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Liver Transplantation after Severe Hepatic Trauma: a Sustainable Practice. A Single-Center Experience and Review of the Literature

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Abstract:	Severe hepatic trauma is a rare indication for liver transplantation (LT). We report our single-center experience of LT for hepatic trauma. Four new cases are discussed in the light of a literature review in order to depict the pathways leading from hepatic trauma to LT and to assess the outcomes of this practice. LT is generally indicated in case of uncontrollable hemorrhage, acute liver failure, or post-traumatic late sequelae. Hepatic vessels thrombosis, sepsis, major hepatic resections and a late referral are factors associated with the progression towards irreversible liver failure. Considering all reported cases, early patient and graft survival reached 68% and 62%, respectively, but in the last decade both have improved to 84%. LT after severe hepatic trauma is a sustainable practice considering the current good outcomes and the ineluctable death of these patients without LT.

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Liver Transplantation after Severe Hepatic Trauma: a Sustainable Practice. A Single-Center Experience and Review of the Literature Damiano Patrono, Andrea Brunati, Renato Romagnoli, and Mauro Salizzoni General Surgery 8 and Liver Transplantation Center, San Giovanni Battista – Molinette University Hospital, A. O. Città della Salute e della Scienza, Turin, Italy Running head: Liver Transplantation after Hepatic Trauma Authors contributions: Damiano Patrono designed and performed the study, collected data and wrote the manuscript; Andrea Brunati helped in collecting the data; Renato Romagnoli critically revised the manuscript; Mauro Salizzoni supervised and critically revised the manuscript. No grant or financial support was received for the publication of this paper **Conflict of interest:** the authors disclose no conflicts of interest **Corresponding author:** Prof. Mauro Salizzoni Professor of Surgery. University of Turin General Surgery 8 and Liver Transplantation Center, San Giovanni Battista – Molinette University Hospital, Turin, Italy Corso Bramante 88, 10126, Torino Tel: 00390116334374 Fax: 00390116336770

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ABSTRACT

Severe hepatic trauma is a rare indication for liver transplantation (LT). We report our single-center experience of LT for hepatic trauma. Four new cases are discussed in the light of a literature review in order to depict the pathways leading from hepatic trauma to LT and to assess the outcomes of this practice. LT is generally indicated in case of uncontrollable hemorrhage, acute liver failure, or post-traumatic late sequelae. Hepatic vessels thrombosis, sepsis, major hepatic resections and a late referral are factors associated with the progression towards irreversible liver failure. Considering all reported cases, early patient and graft survival reached 68% and 62%, respectively, but in the last decade both have improved to 84%. LT after severe hepatic trauma is a sustainable practice considering the current good outcomes and the ineluctable death of these patients without LT. **Keywords:** hemorrhage, liver failure, liver transplantation, sepsis, thrombosis

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FIGURE LEGENDS:

Figure 1. (Case 1) A. Contrast-enhanced computed tomography showing severe dilatation of intrahepatic bile ducts of the liver remnant after right hepatectomy (arrow) and B. Portal vein thrombosis (arrow) and inferior vena cava dilatation (arrowhead).

Figure 2. (Case 4) Contrast-enhanced computed tomography showing the severely swollen and inhomogeneous liver remnant after right hepatectomy.

Figure 3. Clinical scenarios of LT for hepatic trauma

INTRODUCTION

Liver is the most frequently injured abdominal organ (1). The treatment of blunt hepatic trauma has significantly evolved over the last three decades with the introduction and wide acceptance of the concepts of nonoperative management, damage control surgery and the use of interventional radiology (2-6). Nowadays, nonoperative management is the preferred strategy in hemodinamically stable patients (6-9) but surgery, alone or in association with interventional radiology, still plays a major role in the management of severe liver injuries (grade IV and V according to the American Association for the Surgery of Trauma Organ Injury Score) (10), which remains extremely challenging even in experienced hands (11, 12). The main causes of death in these patients are exsanguinating hemorrhage and liver failure leading to multiorgan failure (13). Both these conditions, in principle, can be treated by a timely liver transplantation (LT).

Nevertheless, severe hepatic trauma is a peculiar albeit rare indication for orthotopic LT. LT has been most frequently performed for an uncontrollable hemorrhage requiring a total hepatectomy, or for an acute liver failure (ALF) developing after the first treatment.

Although salvage LT for hepatic trauma represents a well-established practice in all major liver transplant centers, a comprehensive literature review analyzing the different scenarios in which LT becomes the last possible therapeutic option after hepatic trauma has not been carried out so far. Furthermore, the short and long-term results of this practice have not been thoroughly assessed.

In this article we report four more cases of patients who underwent LT at our institution following a severe hepatic trauma; we focused our case reports on the initial trauma management and on how LT eventually resulted as the only viable therapeutic solution. Afterwards, based on our experience and on an accurate review of the literature, we depict the clinical scenarios in which a liver injury can eventually lead to LT and assess the outcomes of this practice. Finally, we highlight some specific factors linked to the indication for LT in these extreme situations.

CASE 1

In June 2002 a 15-year-old female suffered a grade IV right liver injury as a consequence of a horse kick. She was first referred to a peripheral hospital, where she underwent a right hepatectomy. Her postoperative course was complicated by progressive liver failure, portal vein and inferior vena cava thrombosis, biliary leak-related sepsis, and acute renal failure (Figure 1). She was then transferred to our institution on postoperative day (POD) 14, where a relaparotomy was performed in order to drain the bile collections and to assess the hepatic vessels permeability. At reoperation, we observed a complete portal vein and hepatic artery thrombosis, the latter due to some surgical stitches from the previous operation, and a biliary leak coming from the left bile duct, which had been completely severed. The biliary leak was treated by placing a drain into the left bile duct stump, but the portal vein thrombosis invariably recurred after two successive attempts of surgical thrombectomy. Forty-eight hours later, she developed hepatic failure and coagulopathy and became hemodinamically unstable as a result of massive abdominal hemorrhage. The bleeding was only partially controlled by liver packing. She was then placed on the national waiting list for an urgent liver transplantation for acute liver failure. Despite massive fresh frozen plasma transfusions due to ongoing bleeding, her Model for End-stage Liver Disease (MELD) score was 23. Transplantation was carried out two days later (19 days after the trauma) with resection of the retro-hepatic inferior vena cava that was occluded by a thrombus. The post-transplant course was uneventful and she was discharged home on POD 18. More than 10 years after, she is alive and well with a normal hepatic function.

CASE 2

In March 2003 a 20-year-old female with a previous medical history of Thalassemia Major suffered an abdominal trauma from a motorway accident. She underwent an explorative laparotomy in a

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peripheral hospital, where a 5-cm-deep parenchymal tear involving segment 8 was treated by hepatorrhaphy. Due to persistent bleeding and respiratory failure she was transferred to our department on POD 1, where a decision for a re-laparotomy was taken after a CT-scan revealed a large hematoma of the right liver lobe, a dilatation of the bile ducts of the right liver segments and an abundant peritoneal fluid collection. During the operation, we observed a huge hematoma of the right hepatic lobe and a large tear of the right hepatic vein. Hemostasis was achieved through a right hepatectomy. Postoperatively, the patient developed progressive liver failure, acidosis and a systemic inflammatory response syndrome. After having received the pathological report that revealed a severe hepatic iron overload and fibrosis, iron-chelation with desferoxamine was started but could not reverse the deterioration of the hepatic function, which was characterized by hyperbilirubinemia, ascites and encephalopathy. She was placed on the national list for an urgent LT with a MELD score of 32 and was transplanted six days after, i.e. fifteen days after the trauma. Unexpectedly, a previously unrecognized portal vein thrombosis was observed during transplantation. The postoperative course was uneventful except for a transitory early graft dysfunction. She is still alive and well 10 years after the trauma.

CASE 3

In September 2002 a 4-year-old female was rammed by a car and suffered a grade III blunt liver trauma. She was first referred to another institution where, since she was hemodinamically stable, a nonoperative management was initially attempted, in spite of the presence of abundant abdominal effusion. Due to persistent abdominal distension and fever, a percutaneous ultrasound-guided drainage of a bile collection was performed a month later. As the fistula persisted, an explorative laparoscopy was carried out showing a complex injury of the main bile ducts at the hilar plate. Two drains were placed in the hepatic hilar region with the hope of a spontaneous healing of the biliary fistula, but without any positive result. She was eventually treated by a double

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hepaticojejunostomy. In the early postoperative period, she developed several episodes of *Enterococcus Faecium* cholangitis and a moderate liver function impairment. She was finally discharged home and was in good health for the following two years, until she presented a sudden upper gastrointestinal bleeding from large esophageal varices. Biliary ducts dilatation and portal vein thrombosis were ruled out by Doppler ultrasonography and CT-scan, which showed signs of portal hypertension and liver cirrhosis. A liver biopsy was consistent with secondary biliary cirrhosis. She subsequently developed thrombocytopenia and presented several episodes of cholangitis, with blood tests revealing a marked cholestasis. The indication for LT was based on the reiterate episodes of cholangitis in the setting of an established cirrhosis complicated by variceal bleeding, thrombocytopenia and growth delay. LT was carried out in February 2005 using a whole liver allograft. The postoperative course was uneventful and she was discharged home on POD 8. Eight years after LT she is well and attending school regularly.

