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Liver Transplantation Due to Abdominal Trauma

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1. Introduction

1.1 Organ shortage situation in Eurotransplant regions/Germany

An organ transplant is currently the treatment method of choice for a large number of patients with chronic or acute organ failure. However, the shortage of suitable donor organs poses a considerable problem for transplantation medicine not only in Germany (1, 2). The figure of 3,897 available postmortal donated organs in 2009 currently contrasts with the needs of approximately 12,000 patients waiting for a suitable donor organ (3). At the same time, the entries on transplant waiting lists have increased by about 45% in the last 17 years; this upward trend is expected to continue (4, 5). As a result, the shortage of suitable donor organs means that in Germany more than 1,000 patients on the transplant waiting list die every year. According to the German Organ transplant Foundation (DSO), three times as many people are waiting for a kidney transplant than the number of organs that can be procured (6-10). As a result, on average 3 people on the waiting list die every day because no suitable donor organ is available in time (11, 12).

1.2 Liver transplantation as a valuable option due to trauma

The isolated trauma of the liver are a rare event in blunt injuries of severely injured patients; yet liver injuries probably lead to a clear increase in post-trauma mortality due to the complex functioning of this organ. The immunological changes caused by blunt liver trauma are just as difficult to classify as the specific mortality. As the liver injury increases in severity, other organ systems become involved, so that total mortality results from the cumulation of all damaged organs. However, there are definitive indications leading to speculation that liver involvement superproportionally increases total mortality (13-16). The mortality rate after liver trauma documented in the literature has a wide spread and ranges between 7 and 36% (17, 18). This is differentiated between early mortality, mainly due to blood loss, and late mortality. Late mortality is frequently based on secondary complications from intensive medical treatment in connection with immunological failure after a trauma which can cause sepsis/SIRS and multi-organ failure. The actual specific significance of liver injury for the emergency of such complications in this event is to date not yet fully understood.

The liver is crucial to the post-traumatic recovery of a severely injured patient. This is where proteins are formed, which constitute among other things components for coagulation and non-specific defense. It has a decisive effect on inflammatory processes and represents the center of the energy metabolism. Moreover, the Kupffer cells represent the largest macrophage pool in humans. The knowledge that liver damage alone negatively affects both early and late mortality may be an initial approach leading to organ-specific post-traumatic treatment.

In this context, it must be kept clearly in mind that the last two decades have seen a clear paradigm change concerning surgical treatment for liver injuries (19). With the introduction of computer tomography and the availability of clotting factors, conservative treatment of the liver injury became the method of choice for hemodynamically stable patients after blunt liver trauma (20). Different studies have shown that 71-89% of all patients with blunt liver trauma can be successfully conservatively treated. As a result, the survival rate is 85 to 94% (21). There is also agreement that despite all the opportunities for intensive fluid, blood and coagulation substitution, hemodynamically unstable patients must still be operated on (22).

Here, the management of a liver injury aims to control hemorrhage, preserve sufficient hepatic function and prevent secondary complications. If an adequate control of the bleeding cannot be achieved despite exhausting the current therapy options, the indication for liver transplant (LT) needs to be assessed critically in individual cases. These cases are extremely scarce in the clinical daily routine (23).

Nonetheless, LT are carried out due to acutely uncontrollable liver injuries in exceptional cases only. For this, indication is judged critically and discussed controversially due to usually existing secondary injuries, early septic complications, and poor general condition. Due to poor results, LT in these patients is occasionally described as “waste of organs”, however based on insufficient data (24, 25).

Patients with subacute and chronic results of a liver injury need to be considered differently from the acute and due to their initial position very special group of surgically uncontrollable patients with liver trauma. However, they share the fact that also the indication for transplantation for instance in patients with “shock liver” in the context of polytrauma or with induced liver failure after a longer intensive therapy need to be measured (26, 27).

2. Investigate the significance of liver trauma and prognostic factors in severely injured patients

Based on an analysis of the trauma registry data from the German Society of Trauma Surgery (DGU) [Deutsche Gesellschaft für Unfallchirurgie] from 1993 to 2005 (n=24,711), the present study examined whether the participating liver injury in a polytraumatized patient superproportionally increases the incidence of sepsis and multi-organ failure, and whether survival after polytrauma is definitively decreased when the liver is involved.

