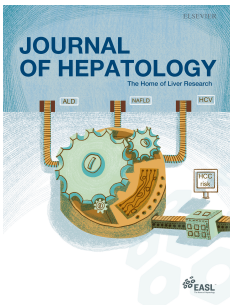


Alternative forms of portal vein revascularization in liver transplant recipients with complex portal vein thrombosis

Yiliam Fundora, Amelia J. Hessheimer, Luca Del Prete, Lorenzo Maroni, Jacopo Lanari, Oriana Barrios, Mathias Clarysse, Mikel Gastaca, Manuel Barrera Gómez, Agnès Bonadona, Julius Janek, Andrea Boscà, Jose María Álamo Martínez, Gabriel Zozaya, Dolores López Garnica, Paolo Magistri, Francisco León, Giulia Magini, Damiano Patrono, Jiří Ničovský, Abdul Rahman Hakeem, Silvio Nadalin, Lucas McCormack, Pilar Palacios, Krzysztof Zieniewicz, Gerardo Blanco, Javier Nuño, Baltasar Pérez Saborido, Juan Echeverri, J. Steve Bynon, Paulo N. Martins, Víctor López López, Murat Dayangac, J. Peter A. Lodge, Renato Romagnoli, Christian Toso, Julio Santoyo, Fabrizio Di Benedetto, Concepción Gómez-Gavara, Fernando Rotellar, Miguel Ángel Gómez-Bravo, Rafael López Andújar, Edouard Girard, Andrés Valdivieso, Jacques Pirenne, Laura Lladó, Giacomo Germani, Matteo Cescon, Koji Hashimoto, Cristiano Quintini, Umberto Cillo, Wojciech G. Polak, Constantino Fondevila

PII: S0168-8278(23)00018-1

DOI: https://doi.org/10.1016/j.jhep.2023.01.007

Reference: JHEPAT 9013

To appear in: *Journal of Hepatology*

Received Date: 17 July 2022

Revised Date: 22 December 2022

Accepted Date: 12 January 2023

Please cite this article as: Fundora Y, Hessheimer AJ, Del Prete L, Maroni L, Lanari J, Barrios O, Clarysse M, Gastaca M, Gómez MB, Bonadona A, Janek J, Boscà A, Álamo Martínez JM, Zozaya G, Garnica DL, Magistri P, León F, Magini G, Patrono D, Ničovský J, Hakeem AR, Nadalin S, McCormack L, Palacios P, Zieniewicz K, Blanco G, Nuño J, Saborido BP, Echeverri J, Bynon JS, Martins PN, López VL, Dayangac M, Lodge JPA, Romagnoli R, Toso C, Santoyo J, Di Benedetto F, Gómez-Gavara C, Rotellar F, Gómez-Bravo MÁ, Andújar RL, Girard E, Valdivieso A, Pirenne J, Lladó L, Germani G, Cescon M, Hashimoto K, Quintini C, Cillo U, Polak WG, Fondevila C, Alternative forms of portal vein revascularization in liver transplant recipients with complex portal vein thrombosis, *Journal of Hepatology* (2023), doi: https://doi.org/10.1016/j.jhep.2023.01.007.

ALTERNATIVE FORMS OF PORTAL VEIN REVASCULARIZATION IN LIVER RECIPIENTS WITH COMPLEX PORTAL VEIN THROMBOSIS: RESULTS OF THE RP4LT COLLABORATIVE STUDY

Extra-anatomical portal vein anastomoses deriving recipient splanchnic blood flow to transplant allograft offer acceptable results, while ones deriving only systemic blood flow to the graft should not be performed.

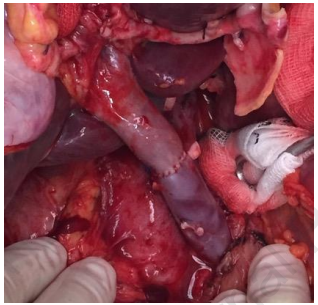
POPULATION

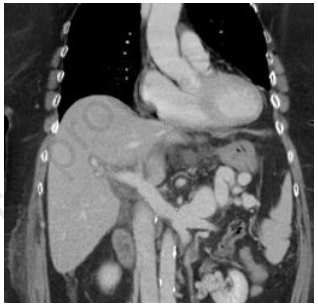
LT recipients with complex PVT undergoing extra-anatomical portal anastomosis:

- Left renal vein N=74
- Left gastric vein N=18
- Pericholedochal vein N=20
- Cavoportal anastomosis N=28

SETTING

Cases submitted from 33 LT centers in 14 countries





OUTCOMES

Acute kidney injury 49%
Refractory ascites 9%
5-y survival:

- Overall 61% patient, 57% graft
- 68% for recipients with physiological PV anastomoses deriving splanchnic flow to graft
- 6.7% for recipients with non-physiological anastomoses deriving systemic flow only

RP4LT Multicenter Study

Fundora Y *et al.* J Hepatol 2023.

seth

ELITA ESOT

ILTS

Alternative forms of portal vein revascularization in liver transplant recipients with complex portal vein thrombosis

Yiliam Fundora[1]*, Amelia J. Hessheimer[1,2,3]*, Luca Del Prete[4], Lorenzo Maroni[5], Jacopo Lanari[6], Oriana Barrios[7], Mathias Clarysse[8], Mikel Gastaca[9], Manuel Barrera Gómez[10], Agnès Bonadona[11], Julius Janek[12], Andrea Boscà[13], Jose María Álamo Martínez[14], Gabriel Zozaya[15], Dolores López Garnica[16], Paolo Magistri[17], Francisco León[18], Giulia Magini[19], Damiano Patrono[20], Jiří Ničovský[21], Abdul Rahman Hakeem[22], Silvio Nadalin[23,36], Lucas McCormack[24], Pilar Palacios[25], Krzysztof Zieniewicz[26,36], Gerardo Blanco[27], Javier Nuño[28], Baltasar Pérez Saborido[29], Juan Echeverri[30], J. Steve Bynon[31], Paulo N. Martins[32], Víctor López López[33], Murat Dayangac[34], J. Peter A. Lodge[22], Renato Romagnoli[20], Christian Toso[19,36], Julio Santoyo[18], Fabrizio Di Benedetto[17], Concepción Gómez-Gavara[16], Fernando Rotellar[15], Miguel Ángel Gómez-Bravo[14], Rafael López Andújar[13], Edouard Girard[11], Andrés Valdivieso[9], Jacques Pirenne[8], Laura Lladó[7], Giacomo Germani[6,36], Matteo Cescon[5], Koji Hashimoto[4], Cristiano Quintini[4], Umberto Cillo[6], Wojciech G. Polak[35,36], and Constantino Fondevila[1,2,3,36]
**Both authors contributed equally to this publication.*

[1]General & Digestive Surgery Service, Hospital Clínic, Barcelona, Spain
[2]General & Digestive Surgery Service, Hospital Universitario La Paz, IdiPAZ, Madrid, Spain
[3]CIBERehd, Instituto de Salud Carlos III, Madrid, Spain
[4]Transplantation Center, Department of General Surgery, Cleveland Clinic, Cleveland, Ohio, USA
[5]Hepatobiliary Surgery & Transplant Unit, Policlinico Sant'Orsola IRCCS, University of Bologna, Italy
[6]Department of Surgery, Oncology, & Gastroenterology, Hepatobiliary & Liver Transplantation Unit, Padua University Hospital, Padua, Italy
[7]Department of Hepato-Biliary and Pancreatic Surgery and Liver Transplantation, Hospital Universitari de Bellvitge, Barcelona, Spain
[8]Abdominal Transplant Surgery, UZ Leuven, KUL, Leuven, Belgium
[9]Hepatobiliary Surgery & Liver Transplantation Unit, Biocruces Bizkaia Health Research Institute, Hospital Universitario Cruces, University of the Basque Country, Bilbao, Spain
[10]Hospital Universitario Nuestra Señora de Candelaria, Santa Cruz de Tenerife, Spain
[11]Grenoble Alpes University, CHU Grenoble Alpes, Digestive Surgery & Liver Transplantation, Grenoble, France
[12]Department of Transplant Surgery, F.D. Roosevelt Hospital, Banská Bystrica, Slovakia
[13]Hepatobiliary Surgery & Transplantation Unit, Hospital Universitario y Politécnico La Fe, Valencia, Spain
[14]Hospital Universitario Virgen del Rocío, Seville, Spain
[15]HPB and Liver Transplant Unit, Clínica Universidad de Navarra; Institute of Health Research of Navarra (IdisNA), Pamplona, Spain
[16]Hospital Universitario Vall d'Hebrón, Barcelona, Spain
[17]Hepato-pancreato-biliary Surgery & Liver Transplantation Unit, Università degli Studi di Modena e Reggio Emilia, Modena, Italy
[18]Hospital Regional Universitario de Málaga, Málaga, Spain
[19]Hôpitaux Universitaires de Genève, Geneva, Switzerland
[20]General Surgery 2U – Liver Transplant Centre, AOU Città della Salute e della Scienza di Torino, Torino, Italy
[21]Centrum Kardiovaskulární a Transplantační Chirurgie, Brno, Czechia
[22]Department of HPB and Liver Transplant Surgery, St. James's University Hospital, Leeds, UK
[23]University of Tübingen, Tübingen, Germany
[24]Hospital Alemán, Buenos Aires, Argentina
[25]Hospital Clínico Universitario de Zaragoza, Zaragoza, Spain
[26]Medical University of Warsaw, Warsaw, Poland
[27]Hospital Universitario de Badajoz, Universidad de Extremadura, Badajoz, Spain
[28]Hospital Universitario Ramón y Cajal, Madrid, Spain
[29] Hepatobiliopancreatic Surgery & Liver Transplant Unit, Hospital Universitario Rio Hortega, Valladolid, Spain
[30]Hospital Universitario Marqués de Valdecilla, Santander, Spain
[31]University of Texas Houston – Memorial Hermann TMC, Houston, Texas, USA
[32]University of Massachusetts – Memorial Medical Center, Worcester, Massachusetts, USA
[33]Department of Surgery & Transplantation, Hospital Clínico Universitario Virgen de la Arrixaca, Murcian Institue of Biosanitary Research (IMIB), Murcia, Spain

