LIVER TRANSPLANTATION AFTER SEVERE HEPATIC TRAUMA: CURRENT INDICATIONS AND RESULTS

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ABSTRACT - Background: The liver is the most injured organ in abdominal trauma. Currently, the treatment in most cases is non-operative, but surgery may be necessary in severe abdominal trauma with busy critical traumatic injuries, especially those that cause uncontrollable bleeding. Despite the damage control approaches in order to achieve hemodynamic stability, many patients develop hypovolemic shock, acute liver failure, multiple organ failure and death. In this context, liver transplantation appears as the lifesaving last resource Aim: Analyze the use of liver transplantation as a treatment option for severe liver trauma. Methods: Were reviewed 14 articles in the PubMed, Medline and Lilacs databases, selected between 2008-2014 and 10 for this study. Results: Were identified 46 cases undergoing liver transplant after liver trauma; the main trauma mechanism was closed/blunt abdominal trauma in 83%, and severe trauma (≥grade IV) in 81%. The transplant can be done, in this context, performing one-stage procedure (damaged organ removed with immediate transplantation), used in 72% of cases. When the two-stage approach is performed, end-to-side temporary portacaval shunt is provided, until new organ becomes available to be transplanted. If two different periods are considered - from 1980 to 2000 and from 2000 to 2014 - the survival rate increased significantly, from 48% to 76%, while the mortality decreased from 52% to 24%. Conclusion: Despite with quite restricted indications, liver transplantation in hepatic injury is a therapeutic modality viable and feasible today, and can be used in cases when other therapeutic modalities in short and long term, do not provide the patient survival chances.

INTRODUCTION

The mortality rate due to liver injuries has fallen significantly in recent years. Surgical cases resulting from these traumas cover only 10% of cases, while 90% are treated conservatively. The main causes of death following severe hepatic trauma are uncontrollable bleeding due to vascular and liver laceration injury and acute liver failure. Both conditions can be treated by selected cases of liver transplantation; however, indications are still well restricted. In cases of severe liver injury (TSAA grade>IV) mortality rates rise to about 46-80%, and liver transplantation should be considered in cases where all other therapies have failed to achieve hemodynamic stability, making it imperative to adopt damage control measures in order to promote temporary hemostasis until an organ becomes available for transplantation (Table 1).
The indications for liver transplantation due to trauma more described in the literature are: uncontrollable continuous bleeding after damage control operation; extensive complex liver lacerations not amenable to surgical correction; extensive lesions of the portal vein, hepatic vein or bile duct that cannot be repaired by surgery; progressive liver failure due to trauma, and hepatic necrosis. In these patients, often the liver transplant is the last therapeutic alternative; however, not all patients are candidates for transplant and that choice should be conducted carefully and individually. Situations such as severe sepsis, multiple organ failure, other serious injuries associated may contraindicate the transplant.

There are two types of procedures described in the literature: transplantation in one and two stages. The in one, is the immediate removal of the native liver with subsequent implantation of a new organ. During the procedure performed in two stages there will be a temporary vascular portocaval shunt type to allow the patient to wait for a new body and avoid congestion in mesenteric splanchnic system. Was found 14 related articles, of Lilacs, between 2008-2014 correlating liver trauma and liver transplantation as a treatment option for severe liver trauma.

The overall survival rate was 63%, and 24% of patients required retransplantation; 65% were transplanted in early to 72 h and the leading cause of postoperative death was 17% of sepsis cases (Table 3).

### METHOD

Survey was conducted in the Pubmed, Medline and Lilacs, between 2008-2014 correlating liver trauma and liver transplantation headings. Was found 14 related articles, of which 10 were selected for theme analysis.

### RESULTS

After making systematic literature review of the literature was identified total of 46 case reports of patients undergoing liver transplant after liver trauma; closed/blunt trauma had a higher prevalence with total of 83%, as well as severe trauma (>grade IV, Table 1) with 81% of the votes. The main indication in 52% of cases was the acute liver failure (OR 0.5, CI: 95%, p=0.1941). The technique in one step was the most frequent in 72% of cases. The characteristics of the sample are shown in Table 2.

The treatment by means of transplantation has undergone significant improvement in recent years (Table 4). In 88% of cases the major trauma mechanism was the closed/blunt type, as well as severe trauma (> grade IV). The main indication for transplant remains acute liver failure. The bleeding transplant indication was a statistically significant decrease from 33% to 8% (OR: 5.75; 95% CI, p= 0.0365). The technique in one step was the most used in the last decade with a significant increase to 92% of cases, with statistical significance (OR: 0.07; 95% CI p=0.0011). Early transplantation remains a vast majority increased to 68%, and this fact is due to the mastery of technique combined with the good results achieved with transplantation as a treatment modality for chronic diseases and even against patients with acute liver failure. The rate of survival increased significantly, from 48% to 76%, the mortality rate from 52% to 24%, and sepsis remained the main cause of death.

