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# Portal Vein Obstruction in Pediatric Liver Transplant Patients: An Evaluation of Self-Reported Management Practices

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## ABSTRACT

**Background and Aims:** Portal vein obstruction (PVO) is a known complication after pediatric liver transplantation (pLT). Effective management strategies are crucial in improving patient outcomes. This study investigated the various practice patterns related to PVO management to clarify the degree of consensus on the diverse facets of care involved in addressing PVO after pLT.

**Methods:** A self-reported evaluation was conducted using a scanned, paper-based survey among specialized pLT centers participating in the Portal vein Obstruction Revascularization Therapy After Liver transplantation (PORTAL) registry. The survey consisted of 30 questions covering the current practices regarding PVO, including experience, team composition, follow-up and screening protocol, assessment criteria, postprocedural care, and radiologic follow-up.

**Results:** The survey was returned by 25 centers (100%) from different regions worldwide. All centers used Doppler ultrasound (DUS) for PVO screening in the outpatient department. Noninvasive diagnostic criteria used during DUS assessment included anastomotic velocity (50%) and anastomotic-to-pre-anastomotic velocity ratio (54%). Digital subtraction angiography was used by 79% of respondents to diagnose portal vein anastomosis stenosis, which led to diagnostic cutoff values including a narrowing of the visual aspect of the anastomosis of  $\geq 50\%$  (80%) and a pressure gradient  $\geq 5$  mmHg (50%). PTA was identified as a standard treatment for PVO. A remarkable heterogeneity was observed in postinterventional anticoagulation and surveillance protocols.

For affiliations refer to page 9.

**Abbreviations:** ASA, acetylsalicylic acid; CT, computed tomography; d, days; DUS, Doppler ultrasound; FU, follow-up; IQR, interquartile range; LL, lifelong usage; LMWH, low-molecular-weight heparin; m, months; MRB, meso-Rex bypass; n, number; pLT, pediatric liver transplantation; PORTAL, Portal vein Obstruction Revascularization Therapy After Liver transplantation; PTA, percutaneous transluminal angioplasty; PTA/stent, percutaneous transluminal angioplasty with stent placement; PVAS, portal vein anastomosis stenosis; PVO, portal vein obstruction; SWE, shear wave elastography; TE, transient elastography; UFH, unfractionated heparin; VKA, vitamin K antagonist; yr, years.

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**Conclusions:** The care for PVO after pLT lacks standardization, resulting in substantial variation across healthcare centers. There is a need to establish a clear consensus on PVO management after pLT to guarantee optimal care.

**Trial Registration:** NL9261.

## 1 | Introduction

Liver transplantation is a well-established and effective treatment for children with end-stage liver disease, metabolic liver diseases, hepatic malignancy, and acute liver failure. Despite advancements in surgical techniques, portal vein obstruction (PVO), which encompasses extrahepatic portal vein occlusion and portal vein anastomosis stenosis (PVAS), is a common complication with a prevalence of 7.6% [1]. The occurrence of a PVO can have detrimental effects on both graft and patient survival [1].

To address this challenge, various strategies have been implemented to decrease the incidence of PVO and enhance its detection. These measures include performing a preventive portoplasty during pediatric liver transplantation (pLT) if the portal vein is hypoplastic, optimizing anticoagulation therapy, and enhancing radiologic surveillance during the immediate postoperative phase as well as during the subsequent follow-up period. A recent systematic review revealed a wide range of treatment strategies addressing PVO, from conservative approaches to endovascular interventions and surgical revascularization [2].

However, the specific management strategies used in daily clinical practice remain unclear at present. To address this knowledge gap and gain valuable insights into existing management strategies, this study investigated the practice patterns in the measures taken to prevent, detect, and manage PVO through an international survey conducted among specialized pLT centers. The study aims to provide a comprehensive understanding of the practice patterns used in preventing and managing PVO, thereby determining the degree of consensus on the care provided to patients undergoing pLT.

## 2 | Materials and Methods

A scanned, paper-based survey was sent to 25 international pLT centers participating in the Portal vein Obstruction Revascularization Therapy After Liver transplantation (PORTAL) registry [3]. This registry serves as a multicenter, retrospective, observational database for pediatric patients diagnosed with and treated for PVO after pLT.

The survey comprised 30 questions encompassing both closed- and open-ended formats (Supporting Information S1: Supplemental Digital Content 1, Materials and Methods). The survey was organized into seven domains: (1) center experience; (2) team composition; (3) care structure; (4) follow-up and screening protocol; (5) assessment criteria; (6) postprocedural care after PVO intervention; and (7) radiologic follow-up after treatment. Some questions allowed for multiple answers. The study is registered in the Dutch Trial Register (registration number NL9261), and approval was obtained via a waiver from the local Medical Ethics Committee (METc2021/072).

## 2.1 | Statistical Analysis

The responses to the survey were analyzed using IBM SPSS Statistics 28 software. Descriptive statistics were used to analyze the quantitative and qualitative data, with quantitative variables reported as median and interquartile range (IQR), where applicable, and categorical variables were reported as absolute and relative frequencies. Subcategories of low-, medium-, and high-volume centers performing pLT were created by using the 25th- and 75th-percentiles of the mean number of yearly performed pLTs during their active program in the period between January 1, 2001 and January 1, 2020.

