




# Hepatic artery reconstruction using an operating microscope in pediatric liver transplantation—Is it worth the effort?

Tomasz Dziodzio<sup>1,2</sup>  | Friederike Martin<sup>1</sup> | Safak Gül-Klein<sup>1</sup>  | Brigitta Globke<sup>1,2</sup> | Paul Viktor Ritschl<sup>1,2</sup> | Maximilian Jara<sup>1</sup> | Karl-Herbert Hillebrandt<sup>1,2</sup> | Maximilian Nösser<sup>1</sup> | Georgios Koulaxouzidis<sup>1</sup> | Uli Fehrenbach<sup>3</sup> | Alexander Gratopp<sup>4</sup> | Stephan Henning<sup>5</sup> | Philipp Bufler<sup>5</sup> | Wenzel Schöning<sup>1</sup> | Moritz Schmelzle<sup>1</sup> | Johann Pratschke<sup>1</sup> | Christian Witzel<sup>1</sup> | Robert Öllinger<sup>1</sup> 

<sup>1</sup>Department of Surgery - Campus Charité Mitte and Campus Virchow-Klinikum, Charité – Universitätsmedizin Berlin, Berlin, Germany

<sup>2</sup>BIH Charité (Digital) Clinician Scientist Program, Berlin Institute of Health (BIH), Berlin, Germany

<sup>3</sup>Department of Radiology, Charité – Universitätsmedizin Berlin, Berlin, Germany

<sup>4</sup>Division of Pulmonology, Immunology and Critical Care Medicine, Department of Pediatrics, Charité – Universitätsmedizin Berlin, Berlin, Germany

<sup>5</sup>Department of Pediatric Gastroenterology, Nephrology and Metabolic Diseases, Charité–Universitätsmedizin Berlin, Berlin, Germany

## Correspondence

Tomasz Dziodzio, Department of Surgery, Campus Charité Mitte - Campus Virchow-Klinikum, Charité - Universitätsmedizin Berlin, Augustenburger Platz 1, 13352 Berlin, Germany.  
Email: tomasz.dziodzio@charite.de

## Abstract

**Introduction:** In pediatric liver transplantation (pLT), hepatic artery thrombosis (HAT) is associated with inferior transplant outcome. Hepatic artery reconstruction (HAR) using an operating microscope (OM) is considered to reduce the incidence of HAT.

**Methods:** HAR using an OM was compared to a historic cohort using surgical loupes (SL) in pLT performed between 2009 and 2020. Primary endpoint was the occurrence of HAT. Secondary endpoints were 1-year patient and graft survival determined by Kaplan–Meier analysis and complications. Multivariate analysis was used to identify independent risk factors for HAT and adverse events.

**Results:** A total of 79 pLTs were performed [30 (38.0%) living donations; 49 (62.0%) postmortem donations] divided into 23 (29.1%) segment 2/3, 32 (40.5%) left lobe, 4 (5.1%) extended right lobe, and 20 (25.3%) full-size grafts. One-year patient and graft survival were both 95.2% in the OM group versus 86.2% and 77.8% in the SL group ( $p = .276$  and  $p = .077$ ). HAT rate was 0% in the OM group versus 24.1% in the SL group ( $p = .013$ ). One-year patient and graft survival were 64.3% and 35.7% in patient with HAT, compared to 93.9% and 92.8% in patients with no HAT (both  $p < .001$ ). Multivariate analysis revealed HAR with SL ( $p = .022$ ) and deceased donor liver transplantation (DDLT) ( $p = .014$ ) as independent risk factors for HAT. The occurrence of HAT was independently associated with the need for retransplantation ( $p < .001$ ) and biliary leakage ( $p = .045$ ).

**Abbreviations:** anti-IL-2, anti-interleukin-2; CIT, cold ischemia time; CT, Computed tomography; DDLT, deceased donor liver transplantation; ENIS, Eurotransplant Network Information System; GRWR, graft-to-recipient weight ratio; GTBWR, graft-to-body weight ratio; HAR, hepatic artery reconstruction; HAT, hepatic artery thrombosis; i.v., intravenous; ITBL, ischemic type biliary lesions; LDLT, living donor liver transplantation; LT, liver transplantation; MELD, model for end-stage liver disease; OM, operating microscope; PELD, pediatric end-stage liver disease; pLT, pediatric liver transplantation; SL, surgical loupes; UNOS, United Network for Organ Sharing; WIT, warm ischemia time;  $\beta$ , standardized beta coefficient.

