruction in complex PVT depends upon the presence of large spontaneous (splenorenal being most common) or previously surgically created portosystemic shunts. Renoportal anastomosis is the reconstruction of choice in case of a pre-existing splenorenal shunt.

Patients with a pre-existing portosystemic shunt (surgical or spontaneous)

Left renal vein to graft portal vein anastomosis

This technique is indicated in patients with a splenorenal shunt (SRS) (spontaneous or surgical): this end-to-end anastomosis between the left renal vein and the graft portal vein (so-called renoportal anastomosis or RPA) drains the splanchnic blood flow to the graft via the left renal vein as illustrated in Fig. 1. Sheil *et al.*[56] described the first case of native left renal vein to graft portal vein anastomosis in a patient with a thrombosed portal vein and a functioning, previously created, surgical end-to-end SRS. Kato *et al.*[57] modified this procedure and used an interposition cadaveric vein graft in 5 patients with a patent surgically created distal SRS.

Table 1 summarises 57 reported cases (1997–2017) of RPA in patients with PVT.[44,47,49,56–67] Thirty-two of these patients had a spontaneous SRS, 13 had a previously created surgical SRS, and in 6 patients, the type of pre-existing shunt (spontaneous or surgical) was not specified. One patient had a pre-existing mesorenal shunt. In 5 cases, RPA was performed in patients without pre-existing SRSs[44,58] (see below, section of non-physiological reconstructions). Considering the analysable data, postoperative variceal bleeding, acute kidney injury, and PVT occurred in 7%, 20%, and 6% of patients, respectively. The postoperative mortality rate was 16% (8/51 analysable cases). Among 51 analysable cases, 41 (81%) patients were alive and well with patent portal flow at the last follow-up visit (2 months to 5 years after surgery).

Large left gastric vein to portal vein anastomosis

Czerniak *et al.*[68] first reported on anastomosis of a large LGV functioning as a spontaneous portosystemic shunt to the graft portal vein (so-called coronary-portal anastomosis) in a patient with complete PVT (Fig. 2). Table 2 summarises the 37 reported cases (1990–2018) of LGV to portal anastomosis.[9,13,22,34,38,40,45,47,52,68–74] All reports were single case reports or small case series (median

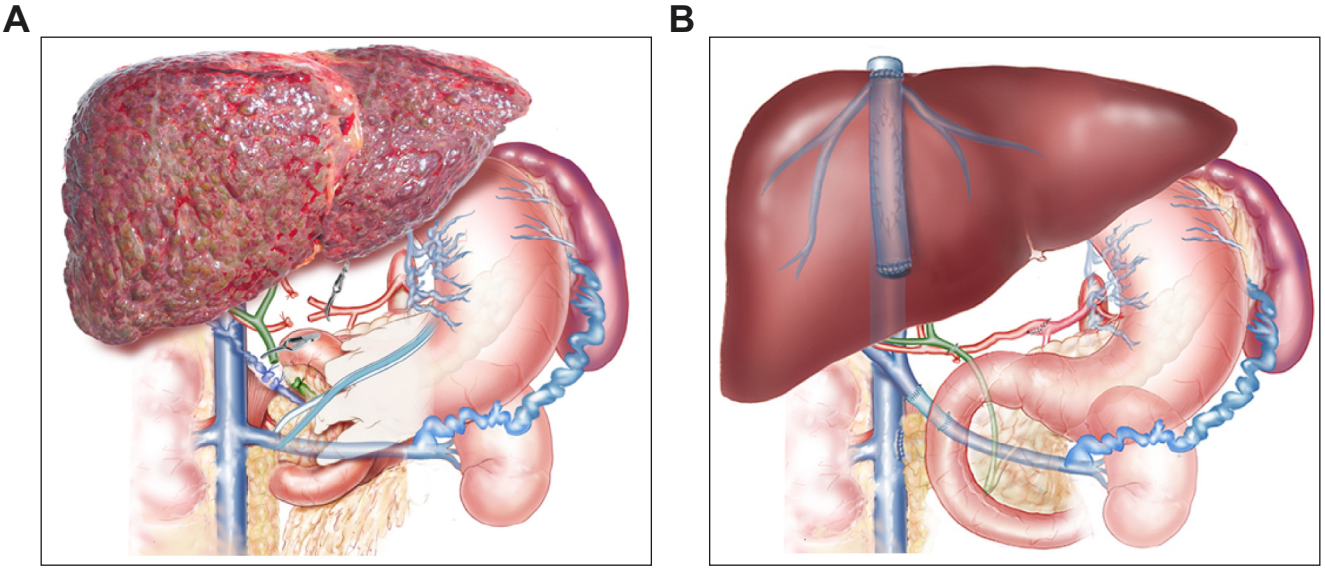

Fig. 1. Reno-portal anastomosis. This reconstruction is physiological because it directs the large spleno-renal shunt into the graft portal vein via the left renal vein (with interposed vein graft). (A) Before transplantation; (B) After transplantation.

