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Outcome after pediatric liver transplantation for staged abdominal wall closure with use of biological mesh—Study with long-term follow-up

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Abstract

Abdominal wall closure after pediatric liver transplantation (pLT) in infants may be hampered by graft-to-recipient size discrepancy. Herein, we describe the use of a porcine dermal collagen acellular graft (PDCG) as a biological mesh (BM) for abdominal wall closure in pLT recipients. Patients <2 years of age, who underwent pLT from 2011 to 2014, were analyzed, divided into definite abdominal wall closure with and without implantation of a BM. Primary end-point was the occurrence of postoperative abdominal wall infection. Secondary end-points included 1- and 5-year patient and graft survival and the development of abdominal wall hernia. In five out of 21 pLT recipients (23.8%), direct abdominal wall closure was achieved, whereas 16 recipients (76.2%) received a BM. BM removal was necessary in one patient (6.3%) due to abdominal wall infection, whereas no abdominal wall infection occurred in the no-BM group. No significant differences between the two groups were observed for 1- and 5-year patient and graft survival. Two late abdominal wall hernias were observed in the BM group vs none in the no-BM group. Definite abdominal wall closure with a BM after pLT is feasible and safe when direct closure cannot be achieved with comparable postoperative patient and graft survival rates.

KEYWORDS

abdominal wall closure, biological mesh, pediatric liver transplantation in infants, porcine dermal collagen acellular graft

Abbreviations: AFS, acceptable-for-size; BM, biological mesh; DDL, deceased donor liver; ENIS, Eurotransplant Network Information System; GRWR, graft-to-recipient weight ratio; HA, hepatic artery; HAT, hepatic artery thrombosis; LDL, living donor liver; LFS, large-for-size; OCT, ornithine transcarbamylase; OS, overall survival; PDCG, porcine dermal collagen acellular graft; PDCG, porcine dermal collagen graft; PELD, pediatric end-stage liver disease; pLT, pediatric liver transplantation; PV, portal vein; PVT, portal vein thrombosis; SM, synthetic mesh.

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1 | INTRODUCTION

pLT has become clinical routine with excellent short- and long-term patient survival.[1-3] Nevertheless, the shortage of size-matched donors in pLT regularly requires the implantation of LFS grafts from adult donors. This donor-recipient size discrepancy is one of the most complex and challenging problems for transplant surgeon.[4,5]

Therefore, especially in very young and small recipients, definite closure of the abdominal wall might be hampered by various factors, such as the graft-to-recipient weight ratio (GRWR), complex vascular reconstructions or post-operatively occurring thromboses of the hepatic artery (HAT) and the portal vein (PVT). These complications are known to be associated with a high morbidity and mortality after pLT.[6-9]

The chance for direct abdominal wall closure in pLT is further constrained by the perioperative fluid management, reperfusion edema of the liver graft, and swelling of the intestines due to clamping of the PV.[10] These factors are commonly associated with an increased abdominal pressure and interfere with the graft perfusion increasing the risk of graft loss after pLT.[11,12] Additionally, the increasing use of liver grafts for critically low-weight recipients with a history of previous abdominal surgeries is leading to a more frequent need for complex abdominal wall reconstructions.[13,14]

Established concepts for abdominal wall closure include definite reconstruction with native tissue or alternatively with BMs or SMs after staged approximation of the abdominal wall fascia.[15,16] We herein describe the outcome of the largest cohort for implantation of PDCG as BM for abdominal wall closure in pLT recipients <2 years of age.

2 | MATERIALS AND METHODS

2.1 | Patients and study design

Patients younger than 2 years of age, who underwent pLT from January 1, 2011 until December 31, 2014 at the Department of Surgery Campus Mitte and Campus Virchow Klinikum, Charité—University Hospital, Berlin, Germany, were enrolled in the study, respectively. Exclusion criterion was death within 30 days. The primary end-point was the occurrence of postoperative abdominal wall infection. Secondary endpoints included 1- and 5-year patient and liver graft survival and the development of abdominal wall hernias. The analysis and reporting of data received institutional review board approval (EA2/150/13).