Christian Witzel and Robert Öllinger contributed equally to this study.

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**Conclusion:** In pLT, the use of an OM is significantly associated to reduce HAT rate, biliary complications, and graft loss and outweighs the disadvantages of delayed arterial perfusion and prolonged warm ischemia time (WIT).

**KEYWORDS**

hepatic artery reconstruction, hepatic artery thrombosis, operating microscope, pediatric liver transplantation, surgical loupes

## 1 | INTRODUCTION

pLT has become clinical routine with a 20-year patient survival of up to 79%.<sup>1</sup> HAR is the most demanding part of the pLT due to the narrow diameter of the corresponding hepatic arteries, especially when segment 2/3 grafts from living donors (LDLT) or split grafts from deceased donors (DDLT) are used. HAT is the most frequent surgical complication after pLT, occurring in up to 30% of cases and requires emergent surgical revision with thrombectomy, de novo HAR, or, if inevitable, retransplantation.<sup>2-9</sup> If treatment is delayed, HAT leads to a fatal outcome with poor patient and graft survival.<sup>10</sup> Additionally, long-term sequelae of early graft ischemia, even if resolved, are associated with graft damage and may impair patient and graft survival.<sup>1,10</sup>

Although HAT has been studied extensively, there are only few data comparing HAR using OM and SL. There is an ongoing debate as to which technique should be preferred.<sup>11,12</sup> In 1992, the Kyoto group first introduced HAR with an OM in living donor LT recipients and hereby reduced HAT incidence to 1.7%.<sup>13</sup> However, increased experience in LDLT, the evolution of surgical techniques and instruments yielded comparable HAT rates in HAR with SL to those achieved with OM.<sup>11,14</sup> While the advantages of the OM are a better vision and increased accuracy of anastomotic sutures,<sup>4</sup> the disadvantages are a higher technical effort. Furthermore, in many cases the necessity of an additional surgeon (plastic surgeon or surgeon with regular experience with the OM) is needed, resulting in a prolonged anastomosis time and higher likelihood for ischemia-related graft deterioration.<sup>15</sup>

Plastic surgery is well established in academic transplant-associated centers with a main focus on vessel reconstruction and microanastomoses. Hence, HAR performed by a plastic surgeon using an OM seems obvious but it is not common in pLT. In 2015, we launched a cross-functional collaboration between transplant and plastic surgeons in our center and ever since, HAR is being performed by a plastic surgeon using an OM. The main aim of this study was to compare HAT rates and complications between patients undergoing HAR by a plastic surgeon using an OM and patients undergoing HAR by a transplant surgeon using SL.

## 2 | PATIENTS AND METHODS

All patients younger than 16 years of age, who underwent pLT from January 1, 2009, to December 31, 2020, at the Department of Surgery, Campus

Charité Mitte and Campus Virchow-Klinikum, Charité—University Hospital, Berlin, Germany were examined in the study. HAR performed with an OM (2015–2020) was compared to a historic cohort using SL (2009–2015). The primary endpoint was the occurrence of HAT. Secondary endpoints were 1-year patient and graft survival and complications.

### 2.1 | Graft types and operation technique

The allocation process of DDLT grafts was organized by Eurotransplant. The LDLT donors were selected by a standardized protocol and accepted by the living donation ethics committee. Liver transplantation was carried out with caval replacement (full-size graft, extended right lobe) or in a piggy-back technique (S 2/3 or S 2/3/4). In both the standard and microsurgical cohorts, the order of anastomoses was as follows: vena cava, portal vein, hepatic artery, and finally bile reconstruction. Vena cava, left hepatic vein, and portal vein were anastomosed using PDS 5-0, 6-0, or 7-0 running sutures. In the SL group, HAR was performed with PDS 7-0 or 8-0 interrupted or running sutures. In the OM group, HAR was performed with interrupted 9-0 or 10-0 silk sutures by a plastic surgeon. The OM (OPMI® Vario 700, Carl Zeiss Meditec AG) was placed on the right side of the patient and the plastic surgeon stood on the left side.