CASE 4

In August 2006, during a motorcycle accident, a 22-year-old male suffered a grade IV liver injury of the posterior right liver segments associated with a grade V lesion of the right kidney. He was initially referred to a peripheral hospital where a right nephrectomy and a liver packing were performed. The packing was removed on POD 3, after which the patient presented a biliary leak exteriorized by the surgical drains, complicated by sepsis and renal failure. Due to the worsening of his conditions despite a broad-spectrum antibiotic therapy he was transferred to our department on POD 11. On arrival, he presented hypotension, tachycardia, fever and anuria. He underwent an explorative laparotomy during which an abundant bile collection was washed out. The liver was oedematous, brown-coloured, and presented a deep necrosis of the right posterolateral segments, the origin of the biliary leak, which was treated by a debridement right hepatectomy. In the postoperative period, we observed a mild but continuous bleeding from the drains and a

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progressively worsening coagulopathy. Five days later he underwent a further laparotomy during which an abundant hemoperitoneum was observed and the abdomen was packed to secure hemostasis; at that moment, the liver remnant was severely swollen and cholestatic (Figure 2). As the hemorrhage was not completely controlled despite the peri-hepatic packing, this had to be repositioned three times during three subsequent operations, but could not achieve a complete hemostasis because of the underlying coagulopathy. Finally, on POD 27, the patient became hemodinamically unstable as a result of the liver failure, so we decided to perform a total hepatectomy associated with a porto-caval shunt and place him on the national list for an emergent LT. An AB0-compatible donor was available the same day, limiting the duration of the anhepatic phase to 19 hours, during which he was treated with continuous veno-venous hemodialysis and infusion of calcium gluconate and glucose. After LT, the abdominal wall closure was achieved with a multistep approach using a Gore-Tex[®] dual-mesh and the vacuum-assisted closure device (VAC[®] Therapy). The postoperative course was complicated by an oropharingeal *Rizhomucor* infection, cytomegalovirus infection, an acute rejection, biliary and urinary tract infections by *Enterococcus* and *Pseudomonas Aeruginosa*. He was discharged home 85 days after LT but, six months later, he developed a pharyngeal B-cell lymphoma, which was treated with Rituximab and an immunosuppression switch from Tacrolimus to Everolimus. One year after LT, he presented several episodes of cholangitis in the setting of bilateral intra-hepatic ischemic-type biliary lesions. We considered retransplantation unfeasible due to the previous surgical and medical history, so he underwent several percutaneous dilatations. Recurrent cholangitis was complicated by pneumonias that led to the development of bronchiectasis colonized by multi-resistant Pseudomonas Aeruginosa. The latter episode of pneumonia was complicated by an untreatable respiratory failure leading to the patient's death in December 2010, 49 months after LT.

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METHODS A systematic interrogation of the PubMed database was performed on December 1 2012 using the terms "hepatic trauma", "liver trauma" and "liver transplantation". Articles reporting recipients of a liver transplantation as a consequence of hepatic trauma were reviewed. References from each article were cross-checked to identify additional articles. Articles reporting cases of multivisceral transplantation, autotransplantation or with insufficient patients' data were excluded. According to Ringe et al. (14), a 2-stage procedure was defined as a LT procedure in which total hepatectomy is performed urgently when a liver allograft is not yet available and a temporary portocaval shunt is performed to avoid splanchnic congestion. While waiting for an allograft, the patient remains anhepatic; when the two stages are completed, the anhepatic phase is followed by the implantation of the liver allograft. Cases in which the patient died before graft implantation were excluded. The data collected were patients demographics, type of injury (blunt or penetrating), Glasgow Coma Scale score, American Association for the Surgery of Trauma Liver Injury Score, indication for transplantation, timing of transplantation, number and type of previous operations, surgical technique, length of follow-up, patient and graft survival and causes of death or retransplantation. A particular effort was made to gather information about factors possibly associated with the need for LT, like portal vein or hepatic artery thrombosis or occlusion, sepsis or major hepatic resection (i.e. resection of three or more Couinaud's segments). Early LTs were defined as those performed as a direct consequence of the injury or for an ALF arising after the initial treatment. All other cases were defined as late LTs. Postoperative mortality and graft loss were defined as those occurring within 30 days after LT or during the hospital stay. Data from the literature were pooled with those of the patients in our series. An analysis was performed comparing patients transplanted with a standard versus a 2-stage procedure and according to different indications. The groups were compared by two-sided Fisher's exact test or Mann-Whitney test, as appropriate.

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RESULTS After excluding a case of auto-transplantation (15), six double reports (13, 14, 16-22) and a case for which no information about the management was provided (23), 30 patients were identified (17, 24-40) and pooled with the four patients in our series, for a total of 34 patients. Table 1 shows a synopsis of the present series. Table 2 summarizes the literature review, which has been split in two periods, 1987 – 2001 and 2002 - 2012. Median age of LT recipients was 24 years (range 4-68) and in 76% of the cases LT was performed after a blunt hepatic injury. The indication for LT was ALF and hemorrhage in 59% and 26% of patients, respectively. Concerning risk factors for acute liver failure, fourteen (41%) patients underwent a major hepatectomy during the first management of injury and 9 (26%) developed a sepsis thereafter; fifteen (44%) patients presented a thrombosis or an occlusion of the portal vein or the hepatic artery which was considered significant in determining the indication for LT. Median length of follow up was 6 months (range 1 - 156months) and in only 15 (48%) cases long-term follow up (i.e. \geq 12 months) was reported. In the whole series, postoperative patient and graft survival rate was 68% and 62%, respectively. For patients transplanted in the last decade, postoperative and long-term patient survival significantly improved to 84% and 79%, respectively. In 9 (26%) cases LT was performed as a 2-stage procedure. Overall, a 2-stage procedure was attempted in 13 patients, four of whom (31%) died before the second stage completion (i.e. graft implantation) and another four (31%) died in the early post-LT period, leading to a procedure-specific 38% survival rate. The most frequent cause of early death was sepsis. Seven patients required re-transplantation and one patient was transplanted three times (38). Death with a functioning graft and primary non function were the most frequent causes of graft loss. No significant difference between early and late LT was observed concerning the rates of postoperative patient survival (67% vs 71%, p = 1) and graft survival (59% vs 71%, p = 0.68). An analysis comparing standard versus 2-stage procedure was performed (Table 3): a 2-stage procedure was carried out most frequently in case of uncontrollable hemorrhage; no difference in patient survival was observed but patients undergoing a 2-stage procedure showed a trend towards a decreased graft survival (72% versus 33%; p = 0.057). Finally, patients were regrouped according

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to the indication for LT (Table 4). Patients transplanted for an uncontrollable hemorrhage were more likely to undergo a 2-stage procedure; in this group postoperative graft survival was 27%.

DISCUSSION

As hemodynamic stability is the main factor determining the treatment, roughly 85% of liver trauma are managed nonoperatively (41). Unstable patients requiring an emergent laparotomy usually present more severe injuries that can be managed with a combination of surgical techniques including bimanual compression, Pringle maneuver, resectional debridement, hepatic resection and liver packing (1). Along with surgical procedures, angiography with transcatheter embolization is a mainstay in liver trauma management, either as a nonoperative hemostasis technique or as an adjunct hemostasis following damage control surgery (42, 43).

The most frequent cause of death after severe hepatic trauma is an exsanguinating hemorrhage from a disrupted liver or an acute liver failure consequence of the injury itself or to the operative procedures used to achieve hemostasis. Although both of these conditions are ideally treatable by LT, only 34 cases have been reported. In 1987, Esquivel et al. reported the first case of post-traumatic LT in a patient with a complex vascular and biliary lesion 66 days after a motor vehicle accident (29). In 1988 (44), Ringe et al. described the two-stage procedure, which was used in this context to treat an injury beyond repair by an expeditious total hepatectomy, in the hope of a readily available liver donor.

Subsequent reports have described a variety of clinical situations that can be grouped in three distinct clinical scenarios (Figure 3). The emergency indication for LT is represented by a massive hemorrhage arising from an injured liver that can be controlled only with a total hepatectomy. In this case, LT is carried out as a two-stage procedure. The longest anhepatic phase mentioned in the literature lasted 66 hours (45) and there are several reports in which an anhepatic period lasting more than 30 hours was tolerated (25, 27). However, it must be noted that survival rate of patients in whom a 2-stage procedure was attempted was 38% and that a reduced postoperative graft survival and a trend towards an increased postoperative mortality were observed in patients reaching the second step. In the second scenario the urgent indication for LT is ALF. As the clinical

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picture deteriorates quickly, clinicians have the choice to list the patient for an urgent LT with the standard technique, or to opt for a two-stage procedure with the aim of improving the hemodynamic state through immediate removal of a toxic liver. As the efficacy of such a strategy is not clear (28), the choice to perform a two-stage procedure in this situation should be carefully evaluated on a case-by-case basis. Finally, the third setting refers to the patients with late post-traumatic sequelae, mostly complex vascular and biliary injuries that are not amenable to a surgical repair or lead to a secondary biliary cirrhosis, in which LT is carried out electively (30).

Although LT was frequently performed in desperate situations, early patient and graft survival rate was 68% and 62%, respectively, increasing to 84% in the last decade. This improvement can be explained by the fact that in comparison with the 1987 – 2001 period, in the last decade the indication for LT was less frequently an uncontrollable hemorrhage and consequently a 2-stage technique was more rarely used. As performing a total hepatectomy to fix an otherwise uncontrollable hemorrhage clearly represents an extreme clinical situation, it is not surprising that a trend towards a reduced postoperative patient and graft survival was observed in this setting (Table 4 and 5).

Our experience reflects the heterogeneity of the scenarios depicted above: patients reported in case 1 and 2 were transplanted for an ALF presenting after a major hepatic resection and favored in one case by sepsis and in the other by an underlying liver disease; case 3 is an example of LT carried out for the late consequences of a traumatic injury to the biliary ducts and of the repair procedure; in case 4 ALF was complicated by reiterate hemorrhage and hemodynamic instability, leading to the need for a 2-stage procedure.