Table 1. Reported series of renoportal anastomosis.

Author, year[ref]	N	Postoperative mortality	Patients alive/ follow-up
Sheil, 1997[56]	1	0	1/1 (5 years)
Kato, 2000[57]	5	1	4/5 (3–41 months)
Marubashi, 2005[58]	3	0	3/3(12–48 months)
Moon, 2008[59]	5	1	4/5 (1–35 months)
Gonzalez-Pinto, 2009[60]	1	0	1/1 (2 months)
Perumalla, 2008[61]	1	0	1/1 (12 months)
Bhangui, 201[44]	17	6	11/17 (3–144 months)
Moon, 2011[62]	1	0	1/1 (8 months)
Awad, 2012[63]	1	0	Yes/1 (N
Matsumoto, 2013[64]	1	0	1/1 (4 months)
Hibi, 2014[47]	6	n.a.	n.a./6
Quintini, 2015[65]	10	0	10/10 (mean: 42.2 ± 21.1 months)
Aktas, 2017[49]	2	0	2/2 (8–36 months)
Nazzal, 2017[66]	2	1	1/2 (11 months
Ozdemir, 2017[67]	1	1	0/1

n.a., not available; N, number of patients.

number of cases per publication = 2) without details regarding the postoperative morbidity. The postoperative mortality (in papers mentioning this outcome) was nil. Long-term results were available in 24 patients, and 22 (92%) patients were reported to be alive and well with a patent portal reconstruction at the last follow-up visit.

Large pericholedochal varix to portal vein anastomosis

In some cases of complex PVT, a large pericholedochal varix running anterolateral to the main bile duct is the only portal inflow to the liver.[75,76] Hiatt *et al.*[77] first reported the use of a pericholedochal varix as portal inflow to the graft.

In this technique, an end-to-end anastomosis is constructed between the graft portal vein and varix (Fig. 3). In this setting, a Roux-en-Y hepaticojejunostomy is logical because of the risk of injury to the sole portal flow available.

Eleven cases (1986–2017) of pericholedochal varix to portal vein anastomosis have been reported in patients with complex PVT[46,79–84] (Table 3). Postoperative mortality was nil and postoperative morbidity could not be clarified. With a follow-up ranging from 12 to 92 months, 9/10 (90%) patients were reported as well with a patent portal reconstruction.

Use of other varices or pre-existing shunts

Other varices have been used to reconstruct the portal inflow to the graft, including the right superior colic vein,[79] ileocolic vein,[85] gastroepiploic vein,[86] or the middle colic vein.[87] The surgical technique is similar to that described for LGV to donor portal vein anastomosis.

Similarly, in the case of pre-existing spontaneous mesenterico-iliac or surgically created mesocaval shunts that cannot be dismantled, cavoportal hemitransposition (see below for the

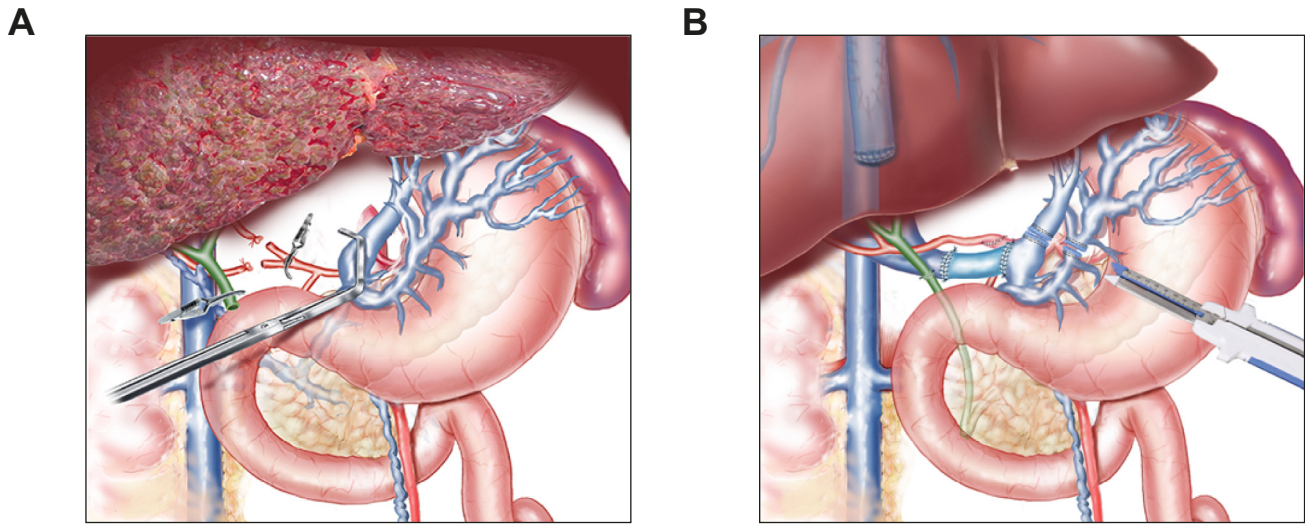

Fig. 2. Coronary-portal anastomosis. This reconstruction is physiological because it directs the large left gastric vein (coronary vein) into the graft portal vein (with interposed vein graft). (A) Initial control in the recipient; (B) After reconstruction of portal inflow.