### 2.2 | Perioperative management

We used a standardized clinical protocol for immunosuppression, using the anti-IL-2 receptor antagonist Basiliximab for induction and on tacrolimus and tapered steroids. All patients were treated with i.v. heparin aiming a postoperative activated partial thromboplastin time of 50 s. In patients without signs of hemorrhage, acetylsalicylic acid was routinely administered (3–5 mg/kg/day) from postoperative day 3 and continued for 6 months. Ultrasound screening of graft perfusion was carried out routinely 4 times per day in the first 3 days after pLT and 2 times per day on days 4–7. CT was carried out in all patients with loss or pathological arterial Doppler signal flow in the ultrasound examination to confirm or exclude HAT.

### 2.3 | Data acquisition and definitions

Electronic records of recipient clinical data were collected from the hospital information system (SAP® SE). Anonymous donor data were

acquired from the ENIS. All patients were tracked for recipient age, gender, height, weight, GRWR (in %), etiology of the liver disease, graft-type (LDLT, DDLT), anastomosis technique (SL/OM), WIT, CIT, length of stay, and complications.

Patient and graft survival, MELD, and PELD were defined according to the UNOS criteria.<sup>16–19</sup> Laboratory MELD was calculated for all recipients, while PELD was calculated for all recipients aged 11 years and younger. The last follow-up was August 1, 2021. The analysis and reporting of data received institutional ethics board approval (EA2/267/20).

## 2.4 | Statistical analysis

Statistical analyses were carried out using IBM SPSS Statistics, version 25 (IBM Corporation). Continuous variables are reported as median and interquartile range, and categorical data as counts and percentages. Continuous variables were tested with the Mann–Whitney *U*-test. A comparison of categorical data was performed using Pearson's chi-square test or Fisher's exact test. Patient and graft survival were analyzed by the Kaplan–Meier method and the log-rank test to compare groups. A multiple logistic regression model was used to determine independent risk factors for HAT and HAT-associated adverse events based on a clinically meaningful variable selection. A *p*-value of less than .05 for two-sided tests was considered statistically significant.

## 3 | RESULTS

Over a 12-year period, 79 pLTs were performed comprising 30 (38.0%) LDLT and 49 (62.0%) DDLT. The main indication for pLT was biliary atresia in 33 (41.8%) patients, followed by congenital metabolic disorders in 12 (15.2%), acute liver failure in 8 (10.1%), cystic fibrosis in 7 (8.9%), malignant tumors in 3 (3.8%), and other entities in 16 (20.3%) patients. The Kasai procedure before pLT was documented in 21 (35%) patients and 9 (11.4%) patients had a history of previous pLT. The median recipient age at pLT was 16.7 (6.1–89.6) months and the median weight was 8.0 (6.0–18.0) kg.

In 23 (29.1%) cases segment 2/3, in 32 (40.5%) a left lobe, in 4 (5.1%) an extended right lobe, and in 20 (25.3%) cases a full-size graft was used. Median PELD at pLT was 28 (28–30) and median MELD was 20 (15–27). Median CIT was 527 (454–605) min in DDLT and 46 (19–65) min in LDLT. Detailed epidemiological data are shown in Table 1.

In 58 (73.4%) cases, HAR was carried out using SL and in 21 (26.6%) cases using an OM. The two groups showed no significant differences with regard to recipient age (11.9 [7.7–99.5] in OM vs. 17.2 [5.9–70.9] months in SL; *p* = .900); recipient weight (8.0 [6.0–10.5] in OM vs. 8.9 [6.0–12.0] kg in SL; *p* = .824), size (69 [63–82] in OM vs. 71 [62–90] cm in SL; *p* = .807) and etiology for pLT (*p* = .197). In the OM group, 9 (42.9%) cases were LDLT and 12 DDLT (57.1%) versus 21 (38.1%) LDLT and 37 (63.8) DDLT in the SL group (*p* = .388).

Back-table arterial and venous reconstruction was performed in 18 (85.7%) of OM cases and in 48 (82.8%) of SL cases (*p* = .606).

