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*Published in:*  
Liver Transplantation

*DOI:*  
[10.1097/LVT.0000000000000257](https://doi.org/10.1097/LVT.0000000000000257)

**IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.**

*Document Version*  
Publisher's PDF, also known as Version of record

*Publication date:*  
2024

[Link to publication in University of Groningen/UMCG research database](#)

*Citation for published version (APA):*

Li, W., Bokkers, R. P. H., Dierckx, R. A. J. O., Verkade, H. J., Sanders, D. H., Kleine, R. D., & van der Doef, H. P. J. (2024). Treatment strategies for hepatic artery complications after pediatric liver transplantation: A systematic review. *Liver Transplantation*, 30(2), 160-169. <https://doi.org/10.1097/LVT.0000000000000257>

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## ORIGINAL ARTICLE

# Treatment strategies for hepatic artery complications after pediatric liver transplantation: A systematic review

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## Abstract

This study aimed to evaluate the effectiveness of different treatments for hepatic artery thrombosis (HAT) and hepatic artery stenosis (HAS) after pediatric liver transplantation. We systematically reviewed studies published since 2000 that investigated the management of HAT and/or HAS after pediatric liver transplantation. Studies with a minimum of 5 patients in one of the treatment methods were included. The primary outcomes were technical success rate and graft and patient survival. The secondary outcomes were hepatic artery patency, complications, and incidence of HAT and HAS. Of 3570 studies, we included 19 studies with 328 patients. The incidence was 6.2% for HAT and 4.1% for HAS. Patients with an early HAT treated with surgical revascularization had a median graft survival of 45.7% (interquartile range, 30.7%–60%) and a patient survival of 61.3% (interquartile range, 58.7%–66.9%) compared with the other treatments (conservative, endovascular revascularization, or retransplantation). As for HAS, endovascular and surgical revascularization groups had a patient survival of 85.7% and 100% (interquartile range, 85%–100%), respectively. Despite various treatment methods, HAT after pediatric liver transplantation remains a significant issue that has profound effects on the patient and graft survival. Current evidence is insufficient to determine the most effective treatment for preventing graft failure.

## INTRODUCTION

Pediatric patients with end-stage liver disease or liver failure primarily undergo liver transplantation (LT) as the

primary treatment. The estimated half-life of graft survival after pediatric liver transplantation (pLT) is currently 31 years. However, hepatic artery complications significantly affect outcomes.<sup>[1]</sup>

**Abbreviations:** HAS, hepatic artery stenosis; HAT, hepatic artery thrombosis; LT, liver transplantation; pLT, pediatric liver transplantation.

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One of the most concerning complications in patients after pLT is hepatic artery thrombosis (HAT), because it is associated with a higher rate of graft loss and the need for retransplantation.<sup>[2]</sup> A previous systematic review indicated that the incidence of early HAT (within 2 mo after pLT) was 8.3% and led to retransplantation in 62% of cases and an overall mortality of 25%.<sup>[3]</sup> Various treatment options, such as immediate retransplantation, surgical or endovascular revascularization, and conservative treatment, have been applied for HAT, but the most effective treatment strategy remains uncertain.<sup>[3]</sup>

Hepatic artery stenosis (HAS) is the second most frequently reported hepatic artery complication, with an incidence of ~5% in pediatric patients.<sup>[4,5]</sup> HAT occurs more frequently, within 1–4 weeks after transplantation, whereas HAS typically develops several months after transplantation. HAS is associated with graft failure, biliary complications, and even death.<sup>[6–9]</sup> As with HAT, the effectiveness of treatment strategies (conservative, surgical, or endovascular) for HAS has not been well identified. Less frequently occurring complications that can affect the arterial perfusion of the liver graft include splenic artery steal syndrome, as well as kinking, compression, spasms, and aneurysms of the hepatic artery.

This systematic review evaluated the effectiveness of the various treatment options for HAT and HAS after pLT.

## METHODS

### Search strategy

A systematic review of the literature was executed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses 2020 guideline. This systematic review was exempt from review by the Institutional Review Board. MEDLINE, Embase, and the Cochrane Library were searched for articles describing treatment of HAT and/or HAS in pediatric patients after LT. The search strategies are included in this article in Appendix 1. Additional studies were selected by screening the references of the included studies found by the search strategy. The search protocol was registered in the PROSPERO database (registration number: CRD42022298757, <https://www.crd.york.ac.uk/prospero/>).

### Study selection

Studies published between January 2000 and January 2023 that investigated the management of HAT and/or HAS after pLT, in which patients were aged younger than 18 years, were selected. Publications were limited to articles reporting original studies (randomized controlled trials, cohort studies, case-control studies, and case reports), and the language was restricted to

English. Treatment methods included immediate retransplantation, conservative treatment (oral anticoagulation, systemic thrombolysis, or hyperbaric oxygen therapy), and revascularization (surgical revascularization or endovascular revascularization). Studies with no data regarding the primary outcomes or unavailable full-text were excluded, as well as studies with a mixed population of children and adults, in which the children's results were not separately reported. We also excluded conference abstracts, reviews, letters to the editors, duplicated articles, and studies with fewer than 5 patients in one of the treatment methods.

The title and abstract screening of studies for inclusion in this review were independently performed by 2 authors (Weihao Li and Dewey H. Sanders). The screening was conducted at EndNote X9 (Thomson Reuters, New York, NY) and Rayyan (<https://www.rayyan.ai/>, Cambridge, MA). The full-text of articles was assessed for relevance according to the inclusion and exclusion criteria by 1 author (Weihao Li). In case of doubt, the articles were sent to the third author (Hubert P.J. van der Doef), and a consensus was reached by means of discussion and arbitration.