[34]Medipol University Hospital Center for Organ Transplantation, Istanbul, Turkey
[35]Division of HPB & Transplant Surgery, Department of Surgery; Erasmus MC Transplant Institute; University Medical Center Rotterdam, Rotterdam, the Netherlands
[36]European Liver and Intestine Transplant Association (ELITA) Board

CORRESPONDING AUTHOR:
Constantino Fondevila, MD, PhD
General & Digestive Surgery Service
Hospital Universitario La Paz
Paseo de la Castellana 261
28046 Madrid, Spain
+34 91 207 1667
constantino.fondevila@salud.madrid.org

KEYWORDS: liver transplantation; portal vein thrombosis; portal hypertension; renoportal anastomosis; cavoportal anastomosis; cavoportal hemitransposition; multivisceral transplantation

WORD COUNT: 3901

FIGURES: 3

TABLES: 5

CONFLICTS OF INTEREST: AJH and CF have received research funding from Guanguong Shunde Innovative Design Institute and Instituto de Salud Carlos III. The remainder of the authors have no conflicts of interest to declare.

FINANCIAL SUPPORT: None.

AUTHOR CONTRIBUTIONS: YF, AJH, and CF contributed to study concept and design. All authors contributed to acquisition of data. YF, AJH, and CF contributed to analysis and interpretation of data and drafting of the manuscript, while the remainder of authors contributed to critical revision of the manuscript for important intellectual content. All authors give their final approval of the version to be published and agree to be accountable for all aspects of the work.

DATA AVAILABILITY: Due to the nature of this research, participants of this study did not agree for their data to be shared publicly, so supporting data is not available.

STRUCTURED ABSTRACT (263 words)

Background: Complex portal vein thrombosis (PVT) is a challenge in liver transplantation (LT). Extra-anatomical approaches to portal revascularization, including renoportal (RPA), left gastric vein (LGA), pericholedochal vein (PCA), and cavoportal (CPA) anastomoses, have been described in case reports and series. The RP4LT Collaborative was created to record cases of alternative portal revascularization performed for complex PVT.

Methods: An international, observational web registry was launched in 2020. Cases of complex PVT undergoing first LT performed with RPA, LGA, PCA, or CPA were recorded and updated through 12/2021.

Results: 140 cases were available for analysis: 74 RPA, 18 LGA, 20 PCA, and 28 CPA. Transplants were primarily performed with whole livers (98%) in recipients with median age 58 years [25-75% interquartile range 49-63], MELD 17 [14-24], and cold ischemia 431 minutes [360-505]. Post-operatively, 49% of recipients developed acute kidney injury (AKI), 16% diuretic-responsive ascites, 9% refractory ascites (29% with CPA, $P<0.001$), and 10% variceal hemorrhage (25% with CPA, $P=0.002$). After median follow-up of 22 months [4-67], patient and graft 1-/3-/5-year survival rates were 71%/67%/61% and 69%/63%/57%, respectively. On multivariate Cox proportional hazards analysis, the only factor significantly and independently associated with all-cause graft loss was non-physiological portal vein reconstruction in which all graft portal inflow arose from recipient systemic circulation (HR 6.639, 95% CI 2.159-20.422, $P=0.001$).

Conclusions: Alternative forms of portal vein anastomosis achieving physiological portal inflow (i.e., deriving at least some splanchnic blood to the transplant graft) offer acceptable post-transplant results in LT candidates with complex PVT. On the contrary, non-physiological portal vein anastomoses fail to resolve portal hypertension and should not be performed.

IMPACT AND IMPLICATIONS

Complex portal vein thrombosis (PVT) is a challenge in liver transplantation. Results of this international, multicenter analysis may be used to guide clinical decisions in transplant candidates with complex PVT. Extra-anatomical portal vein anastomoses deriving at least some recipient splanchnic blood flow to the transplant allograft offer acceptable results. On the other hand, anastomoses that derive only systemic blood flow to the allograft fail to resolve portal hypertension and should not be performed.

ABBREVIATIONS

AKI, acute kidney injury; BMI, body mass index; cDCD, controlled donation after circulatory determination of death; CI, confidence interval; CIT, cold ischemia time; CPA, cavoportal anastomosis; CVA, cerebrovascular accident; DBD, donation after brain death; EBL, estimated blood loss; ELITA, European Liver and Intestine Transplant Association; HAF, hepatic artery flow; HCC, hepatocellular carcinoma; HR, hazards ratio; ICU, intensive care unit; ILTS, International Liver Transplantation Society; LGA, left gastric vein anastomosis; LT, liver transplantation; MELD, model for end-stage liver disease; MVT, multivisceral transplantation; NA, not applicable; NASH, non-alcoholic steatohepatitis; PCA, pericholedochal vein anastomosis; PRBCs, packed red blood cells; PRS, post-reperfusion syndrome; PV, portal vein; PVA, portal vein arterialization; PVF, portal vein flow; PVT, portal vein thrombosis; RPA, renoportal anastomosis; SETH, Sociedad Española de Trasplante Hepático; TBI, traumatic brain injury; TIPS, transjugular intrahepatic portosystemic shunt; WIT, warm ischemia time.

INTRODUCTION

Distinct to other solid organs for transplantation, the liver has dual vascular inflow through the hepatic artery and portal vein (PV), and re-establishment of both inflow sources is a critical objective determining the technical success of liver transplantation (LT). Based on factors associated with end-stage liver disease, non-tumoral PV thrombosis (PVT) has been described in up to 26% and diffuse or complex PVT in nearly to 3% of LT recipients (1), complicating the aforementioned objective in this subset of patients. In reality, these figures underestimate the true prevalence of PVT among potential LT candidates, as PVT has traditionally been an absolute or relative contraindication to LT candidacy. Increasing experience and technical advances over time, however, have allowed more patients with complex PVT to access and benefit from this life-saving procedure.

Several different systems have been developed to classify non-tumoral PVT (2–10). Bhangui and colleagues published a comprehensive and critical review of the literature on LT performed in the context PVT and developed a system correlating anatomical and functional parameters with surgical approach (11). The authors describe non-complex PVT as limited to the PV trunk and/or very distal splenic and/or superior mesenteric veins and complex PVT as complete splanchnic vein thrombosis affecting the portal, splenic, and superior mesenteric veins (Yerdel grade 4, Charco and Jamieson grades 3 and 4) (5,6). While the former may typically be treated with thrombectomy and portoportal reconstruction or placement of an interposition graft from a native PV tributary (anatomical approaches), the latter situation requires application of alternative surgical approaches, including recipient left renal vein to graft PV anastomosis (renoportal anastomosis – RPA), dilated recipient left gastric vein (LGA) or pericholedochal vein (PCA) to graft PV anastomosis, recipient inferior vena cava to graft PV anastomosis (cavoportal anastomosis or cavoportal hemitransposition – CPA), PV arterialization (PVA), and even multivisceral transplantation (MVT) of the liver along with other organs draining to the PV (stomach, pancreas, and small intestine +/- right colon). These approaches have recently been classified as “physiological” when all or some part of the splanchnic blood flow is directed

to the graft PV and "non-physiological" when all graft portal inflow comes from the recipient's systemic circulation (11).

While these various alternative surgical approaches to complex PVT have been described since the 1980s for PCA (12) and 1990s for LGA, RPA, and CPA (13–15), detailed descriptions regarding their clinical application and post-transplant results remain limited to case reports and series, largely produced by a handful of highly experienced centers (16–18). In light of this situation and based on the fact that there is considerable risk for reporting bias in favor of more successful cases, the international, multicenter registry known as RP4LT Collaborative was launched in 2020. The Collaborative's ongoing objective is to record, analyze, and report in anonymized fashion cases of alternative portal revascularization performed in the setting of PVT. The present study is the first report on the Collaborative's findings and focuses solely on extra-anatomical PV reconstructions, to evaluate outcomes and durability of results in terms of resolving portal hypertension and its associated complications.

METHODS

The RP4LT Collaborative was created as a multicenter, international, observational web registry to record cases of LT performed in patients with complex or diffuse PVT. The online registry was officially launched for recording of cases in October 2020. Cases were recorded and updated by study participants through December 2021 for this first analysis. The registry remains active and is sponsored by the European Liver and Intestine Transplant Association (ELITA), the International Liver Transplantation Society (ILTS), and the Spanish Liver Transplant Society (Sociedad Española de Trasplante Hepático – SETH) and was announced multiple times by all three societies to their respective memberships throughout 2020 and early 2021.

Center participation, data collection, and ethics approval

In order to participate in the study and include patients, interested individuals and institutions contacted the principal investigators (YF, AJH) or study sponsor (CF), who confirmed their identity and

their center. Each center was provided with a unique username and password to enter cases in the online platform. Prior to case entry, each center completed an initial survey evaluating center-specific information.

Data was collected via a secure, password-protected, and encrypted online data management system meeting international standards for online databases, including complete anonymization of data. Data collection and analysis were approved by the SETH, the UZ Leuven Institutional Review Board (protocol number S64683), and the Hospital Clínic Barcelona Committee on Ethics in Medical Research (protocol number HCB/2020/0572), the latter of which waived need to obtain written consent. The study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki.