Our results highlight some common features associated with the progression towards hepatic failure and the need for LT.

In the whole series, a major hepatic resection was performed prior to LT in 41% of the cases. Our patients who finally required LT for an ALF had undergone a major hepatic resection, one as the first treatment and two during a subsequent laparotomy. There is no doubt that there are situations

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in which performing a formal hepatic resection is unavoidable and this can yield good results in centers where an experienced hepatobiliary surgeon is readily available (23). Nevertheless, in the trauma setting, performing a major hepatic resection is associated with an increased mortality and morbidity (46, 47), and several Authors claim that it should be avoided as much as possible. For example, it could be argued that a liver packing followed by angiography would have probably been a more sound approach for our patient in case 1. Based on our results, it could be suggested that also in the "second look" operations viable liver parenchyma should be preserved as much as possible, because the hepatic functional reserve could be reduced as a result of hypovolemic shock, sepsis and previously unknown hepatic disease.

Another frequent finding in patients requiring LT for ALF was the presence of a portal vein or hepatic artery thrombosis, which was observed in 26% and 35% of the patients, respectively (Table 2). It is well known that an abrupt interruption of the hepatic arterial inflow can favor the progression towards irreversible ALF, even in a non-traumatic setting (48), and this should be taken into account in case of angiographic embolization, if the arterial supply to large portions of hepatic parenchyma is interrupted (42). Concerning portal vein thrombosis, this can be either one of the factors precipitating ALF, or one of its effects. Portal vein thrombosis can result from the vessel injury itself or from the surgical maneuvers to achieve hemostasis, or be favored by the procoagulating state which results from the activation of the inflammatory pathways after trauma. Alternatively, it can be caused by sinusoidal congestion that has been observed after major hepatic resection in association with liver failure (49) as it was probably the case for our patient in case 3. Finally, sepsis was documented in 26% of the cases. The presence of an inflammatory response in patients with ALF is a negative prognostic factor and, when it is associated with sepsis, the progression towards encephalopathy is more probable (50). The presence of a bile leak clearly represents a predisposing factor for an abdominal sepsis and ALF, as it has been observed after elective hepatic resections (51) and in the trauma setting (37).

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The analysis of the factors linked to the progression towards ALF stresses once more the mainstay importance of the first surgical management and of a timely referral to a center where a whole surgical expertise and all therapeutic means, including LT, are available. Every effort should be made not to get to a desperate situation in which LT remains the only possible therapeutic mean. In conclusion, despite the widespread ongoing problem of organ shortage, the indication for LT after hepatic trauma has to be considered sustainable, in the light of both the current good early survival (utilitarian approach) and the virtual 100% mortality of these patients without LT (survival benefit approach). Three different scenarios characterized by different degrees of urgency and surgical strategy are possible. As a trend towards a reduced patient and graft survival has been observed in patients transplanted for an uncontrollable hemorrhage undergoing a 2-stage procedure, the indication for LT in this setting should be carefully evaluated. Sepsis, hepatic vessels thrombosis and major hepatic resections may favor the progression towards liver failure. Early referral to a specialized center should aim primarily at avoiding the need for LT and the consequent possible complications and secondarily at allowing LT to be performed in a timely fashion when it remains the only therapeutic option.

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References

- Kozar RA, Feliciano DV, Moore EE, Moore FA, Cocanour CS, West MA, Davis JW, McIntyre RC, Jr. Western Trauma Association/critical decisions in trauma: operative management of adult blunt hepatic trauma. J Trauma 2011;71:1-5
- 2. Boone DC, Federle M, Billiar TR, Udekwu AO, Peitzman AB. Evolution of management of major hepatic trauma: identification of patterns of injury. J Trauma 1995;39:344-50
- Brasel KJ, DeLisle CM, Olson CJ, Borgstrom DC. Trends in the management of hepatic injury. Am J Surg 1997;174:674-7
- 4. Feliciano DV, Mattox KL, Jordan GL, Jr. Intra-abdominal packing for control of hepatic hemorrhage: a reappraisal. J Trauma 1981;21:285-90
- Franklin GA, Casos SR. Current advances in the surgical approach to abdominal trauma. Injury 2006;37:1143-56
- 6. Meredith JW, Young JS, Bowling J, Roboussin D. Nonoperative management of blunt hepatic trauma: the exception or the rule? J Trauma 1994;36:529-34; discussion 534-5
- Croce MA, Fabian TC, Menke PG, Waddle-Smith L, Minard G, Kudsk KA, Patton JH, Jr., Schurr MJ, Pritchard FE. Nonoperative management of blunt hepatic trauma is the treatment of choice for hemodynamically stable patients. Results of a prospective trial. Ann Surg 1995;221:744-53; discussion 753-5
- Pachter HL, Hofstetter SR. The current status of nonoperative management of adult blunt hepatic injuries. Am J Surg 1995;169:442-54
- Pachter HL, Knudson MM, Esrig B, Ross S, Hoyt D, Cogbill T, Sherman H, Scalea T, Harrison P, Shackford S, et al. Status of nonoperative management of blunt hepatic injuries in 1995: a multicenter experience with 404 patients. J Trauma 1996;40:31-8

Clinical Transplantation

1		
2 3	10.	Moore EE, Shackford SR, Pachter HL, McAninch JW, Browner BD, Champion HR, Flint
4		
5 6		LM, Gennarelli TA, Malangoni MA, Ramenofsky ML, et al. Organ injury scaling: spleen,
7		liver, and kidney. J Trauma 1989;29:1664-6
8 9	1.1	
10	11.	Asensio JA, Petrone P, Garcia-Nunez L, Kimbrell B, Kuncir E. Multidisciplinary approach
11		for the management of complex hepatic injuries AAST-OIS grades IV-V: a prospective
13 14		study, Seend I Surg 2007:06:214-20
14		study. Scand J Sulg 2007,90.214-20
16 17	12.	Chen RJ, Fang JF, Lin BC, Hsu YP, Kao JL, Chen MF. Factors determining operative
18		mortality of grade V blunt henatic trauma I Trauma 2000:49:886-91
19 20		inoranty of grade v blant nepatie tradina. 5 Tradina 2000, 19:000 91
21	13.	Chen RJ, Fang JF, Lin BC, Wang YD, Chen MF. Factors that influence the operative
22 23		mortality after blunt hepatic injuries. Eur J Surg 1995:161:811-7
24		
25 26	14.	Ringe B, Lubbe N, Kuse E, Frei U, Pichlmayr R. Total hepatectomy and liver
27		transplantation as two-stage procedure Ann Surg 1993.218.3-9
28		numphanianton as two stage procedure. This stag 1990,210.5 9
29 30	15.	Boggi U, Vistoli F, Del Chiaro M, Signori S, Sgambelluri F, Roncella M, Filipponi F,
31		Mosca F. Extracorporeal repair and liver autotransplantation after total avulsion of henatic
32 33		wosed 1. Extracorporeal repair and river automatisplantation after total availation of hepatie
34		veins and retrohepatic inferior vena cava injury secondary to blunt abdominal trauma. J
35 36		Trauma 2006:60:405-6
37		Trauma 2000,00.403-0
38 39	16.	Angstadt J, Jarrell B, Moritz M, Munoz S, Maddrey W, Carabasi A, Yang SL, Radomski J,
40		Buggiere B. Confirmed B. et al. Surgical management of source liver traumer a rale for liver
41 42		Ruggiero K, Gastmend K, et al. Surgical management of severe fiver trauma. a fore for fiver
43		transplantation. J Trauma 1989;29:606-8
44	17	
45	17.	Delis SG, Bakoyiannis A, Selvaggi G, Weppler D, Levi D, Tzakis AG. Liver transplantation
47		for severe hepatic trauma: experience from a single center. World J Gastroenterol
48 49		
50		2009;15:1641-4
51 52	18.	Demirbas A, Fragulidis GP, Karatzas T, Tsaroucha A, Ginzberg E, Weppler D, Nery JR,
53 54		Trakis AG. Pole of liver transplantation in the management of liver trauma. Transplant Proc
55		Tzakis AO. Role of fiver transplantation in the management of fiver trauma. Transplant froe
56 57		1997;29:2848
58		
59 60		17
00		17

- Kodakat SK, Ginsburg R, Gopal PB, Rela M. A case of post-reperfusion syndrome following surgery for liver trauma. Br J Anaesth 2006;96:31-5
 - 20. Lin PJ, Jeng LB, Chen RJ, Kao CL, Chu JL, Chang CH. Femoro-arterial bypass using Gott shunt in liver transplantation following severe hepatic trauma. Int Surg 1993;78:295-7
 - 21. Ringe B, Pichlmayr R, Ziegler H, Grosse H, Kuse E, Oldhafer K, Bornscheuer A, Gubernatis G. Management of severe hepatic trauma by two-stage total hepatectomy and subsequent liver transplantation. Surgery 1991;109:792-5
 - 22. Veroux M, Cillo U, Brolese A, Veroux P, Madia C, Fiamingo P, Zanus G, Buffone A, Gringeri E, D'Amico DF. Blunt liver injury: from non-operative management to liver transplantation. Injury 2003;34:181-6
 - Polanco P, Leon S, Pineda J, Puyana JC, Ochoa JB, Alarcon L, Harbrecht BG, Geller D, Peitzman AB. Hepatic resection in the management of complex injury to the liver. J Trauma 2008;65:1264-9; discussion 1269-70
 - 24. Anderson IB, Kortbeek JB, Al-Saghier M, Kneteman NM, Bigam DL. Liver transplantation in severe hepatic trauma after hepatic artery embolization. J Trauma 2005;58:848-51
 - 25. Angstadt J, Jarrell B, Carabasi A, Yang SL, Moritz M, Radomski J, Munoz S, Maddrey W, Ruggiero R, Gastfriend R, et al. Liver transplantation following severe liver trauma. Transplantation 1988;46:321-2
 - 26. Catalano G, De Simone P, Montin U, Coletti L, Tincani G, Urbani L, Biancofiore G,
 Filipponi F. Severe liver trauma: the transplant surgeon's perspective. A case report.
 Hepatogastroenterology 2008;55:1458-9
 - 27. Chiumello D, Gatti S, Caspani L, Savioli M, Fassati R, Gattinoni L. A blunt complex abdominal trauma: total hepatectomy and liver transplantation. Intensive Care Med 2002;28:89-91