2.1 Investigate the indication of liver transplantation for uncontrollable liver trauma

Our study was aimed to critically question the indication of LT on the basis of blunt and uncontrollable liver trauma; we therefore report our experience with 4 patients who all underwent LT due to accident-caused uncontrollable acute liver trauma at our center along with a comparison and discussion of our results based on the current literature.

2.2 Try to answer the question – Is transplantation a valuable option or just a "waste of organs" in polytraumatized patients with liver injury –

2.2.1 Find new approaches of organ donation improvement

First of all, with regard to the methodology of this work it should be pointed out that in order to respond to the self-declared question posed by this work, various databases and registers, which are listed in detail in the following, were used for analysis.

3. Prognostic factors of liver injury in polytraumatic patients

Based on an analysis of the trauma registry data from the DGU from 1993 to 2005 (n=24,711), the present analyses examined whether the participating liver injury in a polytraumatized patient superproportionally increases the incidence of sepsis and multi-organ failure, and whether survival after polytrauma is definitively decreased when the liver is involved.

It is a standardized and anonymized documentation of severely injured patients at defined phases from time point of accident to hospitals discharge (28). In this analysis the following eligibility criteria were used:

1. Injury Severity Score (ISS) ≥16
2. direct admission from scene to a trauma center
3. no isolated head injury

Injury severity score (ISS) and the severity of individual injuries were determined with the 1998 revision of the Abbreviated Injury Scale (AIS), table 1.

The existence of sepsis was defined based on the criteria of Bone et al. (29). The definition of organ failure followed the SOFA score (Sequential Organ Failure Assessment) (30). An individual organ failure was defined by at least 3 SOFA score points; a multi-organ failure (MOF) was defined as simultaneous failure of at least two organs.

All those patients with a documented liver injury (AIS abdomen <3 and AIS liver 2-5) were assigned to the "liver trauma" group. Patients with abdominal injuries (AIS abdomen 2-5 or AIS liver <3) were placed in the "abdominal non-liver injury" group. All remaining patients who had an AIS abdomen or liver <3 were placed in the third "non-abdominal trauma" group (control group). The restriction to cases with ISS ≥16 guaranteed a minimum injury severity of AIS 3 for the primary region in the respective study groups.

3.1 Statistics (I)

From 1993 until 2001, data were collected and entered on paper sheets. Since 2002, data collection was done with internet-based data entry software with integrated plausibility checks. The anonymized data were analyzed with the statistical program SPSS (Version 14, Chicago, USA). Incidences are presented with counts and percentages, continuous values with mean and standard deviation (SD). Analysis was mainly restricted to descriptive statistics. Statistical tests were avoided due to the multiple comparisons (several groups and outcome parameters), as well as the high sample size which could lead to irrelevant significances. In selected situations only, data from the group with liver trauma were compared statistically against the remaining groups (χ^2 test for incidence rates and U-test for continuous values).

AAST Grade	Injury	Injury Description	AIS-98* Grade
I	hematoma	subcapsular, <10% surface	2
	laceration	capsular tear, <1cm parenchymal depth	2
II	hematoma	subcapsular, 10–50% surface; intraparenchymal hematoma, <10cm in diameter	2
	laceration	capsular tear, 1–3cm parenchymal depth, <10cm length	2
III	hematoma	subcapsular, >50% surface; intraparenchymal hematoma, >10cm in diameter	3
	laceration	>3cm parenchymal depth	3
IV	laceration	parenchymal disruption involving 25–75% of hepatic lobe or 1–3 segments	4
V	laceration	parenchymal disruption involving >75% of hepatic lobe or >3 segments within a single lobe	5
	vascular	hepatic venous injuries	5
VI	vascular	hepatic avulsion	6

*Note–AIS-98 = Abbreviated Injury Scale, 1998 version.

Table 1. American Association for the Surgery of Trauma (AAST) -scale and modified scale for classification of liver injuries

3.2 Transplantation after blunt trauma to the liver

Our study was aimed to critically question the indication of LT on the basis of blunt and uncontrollable liver trauma; we therefore report our experience with 4 patients who all underwent LT due to accident-caused uncontrollable acute liver trauma at our center along with a comparison and discussion of our results based on the current literature.