Study patients

Recipients undergoing a first LT with complex PVT treated with an alternative form of portal revascularization (RPA, LGA, PCA, or CPA) were included for analysis. Exclusion criteria included cases of portoportal or mesoportal anastomoses performed primarily, following surgical thrombectomy, or via use of an interposition graft, as well as cases of PVA, liver re-transplantation, and MVT.

Variables and definitions

Variables related to the donor; graft; and the recipient's pre-, intra-, and post-operative states were recorded for each case. Whether the specific case had previously been reported in the medical literature and the reference of the associated publication was also registered. Graft steatosis was classified as none, mild (<30%), moderate (30-59%), or severe (≥60%). Ascites was classified as none, grade I (mild), grade II (moderate, managed with diuretics), or grade III (severe, refractory to diuretics). Hepatic encephalopathy was classified as none, grade I (mild confusion), grade II (moderate confusion), grade III (marked confusion), or grade IV (coma). Esophageal varices were classified as none, grade I (small, straight), grade II (medium, tortuous), or grade III (>1/3 of esophageal lumen). Post-reperfusion syndrome was defined as decline in mean arterial pressure <30% of baseline for at least 1 minute within 5 minutes of portal reperfusion and/or >0.4 μg/kg/min of epinephrine required during the same time period) (19). Presence of portosystemic shunts and PV collaterals was recorded, and the information

was used to classify the nature of PV reconstruction. Physiological PV reconstructions included anastomoses with hilar PV collaterals (LGA, PCA); RPA performed in the presence of a large (≥8mm), permeable spontaneous or surgical splenorenal shunt; and CPA performed in the presence of a large (≥8mm), permeable spontaneous or surgical mesocaval or mesoiliac shunt (20,21); the remainder of PV reconstructions were considered non-physiological (11). Finally, post-operative acute kidney injury was classified as none, stage I (creatinine increase 1.5-1.9x baseline within first 7 days), stage II (creatinine increase 2-2.9x baseline within first 7 days), or stage III (creatinine increase >3x baseline within first 7 days or initiation of renal replacement therapy) (22).

Data analysis

Categorical variables are described as frequencies and percentages and continuous variables as median [25%– 75% interquartile range], unless otherwise specified. Categorical variables were compared using Pearson chi-square test and continuous variables using Kruskal-Wallis one-way ANOVA. Actuarial survival rates were evaluated according to the Kaplan-Meier method and comparisons between groups made using the Mantel-Cox log-rank test. In order to identify risk factors independently associated with all-cause graft loss as a time-to-event outcome, univariate and multivariate Cox proportional hazards regression models were created to estimate hazards ratios (HR) with 95% confidence intervals (CI). For multivariate analysis, the starting model included predictors with univariate $P<0.2$. Backward stepwise elimination was performed, with $P>0.1$ used as criterion for removal, and stratifying according to transplant center. Missing data were handled by case-wise deletion. A value of $P<0.05$ was considered significant, unless otherwise specified. Statistical analyses were performed with SPSS® Statistics version 25 (IBM®).

RESULTS

Participating center characteristics

Overall, cases were submitted from 33 LT centers in 14 countries on four continents. Median cases recorded per center were 3 (range 1-23). While cases were submitted from 18 high-volume LT centers

(>50 LT/year) (23) and 15 low-volume centers, high-volume centers submitted 77% of cases overall. Six centers (18%) claimed to have active MVT programs at time of case submission.

Case submissions

As of December 2021, a total of 182 cases were recorded in the RP4LT registry. Excluding cases of anatomical PV anastomosis performed using an interposition graft (N=36), PVA (N=1), and unknown form of portal anastomosis (N=5), a total of 140 cases were available for analysis. These included 74 cases of RPA, 18 LGA, 20 PCA, and 28 CPA. Among these, 37 had been described in previous publications (1,18,24–28) and 103 (74%) were novel cases, never before reported in the medical literature (RPA N=55, LGA N=17, PCA N=12, CPA N=19).

Figure 1 depicts the number of cases performed during three consecutive periods. While LT were included that were performed as long ago as 1996, the majority of included cases were performed subsequent to 2010: 1996-2000 N=4 (3%), 2001-2010 N=31 (22%), 2011-2021 N=105 (75%).

Donor and graft characteristics

Table 1 provides overall donor and graft characteristics. Median donor age and BMI were 57 years [40-70] and 25.7 [22.9-28.4], respectively. Donors were 56% men and 92% DBD, and cerebrovascular accident (CVA) was the most common cause of death (58%). In all but three cases, whole liver grafts were used (98%).

Recipient baseline characteristics

Table 2 provides recipient characteristics at baseline. Overall, median recipient age and BMI were 58 years [49-63] and 25.6 [23.2-29.7], respectively. The majority of recipients presented ascites (23% refractory) and some degree of hepatic encephalopathy and esophageal varices, while a minority of patients presented hepatorenal syndrome (7% type I, 10% type II). Median recipient MELD at transplant was 17 [14-24], and the majority of patients were classified Child-Pugh B-C. Portal vein thrombosis was classified as complex in 77% of cases and non-complex (Yerdel grade 3) in the remainder. Slightly fewer than half of all patients (44%) had portal cavernoma. Spontaneous and surgical splenorenal shunts were

present in 59% and 7% of all recipients, respectively. Specifically, among recipients undergoing RPA, 87% were described to have spontaneous splenorenal shunt and another 6% surgical.

Transplant operative characteristics

Table 3 provides intraoperative details associated with LT. Portal thrombectomy was attempted in 32% of cases overall. While thrombectomy was attempted in fewer patients undergoing LGA (6%), it was initially attempted in 68% of patients ultimately undergoing CPA (*P*<0.001). The majority of patients (83%) underwent LT with caval preservation, though this proportion was significantly less (61%) among patients undergoing CPA (*P*<0.001). Venous interposition grafts were used to complete the portal anastomosis in half of all cases; this percentage was higher for cases with RPA (64%, *P*=0.002) and lower for cases with PCA (11%, *P*<0.001). Overall, 12.9% of PV reconstructions were non-physiological; this percentage was significantly higher among recipients undergoing CPA (46.4%, *P*<0.001). Median cold ischemia time was 431 minutes [360-505] and LT warm ischemia time 35 minutes [30-50]. Cold ischemia was significantly longer for cases undergoing CPA (*P*=0.017 vs. RPA, *P*=0.003 vs. LGA), and transplant warm ischemia tended to be longer for cases performed with PCA. Evaluating all cases, LT operative time was 461 minutes [360-540] and tended to be longer for cases undergoing CPA. Nearly all patients underwent intraoperative transfusion of red blood cells (89%) and/or blood products (65% plasma, 61% platelets). Post-reperfusion syndrome arose in 29% of all patients overall.

Outcomes

Table 4 reflects post-transplant events and outcomes. Overall, 28% of patients underwent surgical re-intervention in the immediate post-transplant period, with a trend toward a higher rate of re-intervention (46%) among patients with CPA. Median post-transplant ICU stay was 6 days [3-11] and overall post-operative hospital stay 22 days [14-36]. A slight majority of patients (51%) did not develop any post-transplant AKI, while 13% developed stage 1, 14% stage 2, and 22% stage 3 AKI. Half of all patients remained free of ascites following LT, while a quarter had transient ascites, 16% ascites responsive to ongoing diuretic therapy, and 9% ongoing refractory ascites. Among patients with CPA, ongoing refractory ascites was present in 29% (*P*<0.001). Variceal hemorrhage recurred post-transplant

in 10% of patients overall and a quarter of patients with CPA (*P*=0.002). The overall rate of portal re-thrombosis was 4%. Among all recipients, 41% continued on anticoagulation therapy following LT. Rates of ongoing anticoagulation therapy were lower among patients with LGA (11%, P=0.006) and higher among patients with CPA (71%, *P*<0.001). Only one case of hepatic artery thrombosis was detected in a patient with PCA.

With a median follow-up of 22 months [4-67], patient 1-/3-/5-year survival rates were 71%/67%/61%, respectively, and graft 1-/3-/5-year survival rates (not death censored) 69%/63%/57%, respectively. Figure 2A reflects Kaplan Meier survival curves, stratified according to type of alternative portal anastomosis. At 1/3/5 years, 74%/72%/63% of patients with RPA, 70%/70%/70% of patients with LGA, 85%/79%/79% of patients with PCA, and 52%/42%/33% of patients with CPA, respectively, were surviving (Mantel-Cox log rank *P*=0.020). In terms of graft survival (not death censored), these figures were 74%/68%/60% RPA, 64%/64%/64% LGA, 78%/72%/72% PCA, and 52%/42%/33% CPA (*P*=0.089). Specifically, among recipients with RPA, five cases were recorded in which the recipient had no pre-existing, large splenorenal shunt (spontaneous or surgical) (6.8%). Among these cases, four recipients died near the end of the first post-transplant month, and only one recipient was surviving with a functional transplant allograft at 9.5 months. Excluding these five cases, 1-/3-/5-year survival rates among RPA recipients were 77%/75%/64%, respectively.

Perioperative risk factors for graft loss

Perioperative risk factors for all-cause graft loss were evaluated among the entire 140 patient cohort. Cases of LGA and PCA were considered together for this analysis, based on similarity in terms of physiology of PV reconstruction and post-transplant results. Table 5 depicts the results of uni- and multivariate Cox proportional hazards models, the latter stratified according to transplant center. While CPA was a significant risk factor for graft loss on univariate analysis, it was not included in the multivariate model due to collinearity with the nature of PV reconstruction (physiological vs. non-physiological). In the final multivariate Cox proportional hazards model, the only variable significantly and independently associated with all-cause graft loss was non-physiological PV reconstruction (HR

6.639, 95% CI 2.159-20.422, *P*=0.001). Five-year patient and graft survival rates were 68% and 66%, respectively, in cases of physiological PV reconstruction versus only 6.7% for both patients and grafts in cases with non-physiological PV anastomosis (Figure 2B).