Table 2. Reported cases of use of left gastric vein for portal vein inflow in complex PVT.

Author, year[ref]	N	Outcome (shunt patency, patient last follow-up status, duration)
Czerniak, 1990[68]	1	Patent, well, 3 months
Stieber, 1991[13]	1	Patent, well, 6 years
Orlando, 2004[22]	2	n.a.
Maluf, 2006[69]	1	Patent, well, 24 months
Llado, 2007[34]	5	n.a.
Pan, 2009[38]	4	n.a.
Wu, 2009[70]	3	Patent, well, 21, 36, 36 months after LT
Ramos, 2010[40]	1	n.a.
Kim, 2011[45]	3	Shunt patent, long term in 2, thrombosed in 1 patient, all patients well at last follow up
Ravaioli, 2011[9]	3	n.a., 1 patient died, 2 alive at last follow-up
Hibi, 2014[47]	1	n.a.
Alexopoulos, 2014[71]	5	All shunts patent (1 after surgical revision), all patients well, median follow up 2.3 years
Wang, 2014[72]	1	Patent, well, 1 year
Teixeira, 2016[73]	2	Patent, well, 5 years, 1 month
Safwan, 2016[74]	1	Patent, well, 3 months
Gomez Gavara, 2018[53]	3	Patent and well at 1, 2, 2 years

n.a., not available; PVT, portal vein thrombosis; N, number of patients.

Key point

In patients with complex PVT, a thorough evaluation of the choices for portal inflow should be performed well in advance of LT, whenever possible.

technical aspects) may be a good option.[88] The latter may still qualify as a physiological inflow because cavoportal hemitransposition drains the portal flow via the IVC to the graft (Fig. 4). However, this latter point is still debatable, as this reconstruction may still be considered non-physiological as some of these patients continue to have persistent PHT, leading to bleeding complications and requiring surgical and/or endoscopic interventions even in the long-term.

The reported postoperative mortality of different physiological reconstructions detailed above is very heterogeneous, primarily because of the data being derived from single case reports, or a small case series, and also due to variable follow-up durations. The reported postoperative mortality in the RPA group was 19%, and 0% in the LGV and pericholedochal varices groups (Tables 1–3). However, there could be a significant reporting bias, especially in the review based on case reports, because there is always a tendency to report successful cases, and not the ones in which the patients did not survive after attempts at such procedures for portal inflow.

There are indeed some rare situations where anastomosis between the mesenteric and gonadal vein, followed by RPA are performed for portal inflow. The question remains whether the PHT, which can be documented in the form of collaterals by imaging or by repeat endoscopy, actually resolves in the long run in such cases. If the PHT resolves, only then can this reconstruction be considered truly physiological.

Patients with complex PVT with no pre-existing shunts

Other options of physiological reconstruction in the absence of pre-existing shunts or large varices

A rare situation is the presence of a patent mid-portion of the splenic vein without a large usable portosystemic shunt. In this situation, it is possible to achieve a physiological portal reconstruction as follows: a latero-lateral splenorenal anastomosis is performed (with an interposed vein, artery, or synthetic graft). Then, end-to-end RPA as described above is performed. One such case was performed at our centre (unpublished). Potentially, the same strategy could be used by anastomosing a large inferior mesenteric vein to the left gonadal vein[89] or left renal vein,[90] followed by RPA or, for that matter, any other large collateral to the IVC[91] followed by cavoportal anastomosis (CPA). Ultimately, this would amount to a physiological portal inflow to the graft.

In the presence of a patent proximal splenic vein (in the splenic hilum) without a large usable shunt, the concept of heterotopic LT in the splenic fossa is an option.[92] This was recently reported by our team during retransplantation of a patient with complex PVT.[93]

Regarding the surgical approach used during recipient hepatectomy in patients with diffuse PVT, Lerut *et al.*[94] proposed that the extent of thrombosis and quality of the vessel wall should determine the use of a hilar or infracolic approach to the portomesenteric system. The latter is preferred, especially if the portal vein is reduced to a fibrotic vessel remnant, or if inflammatory portal vein changes are present. Additionally, in the presence of portal phlebitis, a jump graft from the SMV may be preferable as a primary approach, even in grade 3 (Yerdel) PVT, rather than an attempt to dissect out and perform an anastomosis using the portal vein.