From September 1987 to December 2008, our center performed 1,529 LT (6 traumatic and 1,523 others in 4 and 1,475 patients, respectively). Apart from transplant surgery, the clinic's second major focus is on hepatobiliary surgery. In this analysis the following eligibility criteria were used:

1. patients ≥ 18 years;
2. trauma-caused blunt liver injury;
3. uncontrollable clinically situation without transplantation.

The transplantations conformed to the local ethical guidelines and followed the ethical guidelines of the 1975 Declaration of Helsinki. LT was indicated in cases of uncontrollable liver injuries. It was considered contraindicated in cases of irreversible cerebral damage (i.e. slight cerebral edema is not considered a contraindication), absence of uncontrolled extrahepatic infection (i.e. no SIRS), absence of uncontrolled multiple organ failure (MOF) (less than 3 organs including the liver).

In order to offer the best sized organ in a timely fashion, the following surgical procedures were considered for all recipients when available: deceased donor liver transplantation (DDLT) (full size and split-left lateral, left, right, extended right) and living donor liver transplantation (LDLT) (left lateral, left, right).

The conservative management of our patients consisted of: a) causal therapy, b) intense monitoring of hemodynamic, respiratory, renal, neurological, infectious, hepatic and metabolic parameters, c) minimal handling and no sedation whenever possible, d) fluid restriction but enough fluid to assure cerebral perfusion, e) hypercaloric protein-free nutrition, f) intestinal sterilization with Neomycine and Lactulose, g) fresh frozen plasma in cases of coagulation disorder. All patients received immunosuppressive induction with Prednisolone. Maintenance immunosuppression consisted of a dual therapy with calcineurin inhibitors and Prednisolone post-transplant.

We monitored the peri-operative course of each patient and noted short-term and long-term outcomes. The end of follow-up for this study was the end of July 2009.

3.2.1 Statistics (II)

Continuous variables are expressed as mean (±SD) or median (range).

4. Prognostic factors of liver injury in polytraumatic patients

The average age was 39.6±19.5 years, and 72.8% were male. The average ISS was 31.9±12.1 points. Patients with liver trauma were found to be younger (liver 34.9±15.6; abdomen 37.7±18.2) and more frequently female (66.0% vs. 73.5%). The number of blunt traumas was only slightly less in the liver group (91.8%) than in the non-liver abdominal trauma group (93.5%). The incidence of a primary liver injury according to the criteria mentioned was rather small, with 3.1% in the total group studied (abdomen 5.5%).

4.1 Mortality

Mortality in the liver trauma group was significantly increased (34.9%) compared to patients in the abdominal trauma group (12.0%) and patients with no primary liver or abdominal injury (control group 12.0%).

Further analysis of these differences between abdominal trauma group and the control group showed that the higher mortality in the control group is explained by the high mortality of the accompanying head injuries. Thus, a subgroup analysis shows that of the 9,574 trauma patients in the control group, 2,160 patients had suffered a relevant head injury (AIS >3). In this subgroup, mortality even reached 32.8%. The investigation of early mortality showed that 27.3% of patients in the liver trauma group died within the first 24 hours, while this rate was only 6.6% in the non-liver abdominal group.

4.2 Blood transfusion

Compared to patients with non-liver abdominal injuries, patients with severe liver trauma clearly had a greater need for blood transfusions (67.0% vs. 48.0%). The high blood loss in the liver group is correlated with the blood pressure pattern in both the preclinical and emergency room (ER) phases. Initial blood pressure was ≤90mmHg preclinically in 36.4% of the liver group and 30.0% of the abdomen group. Both groups are clearly above the rate in the control group (22.0%). Blood pressure in the liver group could not be raised in any definitive way during initial clinical care (ER phase in contrast to the abdomen group (RR <90mmHg, liver: 32.2% with delta RR 4.2 mmHG; abdomen: 18.2% with delta RR: 11.2mmHG). In the ER, an initial hemoglobin content of less than 8g/dl was much more frequent in the liver group with 38.1% than in the abdomen group with 16.9% and the control group with 13.9%. Analogous to this, the average amount of transfused erythrocyte concentrate (EC) until admission to the intensive care unit was much higher in the group of patients with liver injury (8.6 units) compared to the abdomen group (4.5 units) and the control group (2.1 units).