### Risk of bias and quality assessment

The risk of bias in nonrandomized studies was assessed using the Risk of Bias in Non-randomized Studies of Interventions tool, in conjunction with the Newcastle-Ottawa Scale for nonrandomized studies (case-control or cohort studies).<sup>[10,11]</sup> The results were visualized using the robvis visualization tool in various domains.<sup>[12]</sup> Studies with less than 5 score on the Newcastle-Ottawa Scale were deemed of insufficient methodological quality and excluded from further analysis. Case reports and case series were assessed using the Joanna Briggs Institute Critical Appraisal Checklist for Case Reports and Case Series<sup>[13,14]</sup>; studies were considered to have a low risk of bias if at least 80% of criteria were met, moderate risk if at least 60% of criteria were met, and high risk if <60% of criteria were met.

### Data extraction and validity

Various characteristics of the included studies were analyzed according to predefined parameters: study design, study period, number of transplantations, the use of a magnification loupe for the hepatic artery anastomosis, the anticoagulation protocol after transplantation, screening protocol with Doppler ultrasound imaging, and definitive diagnostic method. Treatment characteristics and outcomes were included when > 5 patients were described. Relevant treatment characteristics were recorded in accordance with a recent systematic review regarding risk factors<sup>[3]</sup>: cytomegalovirus status (donor/

recipient), retransplantation versus primary transplantation, use of arterial conduits, arterial variants and/or reconstructions, operation time, recipient weight, and number of transplants per center. Also recorded as patient characteristics were age and sex of recipients, follow-up time, primary disease, type of liver donor, and time to diagnosis of HAT and/or HAS. The exact time frame for early HAT varied, depending on the specific source. In this review, early HAT was defined as HAT that occurred 14 days after LT.

## Outcome measures

The primary outcome measures were technical success and graft and patient survival. The secondary outcome measures were hepatic artery patency, intraoperative and postoperative complications, and incidence of HAT and HAS. The incidence of HAT and HAS is delineated as a percentage, signifying the proportion of transplanted livers with HAT and HAS in relation to the total number of LTs. Technical success and hepatic artery patency were not analyzed in retransplantation and conservative treatment groups, given the nature of the treatments.

## Data collection and analysis

Data were collected and analyzed by means of descriptive statistics. The identified variables collected from the included studies were entered into a database for subsequent statistical analysis. Data are presented as mean with SD or as median with range. In addition, median with interquartile range are given for the primary outcomes, if applicable.

## RESULTS

### Search strategy

The search strategy identified 3570 articles, of which 1114 were duplicates. After the duplicates were excluded, 2456 articles were eligible for further analysis based on titles, animal studies, reviews, irrelevant studies, and conference abstracts. After title and abstract screening, 148 articles remained, 129 of which were excluded after full-text assessment based on inclusion and exclusion criteria. Accordingly, 19 studies were included in the analyses. [Figure 1](#) illustrates the selection process.

### Risk of bias and quality assessment

The summary of risk of bias assessments of non-randomized studies is shown in Supplemental Figure

S1, <http://links.lww.com/LVT/A509>. The methodological quality scores of the included studies are presented in Supplemental Tables S1, <http://links.lww.com/LVT/A490>, and S2, <http://links.lww.com/LVT/A491>. All studies had an Newcastle-Ottawa Scale score higher than 5 (range, 6–9). One case series study was evaluated using the Joanna Briggs Institute tool (Supplemental Table S3, <http://links.lww.com/LVT/A492>). Owing to the small sample size and heterogeneity of data reported in the studies, meta-analysis was not reliably possible.

## Study characteristics

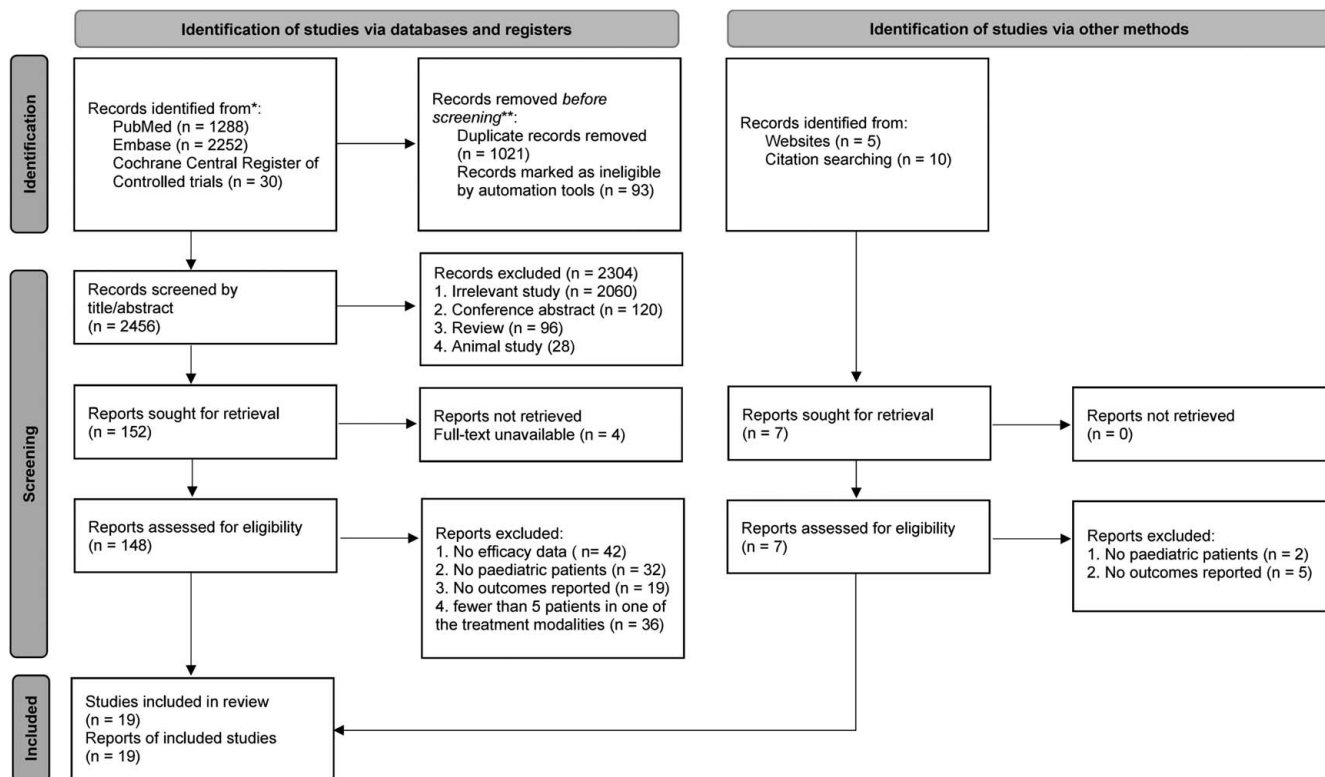
The characteristics of the studies are summarized in [Table 1](#). Of the 19 included studies,<sup>[5,8,15–31]</sup> 11 were retrospective cohort studies,<sup>[8,15,16,19,22–24,26,28,30,31]</sup> 6 were case-control studies,<sup>[5,17,18,20,21,29]</sup> and 1 was a case series study.<sup>[25]</sup> One study was both a case-control study and a retrospective cohort study.<sup>[27]</sup> A total of 356 patients were diagnosed with HAT or HAS, with an incidence of 6.2% for HAT and 4.1% for HAS.

