

Liver Transplantation for Hepatic Trauma: A Study From the European Liver Transplant Registry

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Background. Liver transplantation is the most extreme form of surgical management of patients with hepatic trauma, with very limited literature data supporting its use. The aim of this study was to assess the results of liver transplantation for hepatic trauma. **Methods.** This retrospective analysis based on European Liver Transplant Registry comprised data of 73 recipients of liver transplantation for hepatic trauma performed in 37 centers in the period between 1987 and 2013. Mortality and graft loss rates at 90 days were set as primary and secondary outcome measures, respectively. **Results.** Mortality and graft loss rates at 90 days were 42.5% and 46.6%, respectively. Regarding general variables, cross-clamping without extracorporeal veno-venous bypass was the only independent risk factor for both mortality ($P = 0.031$) and graft loss ($P = 0.034$). Regarding more detailed factors, grade of liver trauma exceeding IV increased the risk of mortality ($P = 0.005$) and graft loss ($P = 0.018$). Moreover, a tendency above the level of significance was observed for the negative impact of injury severity score (ISS) on mortality ($P = 0.071$). The optimal cut-off for ISS was 33, with sensitivity of 60.0%, specificity of 80.0%, positive predictive value of 75.0%, and negative predictive value of 66.7%. **Conclusions.** Liver transplantation seems to be justified in selected patients with otherwise fatal severe liver injuries, particularly in whom cross-clamping without extracorporeal bypass can be omitted. The ISS cutoff less than 33 may be useful in the selection process.

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Despite its protected anatomical localization, the liver is one of the most frequently injured abdominal organs.^{1,2} The term hepatic trauma covers a wide spectrum of both blunt and penetrating injuries involving the liver parenchyma, intraparenchymal and extraparenchymal blood vessels, and bile ducts. Severity of those injuries ranges from small subcapsular hematomas through large intraparenchymal hematomas and lacerations with vascular disruption to complete hepatic avulsion. They are commonly categorized into 6 grades according to the American Association for the Surgery of Trauma classification.³

The strategy of management of patients with hepatic injuries has markedly evolved over the last decades, which is commonly referred to as a "paradigm change."⁴ Historically, majority of patients was managed operatively and high-risk procedures, such as major liver resections, selective hepatic artery ligations, and atriocaval shunts were frequently performed, whereas nonoperative strategies were practically not used. Consequently, the overall mortality rate reached almost 90% in patients with injuries involving major hepatic vessels.⁵ Introduction of damage control strategies, perihepatic packing, and direct repair of vascular injuries dramatically improved patients' prognosis. However, results improved largely due to a widespread utilization of selective nonoperative management strategy, largely attributable to the development of diagnostic imaging, interventional radiology, and endoscopy.⁴⁻⁶

Currently, nonoperative management remains the treatment of choice in hemodynamically stable patients without the signs of peritonitis or concomitant injuries of other organs that require an operative approach. Nonoperative management can be implemented in 29% to 100% of patients with hepatic trauma, depending on the severity of hepatic trauma (excluding only rare cases of hepatic avulsion).⁵⁻¹⁰ Basing on several relatively large reports, the success rate exceeds 85% to 90%^{6,8,11-13} and notably, failure of nonoperative

management does elevate the risk of negative outcomes,¹⁴ yet conflicting reports have also been published.¹⁵ In patients requiring immediate operations, extensive procedures should be avoided and a damage-control strategy should be implemented. The armamentarium comprises procedures, such as perihepatic packing, hepatotomy with direct suture or ligation, selective hepatic artery ligation, and finally, nonanatomical and anatomical resections. Liver transplantation (LT) completes the spectrum of available surgical modalities in extreme and rare cases of massive injuries, when the aforementioned procedures fail to control the hemorrhage and complete hepatectomy needs to be performed, as well as in patients developing acute liver failure.⁴ In the literature, there is very limited data on LT for hepatic trauma, with the largest available case series comprising 12 patients and a total number of reported cases of less than 50.¹⁶⁻¹⁸ Thus, the primary purpose of this study was to assess the results of LT for hepatic trauma.

MATERIALS AND METHODS

Study Design

This was a retrospective study performed on the data of the European Liver Transplant Registry (ELTR), an international database acquiring information from 145 centers across Europe. Data from particular centers are voluntarily submitted and comprise recipient, donor, operative, and outcome variables. Data collection process is regularly audited and the reliability of information included in the ELTR has been confirmed.¹⁹ The study has been approved and performed under the auspices of the European Liver and Intestine Transplant Association.