## 3 | Results

All 25 centers participating in the PORTAL registry returned the survey, which resulted in 23 complete surveys and 2 incomplete surveys (2 domains were missing). Institutions participating in the study originated from Europe (48%,  $n = 12$ ), North America (12%,  $n = 3$ ), South America (16%,  $n = 4$ ), Africa (4%,  $n = 1$ ), and Asia-Pacific (20%,  $n = 5$ ). Table 1 summarizes the center-related characteristics of PORTAL registry participants.

### 3.1 | Low-, Medium-, and High-Volume Centers

Included were 6 low-volume centers (mean yearly performance of  $\leq 8$  pLTs), 11 medium-volume centers (mean yearly performance between 8 and 24 pLTs), and 5 high-volume centers (mean yearly performance of  $\geq 24$  pLTs). Most center-related characteristics did not differ between the volume subgroups (Supporting Information S2: Table 1).

### 3.2 | pLT Techniques

Of the participating centers, 96% ( $n = 24$ ) stated they had a living-donor liver transplantation program. Preventive portoplasty was performed as a standard procedure during pLT for a hypoplastic portal vein in 40% ( $n = 10$ ) of the centers, which was 60% ( $n = 3$ ) of the high-volume centers, 46% ( $n = 5$ ) of the medium-volume centers, and 17% ( $n = 1$ ) of the low-volume centers.

### 3.3 | Screening Protocol After pLT

All 25 centers reported having a radiologic follow-up program in the outpatient department for detecting PVO after pLT. Six of these used an additional, separate screening program for patients with risk factors (Table 2). The described risk factors for PVO included conditions associated with portal vein size, such as biliary atresia and pLT  $< 1$  year, transplantation-related factors (e.g., living-donor liver transplantation, recent portal vein

## Summary

- An obstruction of the portal vein can impact the well-being of children who have undergone a liver transplantation.
- However, this study reveals a lack of consensus regarding the best practices for managing portal vein obstruction, resulting in diverse health care approaches at different centers.
- Establishing a uniform agreement on post-liver transplantation care for portal vein obstruction is crucial to guarantee that all children receive the best optimal care.

**TABLE 1** | Baseline characteristics of PORTAL registry participants.

| Characteristic                                           | Data values |
|----------------------------------------------------------|-------------|
| Start date of the programs (total)                       |             |
| Liver transplantation ( <i>n</i> = 25)                   |             |
| 1982–1992                                                | 48 (12)     |
| 1993–2003                                                | 24 (6)      |
| 2004–2014                                                | 24 (6)      |
| 2015–2021                                                | 4 (1)       |
| Living-donor liver transplantation ( <i>n</i> = 24)      |             |
| 1982–1992                                                | 8 (2)       |
| 1993–2003                                                | 38 (9)      |
| 2004–2014                                                | 46 (11)     |
| 2015–2021                                                | 8 (2)       |
| Performance of preventive portoplasty ( <i>n</i> = 10)   |             |
| 1998–2008                                                | 60 (6)      |
| 2009–2021                                                | 40 (4)      |
| Performance of PTA ( <i>n</i> = 24)                      |             |
| 1998–2008                                                | 29 (7)      |
| 2009–2015                                                | 33 (8)      |
| Unknown start date                                       | 38 (9)      |
| Performance of PTA with stent placement ( <i>n</i> = 20) |             |
| 1998–2008                                                | 30 (6)      |
| 2009–2016                                                | 25 (5)      |
| Unknown start date                                       | 45 (9)      |
| Performance of meso-Rex bypass ( <i>n</i> = 18)          |             |
| 1998–2008                                                | 22 (4)      |
| 2009–2021                                                | 28 (5)      |
| Unknown start date                                       | 50 (9)      |
| Composition of the team ( <i>n</i> = 25)                 |             |
| Pediatric hepatologists                                  | 4 (3–6)     |
| Pediatric radiologists                                   | 4 (3–6)     |
| Interventional radiologists                              | 2 (2–3)     |

(Continues)

**TABLE 1** | (Continued)

| Characteristic                                                                 | Data values |
|--------------------------------------------------------------------------------|-------------|
| Hepato-pancreato-biliary surgeons                                              | 4 (2–5)     |
| Hepato-pancreato-biliary surgeons (who perform meso-Rex bypass)                | 2 (1–2)     |
| Presence of specialized team for PVO ( <i>n</i> = 25)                          | 96 (24)     |
| Presence of specialized multidisciplinary meeting for PVO ( <i>n</i> = 25)     | 88 (22)     |
| Presence of specific protocol for PVO ( <i>n</i> = 25)                         |             |
| Screening                                                                      | 48 (12)     |
| Diagnosis                                                                      | 48 (12)     |
| Indication for treatment                                                       | 48 (12)     |
| Treatment                                                                      | 52 (13)     |
| Postprocedural care                                                            | 52 (13)     |
| Preferred noninvasive imaging method for screening for PVO ( <i>n</i> = 25)    |             |
| Doppler ultrasound                                                             | 100 (25)    |
| Computed tomography                                                            | 60 (15)     |
| Transient elastography                                                         | 12 (3)      |
| Shear wave elastography                                                        | 4 (1)       |
| Preferred noninvasive imaging method as a diagnostic for PVAS ( <i>n</i> = 25) |             |
| Doppler ultrasound                                                             | 96 (24)     |
| Computed tomography                                                            | 80 (20)     |
| Transient elastography                                                         | 8 (2)       |
| Shear wave elastography                                                        | 4 (1)       |

Note: Data are presented as % (*n*) or median (interquartile range).