DISCUSSION

To date, this is the largest comprehensive description of extra-anatomical portal anastomoses performed in the context of LT with complex PVT. Cases were submitted from 33 LT centers in 14 countries, and close to 77% came from centers considered to perform high overall volume of LT. A total of 140 cases of extra-anatomical PV anastomoses were analyzed, among which approximately three quarters were new cases never reported in the medical literature previously. The great majority (75%) were performed over the course of the past decade. Notable study findings include 5-year post-transplant patient survival rates of 61% overall; 68% for patients with physiological PV reconstruction, including 64% for patients with RPA and pre-existing splenorenal shunt (the most common form of alternative portal vein anastomosis); and 33% for patients undergoing CPA. Portal re-thrombosis was not an important issue in this experience, arising in only 4% of patients. Rather, non-physiological PV reconstruction was the only significant, independent predictor of all-cause graft loss during follow-up. These results not only validate the Bhangui system for classifying PVT in the setting of LT but also reinforce the critical importance of including precise cross-sectional imaging of the portosplenomesenteric system in the pre-operative LT work-up. They also suggest that non-physiological PV reconstructions should be contraindicated in patients with complex PVT and no accessible portal vein collaterals, no large portosystemic shunts, and no potential to create surgical shunts intraoperatively, as such non-physiological procedures are associated with dismal post-transplant outcomes (<7% 5-year patient and graft survival).

Prior to this multicenter, international collaborative, the most important resources describing alternative forms of PV anastomosis have been systematic reviews of case reports and series (11,17) and a 2021 publication detailing results of LT performed with RPA by a handful of expert centers (18).

In the most recent literature review, 57 cases of RPA performed between 1997 and 2017 were compiled (11). Among recipients, 20% developed AKI and 6% portal re-thrombosis, and 81% of patients were described to be alive at intervals ranging from 2 months to 5 years post-transplant. The recent publication by Azoulay and colleagues provides a more granular view of RPA outcomes achieved among 57 LT performed at 5 expert centers (3 in France, 1 in Spain, 1 in the United States of America) (18). Authors reported that RPA was feasible in all cases in which it was attempted. Some degree of post-transplant renal functional impairment was observed in 28% of patients and portal re-thrombosis in 14%. Nonetheless, 5-year graft and patient survival rates were 73% and 76%, respectively.

Aside from RPA, the present study describes outcomes of 38 LT with PV anastomoses performed with dilated recipient PV collaterals (LGA, PCA). In the literature published to date, use of PV collaterals to revascularize the LT allograft has been described anecdotally albeit successfully. Bhangui and colleagues compiled 37 cases of LGA reported between 1990 and 2018 and 11 cases of PCA reported between 1986 and 2017 (11). Among these cases, there was limited description of post-operative morbidity, and patient survival was described as being at least 90% for both approaches, though after variable and somewhat unclear lengths of follow-up. Herein, 5-year patient survival rates following LGA and PCA were 70% and 79%, respectively. Considering the standard cut-off of achieving 50% post-transplant survival at 5 years (29), these results appear to be acceptable and justify ongoing use of these approaches, at least in the hands of experienced surgeons.

An approach that does not appear acceptable is that of CPA. Results observed following CPA in this study include 33% patient survival at 5 years, with 68% developing some degree of AKI and 46% requiring surgical re-intervention due to hemorrhage and other complications arising in the immediate post-transplant period. During follow-up, ongoing ascites and recurrent variceal hemorrhage were observed in 39% and 25% of recipients, respectively, reflecting failure of CPA to resolve portal hypertension in a large percentage of cases. Previous reports on CPA have described similar findings, with 30-50% of patients developing post-operative intraabdominal hemorrhage, 30% recurrent variceal hemorrhage, 20-30% PV re-thrombosis, 40-50% chronic renal dysfunction, and <40% surviving beyond

5 years (11,15,30,31). While CPA may often be performed in extreme situations, when no other therapeutic option may appear feasible, such an approach is erroneous. Unless there is a pre-existing mesocaval or mesoiliac shunt or one can be created intraoperatively, CPA should not be performed.

Alternative PV anastomosis was planned pre-operatively in about half of all cases included in this analysis. This does not necessarily reflect that surgeons involved in these cases were careless, as not every portomesenteric vein system is amenable to reconstruction due to extensive calcification or fragility of the vessel wall that might only become fully apparent at the time of surgical exploration. If anything, it reflects the fact that LT centers need a comprehensive strategy for assessing and managing PVT in transplant candidates. Candidates need to be screened for PVT prior to entering the waiting list. Patients without PVT should be reassessed at least every 3 months if not more frequently in the presence of acute clinical event(s) suggestive of thrombosis. In cases with PVT, initial management includes anticoagulation as well as TIPS for non-complex PVT to facilitate antegrade PV flow and limit if not resolve thrombus formation (32,33). Cross-sectional imaging is essential to adequately characterize recipient anatomy, including extent of thrombosis and presence and size of shunts and/or collaterals (Figure 3). Prior to listing for LT, a surgical plan needs to be made were PV thrombectomy to result unsuccessful or unfeasible intraoperatively. Based on preoperative imaging, an alternative approach for achieving physiological graft PV inflow needs to be identified, be it via anastomosis to patent proximal superior mesenteric vein via an interposition graft (non-complex PVT) or to a dilated hilar collateral or systemic vein fed by a large portosystemic shunt (splenorenal, mesocaval, mesoiliac, or other). Finally, in cases with no large hilar or other accessible collaterals nor relevant portosystemic shunts, referral to a center offering MVT is recommended, if available.

Recipient abdominal exenteration and MVT of the liver, pancreas, stomach, small intestine, and right colon is associated with high rates of morbidity, including many infectious complications, and is performed by a select few centers. Nonetheless, MVT is another physiological treatment option for patients with complex PVT. Aside from case reports, one series has been published to date describing outcomes of MVT performed among 25 patients with complex PVT, including 29 adults and two children

(34). Median pre-transplant MELD was 22 (range 7-40), median operative time 10 hours (range 7-16), and median blood transfusion requirement 29 units (range 5-146). There were no operative deaths, and actuarial one- and five-year survival rates were 80% and 72%, respectively. Of note, there were six deaths in the first post-transplant year due to infectious complications. While these outcomes are comparable to if not slightly better than those observed for other physiological PV reconstructions in the present study, they were obtained at a single, highly experienced center. If anything, they should prompt reappraisal of this important therapeutic alternative, which is currently not available in all countries. In patients with complex PVT undergoing LT at these centers, the entire multivisceral allograft may be recovered and serve as a back-up alternative when adequate PV flow cannot be established via other routes intraoperatively (35). In order to avoid severe and life-threatening hemorrhage during dissection and exenteration of the recipient's native organs, techniques of intraoperative embolization of the celiac trunk branches and superior mesenteric artery and staged removal of abdominal organs have been described (36). Such visceral artery embolization, however, has been associated with devastating intraoperative consequences related to migration of embolized material (37) and necessarily commits the surgical team to MVT.

The present study has limitations related to its retrospective nature. While the manner in which cases were recruited may have helped to reduce reporting bias relative to previous studies, such risk remains, and cases of intraoperative death may not have been captured. As well, the fact that data was largely recovered retrospectively means that additional variables of interest (intraoperative PV and hepatic artery flows, native liver and transplant allograft masses, etc.) were not recorded in a large proportion of cases and could not be analyzed. Finally, in spite of ample and repeated diffusion of the existence of the RP4LT Collaborative via different media pathways and societies, the great majority of cases provided came from Europe. Inclusion of cases from Asia, where living donor liver transplantation is more common, was very low. By maintaining the Collaborative open and active, we hope to continue to recruit more cases prospectively and from currently underrepresented regions and settings.

In summary, management of complex PVT in LT candidates and recipients is difficult. Prior to entry on the LT waiting list, detailed cross-sectional imaging is necessary to identify the most appropriate intraoperative strategy were thrombectomy and standard portoportal anastomosis to result unsuccessful. While alternative forms of PV anastomosis, including RPA, LGA, and PCA, appear to offer acceptable results, these cases should be managed by experienced centers or surgeons in order to achieve optimal post-transplant results. Non-physiological PV reconstruction, in which all allograft PV inflow arises from the recipient's systemic circulation, should not be performed. Rather, patients with complex PVT with no large portosystemic shunt nor the potential to create such a shunt nor any large hilar PV collateral might best be managed in centers offering MVT as a back-up alternative.

ACKNOWLEDGMENTS

The authors would like to thank Ms. Adela Mas for assistance with database preparation and management.