Patients meeting inclusion criterion (hepatic trauma as an indication for the procedure) that underwent first LT until mid-2013 were extracted from the ELTR database. All of

the centers were contacted individually to confirm that hepatic trauma was an indication for LT and to acquire more detailed data. The final study cohort consisted of 73 LT recipients performed in 37 centers in the period between 1987 and 2013 (Figure 1). More detailed data were obtained for 24 of 73 (32.9%) patients. Observations were censored at the last available follow-up visit or at 5 years posttransplantation. Causes of death and indications for retransplantation were established.

Risk factors for negative outcomes were evaluated separately in the whole study cohort and in a subgroup of 24 patients with more detailed data. To evaluate potential differences in outcomes associated with recipient age and year of LT, patients were divided into adult (18 years or older) and pediatric (younger than 18 years), as well as into those undergoing LT in the early (1987-1999) and late (2000-2013) years of the study period.

Outcome Measures and Definitions

Death irrespective of cause was set as a primary endpoint of the study and death irrespective of cause or retransplantation was set as a secondary combined end-point of the study. Primary and secondary outcome measure, namely, postoperative (90-day) mortality and graft loss, were calculated based on the 2 endpoints, respectively. In addition to the assessment of early outcomes, 5-year patient and graft survival rates were established.

Primary graft nonfunction (PNF) was defined as graft failure leading to death or retransplantation within the first 7 postoperative days in the absence of a recognized cause. Delayed PNF was defined as graft failure leading to death or retransplantation after the first 7 postoperative days in the absence of a recognized cause. One-stage LT was defined as a hepatectomy immediately followed by graft implantation, while 2-stage LT was defined as a hepatectomy performed without a graft available for transplantation and thus, followed by a period of waiting for an available organ. Procedures were divided according to surgical technique into those with cross-clamping and replacement of the retrohepatic inferior vena cava (IVC) (conventional LTs) (i) without extracorporeal venovenous bypass (VVB) and (ii) with VVB and therefore, preserved outflow from the area drained by the IVC and portal vein, and (iii) into those with

lateral clamping of the vena cava and preserved partial caval flow (piggyback LTs).

Statistics

Quantitative and qualitative data were presented as medians with interquartile ranges and ranges and numbers (percentages), respectively. Fisher exact test, χ^2 test, and Kruskal-Wallis test were used for comparisons, as appropriate. Kaplan-Meier estimator was used to calculate survival rates. Reverse Kaplan-Meier method was used to calculate median follow-up. Survival curves were presented along with number of patients at risk at particular time-points. Logistic regression models were applied to evaluate risk factors for early outcomes. Odds ratios (ORs) were presented with 95% confidence intervals (95% CI). Analyses of the receiver operating characteristics (ROC) curves were performed to establish optimal cutoffs of continuous variables in prediction of particular end-points. Areas under the ROC curves were presented with 95% CI. All tests were 2-tailed. The level of statistical significance was set at 0.05. STATISTICA v. 10 (StatSoft, Inc., Tulsa, OK) statistical software was used for computing statistical analyses.

RESULTS

Baseline characteristics of the 73 LT recipients included in the final study cohort are presented in Table 1. Median follow-up was 5 years. There were 31 deaths in the 90-day postoperative period (including 1 intraoperative) out of a total of 34 deaths, with the postoperative mortality rate of 42.5% (31/73). The 90-day graft loss rate was 46.6% (34/73). Of the 7 patients retransplanted over the 90-day postoperative period, 6 patients underwent 1 retransplantation and 1 patient underwent 2 retransplantations. Two patients were retransplanted beyond the first 90 postoperative days, 1 patient underwent retransplantation for graft failure of unknown cause and another patient underwent 3 retransplantations subsequently for chronic rejection, hepatic artery thrombosis (HAT), and recurrent HAT. In the entire study cohort, patient survival after 5 years was 50.7%. The corresponding rate of graft survival was 44.9%, with a median graft survival of 3.2 months (Figure 2). Causes of death and indications for retransplantations in the 90-day postoperative period are shown in Table 2 and Table 3, respectively.

The rate of postoperative mortality was 55.0% (11/20) for the early period and 37.7% (20/53) in the late period ($P = 0.198$) with the corresponding 90-day rates of graft loss of 65.0% (13/20) and 39.6% (21/53), respectively ($P = 0.068$). Early mortality was similar in adult (42.6% [26/61]) and pediatric (41.7% [5/12]) recipients ($P = 1.000$). Similarly, there was no significant difference in 90-day rate of graft loss between adult (45.9% [28/61]) and pediatric (50.0% [6/12]) recipients ($P = 1.000$).