Patients who fulfilled the criteria of a massive transfusion (number of transfused EC >10 were filtered out of the liver and abdomen groups.

Given that the average number of ECs and the average ISS in both groups of liver and abdominal trauma were almost the same (liver: 20.9 EC, ISS 39.2; abdomen 19.9 EC, ISS 38.5), the possible measured variable of an unequal EC quantity was leveled out. Thus, the high total mortality in the liver group (55.8%) compared to the abdomen group (36.5%) cannot be explained by the number of ECs. The same applies to the increased MOF (96.0% vs. 60.0%) and sepsis rate (72.0% vs. 36.0%) of the survivors.

4.3 Sepsis, organ failure

Compared to the other groups, increased early mortality in the liver group did not lead to a simultaneous reduction in late mortality. Patients with a liver injury showed - apart from the patients with head injuries – an average late mortality of 7.8%. One cause for the increased late mortality in comparison with patients with no liver injury is possibly the high sepsis rate (19.9%), if the first 24 hours were survived.

The increased sepsis rate in the liver group is also reflected in the frequency of organ failure (OF 48.6%) and multi-organ failure (MOF 33.3%). Compared to patients with abdominal injuries with no severe liver trauma, all three characteristics are significantly more fully developed (sepsis 11.0%, OF 33.2%, MOF 16.6%). Patients from the control group also showed a significantly decreased incidence for sepsis and multi-organ failure.

The frequency of a laparotomy is reduced from 71.6% (before 2001) to 60.4% (from 2001). Remarkably, mortality is reduced in the same period from 35.5 to 33.1%. The ISS is almost identical with 39.7 vs. 38.8.

4.4 Severity adjustment

Adjusting for severity with the RISC Score shows that patients with liver trauma die significantly more frequently than expected. The 33.0% mortality observed (95.0% confidence interval 27.6 – 38.4) offsets a prognostic mortality rate of only 23.4%. In the other two groups of injuries, prognosticated mortality hardly deviates at all from the observed mortality. These results could imply that the resuscitation and/or operative management was suboptimal. However, this is not true. Liver trauma is rather underestimated regarding the expected prognostically impact and shows significantly worse mortality rates than in patients without liver injuries. Therefore, severe liver injury should be judged more critically with respect to mortality than the remaining abdominal injuries, with which the RISC prognosis illustrates actual mortality very well.

4.5 Transplantation after blunt trauma to the liver

Six LT were performed in 4 patients with acute liver injury (2 patients were re-transplanted). The demographics and the clinical presentation of these patients are reported individual. There were 3 men and 1 woman, ranging in age from 36 to 50 years (mean and median, 42 years and 41 years, respectively). All patients had uncontrollable liver injuries caused by motor vehicle accidents. After a median (range) follow-up of 32.95 months (10.3-55.6), 2 out of 4 patients are still alive. Half- and 4-year patient survival rates are 50% and 25% with a corresponding graft survival of 25%, respectively.

5. “Liver transplantation due to abdominal trauma” (Discussion)

The aim of this retrospective investigation was to evaluate possible differences in the characteristics early and late mortality, sepsis and multi-organ failure as a function of the area of organ injury. Consideration of purely isolated organ injuries would not do justice to the complexity of a polytrauma, and may possibly lead to conclusions of no clinical relevance. The selection criteria “great severity of injury” of a specific organ system, with no attention paid to the average frequency and severity of additional injuries, would inaccurately illustrate the information value regarding organ-specific characteristics. It is well-known that liver injuries almost always accompany injuries to other organ systems. To consider only isolated liver injuries would lead to the description of a group that does not occur in this form in reality. The present study illustrates a patient group with a most severely injured organ system and the approach chosen was meant to investigate the impact on an organ system, in view of additional injuries, on the development of early mortality, transfusion requirement, sepsis, organ failure and late mortality.