The median number of pLTs performed per year was 31 (range, 10–144), with a study period ranging from 1984 to 2021. The use of magnification loupe was reported in 12 studies ([Table 1](#)).<sup>[5,16,18–20,22,23,25,26,28,29,31]</sup> Doppler ultrasound imaging was performed as part of standard clinical routine in all centers, with varying screening protocols and assessment criteria (Supplemental Table S4, <http://links.lww.com/LVT/A493>). The anticoagulation protocol used was reported in 16 studies, with heparin most frequently used (n = 6).<sup>[16,17,25–28]</sup> Most studies did not report detailed information regarding cytomegalovirus status, retransplantation versus primary transplantation, use of arterial conduits, arterial variants and/or reconstructions, and operation time of transplantation.

## Patient characteristics

The patient characteristics are presented in [Table 2](#). Of the 356 patients detailed in the included studies, 328 met the inclusion and exclusion criteria for subgroup analyses. The primary indication for LT was reported in 180 of the 328 patients, with 95 patients having biliary atresia and 34 having a metabolic disease (unable to distinguish between cirrhotic and noncirrhotic metabolic disease).<sup>[8,15,17,19,20,22,23,26,29,31]</sup> Donor type was reported in 216 of the 328 patients, with 39.4% (85 of 216) of patients having undergone living donor LT.<sup>[5,8,16,17,19,20,22,23,25–28,30]</sup> Missing data prevented us from analyzing the impact of primary indication, donor type, and the other potential risk factors for each treatment.

The time to diagnosis of HAT varied between 0 and 1435 days, and 113 of the total of 283 HAT cases reported a diagnosis within 14 days after



**FIGURE 1** PRISMA flow diagram of primary studies. \*Consider, if feasible to do so, reporting the number of records identified from each database of register searched (rather than the total number across all databases or registers). \*\*If automation tools were used, indicate how many records were excluded by a human and how many were excluded by automation tools. Abbreviation: PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

pLT.<sup>[19,20,24–26,29,30]</sup> Most patients were confirmed to have HAT or HAS through digital subtraction angiography, surgery, and/or CT angiography, with digital subtraction angiography being the most reported diagnostic method. Follow-up data were available for 138 patients, with a median follow-up time of 3.7 years (Table 2).<sup>[15,20,22–25,29–31]</sup>

## Hepatic artery thrombosis

The type of treatments and outcomes of the 283 patients included in subgroup analyses are described in Table 3. Of these patients, 86 received conservative treatment,<sup>[16,17,20,27,31]</sup> 112 underwent surgical revascularization,<sup>[5,15,17,19,21,24,26–28,30]</sup> 41 underwent endovascular revascularization,<sup>[15,18,21,25,30]</sup> and 44 underwent retransplantation.<sup>[5,26,29,31]</sup> Early HAT was reported in 113 patients,<sup>[19,20,24–26,29,30]</sup> with 23 patients in the conservative treatment group,<sup>[20]</sup> 57 in the surgical revascularization group,<sup>[19,24,26,30]</sup> 14 in the endovascular revascularization radiology group,<sup>[25,30]</sup> and 19 in the retransplantation group.<sup>[26,29]</sup> Subsequent anticoagulation therapy was reported in 31 patients following surgical revascularization, and in 15

patients who underwent endovascular revascularization with stent placement.<sup>[18,24]</sup>

Table 4 presents the technical success and graft and patient survival of those with HAT or HAS. Technical success rates were higher in the endovascular revascularization group than in the surgical revascularization group for patients with early HAT and HAT. Patients with early HAT or HAT who underwent surgical revascularization had lower graft survival and patient survival compared with other treatments. In contrast, patients who received conservative treatment had higher graft and patient survival than those who underwent endovascular revascularization or retransplantation. No information regarding the statistical significance was provided, potentially due to biases in the data.