The allocation process of DDL grafts was organized by Eurotransplant. LDL donors were selected by a standardized protocol and accepted by our institutional ethics committee.

Definite abdominal wall closure was aimed in all patients. Delayed primary closure of the abdominal wall is being referred to “direct” abdominal wall closure. According to our standards, post-pLT a SM (Gore Tex® Patch) was inserted in order to reduce intra-abdominal pressure. The size of the SM has been reduced consecutively over time in following operations post-pLT according to the clinical situation and the ultrasonography perfusion results. The indications for implantation of BM were the persistence of abdominal wall defects with impossibility of definite closure, the risk of an abdominal compartment, or potential restrictions in the blood flow of the liver graft. The decision on the timing of BM implantation was made individually regarding the pediatric patient's intraoperative situation. The BM used in our cohort was PDCG (Permacol™; Medtronic).

2.2 | Data collection

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

Patient demographics and clinical characteristics included sex, recipient and donor age at time of pLT, pretransplant PELD score, GRWR (in %), and etiology of the liver disease. Furthermore, previous surgeries before pLT, graft-types (LDL, DDL), median duration of operation (min), the amount of days and surgeries until definite abdominal wall closure, and the duration of total hospitalization (days) were obtained. The standard immunosuppression regimen based on FK 506 (tacrolimus) plus tapered steroids. Patients were followed up until October 2019 in regard to patient and liver graft survival with need for re-transplantation and hernia occurrence.

2.3 | Statistical analysis

All statistical analyses were carried out using IBM SPSS Statistics, version 25 (IBM Corporation). Continuous variables were reported as median and range (minimum and maximum) and categorical data as counts and percentages. Continuous variables were tested for normal distribution with Shapiro-Wilk test and thereafter analyzed with Mann-Whitney *U* test or *t* test. Comparison of categorical data was performed by using Pearson's chi-square test or Fisher's exact test. Survival and time to definite abdominal wall closure were analyzed by the Kaplan-Meier method and the log-rank test to compare groups. Due to the small group sizes and the selection bias (pLT recipients, in whom a native abdominal closure was not possible received a BM implantation) in this exploratory study, the *P*-values are given as an orientation and described as significant for two-sided *P*-values < .05, but are not to be interpreted as confirmatory.

3 | RESULTS

A total of 21 patients were eligible for this study. Patient characteristics are shown in Table 1. Direct abdominal wall closure was achieved in 5 pLT recipients (23.8%), whereas 16 patients received BM implantation (76.2%).

3.1 | Preoperative characteristics

The main underlying etiology of liver disease was biliary atresia (n = 16, 69.6%), followed by acute liver failure (n = 2, 8.7%). The

TABLE 1 Patient characteristics between BM and without BM (no-BM)

	BM (n = 16)	no-BM (n = 5)	*P*-value
Gender (M:W)	6:10	3:2	.611
Recipient age (in days)	179 (94-676)	339 (115-553)	.313
Donor age (in years)	30.4 (0-45)	21.9 (9-50)	.660
Pretransplant PELD	15.7 (0-37)	12.9 (9-24)	1.0
Indications			
Biliary atresia	12 (75)	4 (80)	
Acute liver failure	2 (12.5)	0 (0)	
Hemochromatosis	1 (6.25)	0 (0)	
Byler-syndrome	0 (0)	1 (20)	
OTC deficiency	1 (6.25)	0 (0)	
GBWR in %	3.6 (2.1-6.6)	3.6 (3.1-4.7)	.842
GBWR > 4%	7 (43.8)	1 (20)	.606
Weight (kg)	6.5 (4-12)	6.0 (6-8)	.780
Height (cm)	63 (54-91)	65 (59-78)	.548
Previous abdominal surgeries	9 (56.3)	3 (60)	1.0
Kasai operation	7 (43.8)	3 (60)	.635

Note: Data shown as n (%) or as median (range).

median age at time of pLT was 213 days (range 94-676). Median PELD scores were 15.7 in the BM group and 12.9 in the no-BM group, respectively. Both groups showed a median GRWR of 3.6% with comparable preoperative weight and height. GRWR > 4% was seen in 43.8% in BM group compared to 20% in the no-BM group (P = .606). Furthermore, 12 patients (57.1%) underwent previous abdominal surgeries prior to pLT. Assigned on both groups, a median of one previous abdominal surgery was conducted. Kasai operation had been performed in 43.8% of the cases in the BM group and 60% in the no-BM group (P = .635) (Table 2).