REFERENCES

1. Rodríguez-Castro KI, Porte RJ, Nadal E, Germani G, Burra P, Senzolo M. Management of nonneoplastic portal vein thrombosis in the setting of liver transplantation: A systematic review. Transplantation. 2012;94(11):1145–53.
2. Stieber AC, Zetti G, Todo S, Tzakis AG, Fung JJ, Marino I, et al. The spectrum of portal vein thrombosis in liver transplantation. Ann Surg. 1991;213(3):199–206.
3. Nonami T, Yokoyama I, Iwatsuki S, Starzl TE. The incidence of portal vein thrombosis at liver transplantation. Hepatology. 1992;16(5):1195–8.
4. Gayowski TJ, Marino IR, Doyle HR, Echeverri L, Mieles L, Todo S, et al. A high incidence of native portal vein thrombosis in veterans undergoing liver transplantation. J Surg Res. 1996;60(2):333–8.
5. Yerdel MA, Gunson B, Mirza D, Karayal??in K, Olliff S, Buckels J, et al. PORTAL VEIN THROMBOSIS IN ADULTS UNDERGOING LIVER TRANSPLANTATION. Transplantation [Internet]. 2000 May;69(9):1873–81. Available from: http://journals.lww.com/00007890-200005150-00023
6. Jamieson N V. CHANGING PERSPECTIVES IN PORTAL VEIN THROMBOSIS AND LIVER TRANSPLANTATION. Transplantation [Internet]. 2000 May;69(9):1772–4. Available from: http://journals.lww.com/00007890-200005150-00006
7. Charco R, Fuster J, Fondevila C, Ferrer J, Mans E, García-Valdecasas JC. Portal vein thrombosis in liver transplantation. Transplant Proc. 2005;37(9):3904–5.
8. Bauer J, Johnson S, Durham J, Ludkowski M, Trotter J, Bak T, et al. The role of TIPS for portal vein patency in liver transplant patients with portal vein thrombosis. Liver Transpl [Internet]. 2006 Oct;12(10):1544–51. Available from: http://www.ncbi.nlm.nih.gov/pubmed/17004250
9. Ma J, Yan Z, Luo J, Liu Q, Wang J, Qiu S. Rational classification of portal vein thrombosis and its clinical significance. PLoS One. 2014;9(11):1–7.
10. Sarin SK, Philips CA, Kamath PS, Choudhury A, Maruyama H, Nery FG, et al. Toward a Comprehensive New Classification of Portal Vein Thrombosis in Patients With Cirrhosis.

Gastroenterology [Internet]. 2016;151(4):574-577.e3. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0016508516349757

11. Bhangui P, Lim C, Levesque E, Salloum C, Lahat E, Feray C, et al. Novel classification of non-malignant portal vein thrombosis: A guide to surgical decision-making during liver transplantation. J Hepatol [Internet]. 2019;71(5):1038–50. Available from: https://doi.org/10.1016/j.jhep.2019.08.012

12. Hiatt JR, Quinones-Baldrich WJ, Ramming KP, Lois JF, Busuttil RW. Bile duct varices. An alternative to portoportal anastomosis in liver transplantation. Transplantation [Internet]. 1986 Jul;42(1):85. Available from: http://www.ncbi.nlm.nih.gov/pubmed/3523887

13. Czerniak A, Badger I, Sherlock D, Buckels J. Orthotopic liver transplantation in a patient with thrombosis of the hepatic portal and superior mesenteric veins. Transplantation [Internet]. 1990 Aug;50(2):334–6. Available from: http://www.ncbi.nlm.nih.gov/pubmed/2382299

14. Sheil AG, Stephen MS, Chui AK, Ling J, Bookallil MJ. A liver transplantation technique in a patient with a thrombosed portal vein and a functioning renal-lieno shunt. Clin Transplant [Internet]. 1997 Feb;11(1):71–3. Available from: http://www.ncbi.nlm.nih.gov/pubmed/9067699

15. Tzakis AG, Kirkegaard P, Pinna AD, Jovine E, Misiakos EP, Maziotti A, et al. Liver transplantation with cavoportal hemitransposition in the presence of diffuse portal vein thrombosis. Transplantation [Internet]. 1998 Mar 15;65(5):619–24. Available from: http://www.ncbi.nlm.nih.gov/pubmed/9521194

16. Quintini C, Spaggiari M, Hashimoto K, Aucejo F, Diago T, Fujiki M, et al. Safety and effectiveness of renoportal bypass in patients with complete portal vein thrombosis: An analysis of 10 patients. Liver Transplant [Internet]. 2015 Mar;21(3):344–52. Available from: https://onlinelibrary.wiley.com/doi/10.1002/lt.24053

17. D'Amico G, Hassan A, Diago Uso T, Hashmimoto K, Aucejo FN, Fujiki M, et al. Renoportal anastomosis in liver transplantation and its impact on patient outcomes: a systematic literature review. Transpl Int. 2019;32(2):117–27.

18. Azoulay D, Quintini C, Rayar M, Salloum C, Llado L, Diago T, et al. Renoportal Anastomosis during Liver Transplantation in Patients with Portal Vein Thrombosis. Ann Surg [Internet]. 2021 Feb 10;Publish Ah. Available from: https://journals.lww.com/10.1097/SLA.0000000000004797

19. Blasi A, Hessheimer AJ, Beltrán J, Pereira A, Fernández J, Balust J, et al. Liver Transplant From Unexpected Donation After Circulatory Determination of Death Donors: A Challenge in Perioperative Management. Am J Transplant. 2016;16(6):1901–8.

20. Renzulli M, Dajti E, Ierardi AM, Brandi N, Berzigotti A, Milandri M, et al. Validation of a standardized CT protocol for the evaluation of varices and porto-systemic shunts in cirrhotic patients. Eur J Radiol. 2022;147(October 2021).

21. Dajti E, Renzulli M, Colecchia A, Bacchi-Reggiani ML, Milandri M, Rossini B, et al. Size and location of spontaneous portosystemic shunts predict the risk of decompensation in cirrhotic patients. Dig Liver Dis [Internet]. 2022;54(1):103–10. Available from: https://doi.org/10.1016/j.dld.2020.12.114

22. Kalisvaart M, Schlegel A, Umbro I, De Haan JE, Scalera I, Polak WG, et al. The Impact of Combined Warm Ischemia Time on Development of Acute Kidney Injury in Donation after Circulatory Death Liver Transplantation: Stay Within the Golden Hour. Transplantation. 2018;102(5):783–93.

23. Muller X, Marcon F, Sapisochin G, Marquez M, Dondero F, Rayar M, et al. Defining Benchmarks in Liver Transplantation: A Multicenter Outcome Analysis Determining Best Achievable Results. Ann Surg. 2018;267(3):419–25.

24. Ceulemans B, Aerts R, Monbaliu D, Coosemans W, Verslype C, Van Steenbergen W, et al. Liver transplantation using cavoportal transposition: an effective treatment in patients with complete splanchnic venous thrombosis. Transplant Proc [Internet]. 2005 Mar;37(2):1112–4. Available from: http://www.ncbi.nlm.nih.gov/pubmed/15848638

25. Lladó L, Fabregat J, Castellote J, Ramos E, Torras J, Jorba R, et al. Management of portal vein thrombosis in liver transplantation: Influence on morbidity and mortality. Clin Transplant. 2007;21(6):716–21.

26. Laxague F, Valinoti A, Ramallo D, Casas MA, Quiñones E, McCormack L. Intraoperative Challenge for Vascular Reconstruction in Orthotopic Liver Transplantation Because of Extensive Portal Thrombosis and Intimal Dissection of the Hepatic Artery. ACG Case Reports J. 2020;7(6):e00390.

27. Rotellar F, Cienfuegos JA, Bueno A, Marti P, Valenti V, Zozaya G, et al. Portal revascularization in the setting of cavernous transformation through a paracholedocal vein: A case report. Transplant Proc [Internet]. 2010;42(8):3079–80. Available from: http://dx.doi.org/10.1016/j.transproceed.2010.08.006

28. Guarner P, García R, Al Shwely F, Pérez-Serrano C, Rodríguez S, Torroella A, et al. Unusual Allogeneic Retrohepatic Vena Cava Graft for Renoportal Anastomosis in Orthotopic Liver Transplantation. Liver Transplant. 2020;26(8):1056–9.

29. Schaubel DE, Guidinger MK, Biggins SW, Kalbfleisch JD, Pomfret EA, Sharma P, et al. Survival benefit-based deceased-donor liver allocation. Am J Transplant [Internet]. 2009 Apr;9(4 Pt 2):970–81. Available from: http://www.ncbi.nlm.nih.gov/pubmed/19341419

30. Pinna AD, Nery J, Kato T, Levi D, Nishida S, Tzakis AG. Liver transplant with portocaval hemitransposition: experience at the University of Miami. Transplant Proc [Internet]. 2001;33(1–2):1329–30. Available from: http://www.ncbi.nlm.nih.gov/pubmed/11267311

31. Selvaggi G, Weppler D, Nishida S, Moon J, Levi D, Kato T, et al. Ten-year experience in porto-caval hemitransposition for liver transplantation in the presence of portal vein thrombosis. Am J Transplant. 2007;7(2):454–60.

32. Montalvá E, Rodríguez-Perálvarez M, Blasi A, Bonanad S, Gavín O, Hierro L, et al. Consensus Statement on Hemostatic Management, Anticoagulation, and Antiplatelet Therapy in Liver Transplantation. Transplantation. 2022;106(6):1123–31.

33. Thornburg B, Desai K, Hickey R, Hohlastos E, Kulik L, Ganger D, et al. Pretransplantation Portal Vein Recanalization and Transjugular Intrahepatic Portosystemic Shunt Creation for Chronic Portal Vein Thrombosis: Final Analysis of a 61-Patient Cohort. J Vasc Interv Radiol [Internet]. 2017;28(12):1714-1721.e2. Available from: https://doi.org/10.1016/j.jvir.2017.08.005

34. Vianna RM, Mangus RS, Kubal C, Fridell JA, Beduschi T, Joseph Tector A. Multivisceral transplantation for diffuse portomesenteric thrombosis. Ann Surg. 2012;255(6):1144–50.

35. Tekin A, Beduschi T, Vianna R, Mangus RS. Multivisceral transplant as an option to transplant cirrhotic patients with severe portal vein thrombosis. Int J Surg [Internet]. 2020;82(April 2020):115–21. Available from: https://doi.org/10.1016/j.ijsu.2020.07.010

36. Canovai E, Ceulemans LJ, Gilbo N, Duchateau NM, De Hertogh G, Hiele M, et al. Multivisceral Transplantation for Diffuse Portomesenteric Thrombosis: Lessons Learned for Surgical Optimization. Front Surg. 2021;8(February):1–17.