Combined liver and multivisceral transplantation

The first case of a successful multivisceral transplant (MVT) in a patient with complete thrombosis of the portomesenteric system due to protein C deficiency was reported by Florman *et al.* in 2002.[95] In this case, liver function was normal and there were no signs of PHT before or after MVT.

Tremendous progress has been made in the field of MVT in the last decade; some expert centres have reported good results with MVT in LT

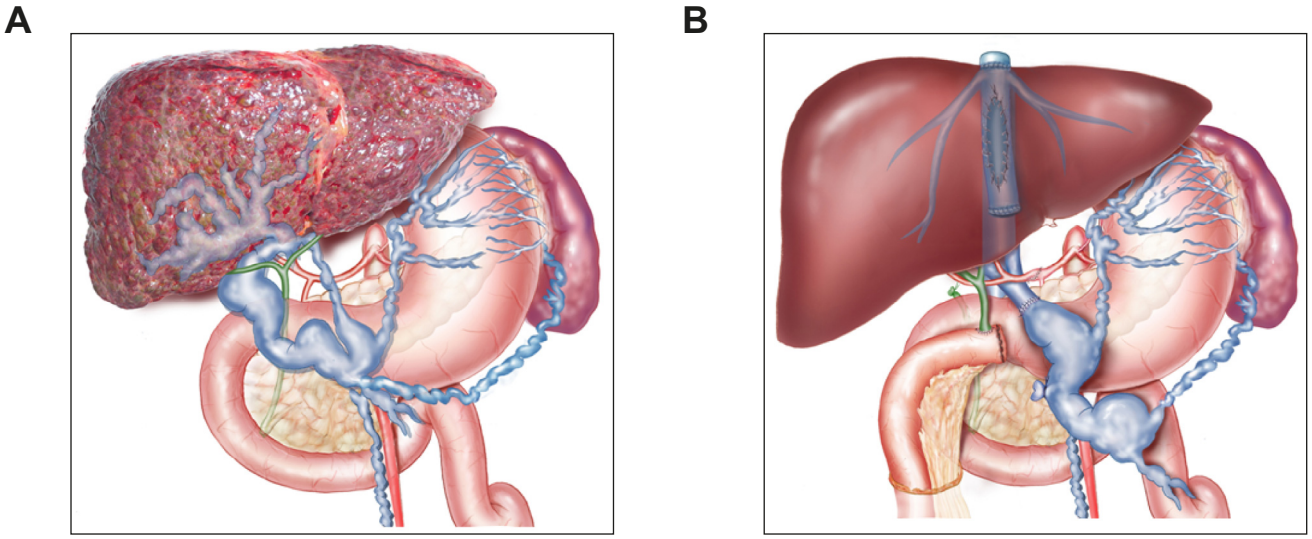

Fig. 3. Pericholedochal varix to portal vein anastomosis. This reconstruction is physiological because it directs the large pericholedochal varix to the graft portal vein. (A) Before transplantation; (B) After transplantation.

Table 3. Reported cases of use of pericholedochal varix to graft portal vein anastomosis.

Author, year[ref]	N	PVT Grade	Biliary reconstruction	Outcome
Hiatt, 1986[77]	1	Yerdel 4	Duct to duct	Patent and well, 12 months
Santoni, 1990[78]	1	Diffuse	n.a.	Died 12 months, patent
Cherqui, 1993[79]	1	Diffuse	n.a.	n.a.
Kniepeiss, 2011[80]	1	Diffuse	n.a.	Patent and well, 6 months
Lee, 2014[81]	1	Yerdel 4	n.a.	Patent and well, 24 months
Kim, 2014[82]	2	Yerdel 4	Roux-en-Y	Patent and well, 22, 21 months
Moon, 2014[46]	2	Diffuse	n.a.	Patent and well, 44, 92 months
Bharathy, 2017[83]	1	Diffuse	Roux-en-Y	Patent and well, 39 months
Yu, 2017[84]	1	Diffuse	Roux-en-Y	Patent and well, (stent), 9 months

n.a., not available; PVT, portal vein thrombosis; N, number of patients.