Out of the analyzed variables, only conventional LT without VVB was a significant risk factor for 90-day mortality ($P = 0.030$) and graft loss ($P = 0.036$, Table 4). Mortality at 90 days was 29.2% (7/24), 36.8% (7/19), and 60.0% (15/25) after piggyback LTs and conventional LTs performed with and without VVB, respectively ($P = 0.077$). In particular, mortality after conventional LTs without VVB was significantly higher than that after piggyback LTs ($P = 0.045$) or after those performed either with conventional technique

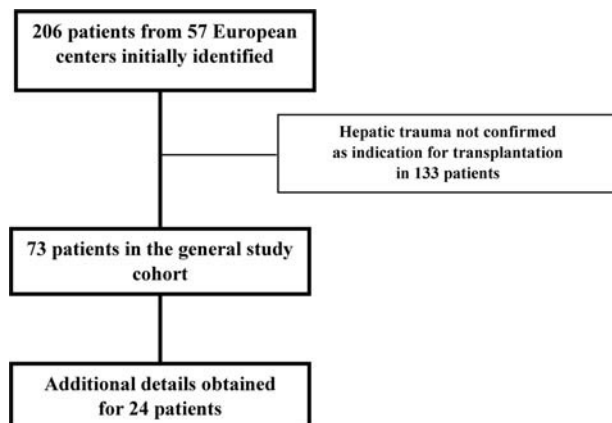


FIGURE 1. Patient selection flowchart.

TABLE 1.**Baseline characteristics of patients undergoing liver transplantation for liver trauma**

Characteristics	Median (range) or n (%)	Interquartile range	Completion rate (%)
Recipient sex:			73 (100.0%)
Male	51 (69.9%)		
Female	22 (31.1%)		
Recipient age, y:		19-40	73 (100.0%)
≥ 18	29 (0-68)		
< 18	61 (83.6%)		
MELD (points)	29 (7-47)	22-34	27 (37.0%)
Bilirubin, mg/dL	11.3 (0.3-37.6)	5.0-17.3	29 (39.7%)
Creatinine, mg/dL	1.8 (0.3-5.5)	1.0-3.1	27 (37.0%)
International normalized ratio	2.1 (1.1-4.7)	1.5-2.5	27 (37.0%)
Period			73 (100.0%)
1987-1999	20 (27.4%)		
2000-2013	53 (72.6%)		
Type of operation			68 (93.2%)
Conventional with venovenous bypass	19 (26.0%)		
Piggyback	24 (32.9%)		
Conventional without venovenous bypass	25 (34.2%)		
Unknown	5 (6.8%)		
Donor age, y	44 (2-85)	26-59	72 (98.6%)

MELD, model for end-stage liver disease.

and VVB or piggyback technique (32.6% [14/43], $P = 0.042$). Similarly, 90-day graft loss rates were 33.3% (8/24), 42.1% (8/19), and 64.0% (16/25) after piggyback LTs and conventional LTs performed with and without VVB, respectively ($P = 0.087$). The 90-day rate of graft loss after conventional LTs without VVB was significantly higher than that after piggyback LTs ($P = 0.046$) and after those performed either with conventional technique and VVB or piggyback technique (37.2% [16/43], $P = 0.045$).

The only significant differences in baseline characteristics between patients undergoing different types of LT was observed for donor age ($P = 0.005$) and recipient sex ($P = 0.015$), with recipients of piggyback LTs being more frequently males and receiving grafts from older donors (Table 5). Although there was a remarkable yet nonsignificant shift from conventional LTs with VVB (41.2% [7/17] to 23.5% [12/51], $P = 0.213$) to those performed with piggyback technique (23.5% [4/17] to 39.2% [20/51], $P = 0.380$), the rate of conventional LTs without VVB was nearly the same in early (35.3% [6/17]) and late (37.3% [19/51]) eras of the study period ($P = 1.000$). Notably, the negative effects of conventional LTs without VVB retained significance both with respect to 90-day mortality (OR, 1.79; 95% CI, 1.06-3.03; $P = 0.031$) and graft loss (OR, 1.80; 95% CI, 1.05-3.09, $P = 0.034$) following adjustment for donor age, recipient sex, and era of transplantation in multivariable model.

More detailed data available for 24 patients are summarized in Table 6. All patients in this subgroup had blunt liver injury. Particular indications along with corresponding grades of trauma are listed in Table 7. A series of univariate logistic regression analyses of the associations between the additionally available factors and postoperative outcomes revealed that grade of liver trauma of V or VI was significantly associated with increased 90-day mortality ($P = 0.005$) and 90-day graft loss ($P = 0.018$, Table 8). Additionally, a statistical tendency toward a negative effect of higher injury

severity score (ISS) ($P = 0.071$) on 90-day mortality was observed. Time interval between injury and LT did not have a significant effect on postoperative mortality ($P = 0.350$) and 90-day rate of graft loss ($P = 0.155$). Moreover, it was not significantly associated with mortality due to infections (OR, 0.96 per 1 day increase; 95% CI, 0.85-1.07; $P = 0.441$). Notably, neither of the 2 patients with concomitant bowel injuries died due to infectious complications in the postoperative period.