Abbreviations: PTA, percutaneous transluminal angioplasty; PVAS, portal vein anastomosis stenosis; PVO, portal vein obstruction.

surgical intervention, and the use of a venous interposition graft), and clinical and/or biochemical risk factors (including platelet count, liver enzymes, and clinical signs of portal hypertension).

The frequency, timing, and duration of screening for PVO after pLT across the follow-up protocols are described in Table 2. Most of the follow-up protocols (79%, *n* = 15) enforced a screening frequency of at least two times within the first year after pLT. This also applied for screening protocols specifically tailored to patients with and without risk factors, because 100% (*n* = 6) and 67% (*n* = 4) of these protocols reported a minimal screening frequency of at least two times in the first year, respectively. One protocol did not include routine follow-up. The median duration of the total follow-up period at pediatric centers extended until patients were the age of 18 years.

### 3.3.1 | Imaging Methods and Diagnostic Criteria

Doppler ultrasound (DUS) was the preferred imaging method for PVO screening in the outpatient department among the 25 centers (100%), and 15 centers (60%) expressed a preference

**TABLE 2** | Timing of radiological screening after transplantation and intervention.

| Screening protocols (total)                       | Timing of screening <sup>a</sup> |         |         |         |         |         | Annually <sup>b</sup><br>> 1 yr | Duration of<br>FU (yr) |
|---------------------------------------------------|----------------------------------|---------|---------|---------|---------|---------|---------------------------------|------------------------|
|                                                   | < 3 m                            | 3 m     | 6 m     | 9 m     | 1 yr    | > 1 yr  |                                 |                        |
| After pLT (outpatient department)                 |                                  |         |         |         |         |         |                                 |                        |
| No incorporation of risk factors ( <i>n</i> = 19) | —                                | 68 (13) | 68 (13) | 63 (13) | 84 (16) | 84 (16) | 74 (14)                         | 18 (7.5–18)            |
| Without risk factors ( <i>n</i> = 6)              | —                                | 67 (4)  | 67 (4)  | 17 (1)  | 83 (5)  | 83 (5)  | 67 (4)                          | 18 (15.8–18)           |
| With risk factors ( <i>n</i> = 6)                 | —                                | 100 (6) | 83 (5)  | 67 (4)  | 67 (4)  | 83 (5)  | 67 (4)                          | 18 (15.8–18)           |
| Postintervention                                  |                                  |         |         |         |         |         |                                 |                        |
| Nonintervention specific ( <i>n</i> = 19)         | 32 (6)                           | 95 (18) | 84 (16) | 47 (9)  | 84 (16) | 89 (17) | 89 (17)                         | 18 (18–18)             |
| PTA specific ( <i>n</i> = 3)                      | 33 (1)                           | 100 (3) | 100 (3) | 33 (1)  | 67 (2)  | 67 (2)  | 33 (1)                          | 5 (2.8–5)              |
| PTA/stent specific ( <i>n</i> = 3)                | 33 (1)                           | 67 (2)  | 100 (3) | 0       | 67 (2)  | 33 (1)  | 0                               | 1 (0.8–3)              |
| MRB specific ( <i>n</i> = 2)                      | 50 (1)                           | 100 (2) | 100 (2) | 50 (1)  | 50 (1)  | 50 (1)  | 50 (1)                          | 9.5 (5.3–13.8)         |

Note: Data are presented as % (*n*) or median (interquartile range).

Abbreviations: FU, follow-up; m, months; MRB, meso-Rex bypass; pLT, pediatric liver transplantation; PTA, percutaneous transluminal angioplasty; PTA/stent, percutaneous transluminal angioplasty with stent placement; yr, year.

<sup>a</sup>Timing of screening related to either liver transplantation or intervention for portal vein obstruction.

<sup>b</sup>Percentage and number of protocols that incorporate at least annual follow-up after the first year post-liver transplantation.

toward using computed tomography (CT) as a complementary or standardized adjuvant to DUS. Elastography was preferred in 16% (*n* = 4) of centers for PVO screening, including transient elastography of the liver in 12% (*n* = 3) and shear wave elastography of both the liver and the spleen in 4% (*n* = 1).

There was a considerable heterogeneity in DUS imaging characteristics and cutoff values used to establish a PVAS diagnosis (Table 3). Reported parameters used for diagnosis included velocity at the portal vein anastomosis (50%, *n* = 12), pre-anastomotic velocity (33%, *n* = 8), postanastomotic velocity (29%, *n* = 7), anastomotic-to-preanastomotic velocity ratio (54%, *n* = 13), and anastomosis diameter (38%, *n* = 9). Although there was a strong agreement on the cutoff value for anastomosis diameter (< 3.0 mm) in diagnosing PVAS, the cutoff values applied for velocity characteristics varied among respondents. CT scans were also used for PVAS diagnosis in 43% (*n* = 10) of respondents, with a median diameter of < 3.0 mm as a cutoff value.