CIT was comparable in both groups (OM 494 [47–648] vs. 438 [12–367] min in the SL group; *p* = .471), whereas WIT (OM 45 [34–63] vs. 36 [22–38] min in the SL group; *p* = .002) and total operating time (OM 451 [420–539] vs. 286 [230–299] min in the SL group; *p* < .001) differed significantly between the groups. Median length of hospital stay differed non-significantly between the two groups (OM 57 [31–71] vs. 44 [29–72] days in the SL group; *p* = .671). One-year patient and graft survival were both 95.2% in the OM group versus 86.2% and 77.8% in the SL group (*p* = .276 and *p* = .077; Figure 1). The causes of 1-year graft loss (*n* = 15) were HAT in 10 recipients (all in the SL group), multi-organ failure in high-urgency LTs due to acute liver failure (*n* = 3), pulmonary artery embolism (*n* = 1), and sepsis (*n* = 1). Retransplantations were performed in 10 (17.2%) cases in the SL group versus 0 (0%) in the OM group (*p* = .042). Portal vein thrombosis (OM 1 [4.7%] vs. 6 [10.3%] in SL; *p* = .429) and bile leakage (OM 2 [9.5%] vs. 5 [8.6%] in SL; *p* = .901) were comparable in both groups. An overview of all complications is shown in Table 2.

HAT occurred in 0 (0%) patients in the OM group versus 14 (24.1%) patients in the SL group (*p* = .013). Two out of 14 HATs (14.3%) were in a retransplant setting and one HAT (7.1%) occurred after LDLT. The median time between pLT and HAT occurrence was 7.5 (1.8–14.3) days. One-year patient and graft survival were 64.3% and 35.7% in the HAT group, compared to 93.9% and 92.8% in the non-HAT group (both *p* < .001; Figure 2). Successful thrombectomy was achieved in four patients (28.6%) with HAT. In further six patients (42.9%), retransplantation was necessary. In four patients (28.6%), HAT was the main cause of patient death.

Multiple regression analysis revealed DDLT (*p* = .014) and HAR with SL (*p* = .022) as an independent risk factor for HAT occurrence (Table 3). HAT was independently associated with the need for retransplantation (*p* < .001) and biliary leakage (*p* = .045) but not with patient mortality (*p* = .140) and ITBL (*p* = .759; Table 4).

## 4 | DISCUSSION

Albeit the evolution of surgical techniques and instruments, HAR remains the most demanding part of pLT, with HAT being one of the most dramatic complications.<sup>7–9</sup> If not resolved within the first 24 h, HAT almost invariably leads to major morbidity, graft loss, and mortality.<sup>10,20</sup> Even if urgently resolved by surgical or radiological thrombectomy, patient and graft outcome remains poor and retransplantation is often required.<sup>21</sup> Consequently, preventing HAT by optimizing anastomosis techniques seems of high importance for successful pLT. In our analysis, HAT occurrence was independently associated with DDLT and HAR with SL. Comparable to our data, HAT rates in pLT are reported to be 6-fold higher after DDLT than LDLT.<sup>22,23</sup> Unfortunately, the causes for increased HAT rates in DDLT are still unknown.<sup>22</sup> In our cohort, HAT rate was 24.1% and occurred only in pLT with HAR using SL. These results are at the upper end of published HAT rates in the literature.<sup>22,24</sup> Possible explanations are not only the already mentioned use of DDLT, but also the inclusion

Variables	OM group (n = 21)	SL group (n = 58)	p-value <sup>a</sup>
<b>General</b>			
Recipient female	12 (70.6)	31 (56.4)	.466
Recipient age (months)	11.9 (7.7–99.5)	17.2 (5.9–70.9)	.900
Retransplantation	1 (4.8)	8 (13.8)	.264
Previous Kasai procedure	8 (38.1)	13 (22.4)	.384
Recipient weight (kg)	8.0 (6.0–10.5)	8.9 (6.0–12.0)	.824
Recipient size (cm)	69 (63–82)	71 (62–90)	.807
PELD (<12 years)	28 (28–35)	30 (27–30)	.139
MELD	19 (16–23)	20 (17–30)	.075
<b>Etiology</b>			
Biliary atresia	10 (47.6)	23 (39.7)	.197
Acute liver failure	0	8 (13.8)	
Cystic fibrosis	4 (19.1)	3 (5.1)	
Congenital metabolic disorder	2 (9.5)	10 (17.2)	
Malignancy	1 (4.8)	2 (3.5)	
Other (including HAT)	4 (19.1)	12 (20.7)	
<b>Graft characteristics</b>			
LDLT	9 (42.9)	21 (38.1)	.388
DDLT	12 (57.1)	37 (63.8)	
Segments 2/3	13 (61.9)	10 (17.9)	<b>&lt;.001</b>
Segments 2/3/4	1 (4.8)	31 (55.4)	
Extended right split	1 (4.8)	3 (5.1)	
Full-size	6 (28.6)	14 (24.1)	
Organ weight (g)	300 (217–379)	329 (220–337)	.557
GTBWR	3.99 (2.76–5.51)	3.24 (2.20–4.17)	.168
<b>Perioperative characteristics</b>			
Back-table vascular reconstruction	18 (85.7)	48 (82.8)	.606
Cold ischemia time (h)	494 (47–648)	438 (12–367)	.471
Warm ischemia time (min)	45 (34–63)	36 (22–38)	<b>.002</b>
Operation time (min)	451 (420–539)	286 (230–299)	<b>&lt;.001</b>
Length of stay (days)	57 (31–71)	44 (29–72)	.671
One-year patient survival <sup>b</sup>	20 (95.2)	50 (86.2)	.276
One-year graft survival <sup>b</sup>	20 (95.2)	44 (77.8)	.077