As vast majority of patients had grade IV and V liver traumas (20/24, 83.3%), a cutoff for the most severe injuries was arbitrarily selected between the 2 grades (≥ 5). An optimal cutoff for ISS in prediction of 90-day mortality derived from analysis of the ROC curve (Figure 3) was 33 points, with area under the curve of 0.800 (95% CI, 0.606-0.994), sensitivity of 60.0%, specificity of 80.0%, positive predictive value of 75.0%, and negative predictive value of 66.7%. Mortality at 90 days posttransplantation was 68.8% (11/16) for patients with liver trauma of grade V or higher, significantly higher than for those with grade IV or less (0.0% [0/7], $P = 0.005$). Graft loss rates at 90 days in the corresponding subgroups of patients were 75.0% (12/16) and 14.3% (1/7), respectively ($P = 0.019$). Patients with ISS over or equal to 33 points had nonsignificantly higher 90-day mortality as compared with those with lower ISS (75.0% [6/8] versus 33.3% [4/12], respectively, $P = 0.170$).

DISCUSSION

Numerous case reports and small case series published in the transplant literature document the continuous use of LT as the only life-saving treatment in rare cases of severe hepatic injuries not amenable to other available treatment modalities.^{16-18,20-31} However, transplant literature is void on larger studies and accordingly, reliable data on both short- and long-term outcomes after LT for trauma have

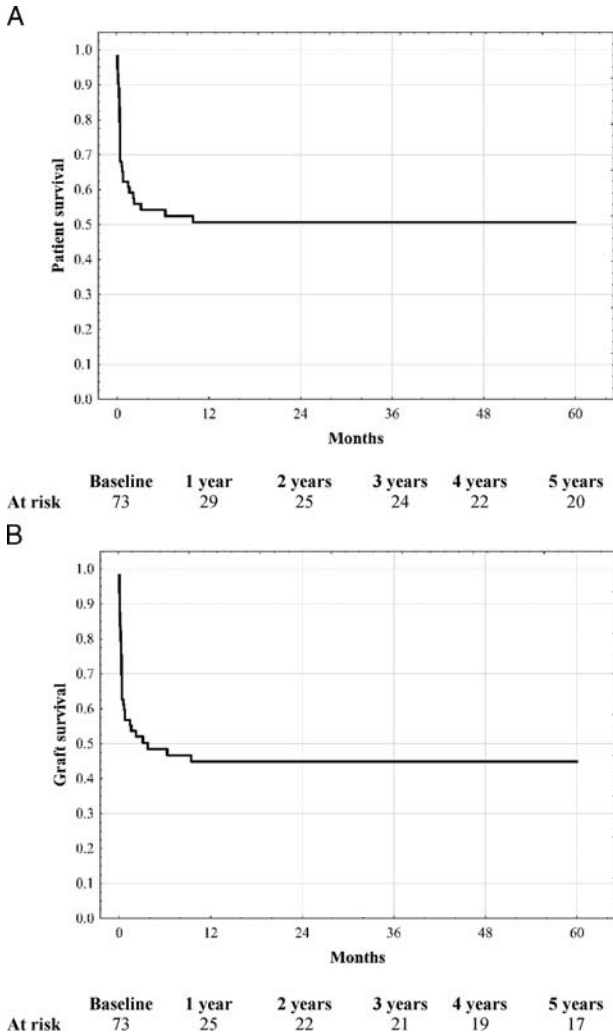


FIGURE 2. Patient (A) and graft (B) survivals after liver transplantations for hepatic trauma. Numbers of patients at risk are presented at the bottom.

been missing to date. To the authors' best knowledge, this is the largest study providing such up-to-date information, as well as an insight into the relevance of several important transplant- and trauma-associated factors in liver trauma patients undergoing LT.