When PVAS was suspected and digital subtraction angiography was used, the radiologic criteria for determining a PVAS involved visually inspecting the anastomosis and measuring the pressure gradient across the anastomosis. Visual inspection of the portal vein anastomosis was used by 79% (*n* = 19) of respondents, and 80% (*n* = 12) used a stenotic ratio of ≥ 50% as a cutoff value to diagnose PVAS. The pressure gradient was used as a criterion by 79% (*n* = 19) of the respondents. The cutoff values for the pressure gradient across the anastomosis used to establish a PVAS diagnosis varied, with 50% (*n* = 9) using a cutoff value of ≥ 5 mmHg and 44% (*n* = 8) using a cutoff value of ≥ 3–4 mmHg.

### 3.4 | Treatment for PVO

Most of the centers were technically able to perform percutaneous transluminal angioplasty (PTA) (96%, *n* = 24) and

additional stent placement (80%, *n* = 20), and 52% (*n* = 13) of the centers were able to perform meso-Rex bypass (MRB) on a transplanted liver (Table 1). These procedures were considered standard care in 83% (*n* = 20), 56% (*n* = 14), and 44% (*n* = 11) of the centers, respectively. All high-volume (100%, *n* = 5) and medium-volume centers (100%, *n* = 11), and most low-volume centers (83%, *n* = 5), had the technical capability to perform PTA (Supporting Information S2: Table 1). The ability to perform MRB in these centers was 80% (*n* = 4), 64% (*n* = 7), and 83% (*n* = 5), respectively. The proportion of centers technically able to perform PTA with stent placement was highest in high-volume centers at 100% (*n* = 5); lower in medium-volume centers at 91% (*n* = 10); and lowest in low-volume centers at 50% (*n* = 3).

Among the respondents who used indicators to assess the technical success of endovascular interventions (83%, *n* = 20), different definitions were used to determine the effectiveness of these interventions (Table 4). The most commonly used parameter was the pressure gradient across the anastomosis (75%, *n* = 18), with a cutoff value of < 3 mmHg applied in 56% (*n* = 10) of these centers. Residual venographic stenosis was used as a criterion by 58% (*n* = 14) of the respondents, with 57% (*n* = 8) using a cutoff value of < 20%–30%. A decrease in the pressure gradient from baseline was used as an indicator of clinical success by 29% (*n* = 7) of respondents, and 86% (*n* = 6) used a cutoff value of a decrease in pressure gradient of ≥ 50%.

### 3.5 | Postprocedural Anticoagulation After PVO Intervention

The routine use of anticoagulation after PVO intervention differed among the centers (Table 5). The types of anticoagulation reported in the protocols included thrombocyte aggregation inhibitors (acetylsalicylic acid [ASA], clopidogrel, and dipyridamole), heparin-based anticoagulation (unfractionated

TABLE 3 | Diagnostic characteristics for portal vein anastomosis stenosis per radiological modality across the collaborating centers.

| Modality (total of respondents)      |  | DUS<br>n = 24         |                               | CT<br>n = 23          |                         | TE/SWE<br>n = 24      |                   | DSA<br>n = 24         |                            |
|--------------------------------------|--|-----------------------|-------------------------------|-----------------------|-------------------------|-----------------------|-------------------|-----------------------|----------------------------|
|                                      |  | Percentage of centers | Cutoff value                  | Percentage of centers | Cutoff value            | Percentage of centers | Cutoff value      | Percentage of centers | Cutoff value               |
| Velocity                             |  |                       |                               |                       |                         |                       |                   |                       |                            |
| Pre-anastomotic (cm/s)               |  | 33                    | 28.50 (20–39.25) <sup>6</sup> | —                     | —                       | —                     | —                 | —                     | —                          |
| Post-anastomotic (cm/s)              |  | 29                    | 17 (15–80) <sup>5</sup>       | —                     | —                       | —                     | —                 | —                     | —                          |
| Anastomotic (cm/s)                   |  | 50                    | 150 (127.5–195) <sup>10</sup> | —                     | —                       | —                     | —                 | —                     | —                          |
| 0–100                                |  |                       | 20 (2)                        |                       |                         |                       |                   |                       |                            |
| 101–150                              |  |                       | 40 (4)                        |                       |                         |                       |                   |                       |                            |
| 151–200                              |  |                       | 40 (4)                        |                       |                         |                       |                   |                       |                            |
| Velocity ratio                       |  | 54                    |                               | —                     | —                       | —                     | —                 | —                     | —                          |
| ≥ 1.5–2:1                            |  |                       | 17 (2)                        |                       |                         |                       |                   |                       |                            |
| ≥ 3:1                                |  |                       | 50 (6)                        |                       |                         |                       |                   |                       |                            |
| ≥ 4:1                                |  |                       | 33 (4)                        |                       |                         |                       |                   |                       |                            |
| Diameter of vessel                   |  | 38                    |                               | 43                    |                         |                       |                   |                       |                            |
| Diameter (mm)                        |  |                       | 3 (3–3) <sup>7</sup>          |                       | 3 (3–3.25) <sup>5</sup> | —                     | —                 | —                     | —                          |
| Stenotic ratio (%)                   |  |                       | > 50 <sup>1</sup>             |                       | > 50 <sup>3</sup>       | —                     | —                 | —                     | —                          |
| Liver stiffness (kPa)                |  | —                     | —                             | —                     | —                       | 4                     | > 10 <sup>1</sup> | —                     | —                          |
| Spleen stiffness (kPa)               |  | —                     | —                             | —                     | —                       | 4                     | > 30 <sup>1</sup> | —                     | —                          |
| Pressure gradient across anastomosis |  | —                     |                               | —                     |                         | —                     |                   | 79                    | ≥ 5 (4–5) <sup>18</sup>    |
| ≥ 3 mmHg                             |  |                       | —                             |                       |                         |                       | —                 |                       | 22 (4)                     |
| ≥ 4 mmHg                             |  |                       | —                             |                       |                         |                       | —                 |                       | 22 (4)                     |
| ≥ 5 mmHg                             |  |                       | —                             |                       |                         |                       | —                 |                       | 50 (9)                     |
| ≥ 6 mmHg                             |  |                       | —                             |                       |                         |                       | —                 |                       | 6 (1)                      |
| Visual inspection of stenosis        |  | —                     | —                             | —                     | —                       | —                     | —                 | 79                    | ≥ 50 (50–50) <sup>15</sup> |
| ≥ 20%                                |  |                       | —                             |                       |                         |                       | —                 |                       | 7 (1)                      |
| ≥ 50%                                |  |                       | —                             |                       |                         |                       | —                 |                       | 80 (12)                    |