37. Nicolau-Raducu R, Livingstone J, Salsamendi J, Beduschi T, Vianna R, Tekin A, et al. Visceral arterial embolization prior to multivisceral transplantation in recipient with cirrhosis, extensive portomesenteric thrombosis, and hostile abdomen: Performance and outcome analysis. Clin Transplant. 2019;33(8):1–7.

FIGURE LEGENDS

Figure 1. Liver transplants performed with alternative portal anastomosis, stratified according to transplant year.

Figure 2. Kaplan Meier survival curves for liver transplant recipients undergoing alternative forms of portal vein anastomoses, stratified according to **(A)** type of anastomosis and **(B)** physiological vs. non-physiological nature of reconstruction.

Figure 3. Pre-transplant coronal CT images of patients with complex portal vein thrombosis and spontaneous splenorenal shunts (white arrow) and dilated perigastric collaterals (black arrow) **(A, B)**; both patients ultimately underwent liver transplantation with left renoportal anastomosis **(C)**. CT venous reconstruction of a patient with complex portal vein thrombosis and spontaneous mesoiliac shunt **(D)**. Post-transplant images of graft portal anastomoses with dilated left gastric vein **(E)** and pericholedochal collaterals **(F)**. Intraoperative image of graft portal vein (white arrow) anastomosis to confluence of pericholedochal collaterals (black arrow), adjacent to completed hepatic arterial anastomosis (asterisk) **(G)**. *Images provided courtesy of G. Blanco, M. Gastaca, S. Nadalin, and F. Rotellar.*

Table 1. Donor and graft characteristics.

	Overall (N=140)	Missing (%)
Donor		
Age (y)	57 [40-70]	0
Sex male	56.6%	2.9
BMI	25.7 [22.9-28.4]	8.6
Type		0
DBD	92.1%	
cDCD	7.2%	
Domino	0.7%	
Cause of death		3.6
CVA	57.8%	
TBI	20.0%	
Anoxic brain injury	18.5%	
Other	3.0%	
NA	0.7%	
Graft		
Type		0
Whole	97.9%	
Right hemiliver	0.7%	
Left hemiliver	0.7%	
Extended right hemiliver	0.7%	
Steatosis		9.3
None	57.5%	
Mild <30%	39.4%	
Moderate 30-59%	2.4%	
Severe >/= 60%	0.8%	

BMI, body mass index; cDCD, controlled donation after circulatory determination of death; CVA, cerebrovascular accident; DBD, donation after brain death; NA, not applicable; TBI, traumatic brain injury.

Table 2. Recipient characteristics at baseline.

	Overall (N=140)	RPA (N=74)	LGA (N=18)	PCA (N=20)	CPA (N=28)	*P*	Missing (%)
Age (y)	58 [49-63]	59 [52-64]	59 [47-61]	56 [52-61]	55 [43-65]	0.770	0
Sex male	75.0%	74.3%	77.8%	85.0%	67.9%	0.589	0
BMI	25.6 [23.2-29.7]	26.5 [23.7-30.9]	25.4 [24.3-28.4]	24.9 [22.6-26.6]	23.8 [21.0-31.9]	0.268	12.1
Etiology						0.146	2.9
Viral hepatitis	34.6%	30.0%	50.0%	40.0%	32.1%		
Alcohol	25.0%	25.7%	38.9%	35.0%	7.1%		
Cholestatic liver disease	3.7%	4.3%	0	0	7.1%		
NASH	4.4%	5.7%	0	0	7.1%		
Other	32.4%	34.3%	11.1	25.0%	46.4%		
HCC	37.8%	34.7%	50.0%	29.4%	42.9%	0.523	3.6
Ascites						0.026	5.0
None	29.3%	35.7%	16.7%	17.6%	28.6%		
Grade I	22.6%	18.6%	55.6%[1]	23.5%	10.7%		
Grade II	24.8%	21.4%	22.2%	23.5%	35.7%		
Grade III	23.3%	24.3%	5.6%	35.3%	25.0%		
Encephalopathy						0.144	3.6
None	46.7%	40.0%	55.6%	42.1%	60.7%		
Grade I	25.2%	25.7%	38.9%	26.3%	14.3%		
Grade II	20.7%	28.6%	5.6%	10.5%	17.9%		
Grade III	5.9%	4.3%	0	15.8%	7.1%		
Grade IV	1.5%	1.4%	0	5.3%	0		
Esophageal varices						0.006	5.7
None	26.5%	27.1%	5.6%	20.0%	45.8%		
Grade I	13.6%	22.9%[1]	5.6%	0	4.2%		
Grade II	43.2%	34.3%	66.7%	65.0%	33.3%		
Grade III	16.7%	15.7%	22.2%	15.0%	16.7%		
Hepatorenal syndrome						0.094	9.3
None	82.7%	85.5%	66.7%	84.2%	85.7%		
Type I	7.1%	4.8%	5.6%	15.8%	7.1%		
Type II	10.2%	9.7%	27.8%	0	7.1%		
Child-Pugh						0.195	18.6
A	11.4%	17.3%	0	16.7%	3.8%		
B	50.0%	53.8%	55.6%	38.9%	46.2%		
C	38.6%	28.8%	44.4%	44.4%	50.0%		
Laboratory MELD score	17 [14-24]	17 [14-23]	16 [14-20]	20 [13-22]	17 [13-25]	0.971	2.1
Complex PVT	76.9%	78.3%	55.6%	84.2%	82.1%	0.128	4.3
Portal cavernoma	44.2%	43.8%	38.9%	52.6%	42.9%	0.855	1.4
Splenorenal shunt						<0.001	4.3
None	34.3%	7.1%[1]	58.8%	100%[1]	42.9%		
Spontaneous	59.0%	87.1%[1]	41.2%	0[1]	39.3%		
Surgical	6.7%	5.7%	0	0	17.9%		
TIPS	3.6%	4.2%	0	10.0%	0	0.249	1.4
Anticoagulation therapy	32.8%	34.2%	22.2%	21.1%	44.4%	0.280	2.1

BMI, body mass index; CPA, cavoportal anastomosis; HCC, hepatocellular carcinoma; LGA, left gastric vein anastomosis; MELD, model for end-stage liver disease; NASH, non-alcoholic steatohepatitis; PCA, pericholedochal vein anastomosis; PVT, portal vein thrombosis; RPA, renoportal anastomosis; TIPS, transjugular intrahepatic portosystemic shunt.

[1]Significant difference on Bonferroni corrected Pearson chi-square post-hoc analysis.

Table 3. Liver transplant center and operative characteristics.

	Overall (N=140)	RPA (N=74)	LGA (N=18)	PCA (N=20)	CPA (N=28)	*P*	Missing (%)
High-volume center	78.6%	72.6%	77.8%	90.0%	89.3%	0.166	0
Thrombectomy attempted	31.4%	24.7%	5.6%	30.0%	67.9%[1]	<0.001	0.7
Alternative anastomosis planned pre-operatively	56.1%	63.4%	44.4%	42.1%	53.3%	0.253	12.1
Technique							0
Caval replacement	17.1%	9.5%	11.1%	20%	39.3%[1]	0.004	
Caval preservation	82.9%	90.5%	88.9%	80%	60.7%[1]		
Interposition graft	51.1%	63.5%[1]	66.7%	10.5%[1]	35.7%	<0.001	0.7
Non-physiological PV reconstruction	12.9%	6.8%	0	0	46.4%[1]	<0.001	0
Organs							0
Liver only	97.1%	94.5%	100%	100%	100%	0.306	
Liver-kidney	2.9%	5.5%	0	0	0		
CIT (min)	433 [360-505]	433 [344-492]	387 [335-435]	400 [340-509]	503 [438-598]	0.002	4.3
Transplant WIT (min)	35 [30-50]	39 [31-52]	30 [28-35]	45 [35-75]	35 [27-40]	0.011	12.9
Operative time (min)	461 [378-540]	457 [354-570]	435 [390-510]	413 [365-495]	517 [463-574]	0.016	3.6
Transfusions							
PRBCs	88.6%	82.6%	88.9%	100%	96.0%	0.094	5.7
Plasma	65.4%	60.9%	38.9%	75.0%	88.0%	0.006	9.3
Platelets	61.4%	58.5%	77.8%	73.7%	48.0%	0.146	9.3
PRS	28.5%	20.0%	16.7%	47.1%	48.0%	0.010	7.1

CIT, cold ischemia time; CPA, cavoportal anastomosis; EBL, estimated blood loss; HAF, hepatic artery flow; LGA, left gastric vein anastomosis; PCA, pericholedochal vein anastomosis; PRBCs, packed red blood cells; PRS, post-reperfusion syndrome; PV, portal vein; PVF, portal vein flow; RPA, renoportal anastomosis; WIT, warm ischemia time.

[1]Significant difference on Bonferroni corrected Pearson chi-square post-hoc analysis.

Table 4. Post-transplant outcomes.