Given the scarcity of organ donors and the risk of mortality over the waiting time, the acceptability of an indication for LT is advocated to be based on the comparativeness of long-term outcomes to those achieved after operations performed for currently widely accepted indications.^{32,33} Nevertheless, the concept of survival benefit, which is related to the prognosis of patients not treated with transplantation, is gaining increased popularity.^{34,35} Given the overall number of patients included in the study cohort and a long median follow up of 5 years, the present study provides reliable estimates on both short- and long-term outcomes after LT for hepatic trauma. The overall 5-year rates of 50.7% and 44.9% for patient and graft survivals are lower than those currently reported after LTs performed for other indications by approximately 20%.³⁶⁻³⁸ Notably, the decline of survival curves was mostly limited to a 90-day postoperative period and postoperative mortality and graft loss rates decreased from 55.0% and 65.0%, respectively, in the early period, to

TABLE 2. Causes of death in 90-day postoperative period after liver transplantations for hepatic trauma

Causes of death	n = 31
Infection	13 (41.9%)
Bacterial	11 (35.5%)
Fungal	2 (6.5%)
Cardiovascular event	4 (12.9%)
Liver complication	3 (9.7%)
PNF	1 (3.2%)
Delayed PNF	1 (3.2%)
Viral hepatitis	1 (3.2%)
Visceral perforation	2 (6.5%)
Multiple organ failure	3 (9.7%)
Pulmonary infection	1 (3.2%)
Intraoperative death	1 (3.2%)
Other	3 (9.7%)
Unknown	1 (3.2%)

37.7% and 39.6%, respectively, in the late period of the study. Although these differences were slightly above the level of significance (probably due to insufficient numbers), they appear to demonstrate a remarkable improvement in perioperative management. Considering the dismal prognosis of these critically injured patients, a lack of alternative treatment, and the fact that the postoperative mortality rate of severe liver trauma patients after other forms of surgical treatment reaches even 50%,³⁹⁻⁴² they seem to support the use of the scarce resource of donor organs. On the other hand, alternate utilization of organs that were allocated to patients with hepatic trauma would probably be associated with approximately 20% better survival outcomes. Thus, the reported rates of postoperative mortality and graft loss indicate the necessity to identify trauma patients in whom LT is most likely to be futile.

The pattern of mortality causes after LT for trauma is characterized by similar or slightly higher frequency of infection-related deaths and slightly lower frequency of cardiovascular events-related deaths as opposed to that reported for LT recipients in general.^{43,44} These discrepancies are presumably due to a relatively high risk of postoperative infections in trauma patients^{41,42,45} and young age of recipients, respectively. In line with LTs under a nontrauma setting,⁴⁶ Primary graft nonfunction predominated among the indications for early retransplantations. The corresponding rate of retransplantations due to HAT was unexpectedly lower than that after first transplantations performed for other indications. More specifically, there was only 1 secondary retransplantation for HAT in the 90-day postoperative period,

TABLE 3. Indications for early retransplantation in 90-day postoperative period after liver transplantations for hepatic trauma

Indications for retransplantation	n = 8
PNF	5 (62.5%)
HAT	1 (12.5%)
Delayed PNF	1 (12.5%)
Unknown	1 (12.5%)

TABLE 4.**Univariate analyses of risk factors for 90-day mortality and graft loss after liver transplantation for hepatic trauma**

Factors	90-day mortality		90-day graft loss	
	OR (95% CI)	P	OR (95% CI)	P
Recipient age	0.99 (0.96-1.02)	0.668	0.99 (0.96-1.02)	0.342
Recipient sex (male)	1.05 (0.63-1.74)	0.860	0.91 (0.55-1.50)	0.700
MELD	0.95 (0.87-1.05)	0.326	0.96 (0.87-1.05)	0.350
Type of operation				
Conventional with veno-venous bypass	0.85 (0.49-1.46)	0.547	0.87 (0.51-1.49)	0.611
Piggyback	0.64 (0.38-1.09)	0.101	0.65 (0.39-1.08)	0.098
Conventional without veno-venous bypass	1.76 (1.06-2.94)	0.030	1.73 (1.04-2.89)	0.036
Donor age	1.00 (0.98-1.03)	0.896	1.01 (0.98-1.03)	0.684
Period of transplantation	0.70 (0.42-1.19)	0.187	0.59 (0.35-1.02)	0.057

ORs are given per: 1 year for recipient and donor age; 1 point for MELD; 2000-2013 versus 1987-1999 for period of transplantation.

preceded by a retransplantation for PNF. Beyond that period, there was 1 second retransplantation for HAT preceded by a first retransplantation due to chronic rejection and followed by a third retransplantation due to recurrent HAT. Given that HAT was not an indication for any of the first retransplantations, hepatic trauma does not seem to increase the risk of this particular complication.