Postprocedural complications were prevalent among the population with HAT, with biliary complications reported in 46 patients (52.9%). Of the 46 patients, 17 had anastomotic stenosis, 1 had extrahepatic bile duct stenosis, 1 had nonanastomotic intrahepatic stenosis, and the complications were not specifically described. Because of limited reporting of intraprocedural complications (3 studies), we could not analyze intraprocedural complications (arterial problems without specific mentioned types).

**TABLE 1** Center-specific characteristics of all hepatic artery complications

References	Study design	Study patients	Transplants (per year)	Study period	Magnification loupe	HAT, % (n =)	HAS, % (n =)
Moreno et al <sup>[15]</sup>	Retrospective cohort	301	35	September 2012 to March 2021	—	4.7 (14)	—
Xu et al <sup>[16]</sup>	Retrospective cohort	110	19	January 2014 to December 2019	Applied <sup>a</sup>	20 (22)	—
Channaoui 2020 <sup>[17]</sup>	Case control	882	32	March 1984 to March 2015	—	3.2 (35)	—
Gautier 2020 <sup>[18]</sup>	Case control	416	100	February 2016 to April 2020	3.5×	4.1 (17)	2.2 (9)
Kutluturk et al <sup>[19]</sup>	Retrospective cohort	175	34	January 2013 to November 2018	8×	4.5 (9)	—
Ma et al <sup>[20]</sup>	Case control	104	144	January 2014 to December 2016	Applied <sup>a</sup>	5.5 (23)	—
Gu et al <sup>[21]</sup>	Case control	330	39	October 2006 to April 2015	—	6.7 (22)	—
Sanada 2013 <sup>[22]</sup>	Retrospective cohort	203	20	May 2001 to November 2011	Applied <sup>a</sup>	—	6.2 (13)
Wakiya et al <sup>[23]</sup>	Retrospective cohort	176	20	May 2001 to April 2010	Applied <sup>a</sup>	0.6 (1)	6.3 (11)
Ackermann et al <sup>[24]</sup>	Retrospective cohort	516	30	January 1988 to December 2007	—	7.3 (44)	—
Sevmis et al <sup>[25]</sup>	Case series	123	—	Since 2001	2.5×	8.1 (10)	—
Warnaar et al <sup>[26]</sup>	Retrospective cohort	232	15	1990–2005	2.5–3×	13.8 (32)	—
Maruzzelli et al <sup>[8]</sup>	Retrospective cohort	99	16	February 2003 to March 2009	—	—	10.1 (10)
Uchida et al <sup>[27]</sup>	Case control + cohort	382	41	January 1996 to December 2005	—	6.7 (27)	—
Yilmaz et al <sup>[28]</sup>	Retrospective cohort	69	10	April 1997 to September 2004	Applied <sup>a</sup>	6.7 (5)	—
Jain et al <sup>[29]</sup>	Case control	166	50	August 1989 to December 1992	3× or greater	6.6 (11)	0.6 (1)
Nishida et al <sup>[30]</sup>	Retrospective cohort	114	19	June 1994 to September 2001	—	9.4 (13)	—
Stringer et al <sup>[31]</sup>	Retrospective cohort	—	40	January 1990 to December 1999	Applied <sup>a</sup>	7.3 (29)	—
Sieders et al <sup>[5]</sup>	Case control	120	10	November 1982 to January 1999	Applied <sup>a</sup>	8.3 (13)	—

<sup>a</sup>Magnification levels not reported; —, unable to retrieve or not reported.

Abbreviations: HAS, hepatic artery stenosis; HAT, hepatic artery thrombosis; n, number of patients.