3.2 | Perioperative outcomes

Implanted donor grafts were 14 LDL grafts (BM group: n = 10, 62.5%; no-BM group: n = 4, 80%) as well as 7 DDL grafts (BM group: n = 6, 37.5%; no-BM group: n = 1, 20%; P = .624).

All 21 recipients underwent staged abdominal wall closure. A BM was implanted as inlay mesh in 16 patients (Figure 1). Until definite abdominal wall closure, a median of 2.5 surgeries and 20 days was needed in the BM group compared to 2 surgeries and 13 days in no-BM group (P = .495; log-rank test: P = .336; Figure 2). Vascular complications after pLT were seen in 37.5% patients, such as HAT in 4 cases (25%) and PVT in 2 cases (12.5%) before BM implantation, and none were seen in the no-BM group (P = .262). No vascular complications have been observed after BM implantation and achieved definite abdominal wall closure.

BM removal was necessary in one patient (6.3%) due to late-onset abdominal wall infection on the 97th postoperative day. This patient suffered from recurrent multi-resistant bacterial sepsis with enterococcus and staphylococcus.

The median duration of hospitalization was 35 days in BM group (range, 26-147 days) compared to 32 days in no-BM group (range, 25-114 days; P = .780).

3.3 | Long-term follow-up

The median follow-up ranged from 14 to 105 months. Overall, 1- and 5-year patient survival was 100% and 95.2% and overall liver graft survival 100% and 85.7%, respectively. Differentiated for both groups, 1- and 5-year patient survival was 100% and 100% in the BM group, compared to 100% and 80% in the no-BM group, respectively (P = 1.0; P = .238). In the BM group, 1- and 5-year liver graft survival was 100% and 87.5% and in the no-BM group 100% and 80% (P = 1.0; P = 1.0). The median patient survival was 76 months (range, 59-105) in the BM group compared to 80.5 months (range, 14-101) in no-BM group (log-rank test, P = .074; Figure 3). One patient died in the no-BM group due to post-transplant lymphoproliferative disorder 14 months after pLT. Whereas both groups showed a 100% 1- and 5-year graft-survival, 5-year graft-survival was 87.5% in the BM group versus 100% in the no BM group (Table 2, Figure 2).

During the observational period of 5 years, 2 patients (12.5%) developed abdominal wall hernia, both of them in the BM group. One patient underwent hernia repair and removal of the BM. In the second case, no intervention addressing the abdominal wall hernia was made. This patient underwent Re-pLT for chronic allograft failure after 62 months. One further patient in the BM group underwent Re-pLT for chronic allograft failure in the absence of abdominal wall hernia after 21 months, resulting in Re-pLT rate of 12.5% in the BM group, compared to 0% in the no-BM group, respectively.

4 | DISCUSSION

pLT in small infants remains challenging. Even though the procedure of pLT has reached clinical routine with favorable outcomes, aspects of size mismatch, previous abdominal surgeries, small dystrophic body constitution, and filigree vessel situations with high risk for thrombosis leading to subsequent need of cautious and staged abdominal wall closure have to be taken under consideration.[15-21] We herein describe the largest series so far on outcomes of patients <2 years of age undergoing pLT with advanced liver disease at our surgical department and a 5-year follow-up.