Analyses of risk factors for poor outcomes in the entire study cohort revealed a major impact of the type of surgical technique used for performing LT, with the worst results being achieved without any form of preservation of the caval flow, either through the piggyback technique or by use of VVB. This may be a result of a selection bias, as the choice of surgical technique might have been related, for instance, to the presence of IVC injuries. However, patients undergoing conventional LTs without VVB received grafts from donors significantly younger than those of piggyback transplant recipients and their median model for end-stage liver disease score was 7 to 9 points lower than that of the remaining recipients. Finally, proportion of patients undergoing conventional LTs without VVB was nearly identical in early and late era of the study period. The results of several previous publications also pointed toward the impact of surgical technique on post-LT outcomes. Superior results were achieved after operations performed with piggyback technique, which

is known to be associated with shorter anhepatic, warm ischemic, and operative times, less blood and plasma transfusions, blood loss, increased hemodynamic stability, and finally, better survival after LT in general,⁴⁷⁻⁵⁰ yet data on the latter are inconsistent.⁵¹ In contrast, conventional LTs without VVB decreases the cardiac preload and output by approximately 50% and mean arterial pressure by more than 30%.⁴⁷ Although majority of LT recipients tolerate these alterations via preserved compensatory mechanisms, this might not be the case for severely injured patients and therefore, results in an unacceptable postoperative mortality rate of 60%. Notably, given that the primary indications for the use of VVB in centers using it selectively during conventional LTs comprise both preexisting hemodynamic instability and intolerance of the cross-clamping, selection bias is rather unlikely reason for the observed differences in outcomes.^{47,48} As a prospective randomized study on the impact of the operative technique on LT outcomes in hepatic trauma patients is practically impossible to perform and there is a great variety of the used techniques among centers,⁵² the limited results of the present study may be a first step in creating a recommendation at least to avoid conventional operations without VVB.

Despite low number of patients for whom additional, more detailed information were available, analysis of particular indications for LTs revealed that hepatic failure was, in

TABLE 5.**Differences in baseline characteristics between patients undergoing liver transplantation of different types**

Factors	Types of liver transplantation			P
	Conventional with venovenous bypass	Piggyback	Conventional without venovenous bypass	
Recipient age:				
≥ 18 years	29 (20-37, 0-51)	30 (20-43, 15-68)	27 (17-44, 2-67)	.678
< 18 years	17 (89.5%)	22 (91.7%)	18 (72.0%)	.128
< 18 years	2 (10.5%)	2 (8.3%)	7 (28.0%)	
Recipient gender:				.015
Male	10 (52.6%)	22 (91.7%)	17 (68.0%)	
Female	9 (47.4%)	2 (8.3%)	8 (32.0%)	
MELD	30 (22-34, 17-44)	32 (24-37, 7-47)	23 (21-30, 16-34)	.234
Donor age	34 (19-45, 14-69)	59 (36-69, 16-85)	42 (34-51, 2-79)	.005
Period of transplantation				.313
1987-1999	7 (36.8%)	4 (16.7%)	6 (24.0%)	
2000-2013	12 (63.2%)	20 (83.3%)	19 (76.0%)	

Data are presented as median (interquartile range, range) or n (%). MELD, Model for End-stage Liver Disease.

TABLE 6.**Additional details available for a subgroup of 24 liver transplant recipients from the study cohort**

Characteristics	Median (range) or n (%)	Interquartile range	Completion rate (%)
AAST Grade of Liver Trauma			23 (95.8%)
VI	2 (8.3%)		
V	14 (58.3%)		
IV	6 (25.0%)		
I	1 ^a (4.2%)		
Unknown	1 (4.2%)		
Injury severity score	25 (16-75)	25-42	20 (83.3%)
Days from trauma to liver transplantation	9.5 (0.0-38.0)	4.0-14.5	24 (100.0%)
Liver transplant indication			24 (100.0%)
Liver failure	18 (75.0%)		
Uncontrollable bleeding	6 (25.0%)		
Isolated liver trauma	8 (33.3%)		24 (100.0%)
Concomitant abdominal injuries:	5 (20.8%)		24 (100.0%)
Spleen	3 (12.5%)		
Bowels	2 (8.3%)		
Pancreas	1 (4.2%)		
Kidney	1 (4.2%)		
Injuries of additional regions:	15 (62.5%)		24 (100.0%)
Head	6 (25.0%)		
Chest	15 (62.5%)		
Pelvis	4 (16.7%)		
Extremities	6 (25.0%)		
Two-stage liver transplantation	6 (25.0%)		24 (100.0%)
Anhepatic time for two-stage operations, n = 6, h	27.5 (14-38.5)	16-36	6 (100.0%)
Cold ischemic time, h	7.6 (2.7-10.9)	6.5-8.7	17 (70.8%)
Interventional treatment before liver transplantation	21 (87.5%)		24 (100.0%)
Packing	12 (50.0%)		
Liver resection	12 (50.0%)		
Parenchymal sutures	4 (16.7%)		
Direct repair	2 (8.3%)		
Biliary anastomosis	1 (4.2%)		
Hepatic artery repair	1 (4.2%)		
Selective hepatic artery ligation	1 (4.2%)		
Arterial embolization (IR)	1 (4.2%)		
External biliary drainage	1 (4.2%)		

^a Liver transplantation due to ongoing ischemia of liver parenchyma.