(Continues)

TABLE 3 | (Continued)

| Modality (total of respondents)  | DUS<br><i>n</i> = 24  |              | CT<br><i>n</i> = 23   |              | TE/SWE<br><i>n</i> = 24 |              | DSA<br><i>n</i> = 24  |              |
|----------------------------------|-----------------------|--------------|-----------------------|--------------|-------------------------|--------------|-----------------------|--------------|
| Parameter                        | Percentage of centers | Cutoff value | Percentage of centers | Cutoff value | Percentage of centers   | Cutoff value | Percentage of centers | Cutoff value |
| ≥ 70%                            |                       | —            |                       | —            |                         | —            |                       | 7 (1)        |
| ≥ 80%                            |                       | —            |                       | —            |                         | —            |                       | 7 (1)        |
| Presence of nonspecific findings |                       |              |                       |              |                         |              |                       |              |
| Turbulence                       | 63                    | —            | —                     | —            | —                       | —            | —                     | —            |
| Collaterals                      | —                     | —            | 74                    | —            | —                       | —            | —                     | —            |
| Cavernoma                        | —                     | —            | 74                    | —            | —                       | —            | —                     | —            |

Note: Data are presented as %, median (interquartile range), or with the specific cutoff value if there was no variation. 1, 3, 5, 6, 7, 10, 15, and 18 are the number of centers that reported these specific parameters. Abbreviations: cm/s, centimeter per second; CT, computed tomography; DSA, Digital subtraction angiography; DUS, Doppler ultrasound; kPa, kilopascal; mm, millimeter; mmHg, millimeter per mercury; *n*, number; SWE, shear wave elastography; TE, transient elastography.

TABLE 4 | Definition of technical success after endovascular radiologic treatment.

| Endovascular criteria for technical success ( <i>n</i> = 24) | Number  |
|--------------------------------------------------------------|---------|
| Pressure gradient anastomosis ( <i>n</i> = 18)               |         |
| < 3 mmHg                                                     | 56 (10) |
| < 4 mmHg                                                     | 17 (3)  |
| < 5 mmHg                                                     | 22 (4)  |
| < 6 mmHg                                                     | 6 (1)   |
| Drop in pressure gradient from baseline ( <i>n</i> = 7)      |         |
| ≥ 50%                                                        | 86 (6)  |
| ≥ 75%                                                        | 14 (1)  |
| Residual venographic stenosis ( <i>n</i> = 14)               |         |
| < 50%                                                        | 29 (4)  |
| < 20%–30%                                                    | 57 (8)  |
| 0%                                                           | 7 (1)   |
| Cutoff value not specified                                   | 7 (1)   |

Note: Data are presented as % (*n*).

Abbreviation: mmHg, millimeter per mercury.

heparin, low-molecular-weight heparin [LMWH]), vitamin K antagonists, and direct oral anticoagulants (rivaroxaban). Among the protocols for PTA (*n* = 21), the most frequently used postprocedural anticoagulation included ASA (52%, *n* = 11) and prophylactic LMWH (52%, *n* = 11). The most frequently chosen anticoagulation type in postprocedural protocols for PTA with additional stent placement (*n* = 19) was ASA (63%, *n* = 12), followed by prophylactic LMWH (42%, *n* = 8). For MRB, all protocols (*n* = 11) included multiple types of anticoagulation, with ASA (82%, *n* = 9) and prophylactic LMWH (55%, *n* = 6) being used the most. The reported total duration of postprocedural anticoagulation varied among the protocols, ranging from 1 to 3 days to lifelong use (Table 6).