To date, the effects of an isolated or primary liver injury on immunological function parameters has not to date been examined in either humans or animals. Only a retrospective evaluation weighted according to organ system can contribute to a more precise understanding of their significance for outcome, sepsis and MOF.

The results presented here show a clear increase in the incidence of sepsis from an MOF and early and late mortality with a severe liver injury. This increase seems to be liver-specific and stands out from the other organ systems investigated. Publications by Strong and Turnkey, which reported a mortality of over 11% of in isolated liver injuries, show a significantly lower mortality after liver trauma. However, these were not assessed in a comparably severely injured collective (31, 32). This stresses the significantly higher survival rates in patients with isolated liver injuries in comparison to poly-traumatized patients.

A review of the literature shows that the classification of more specific e.g. immunological consequences to different organ systems subsequent to polytrauma has not yet been examined. This applies both to experimental and clinical investigations and therefore the results presented here seem debatable, since they are only limited, given the low amount of literature in this regard. Despite the small amount of data, it seems beyond question that the participation of the liver in a traumatic event leads to an increase in mortality. However, there are some indirect references that characterize the liver as being a key organ after a trauma. At the beginning of the 1990s once Tinkhoff et al. had pointed out for the first time a connection between cirrhosis and outcome after trauma, this hypothesis was confirmed by numerous authors. In a matched pairs study, Dangleben et al. proved that cirrhosis of the liver is an independent prognosis marker of mortality, and with this they were able to demonstrate a correlation between mortality and the degree of the cirrhosis (definition according to Child-Turcotte-Pugh). These results were also verified by Christmas et al.: in addition to an increase in mortality and length of hospital stay, they showed a significant increase in the sepsis rate after trauma. Altogether 55% of the patients with cirrhosis of the liver in their study population died from sepsis. 33% of the patients with cirrhosis died compared to only 1% in the non-cirrhosis control group. These studies on cirrhosis of the liver and polytrauma show a close association between liver function and outcome after trauma.

In animal experiments, depending upon the quantity of the liver tissue removed, a liver resection leads to a clear restriction of synthesis efficiency, particularly for coagulation products (33). Furthermore, the clearance function for bacterial endotoxins is drastically reduced. The consequences can be expressed in a decompensated coagulation system, through to a Disseminated Intravascular Coagulation (DIC) in a spontaneous multi-organ failure after sepsis or in refractory shock to the extent that the effects of a liver resection resemble those of traumatic liver destruction (34-36).

However, traumatic liver damage is not necessarily associated with a measurable reduction in liver function. This is why, for example, Perdrizet et al. were able to demonstrate a clear increase in early mortality after reperfusion using a pig model, in which a blunt liver trauma was combined with a hemorrhagic shock. The increase in mortality resulted from continuous post-ischemic shock (37).

The significance of the liver in early trauma events was also demonstrated for example by Perl et al. after a thorax trauma in a mouse model. They showed for the first time a response to thorax trauma by Kupffer cells within 30 minutes. In so doing, the liver formed IL-6, TNF-alpha and IL-10 in high concentrations, without the liver itself being traumatized (38).

It has been proven that a tissue trauma leads to a significant reduction in immunological strength. The liver is a central organ of the reticuloendothelial system (RES) and its significance to the defense against infection has been described several times.

The results shown here from the trauma registry indicate that in the group with severe liver trauma, there is a clear increase in the number of ECs in the early and late phases after trauma. This observation after liver trauma is also supported by other research groups. Thus, for example, the number of transfused ECs constitutes an independent prognosis factor in the post-traumatic period after liver trauma. The authors argue that the blood products possibly lead to an increase in the incidence of sepsis due to their antigenicity (39). Both Moore et al. and Malone et al. showed a clear connection between the number of transfused ECs and the occurrence of post-traumatic organ failure; Malone et al. even showed this correlation within the first 24 hours after trauma (40, 41). Critical in this respect, however, it should be fair to pose the question whether and to what extent the administration of erythrocytes causes immunoparalysis, particularly since trauma patients can develop sepsis and MOF without erythrocytes being administered. Hence, it should be discussed whether the correlation between ECs and mortality must possibly be considered as only an epiphenomenon, e.g. an extended tissue ischemia period. So the number of transfused blood products is also always a marker for injury severity, incidence of shock and length of ischemia time. This cannot be obviously separated by a multivariance analysis. In order to examine this question more closely, two subgroups were formed in the present analysis. Here it shows up remarkably that despite a similar ISS and number of transfused ECs, the patients with severe liver participation continue to predominate, with regard to mortality, sepsis and MOF. In this context, immune modulating substances contribute to a considerable reduction in infectious complications. After polytrauma, proteins such as granulocyte-macrophage colony-stimulating factor (GM-CSF) and interferon gamma can contribute to an improvement in post-traumatic immunoparalysis (42, 43). Patients with immune insufficiency, e.g. also due to liver damage, could benefit from the early use of immune modulating substances.