Clinical Transplantation

28.	Dominguez Fernandez E, Lange K, Lange R, Eigler FW. Relevance of two-stage total
	hepatectomy and liver transplantation in acute liver failure and severe liver trauma. Transpl
	Int 2001;14:184-90
29.	Esquivel CO, Bernardos A, Makowka L, Iwatsuki S, Gordon RD, Starzl TE. Liver
	replacement after massive hepatic trauma. J Trauma 1987;27:800-2
30.	Ginzburg E, Shatz D, Lynn M, Pombo H, Diaz M, Martin L, Livingstone A, Khan MF, Nery
	J, Tzakis A. The role of liver transplantation in the subacute trauma patients. Am Surg
	1998;64:363-4
31.	Hatipoglu S, Bulbuloglu E, Ates M, Kayaalp C, Yilmaz S. Liver Transplantation following
	Blunt Liver Trauma. Transplant Proc 2012;44:1720-1
32.	Heuer M, Kaiser GM, Lendemans S, Vernadakis S, Treckmann JW, Paul A. Transplantation
	after blunt trauma to the liver: a valuable option or just a "waste of organs"? Eur J Med Res
	2010;15:169-73
33.	Honore C, Deroover A, Gilson N, Detry O. Liver transplantation for hepatic trauma:
	Discussion about a case and its management. J Emerg Trauma Shock 2011;4:137-9
34.	Jeng LB, Hsu CH, Wang CS, Chen RJ, Chen SC, Chen MF. Emergent liver transplantation
	to salvage a hepatic avulsion injury with a disrupted suprahepatic vena cava. Arch Surg
	1993;128:1075-7
35.	Ringe B, Pichlmayr R. Total hepatectomy and liver transplantation: a life-saving procedure
	in patients with severe hepatic trauma. Br J Surg 1995;82:837-9
36.	Schnitzbauer AA, Tsui TY, Kirchner G, Scherer MN, Bein T, Schlitt HJ, Obed A. Liver
	transplantation for sclerosing cholangitis in a polytraumatized patient. Nat Clin Pract
	Gastroenterol Hepatol 2009;6:121-6
37.	Sherlock DJ, Bismuth H. Secondary surgery for liver trauma. Br J Surg 1991;78:1313-7
38.	Tucker ON, Marriott P, Rela M, Heaton N. Emergency liver transplantation following
	severe liver trauma. Liver Transpl 2008;14:1204-10
	19

- Veroux M, Madia C, Cillo U, Brolese A, Zanus G, Fiamingo P, Veroux P, D'Amico DF.
 Long-term follow-up after liver transplantation for blunt hepatic trauma. Transplant Proc 2002;34:1226-8
- 40. Plackett TP, Barmparas G, Inaba K, Demetriades D. Transplantation for severe hepatic trauma. J Trauma 2011;71:1880-4
- Kozar RA, Moore FA, Moore EE, West M, Cocanour CS, Davis J, Biffl WL, McIntyre RC, Jr. Western Trauma Association critical decisions in trauma: nonoperative management of adult blunt hepatic trauma. J Trauma 2009;67:1144-8; discussion 1148-9
- 42. Dabbs DN, Stein DM, Scalea TM. Major hepatic necrosis: a common complication after angioembolization for treatment of high-grade liver injuries. J Trauma 2009;66:621-7; discussion 627-9
- Misselbeck TS, Teicher EJ, Cipolle MD, Pasquale MD, Shah KT, Dangleben DA, Badellino MM. Hepatic angioembolization in trauma patients: indications and complications. J Trauma 2009;67:769-73
- 44. Ringe B, Pichlmayr R, Lubbe N, Bornscheuer A, Kuse E. Total hepatectomy as temporary approach to acute hepatic or primary graft failure. Transplant Proc 1988;20:552-7
- 45. Hammer GB, So SK, Al-Uzri A, Conley SB, Concepcion W, Cox KL, Berquist WE, Esquivel CO. Continuous venovenous hemofiltration with dialysis in combination with total hepatectomy and portocaval shunting. Bridge to liver transplantation. Transplantation 1996;62:130-2
- 46. Malhotra AK, Fabian TC, Croce MA, Gavin TJ, Kudsk KA, Minard G, Pritchard FE. Blunt hepatic injury: a paradigm shift from operative to nonoperative management in the 1990s. Ann Surg 2000;231:804-13
- 47. Moore FA, Moore EE, Seagraves A. Nonresectional management of major hepatic trauma.An evolving concept. Am J Surg 1985;150:725-9

- 48. Sato A, Yamada T, Takase K, Matsuhashi T, Higano S, Kaneda T, Egawa S, Takeda K, Ishibashi T, Takahashi S. The fatal risk in hepatic artery embolization for hemostasis after pancreatic and hepatic surgery: importance of collateral arterial pathways. J Vasc Interv Radiol 2011;22:287-93
 - 49. Helling TS. Liver failure following partial hepatectomy. HPB (Oxford) 2006;8:165-74
 - 50. Rolando N, Wade J, Davalos M, Wendon J, Philpott-Howard J, Williams R. The systemic inflammatory response syndrome in acute liver failure. Hepatology 2000;32:734-9
 - 51. Lam CM, Lo CM, Liu CL, Fan ST. Biliary complications during liver resection. World J Surg 2001;25:1273-6

Liver Transplantation after Severe Hepatic Trauma: a Sustainable Practice.

A Single-Center Experience and Review of the Literature

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ABSTRACT

Severe hepatic trauma is a rare indication for liver transplantation (LT). We report our single-center experience of LT for hepatic trauma. Four new cases are discussed in the light of a literature review in order to depict the pathways leading from hepatic trauma to LT and to assess the outcomes of this practice. LT is generally indicated in case of uncontrollable hemorrhage, acute liver failure, or post-traumatic late sequelae. Hepatic vessels thrombosis, sepsis, major hepatic resections and a late referral are factors associated with the progression towards irreversible liver failure. Considering all reported cases, early patient and graft survival rate reaches 68% and 62%, respectively, but in the last decade postoperative results have improved to 84% patient and graft survival rate. Considering all reported cases, early patient and graft survival reached 68% and 62%, respectively, but in the last decade both have improved to 84%. LT after severe hepatic trauma is a sustainable practice considering the current good outcomes and the ineluctable death of these patients without LT. Keywords: hemorrhage, liver failure, liver transplantation, sepsis, thrombosis

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FIGURE LEGENDS:

Figure 1. (Case 1) A. Contrast-enhanced computed tomography showing severe dilatation of intrahepatic bile ducts of the liver remnant after right hepatectomy (arrow) and B. Portal vein thrombosis (arrow) and inferior vena cava dilatation (arrowhead).

Figure 2. (Case 4) Contrast-enhanced computed tomography showing the severely swollen and inhomogeneous liver remnant after right hepatectomy.

Figure 3. Clinical scenarios of LT for hepatic trauma

INTRODUCTION

The liver Liver is the most frequently injured abdominal organ (1). The treatment of blunt hepatic trauma- has significantly evolved over the last three decades with the introduction and wide acceptance of the concepts of nonoperative management, damage control surgery and the use of interventional radiology (2-6). Nowadays, nonoperative management is the preferred strategy in hemodinamically stable patients (6-9) but surgery, alone or in association with interventional radiology, still plays a major role in the management of severe liver injuries (grade IV and V according to the American Association for the Surgery of Trauma Organ Injury Score) (10)), which remains extremely challenging even in experienced hands (11, 12). The main causes of death in these patients are exsanguinating hemorrhage and liver failure evolving leading to multiorgan failure (13)₂; Both these conditions that, in principle, can be treated by a timely liver transplantation (LT).

Nevertheless, severe hepatic trauma is a peculiar albeit rare indication for orthotopic LT. LT has been most frequently performed for an uncontrollable hemorrhage requiring a total hepatectomy, or for an acute liver failure (ALF) developing after the first treatment.

Although salvage LT for hepatic trauma represents a well-established practice in all major liver transplant centers, a comprehensive literature review analyzing the different scenarios in which LT becomes the last possible therapeutic option after hepatic trauma has not been carried out so far. Furthermore, the short and long-term results of this practice have not been thoroughly assessed.

In this article, we report four more cases of patients who underwent LT at our institution following a severe hepatic trauma; we focused our case reports on the initial trauma management and on how LT eventually resulted as the only viable therapeutic solution. Afterwards, based on our experience and on an accurate review of the literature, we depict the clinical scenarios in which a liver injury can eventually lead to LT and assess the outcomes of this practice. Finally, we highlight some specific factors linked to the indication for LT in these extreme situations.