### 3.6 | Postprocedural Follow-Up After PVO Intervention

Most of the centers (83%, *n* = 19) had the same radiologic follow-up protocol for all PVO interventions (Table 2). In addition to these protocols, 3 centers reported intervention-adjusted follow-up protocols, including 3 PTA-, 3 PTA with stent-, and 2 MRB-specific protocols. The frequency and timing of postinterventional screening differed among the centers. The nonintervention-specific, PTA, PTA with stent placement, and MRB postprocedural follow-up protocols consisted of a frequency of ≥ 2 in the first year after the procedure in 89% (*n* = 17), 100% (*n* = 3), 67% (*n* = 2), and 100% (*n* = 2), respectively. The median follow-up duration for nonintervention-specific protocols differed from intervention-specific protocols. The median duration of follow-up was 18 years (IQR, 18–18 years) for nonintervention-specific protocols, 5 years (IQR, 2.8–5 years) for PTA, 1 year (IQR, 0.8–3 years) for PTA with stent placement, and 9.5 years (IQR, 5.3–13.8 years) for MRB.

**TABLE 5** | Frequency and duration of anticoagulants used per intervention across the collaborating centers.

| Intervention protocol<br>Type anticoagulation     | PTA<br>(n = 21)       |                  | PTA with stent<br>placement<br>(n = 19) |                    | MRB<br>(n = 11)       |                 |
|---------------------------------------------------|-----------------------|------------------|-----------------------------------------|--------------------|-----------------------|-----------------|
|                                                   | Protocol <sup>a</sup> | Duration         | Protocol <sup>a</sup>                   | Duration           | Protocol <sup>a</sup> | Duration        |
| Single anticoagulation                            |                       |                  |                                         |                    |                       |                 |
| Prophylactic LMWH                                 | 19 (4)                | 3d–3m            | 11 (2)                                  | 4w–3m              | —                     | —               |
| Therapeutic LMWH                                  | 10 (2)                | 2–3w             | 5 (1)                                   | 3m                 | —                     | —               |
| ASA                                               | 14 (3)                | 3m–LL            | 5 (1)                                   | 3m                 | —                     | —               |
| Total                                             | 43 (9)                | —                | 21 (4)                                  | —                  | —                     | —               |
| Double anticoagulation                            |                       |                  |                                         |                    |                       |                 |
| UFH and prophylactic LMWH                         | 10 (2)                | 1–3d/1w–3m       | 5 (1)                                   | 1d–3d/6m           | 9 (1)                 | 3d/3m           |
| UFH and ASA                                       | 5 (1)                 | Unknown          | —                                       | —                  | 9 (1)                 | 1w/6m           |
| UFH and VKA                                       | —                     | —                | —                                       | —                  | 9 (1)                 | 1w/3m           |
| Prophylactic LMWH and ASA                         | 24 (5)                | 1w–LL/<br>3m–3yr | 11 (2)                                  | 1w/6m              | 18 (2)                | 3m/2w           |
| Prophylactic LMWH and VKA                         | —                     | —                | 5 (1)                                   | 3d/3m              | —                     | —               |
| Therapeutic LMWH and VKA                          | 5 (1)                 | 1w/<br>unknown   | 11 (2)                                  | 3m/LL              | —                     | —               |
| Therapeutic LMWH and ASA                          | 5 (1)                 | 2–4w/LL          | 11 (2)                                  | 2–4w/LL            | —                     | —               |
| ASA and clopidogrel                               | —                     | —                | 11 (2)                                  | 1yr–LL/3–6m        | —                     | —               |
| Total                                             | 48 (10)               | —                | 53 (10)                                 | —                  | 45 (5)                | —               |
| Triple anticoagulation                            |                       |                  |                                         |                    |                       |                 |
| UFH and prophylactic LMWH<br>and VKA              | 5 (1)                 | 7d/6m/LL         | —                                       | —                  | —                     | —               |
| UFH and prophylactic LMWH<br>and ASA              | —                     | —                | 5 (1)                                   | 2w/1m/1m           | 9 (1)                 | 1d/2w/3m        |
| UFH and ASA and dipyridamole                      | —                     | —                | —                                       | —                  | 9 (1)                 | unknown         |
| Therapeutic LMWH and ASA<br>and clopidogrel       | —                     | —                | 5 (1)                                   | 2w/<br>6–12m/6–12m | —                     | —               |
| Prophylactic LMWH and ASA<br>and dipyridamole     | —                     | —                | 5 (1)                                   | 7d/6m/3m           | 18 (2)                | 7d–1m/<br>6m/3m |
| Prophylactic LMWH and<br>therapeutic LMWH and ASA | —                     | —                | —                                       | —                  | 9 (1)                 | 1w/<br>1m/2–6m  |
| Therapeutic LMWH and<br>rivaroxaban and ASA       | 5 (1)                 | 1w/<br>1m/2–6m   | 5 (1)                                   | 1w/1m/2–6m         | 9 (1)                 | 1w/<br>1m/2–6m  |
| UFH and ASA and VKA                               | —                     | —                | 5 (1)                                   | Unknown            | —                     | —               |
| Total                                             | 10 (2)                | —                | 26 (5)                                  | —                  | 55 (6)                | —               |

Note: Data are presented as % (n) or in time units.

Abbreviations: ASA, acetylsalicylic acid; d, days; LL, lifelong; LMWH, low-molecular-weight heparin; m, months; MRB, meso-Rex bypass; PTA, percutaneous transluminal angioplasty; UFH, unfractionated heparin; VKA, vitamin K antagonist; yr, years; w, weeks.

<sup>a</sup>Percentage calculated over total number of protocols that have a postprocedural anticoagulation protocol for this type of intervention.