The evaluation of the data from the trauma registry concerning liver trauma (AIS>2) and treatment before and after 2000 shows the paradigm shift starting in 2000 mentioned in the introduction. The reduction in the rate of laparotomies from 2000 to 11.2% in hospitals affiliated with the trauma registry proves a rethink in care after abdominal injury. This resulted in a reduction in mortality of 2.4% in similar patients (ISS: 39.7 vs. 39.8). In order to better support this advantage of conservative treatment, however, more detailed study is necessary given that both preclinical and clinical care have made progress in the same time period. While in former times an exploratory laparotomy was nearly always performed, now conservative therapy under hemodynamically stable conditions is increasingly being recommended (44). Therefore, the portion in an American (multicenter) study was 47%. With 404 patients, a success rate of 98.5% was reported, where hemorrhaging appeared in only 3.5% of other complications (45).

In another series of 495 conservatively treated patients, the success rate was 94% and the average hospital treatment was 13 days, where only 1.9 EC/patient had to be transfused. The complication rate was 6.2%, whereby there was only 2.8% with hemorrhages. Liver-related deaths or overlooked intestinal injuries were not observed.

Both groups predominantly involved not so serious liver traumas, whereas Moore type IV and V injuries (14%) were rather rare. In a study from Germany up to 2004, only 14% of all patients were treated conservatively. Moreover, the not so serious Type I-III injuries were operated in 2/3 of the cases (31/44), where no liver-related mortality was observed. The authors came to the conclusion that in view of the convincing data from the multicenter studies mentioned and numerous other, at times large patient groups, laparotomy is probably an overtreatment in most patients with Type I-III injuries and seems to be of no real advantage regarding survival, morbidity and duration of treatment (46). Data from this study corroborates this statement.

The matter of the urgent criteria for operating on abdominal and liver trauma is not clearly answered in the literature. The criteria are not uniform and often refer to the term "unstable". It has been shown however by Clarke et al. that mortality increases by 1% every 3 minutes after a trauma involving hematogenic shock, so the time from arrival at the ER to the laparotomy has a crucial effect on the outcome (47).

In addition to acute trauma care following abdominal injury, the therapeutic option of transplant plays a role in chronic hepatic damage rather than in acute injuries. Persistent chronic hepatic damage is mostly seen in the form of "secondary sclerosing cholangitis". The option of transplantation for acute, inoperable hepatic damage also plays an admittedly minor role, but in times of scarce organ availability this should be exercised within reason.

Therefore, treatment of liver trauma has rapidly changed over the past decades. Thus, especially development of the intensive and emergency medicine as well as coagulation substitution reveal a more and more conservative therapy approach against the severity of the injury. To date, merely 10% of the liver trauma patients are surgically treated, 90% follow a conservative therapy regimen. In the process, the overall mortality of 60% could be reduced to about 6% over the past century (48-50).

However, in a few patients with liver injuries it may still occur that they cannot be treated adequately despite exploitation of all conventional surgical measures. Continuous non-controllable acute bleeding, non-reconstructible liver injuries, like e.g. injuries of the liver's veins or the bile duct system, and a liver insufficiency caused by trauma, e.g. shock liver, allow for the consideration of LT (51, 52).