Note: Annotations: Data are presented as *n* (%) or median and interquartile range (Q1–Q3).

Significant *p*-values are shown in bold.

<sup>a</sup>Group comparisons: (1) categorical data: Pearson chi-square test. (2) Continuous variables: Mann-Whitney *U*-test.

<sup>b</sup>Determined by the Kaplan–Meier analysis.

of retransplantations in our study. Regardless of the considerably high HAT rates in the SL group, our data support the idea that HAT occurrence can be significantly reduced, or—as shown in this case-series—entirely avoided in pLT by using an OM.<sup>7–9</sup> Therefore, HAR performed by a plastic surgeon using an OM appears to be a logical step, and many authors suggest the use of an OM for HAR in pLT.<sup>4,13,25,26</sup> Still, its implementation has not fully been established in most pLT programs due to multiple reasons. First, this technique requires higher logistical and personnel

resources, which can be a significant limitation for many centers. The set-up of the OM takes between 5 and 15 min with trained staff. Several aspects must be taken into account, when arranging the anastomotic field: HAR in LDLT can be substantially more complex than in DDLT due to a short and narrow hepatic artery of the graft, vessel size discrepancy between donor and recipient, anatomical variations (e.g., multiple branching) as well as a deep anastomotic field. For this reason, many surgical techniques have been described to facilitate anastomosis in the setting of pLT.<sup>14,27</sup>

**TABLE 1** Epidemiological, clinical, and operative data of pLTs (<16 years of age) performed between 2009 and 2020 divided into hepatic artery reconstruction with OM and SL

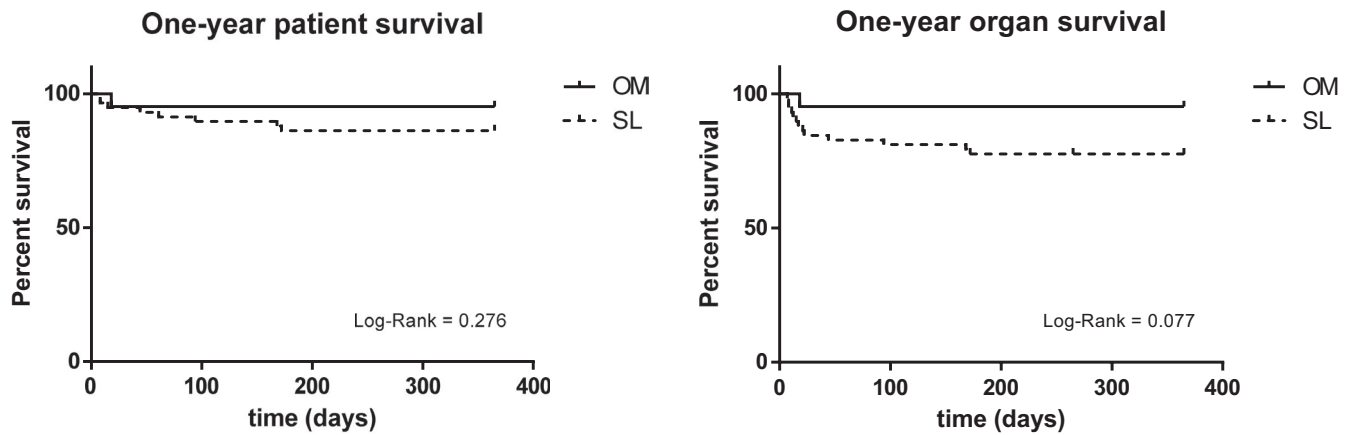


FIGURE 1 One-year patient and graft survival after pediatric liver transplantation performed with OM versus SL