## 4 | Discussion

This is the first self-reported evaluation of practice patterns in the management of PVO in a large group of pLT centers within the global PORTAL registry network. Our study revealed noticeable inconsistencies across most aspects of care for PVO after pLT. Clinical approaches adopted in areas of preventive measures, diagnostic criteria for PVAS, anticoagulation, and follow-up after a PVO intervention were remarkably different

across participating centers. Low-volume centers were less frequently technically equipped to perform PTA with stent placement. Some consistency existed across centers in the types of screening and diagnostic methods used and in the identification of PTA as a standard procedure for PVO.

Preventive portoplasty is a surgical technique used in pLT for reducing the risk of PVO by restoring vessel size discrepancies between donor and recipient portal veins [4]. The reconstruction

**TABLE 6** | Total duration of anticoagulation per postprocedural protocol.

| Intervention protocol (total)             | Total duration of anticoagulation |        |        |        |         |        | Unknown |
|-------------------------------------------|-----------------------------------|--------|--------|--------|---------|--------|---------|
|                                           | < 4 w                             | 1–3 m  | 3–6 m  | 6–12 m | 12 m–LL | LL     |         |
| PTA ( <i>n</i> = 21)                      | 24 (5)                            | 10 (2) | 29 (6) | 10 (2) | 5 (1)   | 19 (4) | 5 (1)   |
| PTA with stent placement ( <i>n</i> = 19) | 0                                 | 11 (2) | 26 (5) | 16 (3) | 11 (2)  | 26 (5) | 11 (2)  |
| MRB ( <i>n</i> = 11)                      | 0                                 | 0      | 45 (5) | 36 (4) | 0       | 9 (1)  | 9 (1)   |

Note: Data are presented as % (*n*).

Abbreviations: LL, lifelong; m, months; MRB, meso-Rex bypass; *n*, number; PTA, percutaneous transluminal angioplasty; w, weeks.

of the portal vein with, for example, branch patches, vein grafts, or vessel caliber-enlarging suture techniques, appears to be a feasible method to decrease the risk of PVO in the literature, especially in children with biliary atresia, because they tend to have a narrow and sclerotic portal vein [4–8]. Nevertheless, we found that only 40% of the centers used preventive portoplasty as a standard procedure for a hypoplastic portal vein, indicating a lack of consensus on the implication of portal vein reconstruction as a preventive measure for PVO. The relatively small number of centers performing this technique might be explained by the limited evidence available on the direct effect of portal vein reconstruction techniques on the occurrence of PVO [4, 8]. As an extension to this study, the used techniques in pLT such as intra-operative blood flow measurements and portal reconstructions should be explored more extensively. A systematic review on described techniques in literature followed with an expert-consensus study on these matters will provide directions to optimal preventive strategies.

This study highlights the common practice to regularly screen for PVO after pLT over an extended period, because the frequency, timing, and duration of screening was consistent across the follow-up protocols. It also emphasizes the strong preference for the use of DUS as a screening tool for PVO. This can be attributed to its convenience, relatively low cost, and lack of exposure to ionizing radiation. Moreover, DUS was frequently preferred as a diagnostic method, and most respondents favored CT and digital subtraction angiography for diagnosing PVAS. However, despite the strong consensus on the diagnostic methods used for PVAS, there was a considerable variation within the DUS parameters and pressure gradient cutoff values that were used. Use of the DUS velocity and diameter parameters, for instance, ranged from 29% to 54% among respondents. This variation reflects the diversity of parameters in the existing literature, because studies use different parameters such as diameter, velocity, and pressure measurements [9–12].

Most center-related characteristics and programs in low-, medium-, and high-volume centers did not differ remarkably, which is especially noteworthy regarding the technical capability to perform PTA and MRB. Nevertheless, an important finding was that in centers with a lower performance of pLT, the performance of preventive portoplasty and the technical capability to perform PTA with stent placement was less, thereby limiting the treatment strategies to address PVO in smaller-volume centers.

Even though most centers were technically able to perform PTA and PTA with additional stent placement and MRB, only the use of PTA was considered a standard procedure for PVO

among these centers. The lack of collective agreement on the standard implementation of PTA with stent placement and MRB can be attributed to the limited studies comparing long-term outcomes of interventions for PVO and the scarcity of reports on the optimal timing of stent placement and MRB to restore portal flow, as well as the technical knowledge and experience of different centers [2, 13, 14]. A comprehensive assessment of the safety and effectiveness of treatment modalities to address PVO will help in obtaining consensus on standardized and optimal care.

Regarding indicators of technical success after endovascular treatment, most respondents used the pressure gradient across the anastomosis (75%, *n* = 18) or residual venographic stenosis (58%, *n* = 14). In the literature, technical success for these indicators is defined as a pressure gradient of < 3–5 mmHg or a residual venographic stenosis of < 20%–30% of the diameter [15]. These described ranges were used in 94% (*n* = 17) and 57% (*n* = 8) of centers, respectively, indicating that the small variation in cutoff values reflects the current literature.