**TABLE 2** Characteristics of included patients treated for hepatic artery complications

References	No.	Male sex, n (%)	Age at LT, y	Recipient weight, kg	Primary disease, n (%)		Living donor, n (%)	Time to diagnosis, d	Definitive diagnosis	Follow-up, y
					BA	MD				
HAT										
Moreno et al <sup>[15]</sup>	11	—	—	—	1 (9.1)	4 (36.4)	0	4 (0–19) <sup>b</sup>	B, C	3 (0.1–8) <sup>b</sup>
Xu et al <sup>[16]</sup>	19	—	—	—	—	—	0	—	B, C	—
Channaoui 2020 <sup>[17]</sup>	35	17 (48.6)	2.2 (0.4–11.2) <sup>b</sup>	—	23 (65.7)	5 (14.3)	2 (5.7)	< 14 or > 14 <sup>a</sup>	A	—
Gautier 2020 <sup>[18]</sup>	15	—	—	—	—	—	—	—	B	—
Kutluturk et al <sup>[19]</sup>	5	2 (40)	0.7 (0.2–5.4) <sup>b</sup>	8 (6–20) <sup>b</sup>	3 (60)	1 (20)	5 (100)	1 (1–7) <sup>b</sup>	C	—
Ma et al <sup>[20]</sup>	23	—	0.7 (0.3–3.3) <sup>b</sup>	6 (3–18) <sup>b</sup>	20 (86.9)	0	0	3.9 ± 2.5 <sup>c</sup>	B, C	3.2 ± 0.9 <sup>c</sup>
Gu et al <sup>[21]</sup>	17	—	—	—	—	—	—	—	A, B	—
Ackermann et al <sup>[24]</sup>	31	—	< 10	< 30	—	—	—	< 14	A, B, C	11.5 (4–17) <sup>b</sup>
Sevmis et al <sup>[25]</sup>	9	6 (66.7)	2.8 (0.6–16) <sup>b</sup>	< 10	—	—	9 (100)	5 (1–12) <sup>b</sup>	B	3 (0–5.8) <sup>b</sup>
Warnaar et al <sup>[26]</sup>	30	13 (43.3)	—	—	12 (40)	10 (33.3)	0	3 (1–10) <sup>b</sup>	C	—
Uchida et al <sup>[27]</sup>	26	5 (19.2)	—	—	—	—	26 (100)	—	B, C	—
Yilmaz et al <sup>[28]</sup>	5	—	13.1 ± 3.1 <sup>a</sup>	—	—	—	1 (20)	< 30	—	—
Jain et al <sup>[29]</sup>	5	2 (40)	1.7 (0.6–3.1) <sup>b</sup>	—	4 (80)	1 (20)	—	5 (1.13) <sup>b</sup>	B	13.9 (0.1–14.4) <sup>b</sup>
Nishida et al <sup>[30]</sup>	10	—	—	—	—	—	1 (10)	5 (1–10) <sup>b</sup>	A, B	2.0 (0.3–7.0) <sup>b</sup>
Stringer et al <sup>[31]</sup>	29	13 (44.8)	3.8 (0.02–16) <sup>b</sup>	—	16 (55.2)	8 (27.6)	—	6 (1–1435) <sup>b</sup>	A, B	3.6 (0.6–7.5) <sup>b</sup>
Sieders et al <sup>[5]</sup>	13	—	—	—	—	—	13 (100)	—	A, B	—
HAS										
Gautier 2020 <sup>[18]</sup>	9	—	—	—	—	—	—	—	B	—
Sanada 2013 <sup>[22]</sup>	13	3 (23.1)	0.8 (0–5.2) <sup>b</sup>	—	9 (69.2)	1 (7.7)	13 (100)	5 (3–16) <sup>b</sup>	B	3.8 (0.7–11.4) <sup>b</sup>
Wakiya et al <sup>[23]</sup>	7	2 (28.6)	—	—	4 (57.1)	1 (14.3)	7 (100)	5 (3–16) <sup>b</sup>	A, B	8.4 (0.1–11.4) <sup>b</sup>
Maruzzelli et al <sup>[8]</sup>	10	6 (60)	6.4 (0.9–13) <sup>b</sup>	—	3 (30)	3 (30)	8 (80)	—	C	—

<sup>a</sup>Twenty-eight patients diagnosed HAT within 14 days and 7 diagnosed HAT beyond 14 days.

<sup>b</sup>Median (range).

<sup>c</sup>Mean ± SD; —, unable to retrieve or not reported.

Abbreviations: A, open surgery; B, digital subtraction angiography; BA, biliary atresia; C, CT angiography; d, day; HAS, hepatic artery stenosis; HAT, hepatic artery thrombosis; LT, liver transplantation; M, male; MD, metabolic disease; n, number of included patients; SASS, splenic artery steal syndrome; y, year.

**TABLE 3** Outcomes for hepatic artery thrombosis

Study	Treatment	Subsequent Anticoagulation	No.	Technical success (%)	Graft survival (%)	Patient survival (%)
<b>Conservative treatment</b>						
Xu et al <sup>[16]</sup>	Heparin + warfarin		19		94.7	94.7
Channaoui 2020	Low-molecular-weight heparin		19		36.8	84.2
Ma et al <sup>[20]b</sup>	Low-molecular-weight heparin		23		87	91.3
Uchida et al <sup>[27]</sup>	Systemic urokinase		13		76.9	76.9
Stringer et al <sup>[31]</sup>	Low-molecular-weight heparin		12		66.7	100
<b>Surgical revascularization</b>						
Moreno et al <sup>[15]</sup>	Reanastomosis (1), HR (4)	—	5	60	60	80
Channaoui 2020 <sup>[17]</sup>	—	—	16	37.5	12.5	75
Kutluturk et al <sup>[19]b</sup>	Thrombectomy + reanastomosis	—	5	60	60	60
Gu et al <sup>[21]</sup>	Thrombectomy	—	11	27.3	—	54.6
Ackermann et al <sup>[24]b</sup>	Thrombectomy (10), reanastomosis (11), HR (10)	Yes <sup>a</sup>	31	61.3	29	54.8
Warnaar et al <sup>[26]b</sup>	Thrombectomy	—	16	37.5	31.3	62.5
Uchida et al <sup>[27]</sup>	Thrombectomy + reanastomosis	—	13	84.6	76.9	76.9
Yilmaz et al <sup>[28]</sup>	Thrombectomy + reanastomosis	—	5	100	—	60
Nishida et al <sup>[30]b</sup>	Thrombectomy + reanastomosis	—	5	100	60	80
Sieders et al <sup>[5]</sup>	Thrombectomy	—	5	40	40	80
<b>Endovascular revascularization</b>						
Moreno et al <sup>[15]</sup>	CDT (4), CDT + PTA (2)	—	6	100	100	83.3
Gautier 2020 <sup>[18]</sup>	PTA (1), PTA + Stent (13), SAE + Stent (1)	Yes <sup>c</sup>	15	100	66.7	86.8
Gu et al <sup>[21]</sup>	PTA	—	6	33.3	—	50
Sevmis et al <sup>[25]b</sup>	CDT (2), CDT + PTA (1), CDT + Stent (6)	—	9	100	77.8	66.7
Nishida et al <sup>[30]b</sup>	CDT	—	5	40	20	80
<b>Retransplantation</b>						
Warnaar et al <sup>[26]b</sup>	Retransplantation		14		35.7	71.4
Jain et al <sup>[29]b</sup>	Retransplantation		5		60	60
Stringer et al <sup>[31]</sup>	Retransplantation		17		94.1	70.6
Sieders et al <sup>[5]</sup>	Retransplantation		8		75	75

<sup>a</sup>Intravenous anticoagulants.