Especially in cases with complicated perioperative course, direct abdominal wall closure bears the risk of increased abdominal pressure. In multiple centers, delayed abdominal wall closure is the method of choice, as it avoids abdominal pressure in the early postoperative period, which is induced by fluid overload, clamping of the PV, and swelling of the liver graft due to ischemia-reperfusion injury. However, after a certain time or number of interventions, definite abdominal wall closure has to be achieved. Assuming an impossibility

TABLE 2 Perioperative outcomes and long-term follow-up compared between patients with BM and without BM (no-BM)

	BM (n = 16)	no-BM (n = 5)	*P*-value
Graft-type			
LDL	10 (62.5)	4 (80)	.624
DDL	6 (37.5)	1 (20)	
Operation time (min) with former Kasai	274 (224-296)	315 (296-335)	.017
Operation time (min) without former Kasai	247 (192-341)	308 (276-340)	.436
Time until definite abdominal wall closure (days)	20 (11-51)	13 (4-41)	.336*
Number of surgeries	2.5 (2-9)	2 (1-7)	.495
Duration of hospitalization (days)	35 (26-147)	32 (25-114)	.780
Vascular complications	6 (37.5)	0 (0)	.262
HAT	4 (25)	0 (0)	.532
PVT	2 (12.5)	0 (0)	1.0
BM removal	1 (6.25)	-	-
Hernia	2 (12.5)	0 (0)	1.0
1-y patient survival	100%	100%	-
5-y patient survival	100%	80%	.238
1-y liver graft survival	100%	100%	-
5-y liver graft survival	87.5%	80%	1.0
Patient survival (months)	76 (59-105)	80.5 (14-101)	.074*

Note: Data shown as n (%) or as median (range).

*Log-rank test.

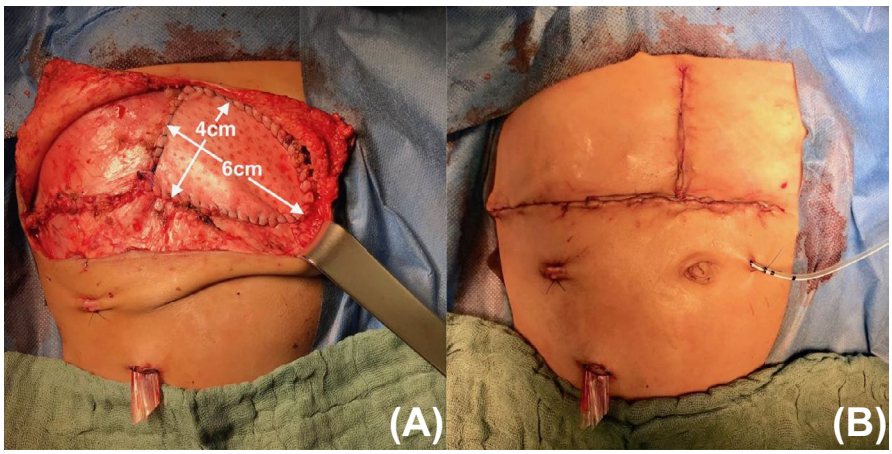

FIGURE 1 A, Abdominal wall of a 18-mo-old infant after Kasai procedure LT and re-LT with segments 2/3 from a 19-y-old donor, GRWR 3,3%: a defect of 6 × 4 cm is being replaced by the use of a BM; (B) abdomen after skin closure

of direct abdominal wall closure, replacement is obligatory and frequent. In these cases, BM and SM for replacement and reconstruction of the abdominal wall integrity are a considerable solution.[14-16,22] The implantation of BM for the treatment of abdominal wall defects is a widely recognized option and is shown to be feasible for transplant recipients.[23,24]

SMs used for replacement and reconstruction of the abdominal wall such as polytetrafluorethylene, polyester, and polypropylene are well established. However, they are being reported for provoking unwanted adhesions, fistula formations, and sincere wound infections.[25-29] In addition, SMs are associated with mesh contraction, chronic pain, inflammation, and seroma.[30] Alternatively, the implantation of BM for the treatment of abdominal wall defects is a widely recognized option in adults and has been shown to be feasible for transplant recipients.[14,16,22,31-33] In pLT recipients, the use of BM has been described; however, case numbers are low, and follow-up data are scarce.[16,22] Based on these results, we decided to test the use BMs for the replacement of the abdominal wall in our pLT recipients.