CASE REPORTS

CASE 1

In June 2002_{τ} a 15-year-old female suffered a grade IV right liver injury as a consequence of a horse kick. She was first referred to another a peripheral hospital, where she underwent a right hepatectomy. Her postoperative course was complicated by progressive liver failure, portal vein and inferior vena cava thrombosis, biliary leak-related sepsis, and acute renal failure (Figure 1). She was then transferred to our institution on postoperative day (POD) 14, where a relaparotomy was performed in order to drain the bile collections and to assess the hepatic vessels permeability. At reoperation, we observed a complete portal vein and hepatic artery thrombosis, the latter due to some surgical stitches from the previous operation, and a biliary leak coming from the left bile duct, which had been completely severed. -The biliary leak was treated by draining exteriorly placing a drain into the left bile duct stump, but the portal vein thrombosis invariably recurred after two successive attempts of surgical thrombectomy. Forty-eight hours after later, as a consequence of she developed hepatic failure and coagulopathy, and she became hemodinamically unstable and developed as a result of massive abdominal hemorrhage. The Bbleeding was only partially controlled by liver packing. She was then placed on the national waiting list for an urgent liver transplantation, the indication being for- acute liver failure. Despite massive fresh frozen plasma transfusions due to ongoing bleeding, her Model for End-stage Liver Disease (MELD) score was 23. Transplantation was carried out two days later (19 days after the trauma) with resection of the retro-hepatic inferior vena cava that was occluded by a thrombus. The Ppost-transplant course was uneventful and she was discharged home on POD 18. More than 10 years after, she is alive and well, with a normal hepatic function.

CASE 2

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In March 2003, a 20-year-old female with a previous medical history significant for of Thalassemia Major suffered an abdominal trauma during from a motorway accident. She underwent an explorative laparotomy in a peripheral hospital, where a 5-cm-deep parenchymal tear involving segment 8 was treated by hepatorrhaphy. Due to ongoing persistent bleeding and respiratory failure she was transferred to our department on POD 1, where a decision for a re-laparotomy was taken after a CT-scan revealed a large hematoma of the right liver lobe, a dilatation of the bile ducts of the right liver segments, and an abundant peritoneal fluid collection. During the operation, we observed a huge hematoma of the right hepatic lobe and a large tear of the right hepatic vein. Hemostasis was achieved through a right hepatectomy. Postoperatively, the patient developed progressive liver failure, acidosis and a systemic inflammatory response syndrome. After having received the pathological report that revealed a severe hepatic iron overload and fibrosis, ironchelation with desferoxamine was started but could not reverse the deterioration of the hepatic function, which was characterized by hyperbilirubinemia, ascites and encephalopathy. She was placed on the national list for an urgent LT with a MELD score of 32 and was transplanted six days afterlater, i.e. fifteen days after the trauma. Unexpectedly, a previously unrecognized portal vein thrombosis was observed during transplantation. The postoperative course was uneventful except for a transitory early graft dysfunction. She is currently still alive and well₅ 10 years after the trauma.

CASE 3

In September 2002, a 4-year-old female was rammed by a car and suffered a grade III blunt liver trauma. She was <u>first</u> referred to another institution where, since she was hemodinamically stable, a nonoperative management was initially attempted, in spite of the presence of abundant abdominal effusion. <u>One month later, dD</u>ue to <u>the persistence persistent of abdominal</u> distension and fever, a percutaneous ultrasound-guided drainage of a bile collection was performed <u>a month later</u>. <u>As the</u>

fistula persisted, Due to the persistence of the biliary leak, an explorative laparoscopy was carried out showing a complex injury of the main bile ducts at the hilar plate. Two drains were placed in the hepatic hilar region with the hope of a spontaneous healing of the biliary fistula, but without any positive result. As the biliary leak persisted, sShe was eventually treated by a double hepaticojejunostomy. In the early postoperative period, she developed several episodes of Enterococcus Faecium cholangitis and a moderate liver function impairment. She was finally discharged home and was in good health for the following two years, until she presented a sudden upper gastrointestinal bleeding from large esophageal varices. Biliary ducts dilatation and portal vein thrombosis were ruled out by Doppler ultrasonography and CT-scan, which showed signs of portal hypertension and liver cirrhosis. A liver biopsy was consistent with secondary biliary cirrhosis. She subsequently developed thrombocytopenia and presented several episodes of cholangitis, with blood tests revealing a marked cholestasis. The indication for LT was based on the reiterate episodes of cholangitis in the setting of an established cirrhosis complicated by variceal bleeding, thrombocytopenia and growth delay. LT was carried out in February 2005 using a whole liver allograft. The postoperative course was uneventful and she was discharged home on POD 8. Eight years after LT₇ she is well and regularly attending school regularly.

CASE 4

In August 2006, during a motorcycle accident, a 22-year-old male suffered a grade IV liver injury of the posterior right liver segments associated with a grade V lesion of the right kidney. He was initially referred to a peripheral hospital where a right nephrectomy and a liver packing were performed. The packing was removed on POD 3, after which the patient presented a biliary leak exteriorized by the surgical drains, complicated by sepsis and renal failure. Due to the worsening of his conditions despite a broad-spectrum antibiotic therapy he was transferred to our department on POD 11. On arrival, he presented hypotension, tachycardia, fever and anuria. He underwent an

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explorative laparotomy during which an abundant bile collection was washed out. The liver was oedematous, brown-coloured, and presented a deep necrosis of the right posterolateral segments, the origin of the biliary leak, which was treated by a debridement right hepatectomy. In the postoperative period, we observed a mild but continuous bleeding from the drains and a progressively worsening coagulopathy. Five days later he underwent a further laparotomy during which an abundant hemoperitoneum was evacuated observed and the abdomen was packed to secure hemostasis; at that moment, the liver remnant was severely swollen and cholestatic (Figure 2). As the hemorrhage was not completely controlled despite the peri-hepatic packing, this had to be re-positioned three times during three subsequent operations, but could not achieve a complete hemostasis because of the underlying coagulopathy. Finally, on POD 27, the patient became hemodinamically unstable as a result of the liver failure, so we decided to perform a total hepatectomy associated with a porto-caval shunt and place him on the national list for an emergent LT. An AB0-compatible donor was available the same day, limiting the duration of the anhepatic phase to 19 hours, during which he was treated with continuous veno-venous hemodialysis and infusion of calcium gluconate and glucose. After LT, the abdominal wall closure was achieved with a multistep approach using a Gore-Tex[®] dual-mesh and the vacuum-assisted closure device (VAC[®] Therapy). The postoperative course was complicated by an oropharingeal *Rizhomucor* infection, cytomegalovirus infection, an acute rejection, biliary and urinary tract infections by *Enterococcus* and Pseudomonas Aeruginosa. He was discharged home 85 days after LT but, six months later, he developed a pharyngeal B-cell lymphoma, which was treated with Rituximab and an immunosuppression switch from Tacrolimus to Everolimus. One year after LT, he presented several episodes of cholangitis in the setting of bilateral intra-hepatic ischemic-type biliary lesions. We considered retransplantation unfeasible due to the previous surgical and medical history, so he underwent several percutaneous dilatations. Recurrent cholangitis was complicated by pneumonias that led to the development of bronchiectasis colonized by multi-resistant Pseudomonas

Aeruginosa. The <u>last-latter</u> episode of pneumonia was complicated by an untreatable respiratory failure leading to the patient's death in December 2010, 49 months after LT.

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METHODS A systematic interrogation of the PubMed database was performed on December 1, 2012, using the terms "hepatic trauma", "liver trauma" and "liver transplantation". Articles reporting recipients of a liver transplantation as a consequence of hepatic trauma were reviewed. References from each article were cross-checked to identify additional articles. Articles reporting cases of multivisceral transplantation, autotransplantation or with insufficient patients' data were excluded. According to Ringe et al. (14), a 2-stage procedure was defined as a LT procedure in which total hepatectomy is performed urgently when a liver allograft is not yet available and a temporary porto-caval shunt is performed to avoid splanchnic congestion. While waiting for an allograft, the patient remains anhepatic; when the two stages are completed, the anhepatic phase is followed by the implantation of the liver allograft. Cases in which the patient died before graft implantation were excluded. The data collected data-were patients demographics, type of injury (blunt or penetrating), Glasgow Coma Scale score, American Association for the Surgery of Trauma Liver Injury Score, indication for transplantation, timing of transplantation, number and type of previous operations, surgical technique, length of follow-up, patient and graft survival, and causes of death or re-transplantation. A particular effort was made to gather informations about factors possibly associated with the need for LT, like portal vein or hepatic artery thrombosis or occlusion, sepsis, or major hepatic resection (i.e. resection of three or more Couinaud's segments). Early LTs were defined as those performed as a direct consequence of the injury or for an ALF arising after the initial treatment. All other cases were defined as late LTs. Postoperative mortality and graft loss were defined as those occurring within 30 days after LT or during the same-hospital stay. Data from the literature were pooled with those of the patients in our series. An analysis was performed comparing patients transplanted with a standard versus a 2-stage procedure and according to different indications. The Ggroups were compared by two-sided Fisher's exact test or Mann-Whitney test, as appropriate.