<sup>b</sup>Early hepatic artery thrombosis.

<sup>c</sup>Heparin infusion was given during the first week after stent placement.

Note: This was followed by the introduction of low-dose aspirin at the onset of oral intake. Once the heparin was discontinued, clopidogrel was added to dual antiplatelet therapy that continued for at least 6 months; —, unable to retrieve.

Abbreviations: CDT, catheter-directed thrombolysis; HR, hepatic reconstruction; n, number of patients; PTA, percutaneous transluminal angioplasty; SAE, splenic artery embolization.

## Hepatic artery stenosis

The treatment outcomes of the 39 patients included in subgroup analyses results can be found in Supplemental Table S5, <http://links.lww.com/LVT/A494>. Of these patients, 25 underwent endovascular revascularization and 14 underwent surgical revascularization.<sup>[8,18,22,23]</sup>

For endovascular therapy, percutaneous transluminal angioplasty was described in 19 patients and percutaneous transluminal angioplasty with stent placement in 6 patients.<sup>[8,18,22]</sup> For surgical revascularization, studies reported reanastomosis in 4 patients and surgical thrombectomy in 10 patients.<sup>[22,23]</sup>



**TABLE 4** Outcomes of patients with HAT or HAS per diagnosis and treatment

Treatment	Technical success (%) <sup>a</sup>	Graft survival (%) <sup>a</sup>	Patient survival (%) <sup>a</sup>
Early HAT (n = 113)			
Conservative treatment (n = 23)		87 <sup>1</sup>	91.3 <sup>1</sup>
Surgical revascularization (n = 57)	60.7 (54.4–71) <sup>4</sup>	45.7 (30.7–60) <sup>4</sup>	61.3 (58.7–66.9) <sup>4</sup>
Endovascular revascularization (n = 14)	70 (55–85) <sup>2</sup>	48.9 (34.5–63.4) <sup>2</sup>	73.4 (70–76.7) <sup>2</sup>
Retransplantation (n = 19)		47.9 (41.8–53.9) <sup>2</sup>	65.7 (62.9–68.6) <sup>2</sup>
HAT (n = 283)			
Conservative treatment (n = 86)		76.9 (66.7–87) <sup>5</sup>	91.3 (84.2–94.7) <sup>5</sup>
Surgical revascularization (n = 112)	60 (38.1–78.8) <sup>10</sup>	50 (30.7–60) <sup>8</sup>	68.8 (60–79.2) <sup>10</sup>
Endovascular revascularization (n = 41)	100 (40–100) <sup>5</sup>	72.3 (55–83.4) <sup>4</sup>	80 (66.7–83.3) <sup>5</sup>
Retransplantation (n = 44)		67.5 (53.9–79.8) <sup>4</sup>	71 (68–72.3) <sup>4</sup>
HAS (n = 39)			
Surgical revascularization (n = 25)	90 (61.5–95) <sup>3</sup>	100 (90–100) <sup>3</sup>	100 (85–100) <sup>3</sup>
Endovascular revascularization (n = 14)	71.4 <sup>2</sup>	57.12 <sup>2</sup>	85.72 <sup>2</sup>

<sup>a</sup>Median (interquartile range is given if applicable).

Abbreviations: <sup>1–10</sup>, number of studies; HAS, hepatic artery stenosis; HAT, hepatic artery thrombosis.

Table 4 summarizes the outcomes after the different treatments. The surgical and endovascular revascularization groups both had a technical success rate exceeding 70% and a patient graft survival rate exceeding 80%, but the graft survival rates were lower in patients who had undergone endovascular revascularization.

The primary patency rate was between 33.3% and 80% for endovascular revascularization and was 28.6% for surgical revascularization. Both treatment groups had a secondary patency of 100%. In the endovascular revascularization group of 25 patients, 5 postprocedural biliary complications were reported (3 nonanastomotic stenoses, and 2 were not specifically mentioned). In the surgical revascularization group of 16 patients, 8 postprocedural complications were reported (3 nonanastomotic stenoses, 4 intrahepatic bile duct stenosis, and 1 hepatic vein stenosis). One study in the endovascular revascularization group reported 2 intraprocedural complications including 1 pseudoaneurysm and 1 HAT.

## DISCUSSION

In this review, we examined the different treatment options for HAT and HAS after pLT. HAT remains a significant contributor to graft loss and even mortality. Surgical revascularization was the primary treatment for most of the patients with HAT, but technical success, graft survival, and patient survival outcomes were poor, particularly in patients with early post-transplant HAT. In patients with HAS, the surgical and endovascular revascularization groups both had technical success rates exceeding 70% and patient survival rates exceeding 80%. However, the endovascular revascularization group had lower graft survival rates compared with the surgical group.

Despite a lower number of patients in the conservative, endovascular revascularization, and immediate retransplantation groups, their outcomes were better than those of surgical revascularization for HAT. However, due to insufficient information about patient characteristics and treatment selection criteria, we cannot rule out selection bias. We are, therefore, unable to make a recommendation for the most effective treatment option for HAT based on these results.

Immediate retransplantation was once the favored option for HAT, but recent literature on this treatment choice is lacking since 2010.<sup>[32]</sup> Surgical revascularization appears to be the most commonly used treatment for HAT based on current literature, whereas endovascular revascularization is a relatively new treatment option, with only 3 reported studies in the past decade. For HAS, surgical and endovascular treatments have both been reported, with favorable outcomes in technical success and patient survival.