TABLE 2 Comparison of complications after pLT for hepatic artery reconstruction with an OM versus SL

Variables	OM group (n = 21)	SL group (n = 58)	p-value <sup>a</sup>
HAT	0 (0.0)	14 (24.1)	<b>.013</b>
Time until HAT (days)	-	7.5 (1.8–14.3)	-
Portal vein thrombosis	1 (4.7)	6 (10.3)	.429
Acute rejection	4 (19.0)	10 (17.2)	.853
Biliary leakage	2 (9.5)	5 (8.6)	.901
ITBL	2 (9.5)	4 (6.9)	.697
Need for retransplantation	0 (4.8)	10 (17.2)	<b>.042</b>

Note: Annotations: Data presented as n (%) or median and interquartile range (Q1–Q3).

Significant p-values are shown in bold.

<sup>a</sup>Group comparisons: (1) categorical data: Pearson chi-square test. (2) Continuous variables: Mann-Whitney U-test.

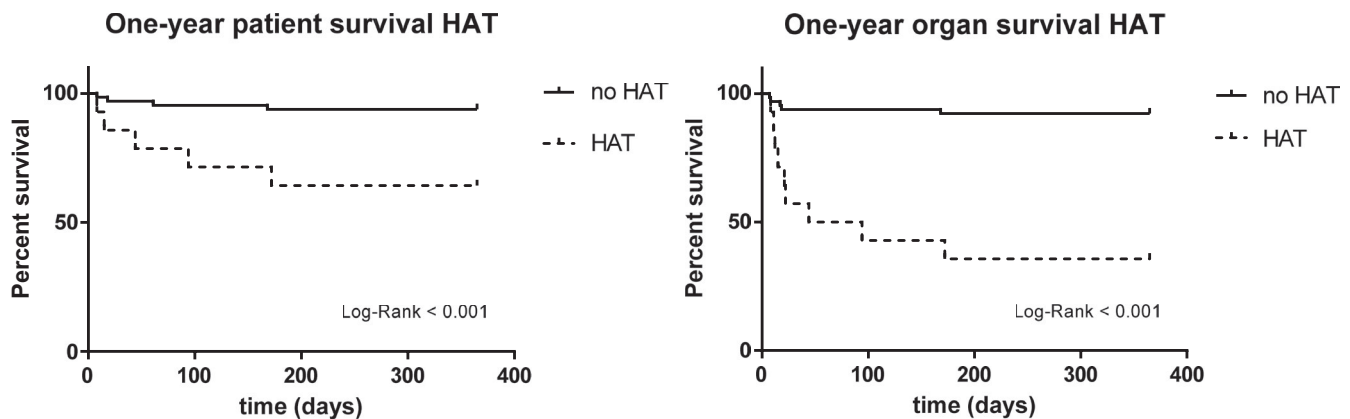


FIGURE 2 One-year patient and graft survival after pediatric liver transplantation with HAT versus no HAT

Some historical results suggested that reconstruction of all artery branches in pLT is not always necessary, as an adequate graft supply can often be achieved by anastomosis of one main artery.<sup>28</sup> Our center's strategy is to perform HAR of all hepatic branches if anatomically possible. In addition—to reduce WIT—the reconstruction of multiple branches is preferably performed in the back-table setting without the OM. In one particular case, we used the following strategy: The accessory hepatic artery branch in the donor was clipped 1 month prior to LDLT. After sonographic

exclusion of a perfusion damage and confirmation of collateralization, the subsequent transplantation was successfully performed without the need of a back-table artery reconstruction. During the pLT, all OM anastomoses were performed with an interrupted technique. This approach allows a good visualization of the anastomotic field, low traction on the anastomosis, and the avoidance of a purse-string effect. Apart from the technical aspects, a relevant part of transplantations takes place on weekends or at night and may result in insufficient availability of plastic surgeons.

**TABLE 3** Multiple linear regression analyses of perioperative independent risk factors for the development of HAT

Variables	$\beta$	<i>p</i> -value
Donor type (DDLT)	0.321	<b>.014</b>
Graft type (split)	0.042	.760
Retransplantation	0.043	.690
Back-table vascular reconstruction	0.148	.240
HAR with SL	0.255	<b>.022</b>
Acute rejection	0.035	.754

Note: Annotations: Enter method. Adjusted  $R^2 = .116$ .  
Significant *p*-values are shown in bold.