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RESULTS After excluding a case of auto-transplantation (15), six double reports (13, 14, 16-22) and a case for which no information about the management was provided (23), 30 patients were identified (17, 24-40) and pooled with the four patients in our series, for a total of 34 patients. Table 1 shows a synopsis of the present series. Table 2 summarizes the literature review, which has been split in two periods, 1987 – 2001 and 2002 - 2012. Median age of LT recipients was 24 years (range 4-68) and in 76% of the cases LT was performed after a blunt hepatic injury. The indication for LT was ALF and hemorrhage in 59% and 26% of patients, respectively. Concerning risk factors for acute liver failure, fourteen (41%) patients underwent a major hepatectomy during the first management of injury and 9 (26%) developed a sepsis thereafter; fifteen (44%) patients presented a thrombosis or an occlusion of the portal vein or the hepatic artery which was considered significant in determining the indication for LT. Median length of follow up was 6 months (range 1 - 156months) and in only 15 (48%) cases long-term follow up (i.e. \geq 12 months) was reported. In the whole series, postoperative patient and graft survival rate was 68% and 62%, respectively. ForIn patients transplanted in the last decade, postoperative and long-term patient survival significantly improved to 84% and 79%, respectively. In 9 (26%) cases LT was performed as a 2-stage procedure. Overall, a 2-stage procedure was attempted in 13 patients, four of whom (31%) died before the second stage completion (i.e. graft implantation) and another four (31%) died in the early post-LT period, leading to a procedure-specific 38% survival rate. The most frequent cause of early death was sepsis. Seven patients required re-transplantation and one patient was transplanted three times (38). Death with a functioning graft and primary non function were the most frequent causes of graft loss. No significant difference between early and late LT was observed concerning the rates of postoperative patient survival (67% vs 71%, p = 1) and graft survival (59% vs 71%, p = 0.68). An analysis comparing standard versus 2-stage procedure was performed (Table 3): a 2-stage procedure was carried out most frequently in case of uncontrollable hemorrhage; no difference in patient survival was observed but patients undergoing a 2-stage procedure showed a trend towards a decreased graft survival (72% versus 33%; p = 0.057). Finally, patients were regrouped according

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to the indication for LT (Table 4). Patients transplanted for an uncontrollable hemorrhage were more likely to undergo a 2-stage procedure; in this group postoperative graft survival was 27%.

DISCUSSION

As hemodynamic stability is the main factor determining the treatment, roughly 85% of liver trauma are managed nonoperatively (41). Unstable patients requiring an emergent laparotomy usually present more severe injuries, which that can be managed with a combination of surgical techniques including bimanual compression, Pringle maneuver, resectional debridement, hepatic resection and liver packing (1). Along with surgical procedures, angiography with transcatheter embolization is a mainstay in liver trauma management, either as a nonoperative hemostasis technique; or as an adjunct hemostasis following damage control surgery (42, 43).

The most frequent cause of death after severe hepatic trauma is an exsanguinating hemorrhage from a disrupted liver or an acute liver failure <u>consequent to</u><u>consequence of</u> the injury itself or to the operative procedures used to achieve hemostasis. Although both of these conditions are ideally treatable by LT, only 34 cases have been reported. In 1987, Esquivel et al. reported the first case of post-traumatic LT in a patient with a complex vascular and biliary lesion 66 days after a motor vehicle accident (29). In 1988 (44), Ringe et al. described the two-stage procedure, which was used in this context to treat an injury beyond repair by an expeditious total hepatectomy, in the hope of a readily available liver donor.

Subsequent reports have described a variety of clinical situations that can be grouped in three distinct clinical scenarios (Figure 3). The emergency indication for LT is represented by a massive hemorrhage arising from an injured liver that can be controlled only with a total hepatectomy. In this case, LT is carried out as a two-stage procedure. The longest anhepatic phase mentioned in the literature lasted 66 hours (45) and there are several reports in which an anhepatic period lasting more than 30 hours was tolerated (25, 27). <u>However, Fi</u>t must be noted, <u>however</u>, that survival rate of patients in whom a 2-stage procedure was attempted was 38% and <u>that</u>, <u>in patients reaching the second step</u>, a reduced postoperative graft survival and a trend toward<u>s</u> an increased postoperative mortality were observed in patients reaching the second step. In the second scenario the urgent

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indication for LT is ALF. As the clinical picture deteriorates quickly, clinicians have the choice to list the patient for an urgent LT with the standard technique, or to opt for a two-stage procedure with the aim of improving the hemodynamic state through immediate removal of a toxic liver. As the efficacy of such a strategy is not clear (28), the choice to perform a two-stage procedure in this situation should be carefully evaluated on a case-by-case basis. Finally, the third setting refers to the patients with late post-traumatic sequelae, mostly complex vascular and biliary injuries that are not amenable to a surgical repair or lead to a secondary biliary cirrhosis, in which LT is carried out electively (30).

Although LT was frequently performed in desperate situations, early patient and graft survival rate was 68% and 62%, respectively, increasing to 84% in the last decade. This improvement can be explained by the fact that <u>, compared toin comparison with</u> the 1987 – 2001 period, in the last decade the indication for LT was less frequently an uncontrollable hemorrhage and; consequently; a 2-stage technique was more rarely used. As performing a total hepatectomy to fix an otherwise uncontrollable hemorrhage clearly represents an extreme clinical situation, it is not surprising that a trend towards a reduced postoperative patient and graft survival was observed in this setting (Table 4 and 5).

Our experience reflects the heterogeneity of the scenarios depicted above: patients reported in case 1 and 2 were transplanted for an ALF presenting after a major hepatic resection and favored in one case by sepsis and in the other by an underlying liver disease; case 3 is an example of LT carried out for the late consequences of a traumatic injury to the biliary ducts and of the repair procedure; in case 4 ALF was complicated by reiterate hemorrhage and hemodynamic instability, leading to the need for a 2-stage procedure.

Our results highlight some common features associated with the progression towards hepatic failure and the need for LT.

In the whole series, a major hepatic resection was performed prior to LT in 41% of the cases. Our patients who finally required LT for an ALF had undergone a major hepatic resection, one as the

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first treatment and two during a subsequent laparotomy. There is no doubt that there are situations in which performing a formal hepatic resection is unavoidable and this can yield good results in centers where an experienced hepatobiliary surgeon is readily available (23). Nevertheless, in the trauma setting, performing a major hepatic resection is associated with an increased mortality and morbidity (46, 47), and several Authors claim that it should be avoided as much as possible. For example, it could be argued that a liver packing followed by angiography would have probably been a more sound approach for our patient in case 1. Based on our results, it could be suggested that also in the "second look" operations viable liver parenchyma should be preserved as much as possible, because the hepatic functional reserve could be reduced as a result of hypovolemic shock, sepsis and previously unknown hepatic disease.

Another frequent finding in patients requiring LT for ALF was the presence of a portal vein or hepatic artery thrombosis, which was observed in 26% and 35% of the patients, respectively (Table 2). It is well known that an abrupt interruption of the hepatic arterial inflow can favor the progression towards irreversible ALF, even in a non-traumatic setting (48), and this should be taken into account in case of angiographic embolization, if the arterial supply to large portions of hepatic parenchyma is interrupted (42). Concerning portal vein thrombosis, this can be either one of the factors precipitating ALF, or one of its effects. Portal vein thrombosis can result from the vessel injury itself or from the surgical maneuvers to achieve hemostasis, or be favored by the procoagulating state which results from the activation of the inflammatory pathways after trauma. Alternatively, it can be caused by sinusoidal congestion that has been observed after major hepatic resection in association with liver failure $(49)_{\overline{2}}$ as it was probably the case for our patient in case 3. Finally, sepsis was documented in 26% of the cases. The presence of an inflammatory response in patients with ALF is a negative prognostic factor and, when it is associated with sepsis, the progression towards encephalopathy is more probable (50). The presence of a bile leak clearly represents a predisposing factor for an abdominal sepsis and ALF, as it has been observed after elective hepatic resections (51) and in the trauma setting (37).

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(46, 47) The analysis of the factors linked to the progression towards ALF stresses once more the mainstay importance of the first surgical management and of a timely referral to a center where a whole surgical expertise and all therapeutic means, including LT, are available. Every effort should be made not to get <u>in-to</u> a desperate situation in which LT remains the only possible therapeutic mean.

In conclusion, despite the widespread ongoing problem of organ shortage, the indication for LT after hepatic trauma has to be considered sustainable, in the light of both the current good early survival (utilitarian approach) and the virtual 100% mortality of these patients without LT (survival benefit approach). Three different scenarios characterized by different degrees of urgency and surgical strategy are possible, characterized by different degrees of urgency and surgical strategy. As a trend towards a reduced patient and graft survival has been observed in patients transplanted for an uncontrollable hemorrhage undergoing a 2-stage procedure, the indication for LT in this setting should be carefully evaluated. Sepsis, hepatic vessels thrombosis and major hepatic resections may favor the progression towards liver failure. Early referral to a specialized center should aim primarily at avoiding the need for LT and the consequent possible complications; and secondarily at allowing LT to be performed in a timely fashion when it remains the only therapeutic option.