The most significant inconsistency in care for PVO was observed in the choice of anticoagulation protocols, including the type and duration, across different centers. Although ASA and prophylactic LMWH were the most frequently used for all postprocedural anticoagulation protocols, their use varied between 42% and 82%, and additional anticoagulation types with varying mechanisms of action were also prescribed. Moreover, the total duration of anticoagulation ranged from 1 to 3 days to lifelong use, indicating a lack of consensus regarding postprocedural anticoagulation. This lack of agreement on postprocedural anticoagulation is reflected by the results of a systematic review and reports from a consensus guideline [2, 16].

It is important to acknowledge the limitations of this study. First, because this is a survey-based study, the reported results should not be interpreted as direct evidence of appropriate care. Rather, the described variations in management reflect the degree of consensus among centers. Second, the current study relied on self-reported data, which introduces the potential for reporting and recall bias. Third, the responses, ranging from completed to incomplete/missing surveys, may not provide a representative picture.

In conclusion, this study highlights the complex heterogeneity observed in the current approach to managing PVO after pLT, presumably due to the variations in definitions and diverse range of management strategies documented in the existing literature. It is important to emphasize these variations across international pLT centers, because these differences in clinical

approaches toward PVO may directly impact patient care and outcomes. There is a need to establish a clear consensus on PVO management after pLT to guarantee optimal care.

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**Lydia Sieben:** formal analysis, methodology, project administration, validation, writing – original draft. **Bader A. Alfares:** conceptualization, data curation, formal analysis, methodology, writing – original draft. **Ruben H. de Kleine:** conceptualization, data curation, writing – review and editing. **Barbara E. Wildhaber:** conceptualization, data curation, writing – review and editing. **Thomas Casswall:** conceptualization, data curation, writing – review and editing. **Greg Nowak:** conceptualization, data curation, writing – review and editing. **Martin Delle:** conceptualization, data curation, writing – review and editing. **Denise Aldrian:** conceptualization, data curation, writing – review and editing. **Valeria Berchtold:** conceptualization, data curation, writing – review and editing. **Georg F. Vogel:** conceptualization, data curation, writing – review and editing. **Piotr Kaliciński:** conceptualization, data curation, writing – review and editing. **Malgorzata Markiewicz-Kijewska:** conceptualization, data curation, writing – review and editing. **Adam Kolesnik:** conceptualization, data curation, writing – review and editing. **Jesús Quintero:** conceptualization, data curation, writing – review and editing. **Maria Mercadal Hally:** conceptualization, data curation, writing – review and editing. **Mauricio Larrarte King:** conceptualization, data curation, writing – review and editing. **Paolo Marra:** conceptualization, data curation, writing – review and editing. **Michela Bravi:** conceptualization, data curation, writing – review and editing. **Domenico Pinelli:** conceptualization, data curation, writing – review and editing. **Mureo Kasahara:** conceptualization, data curation, writing – review and editing. **Seisuke Sakamoto:** conceptualization, data curation, writing – review and editing. **Hajime Uchida:** conceptualization, data curation, writing – review and editing. **Vidyadhar Mali:** conceptualization, data curation, writing – review and editing. **Marion Aw:** conceptualization, data curation, writing – review and editing. **Stéphanie Franchi-Abella:** conceptualization, data curation, writing – review and editing. **Emmanuel Gonzales:** conceptualization, data curation, writing – review and editing. **Florent Guérin:** conceptualization, data curation, writing – review and editing. **Guillermo Cervio:** conceptualization, data curation, writing – review and editing. **Julia Minetto:** conceptualization, data curation, writing – review and editing. **Sergio Sierre:** conceptualization, data curation, writing – review and editing. **Martín Santibañes:** conceptualization, data curation, writing – review and editing. **Victoria Ardiles:** conceptualization, data curation, writing – review and editing. **Jimmy Walker Uño:** conceptualization, data curation, writing – review and editing. **Helen Evans:** conceptualization, data curation, writing – review and editing. **David Duncan:** conceptualization, data curation, writing – review and editing. **John McCall:** conceptualization, data curation, writing – review and editing. **Steffen Hartleif:** conceptualization, data curation, writing – review and editing. **Ekkehard Sturm:** conceptualization, data curation, writing – review and editing. **Jai V. Patel:** conceptualization, data curation, writing – review and editing. **Marumbo Mtegha:** conceptualization, data curation, writing – review and editing. **Raj Prasad:** conceptualization, data curation, writing – review and editing. **Cristina T. Ferreira:** conceptualization, data curation, writing – review and editing. **Luiza S Nader:** conceptualization, data curation, writing – review and editing. **Marco Farina:** conceptualization, data curation, writing – review and editing. **Catalina Jaramillo:** conceptualization, data curation, writing – review and editing. **Manuel I. Rodriguez-Davalos:** conceptualization, data curation, writing – review and editing. **Peter Feola:** conceptualization, data curation, writing – review and editing. **Amit A. Shah:** conceptualization, data curation, writing – review and editing. **Phoebe M. Wood:** conceptualization, data curation, writing – review and editing. **Michael R. Acord:** conceptualization, data curation, writing – review and editing. **Ryan T. Fischer:** conceptualization, data curation, writing – review and editing. **Bhargava Mullapudi:** conceptualization, data

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The authors have nothing to report.

## Conflicts of Interest

The authors declare no conflicts of interest.

## Data Availability Statement

The authors have nothing to report.

## Transparency Statement

The lead author Hubert P. J. van der Doef affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

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### **Supporting Information**

Additional supporting information can be found online in the Supporting Information section.