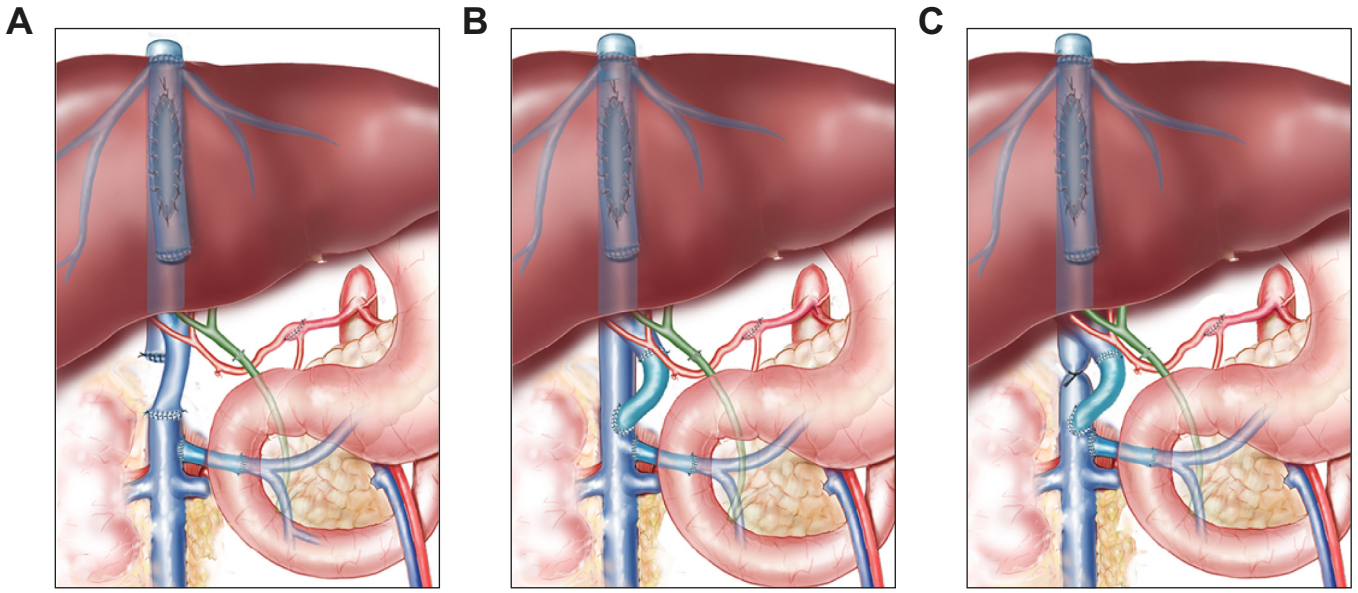

Fig. 4. Cavo-portal anastomosis after graft implantation. (A) With division of the vena cava (the whole caval flow is directed to the graft); (B) Without calibration of the inferior vena cava; (C) With calibration of the inferior vena cava (part of the caval flow is directed to the graft). In case of a mesocaval shunt that cannot be dismantled (as illustrated here), these reconstructions are physiological. Otherwise, these reconstructions are non-physiological.

Key point

Cavoportal anastomosis is the reconstruction of choice in case of portocaval shunt that cannot be dismantled.

recipients with diffuse PVT, in whom no other option is available to establish mesenteric drainage and physiological portal inflow to the graft[95,96] (Table 4). In the largest series published by Vianna *et al.*,[96] relatively good long-term survival was reported in 25 patients with diffuse PVT who underwent MVT (patient and graft survival were 80%, 72%, and 72% at 1, 3, and 5 years, respectively). However, 7 patients (28%) died at a median of 5 months (range, 1–22 months) and surgical complications were encountered in 14 patients (56%).

Pooled data shows 5-year survival rates for MVT (5-year actuarial patient and graft survival 60% and 50%, respectively), and intestinal transplant (actuarial patient survival rates are 76% and 56% at 1 and 5 years, respectively), are indeed improving over time.[97,98]

Notably, in addition to total hepatectomy, MVT requires massive evisceration (of the stomach, pancreaticoduodenal complex, spleen, small intestine, and portion of the large intestine) to place the multivisceral graft. The intestinal component of the MVT is also associated with additional risks of rejection, chronic diarrhoea, and graft versus host disease.

Key point

MVT is theoretically the ideal treatment in complex PVT with no pre-existing portacaval shunt (spontaneous or surgical) but is still limited to highly specialised centres.

Non-physiological reconstructions

These reconstructions pertain to patients with complex PVT and no large accessible portosystemic shunt (spontaneous or surgical).

Cavoportal anastomosis (cavoportal hemitransposition)

The use of CPA in patients with diffuse PVT was first described by Tzakis in 1998.[99] Fig. 4 illustrates the various techniques used to establish caval inflow to the graft.