LT then remains the only available life-saving procedure for these patients. However, not all patients are suitable candidates for LT. Pre-transplant neurological status, severe sepsis, MOF, and accompanying severe injuries may all be contraindications to LT. Furthermore, there is a fundamental difference whether a patient is transplanted due to acute non-controllable liver injury or due to subacute (e.g. shock liver) respectively chronic (e.g. secondary biliary cirrhosis) liver mutation after occurred trauma. Ultimately, only a fraction of patients with uncontrollable liver trauma are deemed to be candidates for transplantation. Like those patients who die before LT, mortality after LT is usually secondary to hemodynamically instability, infections and MOF (53, 54).

The underlying severity of the injury and the occasionally life-threatening other injuries are reflected by the results in our patients who received a LT due to trauma all from a motor-vehicle accident. These patients differ fundamentally from the majority of our other liver transplant patients in the peri-operative prognosis. Based on our clinical experience, the most relevant preoperative prognostic factors negatively influencing the post-transplant outcome have been the hemodynamic, secondary injuries and the recipient age. There are diverging opinions about the role of the MELD score as a prognostic factor for the postoperative outcome in such cases.

The results following LT for uncontrollable traumatic liver injuries are substantially worse than those of LT for sub-acute/chronic and elective indications. In fact, the general patient survival rates are approximately 50-75%. Unfortunately, the few reported cases in the current literature are quite inhomogeneous, reflecting different transplant eras, clinical experience, LT techniques/procedures, and clinical conditions of the patients prior to undergoing LT. In addition these case reports mostly outline the clinical course of liver transplant patients following trauma. While accurate comparison of the clinical presentation of patients across various case reports is not always possible, we can say, based on the available data in 3 case series, that the clinical conditions of our patients appear to be similar to those reported (55-57).

Delis et al. also describe 4 patients with liver trauma in their work who were transplanted in the course of their disease. Non-uniform genesis of these patients are reflected in a range of relatively positive GCS scores. These may be explained by the fact that 3 of the above-mentioned patients had gun-shot liver injuries and hence no, as common in blunt liver injuries, large-area, complex liver injuries. Furthermore, one patient was transplanted after two years due to secondary biliary cirrhosis caused by trauma. This explains the fairly good results in this group with a patient survival rate of 75% after more than 9 years.

Altogether 3 patients with liver injuries due to car accidents, that were hepatectomized pre-operatively due to massive unsalvageable liver trauma, are described by Ringe et al. This quite more homogenous patient population is better comparable to our study and demonstrated a patient survival rate geared to our results. Thereby, Ringe postulates a bilateral approach in patients where no sufficient hemostasis after liver trauma is achievable. After an indication for total hepatectomy depending on hemodynamic parameters, a than obligatory liver transplantation is carried out as soon as possible. In his works, however, also patients are described that could not be allocated with an adequate organ in time due to the present lack of donor organs.

Also comparable with our results are those published in the 1980ies by Esquivel et al. on 2 traffic accident victims with nonreconstructable injuries to the portal vein and following nonfunctional hepatic remnants. In literature, these are the first published cases of liver transplantations after liver trauma.

The majority of our patients demonstrated one or more of negative prognostic factors. This study covers all recorded liver transplantations for otherwise uncontrollable liver trauma due to motor-vehicle accidents at our hospital. These cases often had poor general prognoses. Despite the acute condition of our patients, our results, patient survival rate is 50% with a corresponding graft survival of 25%, are among the first reports on survival rates in a homogenous series to date in the literature.

6. Conclusion

6.1 Investigate the significance of liver trauma and prognostic factors in severely injured patients

In our opinion, unstable patients should be identified by the following parameters: 1) location of the source of bleeding, i.e., free fluid in the abdomen in the initial ultrasound, if need be with an increase in the course of action; 2) volume loss, i.e., substitution is required for hemodynamic stability when systolic blood pressure falls below 80 - 90 mmHG; 3) signs of systemic hypoperfusion with negative base excess and pH and where applicable with an initial hemoglobin under 8 mg/dl with signs of consumptive coagulopathy.

Knowledge of the additional dangers documented here as they can arise from a liver injury and may possibly be positively affected by e.g. a specific coagulation treatment and an early substitution of ECs. The immunological changes to be expected from a liver injury in the meantime may possibly even reinforce the frequently described post-trauma immunosuppression.