AAST, American Association for the Surgery of Trauma; IR, interventional radiology.

majority of cases, most probably associated with prior surgical treatment, namely, resection, packing, and sutures. Moreover, a significant risk factor for poor outcomes of potential clinical relevance in decision-making processes was identified. Although grade of liver trauma has been frequently found to be strongly associated with outcomes of patients in general,^{3,6,39,41} this is not the case for those undergoing LT.^{16,17} Accordingly, this is the first study showing a major difference in postoperative mortality and graft loss rates between LT recipients depending on the severity of liver injury.

In contrast to the grade of liver trauma, there was only a statistical tendency slightly above the level of significance between the overall severity of injury reflected by the ISS and postoperative mortality. Notably, the ISS has been previously proven to be associated with mortality of both trauma patients in general^{15,3-55} and in those with hepatic injuries,^{6,39} however not in the setting of LT.¹⁶ Interestingly, the area under the ROC curve of 0.800 for ISS in prediction of mortality was only slightly lower than that found by Haider et al¹⁴ in

an analysis of the National Trauma Data Bank (>630 thousand patients). Despite the lack of statistical significance most probably related to the number of patients, the ISS cutoff of 33 identified patients with postoperative mortality of 75%, the worst among all of the established subgroups. Therefore, liver trauma patients with ISS over or equal to 33 should be selected for LT with extreme caution to avoid futile procedures. Because ISS is defined as the sum of squares of the highest Abbreviated Injury Scale scores for the 3 most severely injured regions,⁵⁶ it exceeds 33 for any patient with grade V liver injury and any nonabdominal additional injury of Abbreviated Injury Scale over or equal to 3. However, regardless of the significant impact of the overall severity of trauma, the presence of concomitant injuries did not seem to affect posttransplant outcomes by itself and should not be considered as contraindication for LT.

Finally, the presented results indicate an overall acceptability of a strategy based on a 2-stage LT procedure in extreme cases of uncontrollable bleeding or hemodynamic instability

TABLE 7.
Grades of hepatic trauma according to indication for liver transplantation

Indication	AAST liver trauma grade				
	I	IV	V	VI	N/A
Uncontrollable bleeding	—	1	5	—	—
Posthepatectomy liver failure, including:					
Right hemihepatectomy	—	3 ^a	3	—	1
Extended right hemihepatectomy	—	—	1 ^b	—	—
Left hemihepatectomy	—	—	1	—	—
Hepatic necrosis, preceded by:					
Packing and sutures	—	1	2	—	—
Packing	—	1	1	1	—
Sutures	—	—	1 ^c	—	—
Packing and hepatic artery ligation	—	—	—	1	—
Unspecified cause	1	—	—	—	—

^aIncluding 1 patient with portal vein thrombosis and iatrogenic stenosis of the inferior vena cava; 1 patient with iatrogenic injury of the left hepatic artery, portal vein thrombosis and inferior vena cava thrombosis; and 1 patient with portal vein thrombosis.

^bWith repair of the inferior vena cava and approximately 2 hours of intermittent Pringle maneuver, complicated by stenosis of the inferior vena cava.

^cWith repair of the injury of proper hepatic artery.

requiring urgent hepatectomy, when a donor organ is not immediately available. Introduced by Ringe et al⁵⁷ more than 2 decades ago, its use has been reported under such circumstances, also in nontrauma patients developing hemodynamic instability with the longest anhepatic time of 67 hours.⁵⁸⁻⁶⁰ Notably, a nonsignificant increase in 90-day risk of graft loss after 2-stage transplantations was found in the present study. Although a lack of significance with respect to the risk of graft loss may be related to a low number of patients undergoing 2-stage operations, this is not the case for postoperative mortality, which was identical after 1- and 2-stage operations. On the other hand, the pretransplant mortality of approximately 20% to 30% has been reported

previously.^{17,18} However, the outcome would most certainly be fatal in all of these patients without hepatectomy and subsequent transplantation. Nevertheless, the presented results are limited to patients who actually survived the period between the first and second stage and should be interpreted as the most favorable scenario. Thus, it is the surgeon who faces this very difficult decision to perform a hepatectomy without an organ available for transplantation.