A total of 28 series have described CPA in 86 adult patients (89 procedures) for grade 4 PVT as defined by Yerdel (Table S3).[9,30,32,34,37,38,43,44,99–121] Not all series reported complete information regarding the technique, incidence of complications, morbidity and long-term outcomes following CPA. Among those in which details were available, 46 (68%) procedures were performed with termino-terminal CPA, whereas 22 (32%) were termino-lateral CPA with ligation of the retrohepatic IVC. Eight (12%) patients (among those in whom details were available) were reported to have developed PVT, and 11 (16%) had cavomesenteric thrombosis post-CPA. This high incidence of cavomesenteric and portal thrombosis might be related to slower caval flow entirely directed into the graft. A total of 30–50% of patients have been reported to develop intra-abdominal bleeding after cavoportal hemitransposition. Endoscopic sclerotherapy or band ligation for bleeding oesophageal varices, laparotomy for control of intra-abdominal bleeding, gastric devascularisation, and splenectomy have all been reported for the control of post-CPA bleeding in these patients.[44,122,123] Most recipients had ascites after LT (which resolved spontaneously in most). Thirteen patients died during the postoperative period (15%), including 2 of pulmonary embolism, and 48 (63%) were reported to be alive at the last follow-up visit in these series. However, the reported follow-up was short in most series, except for the series by Selvaggi *et al.*[101] (3 days–10 years).

Renoportal anastomosis

We consider that RPA (in the absence of large retroperitoneal or renoportal collaterals) can better ensure portal perfusion at a flow rate matching the portal vein than CPA, while providing optimal coaxiality and congruence of the anastomosed vessels, and preserving retrohepatic IVC flow.[44] Furthermore, an RPA can obviate or reduce the specific and frequent complications associated with CPA, such as lower torso oedema, pulmonary embolism, and deep vein thrombosis. Due to the so-called *siphon effect*, it can also be hypothesised that over a period of time, the splanchnic blood flow with high-pressure will be redirected to the low-pressure caval system via the RPA, thus decompressing the portal system and resolving some persistent PHT after this non-physiological establishment of portal flow.[124,125] However, the *siphon effect*, described in selective portacaval shunts, remains to be demonstrated in the LT setting.

Portal vein arterialisation

In the setting of PVT, PVA can be utilised in 2 ways: either arterialisation of a portal reconstruction to augment portal vein flow (where native physiological portal vein flow is also present), or arterialisation of the portal vein without any portal flow from the native system (salvage technique in complex PVT). Fourteen cases of salvage PVA have been reported in the literature. Nine of these procedures were performed for primary complex PVT, and 5 were performed for diffuse PVT after LT.[18,126–133]

PVA actually represents a non-physiological vascular perfusion of the liver, which is deprived of hepatotrophic splanchnic-derived factors. In addition, "over-arterialisation" can result in liver fibrosis and aneurysmal dilatation of intrahepatic portal branches.

Peri-transplantation medical management of patients with complex PVT

In the setting of LT in patients with PVT, the following 3 major perioperative questions need to be addressed: i) How to prevent the progression from non-complex to complex PVT? ii) How to treat pre- and (possible) post-LT residual PHT? and, iii) How to prevent inflow thrombosis of the reconstructed portal vein after LT?

Table 4. Reported cases of multivisceral transplantation for PVT.

Author, year[ref]	N	Disease	Complications	Outcome
Florman, 2002[95]	1	Protein C deficiency without cirrhosis	Acute rejection	Patent PV, well at 17 months
Vianna, 2015[96]	25		Morbidity = 57%	Mortality = 28%, patient and graft survival: 80%, 72%, and 72% at 1, 3, and 5 years
Meira Filho, 2015[97]	2	Cryptogenic cirrhosis NASH cirrhosis	Ischaemic cholangiopathy Graft *vs.* host disease	Died of infection at 8 months Died of graft *vs.* host disease at 34 days
Ceulemans, 2015[98]	3	Antiphospholipid syndrome, no cirrhosis Neuroendocrine tumour, no cirrhosis Alcoholic cirrhosis	Remaining left colon ischaemia, rejection, aspergillosis Resection of distal ileum, acute rejection Mycotic aneurysm	1 died, 2 survived, 7 and 7 months

NASH, non-alcoholic steatohepatitis; PVT, portal vein thrombosis; N, number of patients.

Up to 31% of patients who are found to have PVT at the time of LT, had PVT at the time of initial listing. This underlines the importance of screening for PVT in cirrhotic patients and potential candidates for LT, as well as the importance of administering anticoagulants to prevent progression to complex PVT.[134] The dose of anticoagulants should be modified as the patient moves up the waiting list. In patients in whom anticoagulant use is contraindicated, or PVT progresses while on anticoagulants, a TIPS may be attempted[134–137] with the same objective *i.e.* to prevent thrombus progression and/or promote recanalisation of the portal vein to allow for standard porto-portal reconstruction at the time of transplant. As proposed in the EASL Clinical Practice Guidelines, TIPS may be considered early in patients with grade 3 (Yerdel) PVT, since it is unlikely that TIPS will be feasible if the PVT progresses to grade 4.[11] Notably, in the only relevant series of pre-LT portal vein recanalisation by TIPS, none of the 61 reported patients had complex PVT as defined here.[138]