	Overall (N=140)	RPA (N=74)	LGA (N=18)	PCA (N=20)	CPA (N=28)	*P*	Missing (%)
Surgical re-intervention	28.1%	30.1%	11.1%	10.0%	46.4%	0.014	0.7
ICU stay (days)	6 [3-11]	7 [3-12]	5 [3-7]	4 [3-6]	10 [4-22]	0.014	5.7
Hospital stay (days)	22 [14-36]	22 [13-32]	20 [15-29]	16 [9-33]	28 [18-51]	0.088	2.9
AKI						0.170	6.4
No	51.1%	48.5%	61.1%	78.9%	32.1%		
Stage 1	13.0%	13.6%	5.6%	5.3%	21.4%		
Stage 2	13.7%	13.6%	16.7%	10.5%	14.3%		
Stage 3	22.1%	24.2%	16.7%	5.3%	32.1%		
Ascites						0.002	7.1
No	49.2%	54.4%	31.3%	55.6%	42.9%		
Transient	24.6%	27.9%	25.0%	22.2%	17.9%		
Diuretic-responsive	16.2%	10.3%	43.8%[1]	22.2%	10.7%		
Refractory	10.0%	7.2%	0	0	28.6%[1]		
Variceal hemorrhage	9.6%	8.6%	0	0	25.0%[1]	0.009	3.6
Re-thrombosis	3.9%	4.5%	0	5.3%	4.0%	0.839	8.6
Anticoagulation therapy	40.9%	40.3%	11.1%[1]	26.3%	71.4%[1]	<0.001	2.1
Re-transplantation	7.2%	6.9%	5.6%	15.0%	3.6%	0.487	1.4

AKI, acute kidney injury; CPA, cavoportal anastomosis; ICU, intensive care unit; LGA, left gastric vein anastomosis; PCA, pericholedochal vein anastomosis; RPA, renoportal anastomosis.

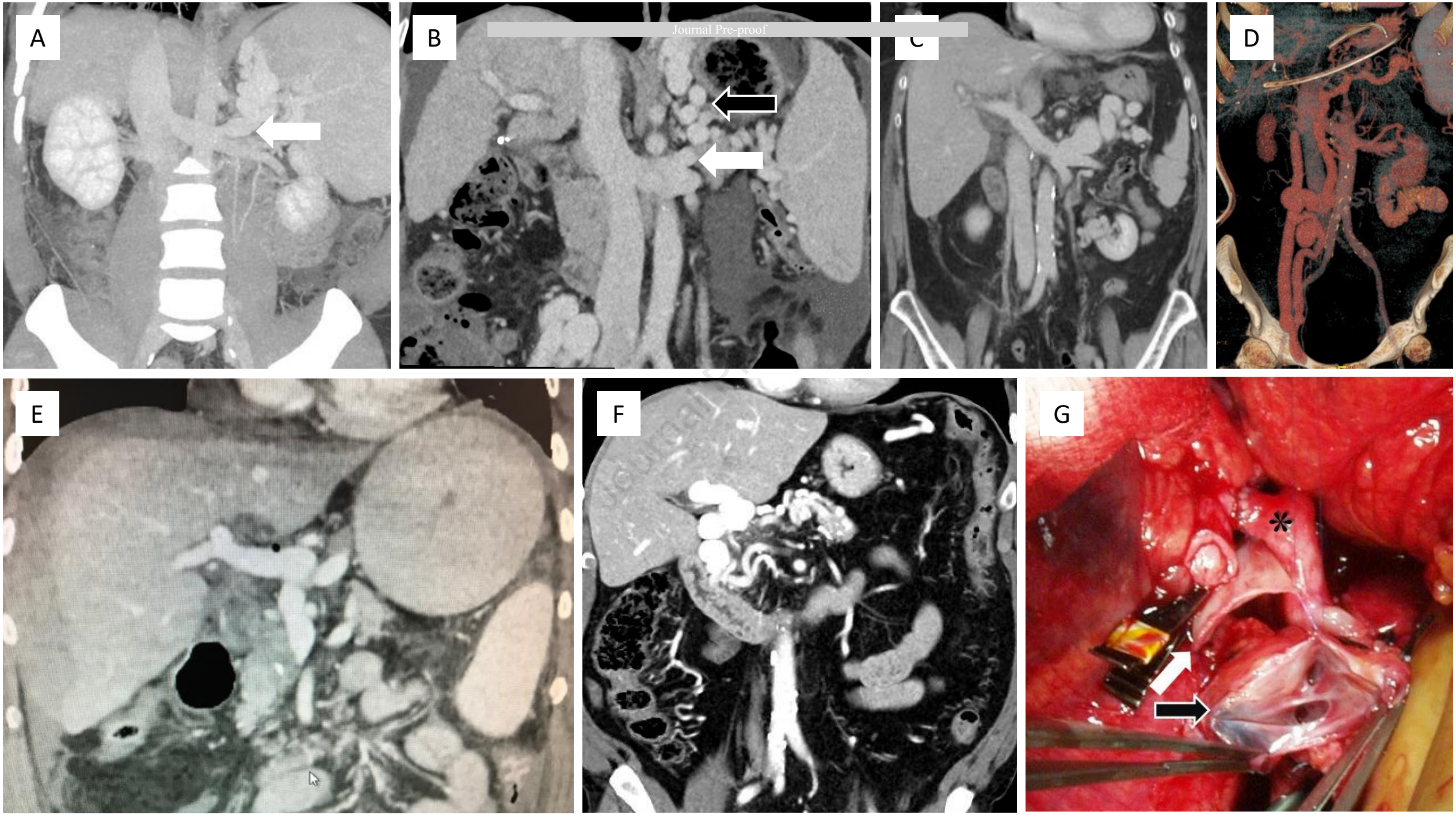
[1]Significant difference on Bonferroni corrected Pearson chi-square post-hoc analysis.

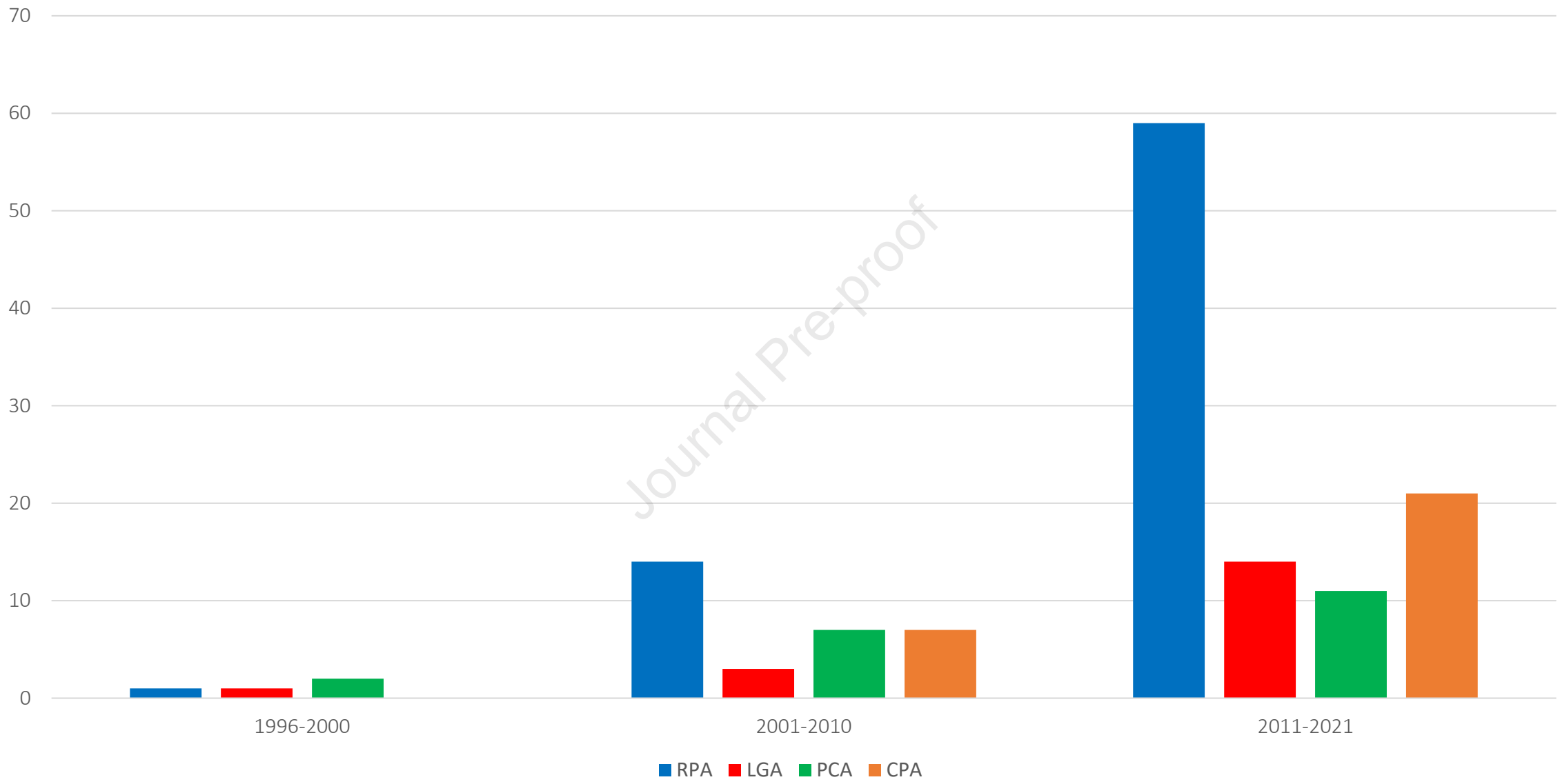
Table 5. Univariate and multivariate Cox proportional hazards analyses evaluating perioperative risk factors for graft loss among liver recipients with complex portal vein thrombosis undergoing alternative forms of portal vein anastomosis.