The presented results indicate that LT should be always taken under consideration in patients with hepatic trauma of grade < V and ISS <33, when all other therapeutic options fail. This comprises both patients with uncontrollable bleeding and those developing liver failure, predominantly related to prior interventional treatment. Patients with grade V injuries may cautiously be considered as potential candidates for LT only if their ISS does not exceed 33 points (without any concomitant nonabdominal injury of grade 3 or higher). Notably, long period of time elapsed since the occurrence of trauma does not appear to be a contraindication, given no significant impact on the risk of overall and infection-related mortality found in the present study.

Several limitations of the present study need to be acknowledged. First, it suffers from the flaws of its retrospective character. Second and more important, only general data were available for a whole cohort of 73 patients and thus, analysis of more detailed risk factors were based on a limited number of patients. Therefore, the results of analyses performed in the smaller subset of patients need to be interpreted with caution. Nevertheless, several important predictors of mortality were identified despite this limitation. However, the numbers precluded the use of multivariable models in analyses of more detailed factors. Finally, the recommendation on avoiding the conventional transplantations without VVB requires further validation.

In conclusion, LT seems justified in selected patients with otherwise fatal liver injuries, providing an approximately 50% chance for survival. The group of optimal candidates

TABLE 8.
Univariate analyses of risk factors for 90-day mortality and graft loss based on additionally available variables in a subgroup of 24 recipients of liver transplantation for hepatic trauma

Factors	90-day mortality		90-day graft loss	
	OR (95% CI)	P	OR (95% CI)	P
AAST liver trauma grade ≥ V	— ^a	0.005 ^a	4.24 (1.28-14.09)	0.018
Injury severity score	1.09 (0.99-1.19)	0.071	1.06 (0.98-1.14)	0.151
Time between trauma and liver transplantation	0.95 (0.86-1.05)	0.350	0.92 (0.83-1.03)	0.155
Uncontrollable bleeding as indication for liver transplantation	1.00 (0.40-2.52)	0.999	2.24 (0.70-7.20)	0.177
Isolated liver injury	0.68 (0.29-1.63)	0.390	1.14 (0.48-2.72)	0.770
Two-stage liver transplantation	1.00 (0.40-2.52)	0.999	2.24 (0.70-7.20)	0.177
Cold ischemic time	1.00 (0.62-1.60)	0.992	0.86 (0.51-1.45)	0.572
Associated injuries:				
Head	1.58 (0.60-4.16)	0.353	1.27 (0.48-3.33)	0.634
Chest	1.73 (0.73-4.11)	0.213	1.10 (0.48-2.53)	0.831
Extremities	1.58 (0.60-4.16)	0.353	1.27 (0.48-3.33)	0.634
Surgical treatment before liver transplantation:				
Packing	0.71 (0.32-1.61)	0.416	0.49 (0.21-1.16)	0.106
Liver resection	0.50 (0.21-1.17)	0.109	0.71 (0.31-1.61)	0.410

Odds ratios are given per: 1 day for time interval between trauma and transplantation, 1 point for injury severity score, and 1 hour for cold ischemic time.

^aIncalculable due to no mortality in patients with liver trauma of AAST grade < V, P value derived from Fisher exact test.

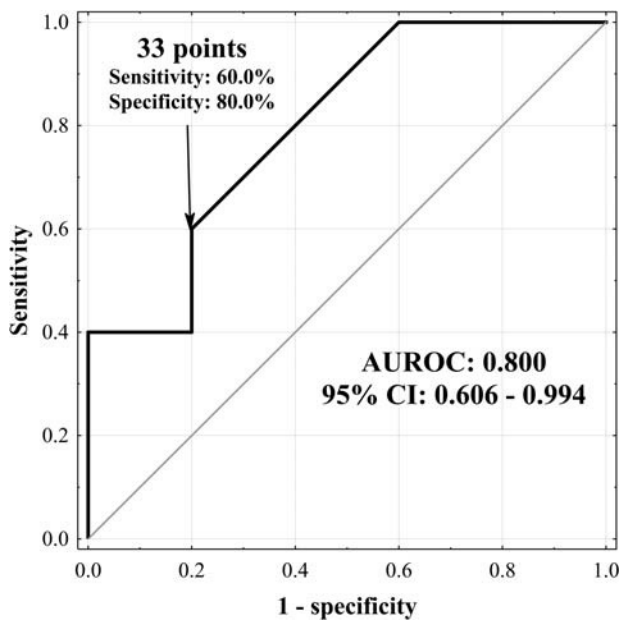


FIGURE 3. Receiver operating characteristics curve for injury severity score in prediction of 90-day mortality after liver transplantation for hepatic trauma.

comprise patients with severity of liver trauma not exceeding grade IV and potentially, those with ISS under 33. Transplantations performed with preservation of the caval outflow throughout the operations are associated with superior outcomes and thus, the use of conventional technique without VVB should be avoided if possible.

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