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References

- Kozar RA, Feliciano DV, Moore EE, Moore FA, Cocanour CS, West MA, Davis JW, McIntyre RC, Jr. Western Trauma Association/critical decisions in trauma: operative management of adult blunt hepatic trauma. J Trauma 2011;71:1-5
- 2. Boone DC, Federle M, Billiar TR, Udekwu AO, Peitzman AB. Evolution of management of major hepatic trauma: identification of patterns of injury. J Trauma 1995;39:344-50
- Brasel KJ, DeLisle CM, Olson CJ, Borgstrom DC. Trends in the management of hepatic injury. Am J Surg 1997;174:674-7
- 4. Feliciano DV, Mattox KL, Jordan GL, Jr. Intra-abdominal packing for control of hepatic hemorrhage: a reappraisal. J Trauma 1981;21:285-90
- Franklin GA, Casos SR. Current advances in the surgical approach to abdominal trauma. Injury 2006;37:1143-56
- 6. Meredith JW, Young JS, Bowling J, Roboussin D. Nonoperative management of blunt hepatic trauma: the exception or the rule? J Trauma 1994;36:529-34; discussion 534-5
- Croce MA, Fabian TC, Menke PG, Waddle-Smith L, Minard G, Kudsk KA, Patton JH, Jr., Schurr MJ, Pritchard FE. Nonoperative management of blunt hepatic trauma is the treatment of choice for hemodynamically stable patients. Results of a prospective trial. Ann Surg 1995;221:744-53; discussion 753-5
- Pachter HL, Hofstetter SR. The current status of nonoperative management of adult blunt hepatic injuries. Am J Surg 1995;169:442-54
- Pachter HL, Knudson MM, Esrig B, Ross S, Hoyt D, Cogbill T, Sherman H, Scalea T, Harrison P, Shackford S, et al. Status of nonoperative management of blunt hepatic injuries in 1995: a multicenter experience with 404 patients. J Trauma 1996;40:31-8

Clinical Transplantation

1		
2 3	10.	Moore EE, Shackford SR, Pachter HL, McAninch JW, Browner BD, Champion HR, Flint
4 5		LM Gennarelli TA Malangoni MA Ramenofsky ML et al Organ injury scaling: spleen
6		Livi, Semiarem 177, Malangom M77, Ramenorsky WL, et al. Organ injury seating. spreen,
7 8		liver, and kidney. J Trauma 1989;29:1664-6
9	11	Asensio IA Petrone P. Garcia-Nunez I. Kimbrell B. Kuncir F. Multidisciplinary approach
10		
12		for the management of complex hepatic injuries AAST-OIS grades IV-V: a prospective
13 14		study. Scand J Surg 2007:96:214-20
15		
16 17	12.	Chen RJ, Fang JF, Lin BC, Hsu YP, Kao JL, Chen MF. Factors determining operative
18		mortality of grade V blunt hepatic trauma. J Trauma 2000:49:886-91
19 20		
21	13.	Chen RJ, Fang JF, Lin BC, Wang YD, Chen MF. Factors that influence the operative
22 23		mortality after blunt hepatic injuries. Eur J Surg 1995;161:811-7
24		
25 26	14.	Ringe B, Lubbe N, Kuse E, Frei U, Pichlmayr R. Total hepatectomy and liver
27		transplantation as two-stage procedure. Ann Surg 1993;218:3-9
28 29		
30	15.	Boggi U, Vistoli F, Del Chiaro M, Signori S, Sgambelluri F, Roncella M, Filipponi F,
31 32		Mosca F. Extracorporeal repair and liver autotransplantation after total avulsion of hepatic
33		
34 35		veins and retrohepatic inferior vena cava injury secondary to blunt abdominal trauma. J
36		Trauma 2006;60:405-6
37 38		
39	16.	Angstadt J, Jarrell B, Moritz M, Munoz S, Maddrey W, Carabasi A, Yang SL, Radomski J,
40 41		Ruggiero R, Gastfriend R, et al. Surgical management of severe liver trauma: a role for liver
42		
43 44		transplantation. J Trauma 1989;29:606-8
45	17.	Delis SG, Bakoyiannis A, Selvaggi G, Weppler D, Levi D, Tzakis AG. Liver transplantation
46 47		
48		for severe hepatic trauma: experience from a single center. World J Gastroenterol
49 50		2009;15:1641-4
50 51		
52	18.	Demirbas A, Fragulidis GP, Karatzas T, Tsaroucha A, Ginzberg E, Weppler D, Nery JR,
53 54		Tzakis AG. Role of liver transplantation in the management of liver trauma. Transplant Proc
55 56		
ออ 57		1997;29:2848
58 50		
59		

- Kodakat SK, Ginsburg R, Gopal PB, Rela M. A case of post-reperfusion syndrome following surgery for liver trauma. Br J Anaesth 2006;96:31-5
 - 20. Lin PJ, Jeng LB, Chen RJ, Kao CL, Chu JL, Chang CH. Femoro-arterial bypass using Gott shunt in liver transplantation following severe hepatic trauma. Int Surg 1993;78:295-7
 - Ringe B, Pichlmayr R, Ziegler H, Grosse H, Kuse E, Oldhafer K, Bornscheuer A, Gubernatis G. Management of severe hepatic trauma by two-stage total hepatectomy and subsequent liver transplantation. Surgery 1991;109:792-5
- 22. Veroux M, Cillo U, Brolese A, Veroux P, Madia C, Fiamingo P, Zanus G, Buffone A, Gringeri E, D'Amico DF. Blunt liver injury: from non-operative management to liver transplantation. Injury 2003;34:181-6
- Polanco P, Leon S, Pineda J, Puyana JC, Ochoa JB, Alarcon L, Harbrecht BG, Geller D, Peitzman AB. Hepatic resection in the management of complex injury to the liver. J Trauma 2008;65:1264-9; discussion 1269-70
- 24. Anderson IB, Kortbeek JB, Al-Saghier M, Kneteman NM, Bigam DL. Liver transplantation in severe hepatic trauma after hepatic artery embolization. J Trauma 2005;58:848-51
- 25. Angstadt J, Jarrell B, Carabasi A, Yang SL, Moritz M, Radomski J, Munoz S, Maddrey W, Ruggiero R, Gastfriend R, et al. Liver transplantation following severe liver trauma. Transplantation 1988;46:321-2
- 26. Catalano G, De Simone P, Montin U, Coletti L, Tincani G, Urbani L, Biancofiore G,
 Filipponi F. Severe liver trauma: the transplant surgeon's perspective. A case report.
 Hepatogastroenterology 2008;55:1458-9
- 27. Chiumello D, Gatti S, Caspani L, Savioli M, Fassati R, Gattinoni L. A blunt complex abdominal trauma: total hepatectomy and liver transplantation. Intensive Care Med 2002;28:89-91

Clinical Transplantation

28.	Dominguez Fernandez E, Lange K, Lange R, Eigler FW. Relevance of two-stage total
	hepatectomy and liver transplantation in acute liver failure and severe liver trauma. Transpl
	Int 2001;14:184-90
29.	Esquivel CO, Bernardos A, Makowka L, Iwatsuki S, Gordon RD, Starzl TE. Liver
	replacement after massive hepatic trauma. J Trauma 1987;27:800-2
30.	Ginzburg E, Shatz D, Lynn M, Pombo H, Diaz M, Martin L, Livingstone A, Khan MF, Nery
	J, Tzakis A. The role of liver transplantation in the subacute trauma patients. Am Surg
	1998;64:363-4
31.	Hatipoglu S, Bulbuloglu E, Ates M, Kayaalp C, Yilmaz S. Liver Transplantation following
	Blunt Liver Trauma. Transplant Proc 2012;44:1720-1
32.	Heuer M, Kaiser GM, Lendemans S, Vernadakis S, Treckmann JW, Paul A. Transplantation
	after blunt trauma to the liver: a valuable option or just a "waste of organs"? Eur J Med Res
	2010;15:169-73
33.	Honore C, Deroover A, Gilson N, Detry O. Liver transplantation for hepatic trauma:
	Discussion about a case and its management. J Emerg Trauma Shock 2011;4:137-9
34.	Jeng LB, Hsu CH, Wang CS, Chen RJ, Chen SC, Chen MF. Emergent liver transplantation
	to salvage a hepatic avulsion injury with a disrupted suprahepatic vena cava. Arch Surg
	1993;128:1075-7
35.	Ringe B, Pichlmayr R. Total hepatectomy and liver transplantation: a life-saving procedure
	in patients with severe hepatic trauma. Br J Surg 1995;82:837-9
36.	Schnitzbauer AA, Tsui TY, Kirchner G, Scherer MN, Bein T, Schlitt HJ, Obed A. Liver
	transplantation for sclerosing cholangitis in a polytraumatized patient. Nat Clin Pract
	Gastroenterol Hepatol 2009;6:121-6
37.	Sherlock DJ, Bismuth H. Secondary surgery for liver trauma. Br J Surg 1991;78:1313-7
38.	Tucker ON, Marriott P, Rela M, Heaton N. Emergency liver transplantation following
	severe liver trauma. Liver Transpl 2008;14:1204-10
	20

- Veroux M, Madia C, Cillo U, Brolese A, Zanus G, Fiamingo P, Veroux P, D'Amico DF.
 Long-term follow-up after liver transplantation for blunt hepatic trauma. Transplant Proc 2002;34:1226-8
- 40. Plackett TP, Barmparas G, Inaba K, Demetriades D. Transplantation for severe hepatic trauma. J Trauma 2011;71:1880-4
- Kozar RA, Moore FA, Moore EE, West M, Cocanour CS, Davis J, Biffl WL, McIntyre RC, Jr. Western Trauma Association critical decisions in trauma: nonoperative management of adult blunt hepatic trauma. J Trauma 2009;67:1144-8; discussion 1148-9
- 42. Dabbs DN, Stein DM, Scalea TM. Major hepatic necrosis: a common complication after angioembolization for treatment of high-grade liver injuries. J Trauma 2009;66:621-7; discussion 627-9
- Misselbeck TS, Teicher EJ, Cipolle MD, Pasquale MD, Shah KT, Dangleben DA, Badellino MM. Hepatic angioembolization in trauma patients: indications and complications. J Trauma 2009;67:769-73
- 44. Ringe B, Pichlmayr R, Lubbe N, Bornscheuer A, Kuse E. Total hepatectomy as temporary approach to acute hepatic or primary graft failure. Transplant Proc 1988;20:552-7
- 45. Hammer GB, So SK, Al-Uzri A, Conley SB, Concepcion W, Cox KL, Berquist WE, Esquivel CO. Continuous venovenous hemofiltration with dialysis in combination with total hepatectomy and portocaval shunting. Bridge to liver transplantation. Transplantation 1996;62:130-2
- 46. Malhotra AK, Fabian TC, Croce MA, Gavin TJ, Kudsk KA, Minard G, Pritchard FE. Blunt hepatic injury: a paradigm shift from operative to nonoperative management in the 1990s. Ann Surg 2000;231:804-13
- 47. Moore FA, Moore EE, Seagraves A. Nonresectional management of major hepatic trauma.An evolving concept. Am J Surg 1985;150:725-9