The GRWR is playing an important role for estimating possible complications, for example, LFS grafts may cause abdominal compartment syndrome and vascular complications.[34,35] Transplantation of the left-lateral segments in pediatric patients under 10kg often results in a LFS situation, since here GRWR is higher than the recommended range between 0.8% and 4% (AFS).[36-38] Not surprisingly,

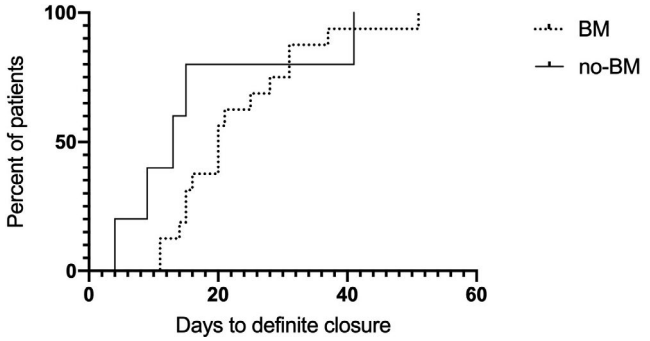

FIGURE 2 Time until definite abdominal wall closure in days in patients with and without BM

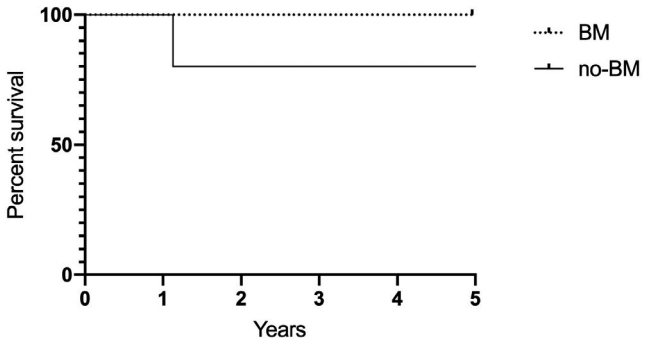

FIGURE 3 One- and 5-y survival in patients with and without BM

GRWR > 4% was seen more frequently in the BM group, although data did not reach statistical significance, probably due to the small case number. Lacking space for the liver graft implicates a temporary abdominal wall closure, may resulting in staged and delayed final closure, as seen in prolonged time until abdominal wall closure in both groups.[30,39,40]

Vascular complications in patients after pLT weighing <10 kg are common with an overall incidence ranging from 4.7% to 30%.[41-43] Being the most common cause of early graft failure, all measures must be undertaken to reduce the risk of thrombosis. In all cases with occurrence of vascular complications after pLT, a BM was used for definite abdominal wall closure. In total, no vascular complications occurred in the BM group after definite abdominal wall closure, but have occurred after pLT, whereas no vascular complications occurred in the no-BM group before and after definite abdominal wall closure. Especially in cases with vascular complications, we considered the use of a BM as meaningful, though prospective data are lacking.

The necessity of BM removal is rare and has been described previously.[34,35] In our series, one BM removal was necessary due to superficial wound healing disorder above the mesh on the 97th postoperative day without any intra-abdominal affection and impairment of graft function. Compared to the infection rate of SM, the percentage of BM removal is considerably low and favors the use thereof, similarly as in adults.[44-46]

A critical view may highlight that the percentage of patients receiving a BM in our cohort was probably too high. However, our results are favorable and the hernia rate was low. In recent years, we have accomplished to find a balance of BM use or direct closure of the abdominal wall in pLT recipients <2 years with a ratio close to 1:1. In general, it has to be mentioned that data on definite abdominal wall closure after pLT in infants <2 years are scarce and no sincere conclusions can yet be drawn. Certainly, our study is limited by its retrospective design and a relatively small cohort. Nevertheless, PDCG as one possibility of BM seems to be promising and a feasible approach for difficult abdominal closure after pLT with previous surgeries. Finally, more data comparing BM with SM and direct closure in pLT recipients are needed.

5 | CONCLUSION

Reconstruction of the abdominal wall with BM is feasible and safe in pLT recipients <2 years of age, if a staged approach does not conclude in a direct closure of the abdominal wall with low rates of abdominal wall infections and excellent patient and liver graft survival.

CONFLICT OF INTEREST

No benefits in any form have been received or will be received from a commercial party related directly or indirectly to the subject of this article. The authors have no conflicts of interest to disclose with regard to this manuscript.

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