In patients with a history of variceal bleeding or in those with grade 3 varices, a protocol of aggressive variceal eradication by endoscopic variceal ligation or sclerotherapy is indicated during the waiting period for LT.[80] The embolisation of large spontaneous portosystemic shunts for refractory hepatic encephalopathy[139] should be avoided in patients listed for transplantation, as such an intervention might take away the last possibility of providing allograft vascularisation as described above. Finally, long-term warfarin treatment has been proposed to prevent post-LT PVT, particularly for patients with non-physiological portal inflow reconstruction, as well as patients with documented hypercoagulable states.[44,47] Anticoagulation does tend to make follow-up in post-LT patients complex, due to drug-drug interactions (including with immunosuppression) and interference with surgical or endoscopic interventions (if required or during biopsies). Lerut *et al.*[94] previously pointed out that anticoagulation may not be necessary in all patients after LT, but probably should be reserved for those patients in whom a complete thrombectomy could not be achieved during LT, or in whom early post-LT PVT develops. In patients with a hypercoagulable state or a metabolic defect, there may not be a need for anticoagulation after LT, as the new liver will immediately correct the situation.

Discussion

Based on the available knowledge and our own experience,[44,52,53] a new and simple classification system has been proposed which could serve as a guide to multidisciplinary decision-making before and during LT in patients with diffuse PVT, something that is lacking in the existing classification systems. This classification, which is relatively unique because of its incorporation of stage-based management recommendations, dichotomises PVT into non-complex or complex PVT. Further, the portal inflow reconstruction can be classified as physiological or non-physiological, based on whether it addresses the pre-existing prehepatic PHT from a functional/haemodynamic standpoint. The inflow could be considered physiological when the splanchnic blood flow can be redirected to the liver (both in non-complex and complex PVT), and non-physiological if the prehepatic PHT persists even after LT due to the absence of any spontaneous or surgically created portosystemic shunt redirected to the graft. In cases of complex PVT, a large shunt (spontaneous or surgical), if available, could help achieve a physiological portal inflow, thus helping to ameliorate and correct prehepatic PHT in the short/mid-term after LT. An algorithm is proposed for portal inflow reconstruction during LT in patients with PVT (Fig. 5).

Key point

Anticoagulation should be applied after LT to prevent thrombosis of the portal reconstruction.

While, in some transplant units, LT is contraindicated in patients with complex PVT and no accessible large portosystemic shunt,[140] it would be preferable to resort to non-physiological reconstruction on a case-by-case basis. MVT should be limited to highly specialised units.

Some areas of uncertainty remain in the field of LT in patients with complex PVT. These include: the unknown proportion of patients with complex PVT excluded from LT at the time of evaluation; the exact influence of complex PVT and/or persistent PHT on short and long-term patient and graft survival after LT[4]; the impact on outcomes of the donor characteristics[141] and of the actual portal