**TABLE 4** Multiple linear regression showing adverse events associated with HAT

Variables	$\beta$	<i>p</i> -value
Biliary leakage	0.207	<b>.045</b>
Portal vein thrombosis	0.181	.088
Need for retransplantation	0.367	<b>&lt;.001</b>
Mortality	0.154	.140
ITBL	0.030	.759

Note: Annotations: Enter method. Adjusted  $R^2 = .265$ .  
Significant *p*-values are shown in bold.

After 2015 also in our center, 6 out of 27 pLTs (22.2%) were performed without a plastic surgeon and using SL due to staffing constraints (all DDLTs with recipients aged >1 year). Transplant surgeons with experience in microanastomoses with the OM are an option for such situations, especially in regions and centers with high numbers of LDLTs and pediatric LTs. The handling of an OM requires regular training and plastic surgeons perform microanastomoses on a daily basis, thus this approach makes sense at least in regions and centers, where microanastomoses are less common. Another reason for the limited use of the OM for HAR is the prolonged anastomosis time. Reconstruction with an OM requires initial portal vein reperfusion only, as WIT might become too long. So far, no single publication has demonstrated an advantage of simultaneous or portal first reperfusion,<sup>29</sup> but the general perception in the field is that longer WIT is associated with ischemia/reperfusion injury and may cause secondary complications like ITBL.<sup>30–32</sup> Within our cohort, WIT and operation time were significantly longer in the OM group when compared to the SL group. However, the rate of ITBL (OM 9.5% vs. 6.9% in the SL group) did not differ significantly between groups. Our data strengthen the suggestion that the advantage of a precise anastomosis through the use of an OM by a plastic surgeon in pLT outweighs the presumed disadvantages caused by a prolonged WIT, has no detrimental effect on graft function, biliary complications, and prevents the occurrence of HAT. The median time to clinical manifestation of HAT was 7.5 days with a range of 1.8–14.3 days. These results are in line with published data.<sup>32,33</sup> In four patients, thrombectomy was successful with no adverse

effects on the graft and patient. In all four cases, early diagnosis of HAT was critical for successful revascularization. Based on the results of our analysis, we have adjusted the protocol of routine postoperative ultrasound examinations and the patients are now examined routinely until postoperative day 14 and a CT scan is performed if the ultrasound result is inconclusive.

Certainly, our study has limitations. First, the single-center, observational, retrospective study design and the comparison of a modern OM technique to a historical control with SL are relevant limitations to the generalizability of our findings that we are well aware of. Therefore, our findings cannot be immediately extrapolated to all pLTs. Second, the cohorts differed in etiology for transplantation and we did not differentiate between high-urgency and non-high-urgency transplantations. Third, the observation period of 12 years may be a disadvantage, as transplant surgeons change over time. In our center, two transplant surgeons with an expertise of more than 300 LTs and more than 50 pLTs performed all pLTs, and as of 2015, HARs were performed by two additional plastic surgeons. Despite the limitations mentioned above, our manuscript demonstrates the advantages of HAR using OM.

## 5 | CONCLUSION

HAR using OM was identified as an independent risk factor for HAT. Despite increased personnel and logistical resources, a collaboration between transplant and plastic surgeons and the use of an OM are associated with reduced rates of HAT, subsequent biliary complications, and graft loss and outweigh the disadvantages of delayed arterial perfusion and prolonged WIT.

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## CONFLICT OF INTEREST

The authors declare no conflicts of interest.

## AUTHOR CONTRIBUTION

All authors have made substantial contributions to the study and approved the submitted manuscript. TD collected the data, drafted and wrote the manuscript, designed and performed the research. PVK, MJ, and KHH collected data. FM, SGK, SK, and MN performed the statistical analysis and revised the manuscript. UF, GK, AG, PB, SH, WS, MS, and JP analyzed and critically revised the manuscript. CW and RÖ designed the research, interpreted the data, and critically revised the manuscript.

## DATA AVAILABILITY STATEMENT

Data are available on request due to privacy/ethical restrictions.



## ORCID

Tomasz Dziodzio  <https://orcid.org/0000-0002-3337-4573>

Safak Gül-Klein  <https://orcid.org/0000-0003-1013-7126>

Robert Öllinger  <https://orcid.org/0000-0002-4499-1673>

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