The incidence of HAT and HAS remained stable at 6.2% and 4.1%, respectively, which is comparable to the incidence reported in a systematic review in 2009 (8.3% for early HAT).<sup>[3]</sup> This review revealed inconsistencies in Doppler ultrasound surveillance and preventive anticoagulant protocols. Moreover, the complexity of pLT has increased, and more high-risk patients, such as low-weight pediatric patients and patients with noncirrhotic metabolic disease, have recently been undergoing transplantation.<sup>[33]</sup> It remains unclear whether the differences in transplantation techniques, high-risk transplant recipients, or preventative measures, such as Doppler ultrasound screening and anticoagulation treatment, will affect the comparability in the incidence of HAT and HAS.

This study has several limitations, primarily due to the lack of large, prospective controlled studies in the field of pLT. This review relied mainly on small retrospective

cohort studies, resulting in missing data for various parameters, including biochemical and clinical characteristics. Another limitation in our review is the lack of consistent data on patients' preprocedural health status, potentially introducing selection bias and affecting the effectiveness of the treatments. Moreover, data polling from included studies was difficult due to the missing data. Additionally, the use of inconsistent definitions for diagnosis and outcomes may have led to selection bias and poor reproducibility.

These limitations underscore the importance of future research on HAT and HAS after pLT. A large multicenter study or real-world registry could be established to evaluate the efficacy of all treatment protocols and assess imaging and clinical characteristics for the diagnosis and indications for treatment. Second, position statements are needed to standardize the screening, preventive measures, and treatment indications for HAT and HAS after LT.

In conclusion, this systematic review comprehensively assessed the occurrence and treatment options for HAT and HAS after pLT. Despite the availability of different treatment options, HAT remains a significant contributor to graft loss and mortality. Our review indicates that surgical revascularization was the primary treatment for most of the patients with HAT, but technical success, graft survival, and patient survival outcomes are poor, particularly in patients with early post-transplant HAT. For HAS, endovascular and surgical revascularization showed similar outcomes. Thus, no definitive recommendation can be made regarding the preferred treatment for HAT and HAS based on these findings.

#### DATA AVAILABILITY STATEMENT

The data that support the findings of this systematic review are available from the original sources cited in the manuscript. All articles and other sources used in this review are publicly available through their respective publishers or databases.

#### FUNDING INFORMATION

Reinoud P.H. Bokkers receives funding from I Netherlands Organization for Health Research and Development, the Dutch Ministry of Economic Affairs and Climate Policy, and an unrestricted research grant from Siemens Healthineers. Weihao Li is supported by the China Scholarship Council (CSC no. 202207720114).

#### CONFLICTS OF INTEREST

The authors have no conflicts to report.

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#### REFERENCES

- de Ville de Goyet J, Baumann U, Karam V, Adam R, Nadalin S, Heaton N, et al. European Liver Transplant Registry: Donor and transplant surgery aspects of 16,641 liver transplantations in children. *Hepatology*. 2022;75:634–45.
- Maksoud-Filho JG, Tannuri U, Gibelli NEM, de Pinho-Appezato ML, da Silva MM, Ayoub AAR, et al. Intimal dissection of the hepatic artery after thrombectomy as a cause of graft loss in pediatric living-related liver transplantation. *Pediatr Transplant*. 2008;12:91–4.
- Bekker J, Ploem S, de Jong KP. Early hepatic artery thrombosis after liver transplantation: A systematic review of the incidence, outcome and risk factors. *Am J Transplant*. 2009;9:746–57.
- Moray G, Boyvat F, Sevmiş Ş, Karakayalı F, Ayvaz I, Dalgıç A, et al. Vascular complications after liver transplantation in pediatric patients. *Transplant Proc*. 2005;37:3200–2.
- Sieders E, Peeters PMJG, TenVergert EM, de Jong KP, Porte RJ, Zwaveling JH, et al. Early vascular complications after pediatric liver transplantation. *Liver Transpl*. 2000;6:326–32.
- Ebel NH, Hsu EK, Dick AAS, Shaffer ML, Carlin K, Horslen SP. Decreased incidence of hepatic artery thrombosis in pediatric liver transplantation using technical variant grafts: Report of the Society of Pediatric Liver Transplantation Experience. *J Pediatr*. 2020;226:195–201.e1.
- Le L, Terral W, Zea N, Bazan HA, Smith TA, Loss GE, et al. Primary stent placement for hepatic artery stenosis after liver transplantation. *J Vasc Surg*. 2015;62:704–9.
- Maruzzelli L, Miraglia R, Caruso S, Milazzo M, Mamone G, Gruttadauria S, et al. Percutaneous endovascular treatment of hepatic artery stenosis in adult and pediatric patients after liver transplantation. *Cardiovasc Intervent Radiol*. 2010;33:1111–9.
- Piardi T. Vascular complications following liver transplantation: A literature review of advances in 2015. *World J Hepatol*. 2016;8:36–57.
- Sterne JA, Hernán MA, Reeves BC, Savović J, Berkman ND, Viswanathan M, et al. ROBINS-I: A tool for assessing risk of bias in non-randomised studies of interventions. *BMJ*. 2016;355:i4919.
- Wells G, Shea B, O'Connell D, Peterson J, Welch V, Losos M The Newcastle-Ottawa Scale (NOS) for assessing the Quality of nonrandomised studies in Meta-analyses. 2014. Accessed December 5, 2022. [http://www.ohrica/programs/clinical\\_epidemiology/oxford.htm](http://www.ohrica/programs/clinical_epidemiology/oxford.htm)
- McGuinness LA, Higgins JPT. Risk-of-bias VISualization (robvis): An R package and Shiny web app for visualizing risk-of-bias assessments. *Res Synth Methods*. 2021;12:55–61.
- Munn Z, Barker TH, Moola S, Tufanaru C, Stern C, McArthur A, et al. Methodological quality of case series studies: An introduction to the JBI critical appraisal tool. *JBI Evid Synth*. 2020;18:2127–33.
- Moola S, Munn Z, Tufanaru C, Aromataris E, Sears K, Sfetcu R, et al. Chapter 7: Systematic reviews of etiology and risk. In: Aromataris E, Munn Z, eds. *JBI Manual for Evidence Synthesis*. JBI. 2020. Accessed December 5, 2022. <https://synthesismanual.jbi.global>
- Moreno NF, Hernandez JA, Huang CS, Desai MS, Haug AB, Cleveland H, et al. Our evolution in the treatment of hepatic