	Univariate hazards ratio	95% CI	*P*	Multivariate hazards ratio	95% CI	*P*
Donor age	1.008	0.994-1.022	0.266			
Donor sex male	1.244	0.728-2.128	0.575			
Donor BMI	1.055	1.001-1.112	0.046			
Donor type						
DBD	*Reference category*					
cDCD	1.270	0.456-3.536	0.647			
Donor cause of death						
CVA	*Reference category*					
TBI	1.090	0.561-2.117	0.800			
Anoxic brain injury	1.127	0.580-2.192	0.724			
Other	1.283	0.301-5.421	0.736			
Graft type						
Whole	*Reference category*					
Partial	0.505	0.071-3.657	0.498			
Recipient age	1.005	0.983-1.028	0.633			
Recipient sex male	1.791	0.905-3.547	0.094			
Recipient BMI	0.975	0.924-1.029	0.361			
Recipient etiology						
Viral hepatitis	*Reference category*					
Alcohol	0.794	0.400-1.576	0.510			
Cholestatic liver disease	1.038	0.242-4.449	0.960			
NASH	1.150	0.341-3.879	0.822			
Other	0.845	0.442-1.615	0.611			
Recipient HCC	0.868	0.498-1.514	0.618			
Recipient MELD	0.990	0.954-1.027	0.584			
Recipient complex PVT	1.172	0.605-2.269	0.638			
Recipient cavernoma	1.286	0.768-2.155	0.339			
Recipient splenorenal shunt	0.939	0.543-1.623	0.822			
Recipient TIPS	0.367	0.051-2.658	0.321			
Center volume						
High	*Reference category*					
Low	1.242	0.669-2.307	0.493			

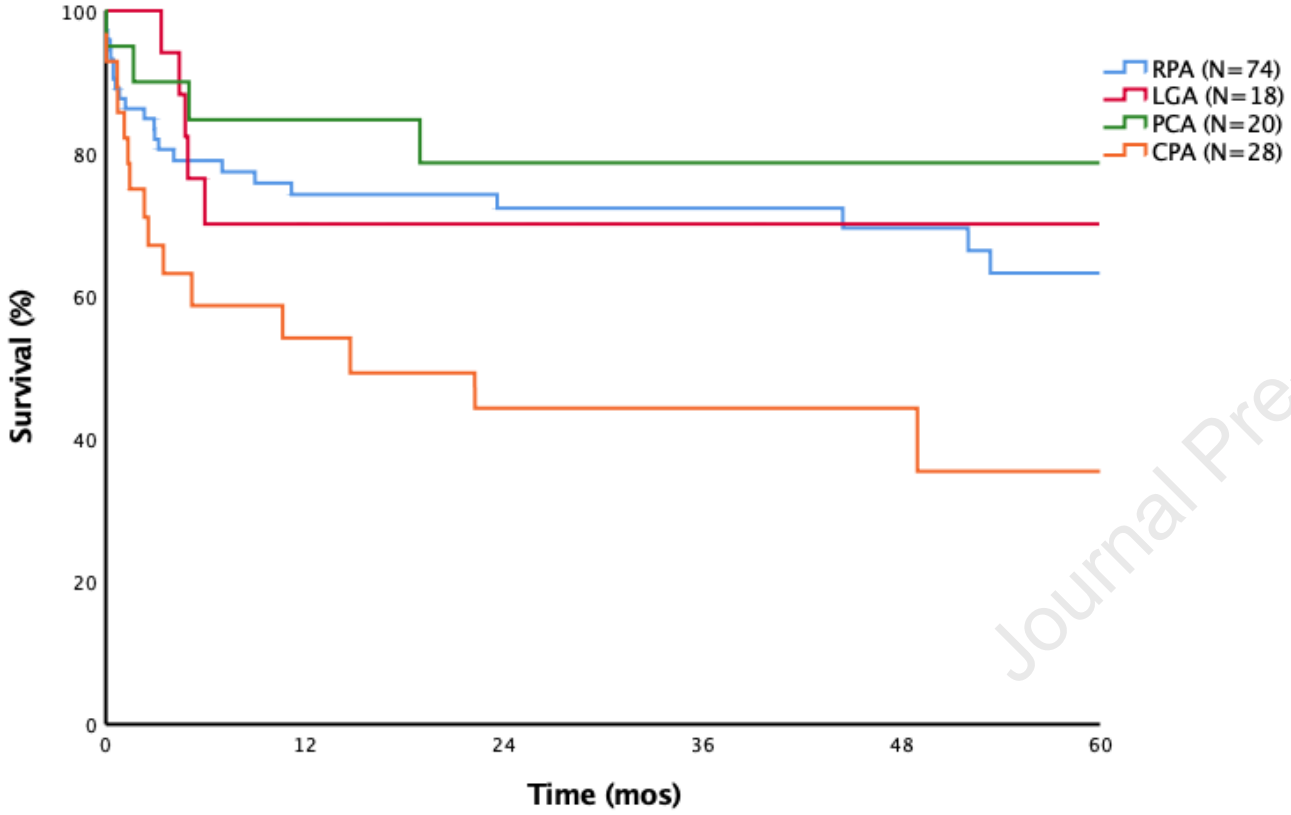
PV anastomosis						
RPA	*Reference category*					
LGA or PCA	0.825	0.435-1.567	0.557			
CPA	1.881	1.005-3.520	0.048			
Interposition graft	0.805	0.480-1.350	0.410			
Non-physiological PV reconstruction	4.854	2.695-8.742	<0.001	**6.639**	**2.159-20.422**	**0.001**
CIT	1.002	1.000-1.004	0.109			
Transplant WIT	1.000	0.986-1.015	0.968			

BMI, body mass index; cDCD, controlled donation after circulatory determination of death; CI, confidence interval; CIT, cold ischemia time; CPA, cavoportal anastomosis; CVA, cerebrovascular accident; DBD, donation after brain death; HCC, hepatocellular carcinoma; LGA, left gastric vein anastomosis; MELD, model for end-stage liver disease; NASH, non-alcoholic steatohepatitis; PCA, pericholedochal vein anastomosis; PV, portal vein; PVT, portal vein thrombosis; RPA, renoportal anastomosis; TBI, traumatic brain injury; TIPS, transjugular intrahepatic portosystemic shunt; WIT, warm ischemia time.



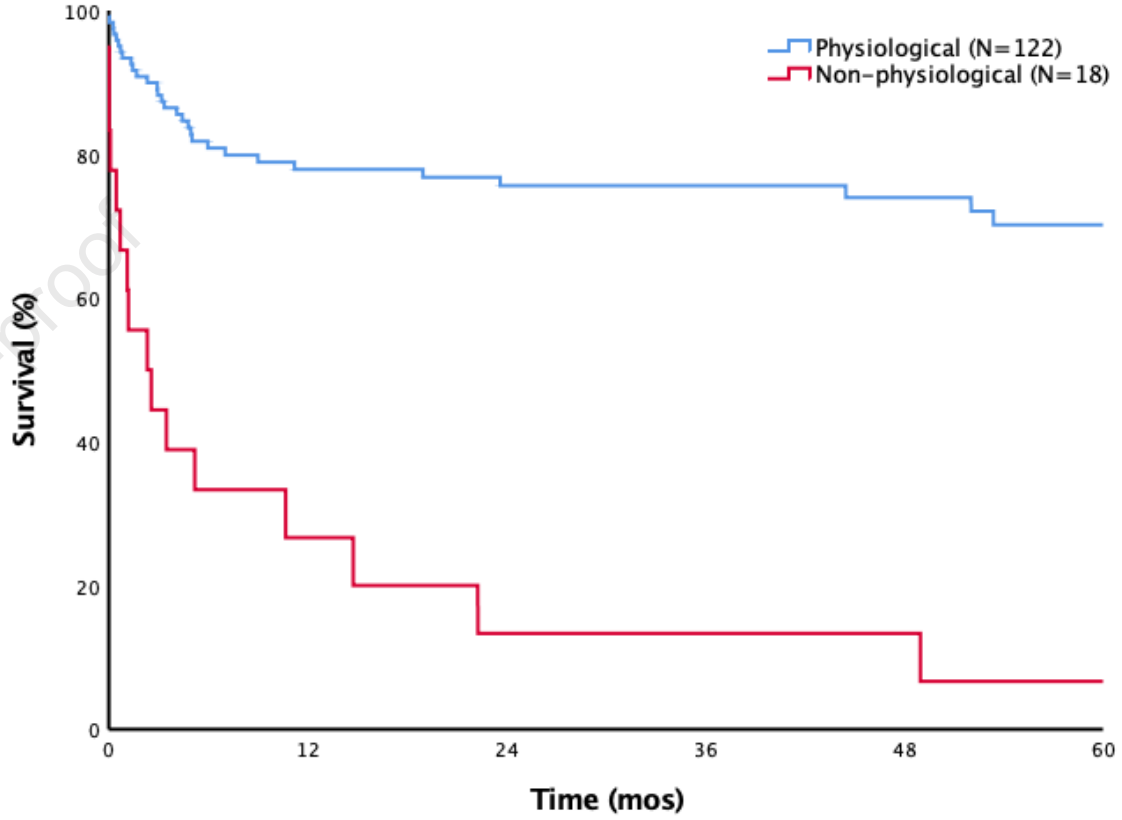


A



RPA	74	45	37	29	24	20
LGA	18	9	7	4	3	3
PCA	20	14	13	12	12	12
CPA	28	12	9	9	5	3

B



P	122	76	64	50	42	37
NP	18	4	2	2	2	1

HIGHLIGHTS

- An international, observational web registry was created to record cases of complex portal vein thrombosis undergoing first liver transplantation performed with an extra-anatomical portal vein reconstruction; 140 cases are analyzed.
- Extra-anatomical portal vein reconstructions that derive recipient splanchnic blood flow to the transplant allograft offer acceptable post-transplant results (5-year patient survival 68%).
- Portal vein reconstructions deriving only systemic blood flow to the graft result in dismal post-transplant survival (<7% at 5 years) and should not be performed.