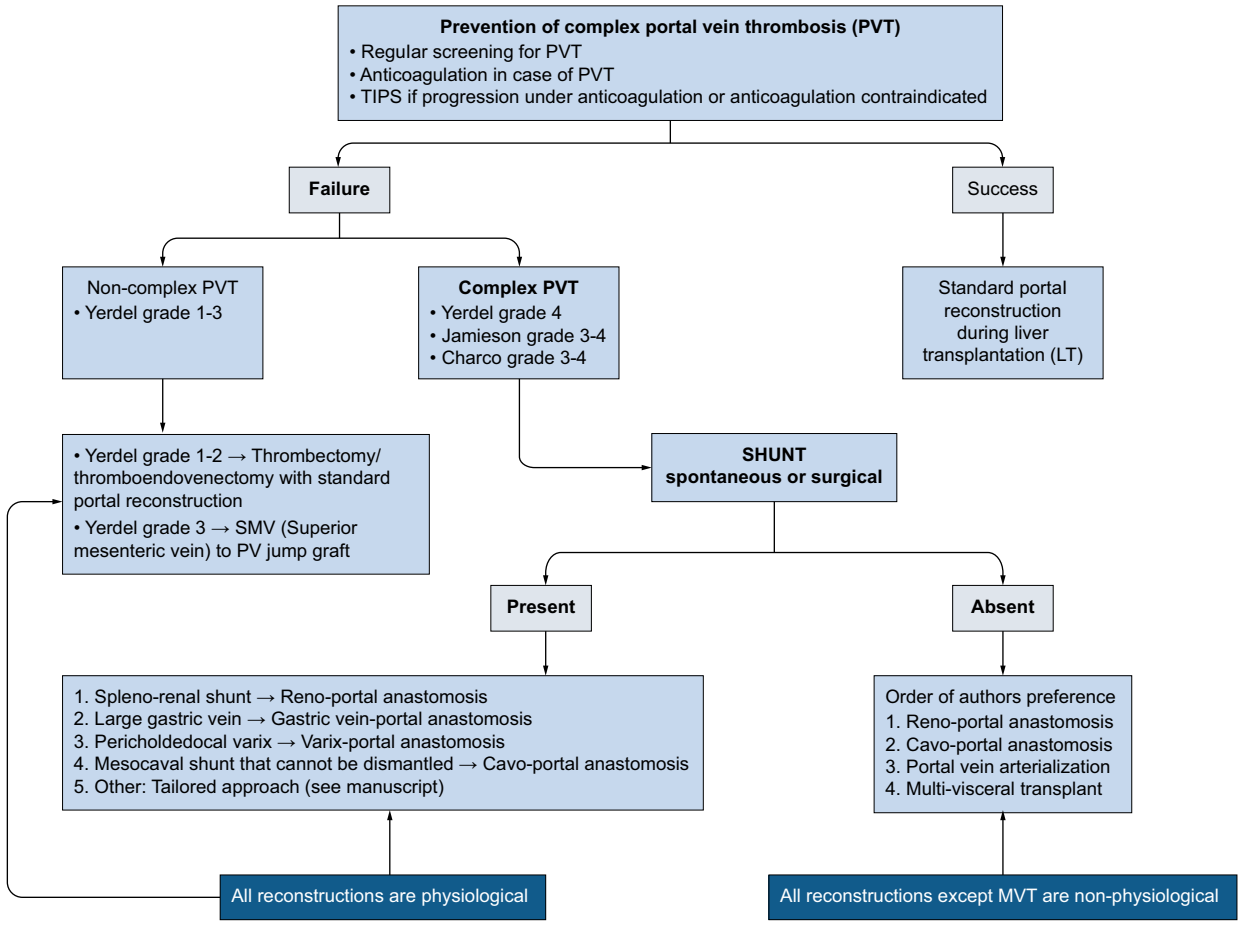

Fig. 5. Proposed algorithm for the management of non-malignant portal vein thrombosis in the setting of liver transplantation.

vein flow.[142] Sufficient long-term results (at 5 years) of LT for complex PVT in large series are awaited to justify the procedure in the ongoing era of worsening organ shortage.

Another question that arises is whether, given the worse post-transplant outcomes in patients with complex PVT compared to those with less severe PVT (grade 1/2 Yerdel)[8], the latter patients should be prioritised for liver allocation, before they progress to complex PVT. In their study evaluating a survival benefit based system for allocating deceased-donor livers to chronic liver failure patients, Schaubel *et al.*[143] found that the presence of PVT was one of the major factors that influenced outcomes of LT (hazard ratio 1.32), and should thus be considered when assessing transplant benefit in organ allocation. Some studies have shown that a policy initiative for early access to deceased donor LT in patients with PVT with both, a very low (<12)[144] or very high model for end-stage liver disease (MELD) score (>30)[145] may not be appropriate in terms of transplant benefit. However, decompensated cirrhotic patients with PVT may benefit from having an LT before they reach an MELD score of 30.[146] It is well known that higher mortality in high MELD score patients with complex PVT is not related *per se* to the PVT grade, but more to the degree of sickness, and medical and surgical (more blood loss during transplant) complications that arise as a result.

In the living donor (LDLT) setting however, the principles may be different. It is of primary importance to respect the risk-benefit equipoise in the LDLT setting – donor safety is of prime importance. However, in experienced centres, where donor morbidity is very low,[147] it may be reasonable to consider decompensated cirrhotics with PVT grade 1-3 (Yerdel) for an early LDLT,[148] because technical issues are known to make LDLT in complex PVT difficult, and outcomes significantly worse.[32,149] Overall, the concept of transplant benefit could guide prioritisation of patients with PVT for LT.

In conclusion, although challenging, good outcomes are possible in patients with complex PVT if the appropriate surgical technique is chosen to ensure portal inflow and resolution of PHT after LT. We believe our proposed classification of PVT in candidates for LT will help clinicians tailor the surgical strategy to an individual patient, in order to provide portal inflow to the graft, together with control of prehepatic PHT whenever feasible. In addition, it could improve teaching and research in the field through comprehensive description for cohort selection and analyses, as well as helping to predict outcomes of LT (especially with

respect to vascular complications) in a subset of patients with the most severe forms of PVT.

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Conflict of interest

The authors declare no conflicts of interest that pertain to this work.

Please refer to the accompanying ICMJE disclosure forms for further details.

Authors' contributions

Study concept and design: CL, CS, DA. Acquisition of data; analysis and interpretation of data: PB, CL, CS, EL, DA. Drafting of the manuscript: PB, CL, DA. Critical revision of the manuscript for important intellectual content: CS, ELe, El, CF. Final approval of the manuscript: PB, CL, ELe, CS, EL, CF, DA.

Supplementary data

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