- artery and portal vein thrombosis in pediatric liver transplantation: Success with catheter-directed therapies. *Pediatr Transplant*. 2022;26:e14306.
16. Xu M, Dong C, Sun C, Wang K, Zhang W, Wu D, et al. Management and outcome of hepatic artery thrombosis with whole-liver transplantation using donors less than one year of age. *J Pediatr Surg*. 2022;57:656–65.
  17. Channaoui A, Tambucci R, Pire A, de Magnée C, Sokal E, Smets F, et al. Management and outcome of hepatic artery thrombosis after pediatric liver transplantation. *Pediatr Transplant*. 2021;25:e13938.
  18. Gautier S, Monakhov A, Tsirolnikova O, Mironkov B, Voskanov M, Dzhambekov T, et al. Time is of the essence: A single-center experience of hepatic arterial supply impairment management in pediatric liver transplant recipients. *Pediatr Transplant*. 2021;25:e13934.
  19. Kutluturk K, Sahin TT, Karakas S, Unal B, Gozukara Bag HG, Akbulut S, et al. Early hepatic artery thrombosis after pediatric living donor liver transplantation. *Transplant Proc*. 2019;51:1162–8.
  20. Ma N, Song Z, Dong C, Sun C, Meng X, Zhang W, et al. Risk factors of hepatic artery thrombosis in pediatric deceased donor liver transplantation. *Pediatr Surg Int*. 2019;35:853–9.
  21. Gu LH, Li FH, Xia Q, Fang H, Zhang SJ, Han LZ. Diagnosis and outcomes of collateral arterial formation after irreversible early hepatic artery thrombosis in pediatric liver recipients. *Hepatobiliary Pancreat Dis Int*. 2017;16:39–44.
  22. Sanada Y, Wakiya T, Hishikawa S, Hirata Y, Yamada N, Okada N, et al. Risk factors and treatments for hepatic arterial complications in pediatric living donor liver transplantation. *J Hepatobiliary Pancreat Sci*. 2014;21:463–72.
  23. Wakiya T, Sanada Y, Mizuta K, Urahashi T, Ihara Y, Yamada N, et al. A comparison of open surgery and endovascular intervention for hepatic artery complications after pediatric liver transplantation. *Transplant Proc*. 2013;45:323–9.
  24. Ackermann O, Branchereau S, Franchi-Abella S, Pariente D, Chevret L, Debray D, et al. The long-term outcome of hepatic artery thrombosis after liver transplantation in children: Role of urgent revascularization. *Am J Transplant*. 2012;12:1496–503.
  25. Sevmis S, Karakayali H, Tutar NU, Boyvat F, Ozcay F, Torgay A, et al. Management of early hepatic arterial thrombosis after pediatric living-donor liver transplantation. *Transplant Proc*. 2011;43:605–8.
  26. Warnaar N, Polak WG, de Jong KP, de Boer MT, Verkade HJ, Sieders E, et al. Long-term results of urgent revascularization for hepatic artery thrombosis after pediatric liver transplantation. *Liver Transpl*. 2010;16:847–55.
  27. Uchida Y, Sakamoto S, Egawa H, Ogawa K, Ogura Y, Taira K, et al. The impact of meticulous management for hepatic artery thrombosis on long-term outcome after pediatric living donor liver transplantation. *Clin Transplant*. 2009;23:392–9.
  28. Yilmaz A, Arikan C, Tumgor G, Kilic M, Aydogdu S. Vascular complications in living-related and deceased donation pediatric liver transplantation: Single center's experience from Turkey. *Pediatr Transplant*. 2007;11:160–4.
  29. Jain A, Costa G, Marsh W, Fontes P, Devera M, Mazariegos G, et al. Thrombotic and nonthrombotic hepatic artery complications in adults and children following primary liver transplantation with long-term follow-up in 1000 consecutive patients. *Transpl Int*. 2006;19:27–37.
  30. Nishida S, Kato T, Levi D, Naveen M, Berney T, Vianna R, et al. Effect of protocol Doppler ultrasonography and urgent revascularization on early hepatic artery thrombosis after pediatric liver transplantation. *Arch Surg*. 2002;137:1279–83.
  31. Stringer MD, Marshall MM, Muiesan P, Karani JB, Kane PA, Mieli-Vergani G, et al. Survival and outcome after hepatic artery thrombosis complicating pediatric liver transplantation. *J Pediatr Surg*. 2001;36:888–91.
  32. Singhal A, Stokes K, Sebastian A, Wright HI, Kohli V. Endovascular treatment of hepatic artery thrombosis following liver transplantation. *Transpl Int*. 2010;23:245–56.
  33. Kohli R, Cortes M, Heaton ND, Dhawan A. Liver transplantation in children: State of the art and future perspectives. *Arch Dis Child*. 2018;103:192–8.

**How to cite this article:** Li W, Bokkers RPH, Dierckx RAJO, Verkade HJ, Sanders DH, de Kleine R, et al. Treatment strategies for hepatic artery complications after pediatric liver transplantation: A systematic review. *Liver Transpl*. 2024;30:160–169. <https://doi.org/10.1097/LVT.000000000000257>