### TABLE 1 - Classification of liver trauma as proposed by TSAA

| Lesion grade | Description |
|--------------|-------------|
| I            | Hematoma, subcapsular not expansive, <10% of surface area |
| Laceration   | Capsular laceration at a bleeding, <1 cm deep parenchymal |
| II           | Hematoma, subcapsular not expansive, 10-50% surface area: intraparenchymal, non-expansive, <10 cm diameter |
| Laceration   | Capsular tear, active bleeding: 1-3 cm deep in the parenchyma, <10 cm in length |
| III          | Hematoma, subcapsular, >50% of surface area or expansion. Intraparenchymal hematoma, >10 cm or expanding |
| Laceration   | >3 cm in depth |
| IV           | Hematomas roto with active bleeding |
| Laceration   | Parenchymal disruption involving 25-75% of hepatic lobe or 1-3 segments (Couinaud) in the same lobe |
| V             | Laceration | Parenchymal break involving >75% of hepatic lobe or >3 segments (Couinaud) in the same lobe |
| Vascular     | Vascular, liver avulsion |
| VI Vascular   | Liver avulsion |

### TABLE 2 - Liver transplantation after liver trauma: characteristic of the sample

| n=46 |
|------|
| Gender | Male 24 (52%) | Female 19 (41%) | Non specified 3 (7%) |
| Trauma mechanism | Closed 38 (83%) | Penetrating 5 (11%) | Non specified 3 (7%) |
| Grade | IV 15 (33%) | V 19 (41%) | VI 3 (7%) | Non specified 5 (11%) |
| Technique | 1 step 33 (72%) | 2 steps 13 (28%) |
| Indications | Acute failure 24(52%) | Hemorrhage 9 (19%) |
| Biliary fistula 2 (5%) | Secondary biliary cirrhosis 2 (5%) |
| Portal vein thrombosis 1 (2%) | Hepatic necrosis 8 (17%) |

### TABLE 3 - Evolution of patients with liver transplant after liver trauma (n=46)

| n (%) |
|------|
| Postoperative survival rate 29 (63%) |
| Postoperative mortality rate 17 (37%) |
| Retransplants 11 (24%) |
| Waiting time to transplant | Precocious (<72 h) 30 (65%) | Late (>72 h) 16 (35%) |
| Cause of death | Sepsis 8 (17%) | PNM 3 (7%) |
| Mesenteric ischemia 1 (2%) | CMV infection 1 (2%) |
| Cerebral edema 1 (2%) | Multiple organ failure 1 (2%) |
| Hepatic failure 1 (2%) | Non specified 1 (2%) |
cause of postoperative death, covering half of patients who progressed to death, compared the two periods analyzed.

It is observed that the main indication for technical mode in one step was bleeding after damage control with 52%, highlighting the cases of hepatic necrosis in second place with 24%, with statistical significance (OR: undefined CI: 95% p=0.0162). While the main indication, statistically significant for the technique in two steps was acute liver failure with 77% (OR: 0.13; 95% CI p=0.00001, Table 5).

**TABLE 5** - Indications according to the technical modality adopted

| Indications          | 1 step (n=33) | 2 steps (n=13) | TOTAL | p      |
|----------------------|---------------|----------------|-------|--------|
| Hemorrhage           | 17 (52%)      | 3 (23%)        | 20    | 0.0759 |
| Acute liver failure  | 3 (9%)        | 10 (77%)       | 13    | 0.0000 |
| Biliary fistula      | 2 (6%)        | 0              | 2     | 0.5101 |
| Secondary biliary cirrhosis | 2 (6%) | 0              | 2     | 0.5101 |
| Portal vein thrombosis | 1 (3%)   | 1              | 1     | 0.7173 |
| Hepatic necrosis     | 8 (24%)       | 0              | 8     | 0.0162 |
| TOTAL                | 33            | 13             | 46    |        |

Discusión

Mortality rates related to trauma have a strong association with the lethal triad of trauma and the widespread intense inflammatory response. In considering the complexity of trauma patients that may require liver transplantation, which usually are used massive transfusion protocols and mechanical ventilation while waiting for a transplant, justified the worst survival rates in three months when compared to patients transplanted for other indications. However with the advent of greater technical mastery, anesthetic support and care in intensive care, it can be observed reduction in mortality compared to the results obtained in the 80s and 90s when it started the transplants after trauma

In 1987, it was reported the first case of liver transplant after liver trauma in a patient with vascular and biliary complex injuries after a car accident, using transplantation in one step, which consists of removing the native liver and immediate implementation of the donor liver. In 1988, the transplantation was described in two steps, which is the total hepectectomy followed terminolaterally portocaval shunt, and a second procedure for implementation of the donor liver with the scope to win time while the donor is found. In most studies, patients tolerated up to 36 h without liver after trauma, with reports of a case that remained for 66 h in anhepatic situation. Despite the low survival rate of the procedure into two steps, it was possible to save up to approximately 25% more patients, making more acceptable procedure for acute cases, especially progressive liver failure and uncontrollable hemorrhage.