6.2 Investigate the indication of liver transplantation for uncontrollable liver trauma

In conclusion, we largely agree with the aforementioned reports. The therapeutic option of liver transplantation also needs to be accessible for patients with liver injuries caused by trauma. However, not least due to the mentioned poor transplantation results in severely injured patients, indication for transplantation needs to be critically proposed by the attending surgeons.

6.3 Try to answer the question – Is transplantation a valuable option or just a "waste of organs" in polytraumatized patients with liver injury –

It is essential to sensibly and appropriately allocate the organs so that the shortage of donor organs is not further enlarged. In patients where no hemodynamic stabilization can be achieved despite exhaustion of all extensive care measures, transplantation should not be considered any further. Although, there is a fundamental difference regarding the timeframe after trauma during which patients are to be transplanted. It has shown, that especially patients with acute, non-controllable liver injuries as described by us have clinically changed for the worse rapidly after transplantation and have died in MOF. Therefore, we postulate that indication for transplantation in these patients may only be provided after critically reviewing every single case as not to "waste of organs".

6.4 Identifying new approaches to improving organ donation

It should be noted that the success of transplantation medicine with a simultaneously increasing shortage of donor organs will only be assured if all available resources are exploited. Increasing acceptance of "expanded criteria donor" organs appears more justified than ever under these circumstances, but also with sustained good results despite constantly deteriorating organ quality. Approaches to increase the transplant quality, not only of extended criteria donor (ECD) organs, offer further developed possibilities that support perfusion such as machine perfusion and optimized perfusion solutions. Moreover, shortened ischemic periods are achieved through further improved logistics and allocation processes, which together with individualized, medicinal immune suppression ultimately benefit the transplant and the organ recipient. In addition to this continuously improving and thus optimized use of postmortal organs, it must also be the common objective of the medical profession and politics to increase the overall number of donor organs and to improve their quality.

In order to achieve this, priority should be given to an improved exploitation of the existing organ donation potential through hospital-based advising, for example by a contact person for organ donation at each intensive care unit. Information and advising by Eurotransplant and the transplant centers for physicians, nursing staff and the population are of key importance here. Furthermore, to an ever great extent it will be the task of all parties involved in the field of transplantation to present organ donation, the allocation and transplantation of organs, and all the decisive aspects relating to the readiness of organ donation such as trust, safety and equity in a transparent manner. Conducting advisory discussions on the topic of organ donation with the relatives of the deceased is a special task for physicians. One measure should include involving a physician with special communicative expertise. It remains to be hoped that in this way a higher acceptance rate for organ donation will be more successfully achieved throughout all population groups in the future. In tapping into all resources and approaches for the optimized exploitation of donated postmortal organs, it should be possible to assure the medical care mandate of transplantation medicine in Germany in the future as well.

Based on previous studies, the recording of organ donors with "expanded criteria" in a targeted analysis is useful and necessary for new ways of improving organ donation. Further local, national and international analyses are additionally necessary to identify the limits to expanding donor acceptance criteria.

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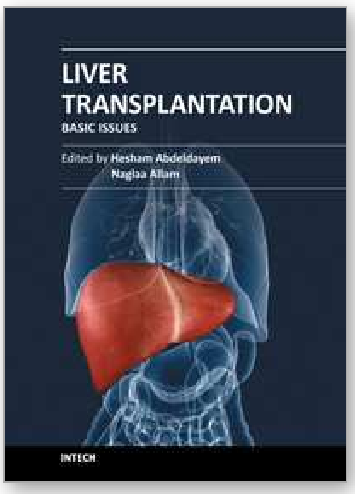

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This book covers a wide spectrum of topics including history of liver transplantation, ischemia-reperfusion injury, immunology of liver transplantation, viral hepatitis and liver transplantation, other indications for liver transplantation, prognostic factors and perioperative period. The authors of the chapters are experts in their respective fields. They are proponents covering different aspects of liver transplantation and come from many centers across the world. The interdisciplinary approach and the authority of the contributors resulted in a valuable reference to anyone interested in developing a global view in liver transplantation including medical students, residents, fellows, nurses, and practicing physicians and surgeons as well as researchers in the field of liver transplantation.