48.	Sato A, Yamada T, Takase K, Matsuhashi T, Higano S, Kaneda T, Egawa S, Takeda K,
	Ishibashi T, Takahashi S. The fatal risk in hepatic artery embolization for hemostasis after
	pancreatic and hepatic surgery: importance of collateral arterial pathways. J Vasc Interv
	Radiol 2011;22:287-93

- 49. Helling TS. Liver failure following partial hepatectomy. HPB (Oxford) 2006;8:165-74
- 50. Rolando N, Wade J, Davalos M, Wendon J, Philpott-Howard J, Williams R. The systemic inflammatory response syndrome in acute liver failure. Hepatology 2000;32:734-9
- 51. Lam CM, Lo CM, Liu CL, Fan ST. Biliary complications during liver resection. World J Surg 2001;25:1273-6

Table 1. Synopsis of the present series

Pt	Mechanism of injury	Grade	First treatment	Complications	Secondary treatment	Evolution	Indication for LT	Interval from trauma to LT	Surgical technique	IS	Length of follow-up	Status
1	Horse kick	IV	Right hepatectomy	Biliary leak, sepsis, hepatic artery injury; portal vein	Portal vein thrombectomy, external	Acute liver failure, hemorrhage requiring	ALF	19 days	1-stage	Tac, steroids	(years) 10.5	Alive
2	Motorway accident	Ш	Hepatorrhaphy	and IVC thrombosis, ARF Hemorrhage, ARF, respiratory failure	biliary drainage Right hepatectomy	repacking Acute liver failure, portal vein thrombosis	ALF	15 days	1-stage	CyA, AZA, steroids	10	Alive
3	Motorway accident	Ш	Nonoperative management	Biliary leak, sepsis	Laparoscopic drainage, hepatico - jejunostomy	Recurrent cholangitis; secondary biliary cirrhosis	Secondary biliary cirrhosis	28 months	1-stage	Tac, steroids	8	Alive
4	Motorcycle accident	IV	Liver packing	Biliary leak, sepsis	Right hepatectomy	Acute liver failure, hemorrhage requiring renacking	ALF	27 days	2-stage	Tac, steroids	4	Dead

Abbreviations: Pt, patient; LT, liver transplantation; IS, immunosuppression; IVC, inferior vena cava; ALF, acute liver failure; ARF, acute renal failure; Tac, tacrolimus; CyA, cyclosporine A, AZA, azathioprine

	Table 2. Liver Transplantation after Hepa	atic Trauma Overall	1987 – 2001	2002 – 2012	р
1		n = 34	n = 15	n = 19	
2	Age (years)	24 (4-68)	21.5 (6 – 43)	26 (4 – 68)	ns 0.010
3	Male	17 (50%)	8 (53%)	6 (37%)	0.019
1	Female	14 (41%)	4 (27%)	13 (68%)	
5	Not specified	3 (9%)	3 (20%)	13 (00,0)	
5	AAST grade	3 (370)	3 (20/0)	Ŭ	ns
7		4 (12%)	1 (7%)	3 (16%)	
2	IV	12 (35%)	3 (20%)	9 (47%)	
	V	14 (41%)	7 (47%%)	7 (39%)	
1	VI	1 (3%)	1 (7%)	0	
10	Not specified	3 (9%)	3 (20%)	0	
1	Mechanism of injury	. ,	. ,		ns
12	Blunt	26 (76%)	10 (67%)	16 (84%)	
13	Penetrating	5 (15%)	2 (13%)	3 (16%)	
14	Not specified	3 (9%)	3 (20%)	0	
15	Indication				0.007
16	Acute Liver Failure	20 (59%)	5 (33%)	15 (79%)	
17	Hemorrhage	9 (26%)	7 (47%)	2 (11%)	
17	Biliary fistula	2 (6%)	2 (13%)	0	
18	Secondary biliary cirrhosis	2 (6%)	1 (7%)	1 (5%)	
19	Liver gangrene	1 (3%)	0	1 (5%)	
20	Timing				ns
21	Early	27 (79%)	10 (67%)	17 (89%)	
22	Late	7 (21%)	5 (33%)	2 (11%)	
23	Number of previous operation	2 (0 – 8)	2 (0 – 4)	2 (1 – 8)	ns
24	Packing	20 (59%)	8 (53%)	12 (63%)	ns
25	Major hepatic resection	14 (41%)	4 (27%)	10 (53%)	ns
20	Angiographic embolization	6 (18%)	2 (13%)	4 (21%)	ns
20	Portal vein occlusion	8 (26%)	5 (33%)	3 (16%)	ns
27	Hepatic artery occlusion	12 (35%)	6 (40%)	6 (32%)	ns
28	Sepsis	9 (26%)	3 (20%)	6 (32%)	ns
29	Technique				0.025
30	1-stage	25 (74%)	8 (53%)	17 (89%)	
31	2-stage	9 (26%)	7 (47%)	2 (11%)	
32	Length of follow up (months)*	6 (1 – 156)	1 (1 – 67)	36 (1 – 156)	0.006
33	Follow up \geq 12 months*	15 (48%)	2 (17%)	13 (68%)	0.009
84	Postoperative patient survival	23 (68%)	7 (47%)	16 (84%)	0.03
25	Postoperative graft survival	21 (62%)	5 (33%)	16 (84%)	< 0.01
	Overall patient survival	22 (65%)	/ (4/%)	15 (79%)	0.07
30	Overall graft survival	17 (50%)	4 (27%)	13 (68%)	0.04
37	Re-transplantation	8 (24%)	5 (33%)	3 (16%)	ns
38	Cause of death		2 (2021)	2 (4 4 9 ()	ns
39	Sepsis	5 (15%)	3 (20%)	2 (11%)	
40	Pneumonia	2 (6%)	1 (7%)	1 (5%)	
41	Bowel Ischemia	1 (3%)	1 (7%)	0	
12	CMV infection	1 (3%)	1 (7%)	0	
13	Cerebral edema	1 (3%)	0	1 (5%)	
1/	Multi-organ failure	1 (3%)	1(7%)	0	
+++	Not specified	1 (3%)	1(/%)	U	n -
C+	Cause of grait loss	0 (2004)	6 (400/)	2 (1 (0/)	115
16	Death with functioning graft	9 (26%)	ь (40%)	3 (10%)	
17	Chronic rejection	5 (15%) 1 (20/)	4 (27%)	1 (5%)	
18	Unionic rejection Hopatic artery thrombosic	⊥(3%) 1(2%)	U 1 (70/)	T (2%)	
19	nepatic aftery thrombosis	1 (3%)	1 (<i>1</i> %)		

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Data are expressed as number (prevalence) or median (range). Length of follow up was not available in three cases (*). Abbreviations: AAST, American Association for the Surgery of Trauma; CMV, cytomegalovirus. Data in the two periods are compared with Fisher's exact or Mann-Whitney test, as appropriate.

Table 3.	1-stage	versus	2-stage	procedure
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	1-stage (n = 25)	2-stage (n = 9)	р
	N (%)	N (%)	
Indication			0.036
Acute Liver Failure	17 (68%)	3 (33%)	
Hemorrhage	3 (12%)	6 (67%)	
Biliary fistula	2 (8%)	0	
Secondary biliary cirrhosis	2 (8%)	0	
Liver gangrene	1 (4%)	0	
Timing			ns
Early	19 (76%)	8 (89%)	
Late	6 (24%)	1 (11%)	
Postoperative patient survival	18 (72%)	5 (56%)	ns
Postoperative graft survival	18 (72%)	3 (33%)	0.057

Data are compared with Fisher's exact test.

vival th Fisher's exact test.

Table 4. Surgical technique and outcome according to indication for LT								
	ALF (n = 20)	Hemorrhage (n = 9)	Other (n = 5)	р*				
	N (%)	N (%)	N (%)					
Surgical technique				0.008				
1-stage	17 (85%)	3 (33%)	5 (100%)					
2-stage	3 (15%)	6 (76%)	0					
Postoperative outcome								
Patient survival	15 (75%)	4 (44%)	4 (80%)	0.27				
Graft survival	15 (75%)	2 (22%)	4 (80%)	0.019				
			ALE A	E 11				

(*) Two-sided Fisher exact test. Abbreviations: LT, Liver Transplantation; ALF, Acute Liver Failure.

2.5%) 2.75%



Figure 1. (Case 1) A. Contrast-enhanced computed tomography showing severe dilatation of intra-hepatic bile ducts of the liver remnant after right hepatectomy (arrow) and B. Portal vein thrombosis (arrow) and inferior vena cava dilatation (arrowhead). 249x111mm (150 x 150 DPI)



Figure 2. (Case 4) Contrast-enhanced computed tomography showing the severely swollen and inhomogeneous liver remnant after right hepatectomy. 166x130mm (150 x 150 DPI)



169x170mm (150 x 150 DPI)