Three different scenarios are described in the statement of transplantation: massive bleeding due to liver damage controllable only with full hepectectomy; liver failure with progressive clinical deterioration in the days following the trauma; and irreparable vascular or biliary injury or evolve secondary to cirrhosis, which is usually later. Different approaches are adopted in accordance with the indication for the procedure. In the first group, in large and uncontrollable bleeding is indicated transplant in two steps with immediate withdrawal of the injured liver that usually leads to hemodynamic instability arising from massive bleeding as a compatible donor is sought, so keeping the patient with temporary portocaval shunt type. In the second group, the progressive failure of the body, can be chosen to perform the transplant by the standard technique, or in the case of severe hemodynamic instability, the technique in two steps, with the intention of faster improvement of symptoms after removal of insufficient liver. In the third scenario the indication is transplant elective procedure by one step, since they are patients with late post-traumatic sequelae as demonstrated in Table 5.

The two steps technique is valuable procedure in severe acute cases. Despite the length of anhepatic situation, this type is often the only and last alternative therapy in the hope till a compatible donor is found and the patient has a chance to survive, and get restabilisation during anhepatic after hepectectomy, being observed amazing long-term success rates with survival up to two decades.
It is not surprising that patients undergoing the procedure in two steps have been, in the vast majority (69%), early transplant on within 72 h, since this therapy is recommended in acute cases, as discussed above. Conversely, patients undergoing transplantation in one step, in addition to cover the majority of transplant patients (n = 33) had a greater number of late transplantation (n = 12), since this is the technique of choice for elective procedures and chronic complications when a compatible donor was previously chosen.2,7

Regarding retransplantation were identified a total of 11 cases in which the main causes were of cholestasis and repeated cholangiitis due to ischemic lesions of the bile duct, hepatic artery thrombosis, primary graft failure, and late failure of the transplanted organ by diabetes.7,10,14

Current survival after transplantation for liver trauma is about 76% while two decades ago was around 48%. Sepsis is still the main cause of mortality after transplantation (50%), despite a significant drop in the total number of cases over the past 10 years. This increase in survival rates may be attributed to the fact that 20 years ago the signs were smaller and less frequent.10

The patients submitted to the standard procedure in one step survival rate is around 70%, while with the two steps is 54%. Such data are justified by the selection of cases where every mode has been indicated. The cases undergoing treatment in two steps usually end up being more severe cases that end up presenting progressive organ failure and therefore have a worse prognosis, increasing with it the mortality.10

Another important factor is the transplantation in patients who develop liver necrosis in the days following the trauma; necrotic liver has been seen as toxic agent leading to increased hemodynamic instability. Therefore, total hepatectomy followed by transplantation in two steps is also indicated in these patients. However, the ethical implications of this approach are key, leaving the post-trauma liver transplantation as the only solution, which is, however, entirely dependent on the availability of a adequate donor.5

The ethical issue also includes the context of patients received grafts from living donors. Because of the many implications and repercussions that this theme will bring, not being the focus of this study, was identified only one report from a living donor for a patient who received the right lobe of his brother. They were not identified in the review other cases.5

With the increase in the number of organ donors, as well as transplants performed in the last decade, today is considered even in cases of trauma such as early as possible approach with the procedure in one step with significant increase in survival.10

In this context, liver failure is a challenge that requires urgent liver transplantation, since it leads to worsening of the clinical condition and hemodynamic stability, leading to complications such as cerebral edema and increased intracranial pressure, which can lead to irreversible brain damage to the patient. Thus, was developed an extracorporeal liver support system, that controls these complications, helping to keep patients stable until a suitable donor was found for the viable and available for transplantation. The methods used for extracorporeal support can be classified between biological and non-biological. The bioartificial system uses primary porcine hepatocytes or processed human hepatocytes that are housed within a bioreactor through which blood is pumped into the extracorporeal circuit. The difficulty of finding a compatible donor quickly, coupled with the inability to maintain stable patient in anhepatic stage for long periods of time, they become a major problem in the management of these patients. Thus, it appears as support therapy an alternative, by increasing the survival time where the transplant precociously cannot be performed.18

Despite not having been found in the present review any study that uses this type as the device bridge method for patients who have their organs removed as a result of the trauma extent and therefore were subjected to the use of this type of device, it may have relevant role in increasing survival during anhepatic phase, as well as the waiting time on the list and may allow patients who previously could not afford to wait for longer times in the list, are likely to be transplanted.

**CONCLUSION**

Liver transplantation, despite having very limited information on the stage of hepatic injury, is therapeutic modality viable and feasible on these days and can be used in cases where surgical treatment as well as other therapeutic modalities, do not offer the patient chances of survival to short and long term.

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