Title:
The outcome of Living Donor Liver Transplant recipients with Recent Episodes of Spontaneous Bacterial Peritonitis

Authors:
Vinayak Nikam, Manish Srivastava

DOI: 10.17235/reed.2020.6780/2019
Link: PubMed (Epub ahead of print)

Please cite this article as:

This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.
OR 6780

The outcome of living donor liver transplant recipients with recent episodes of spontaneous bacterial peritonitis

Vinayak Nikam and Manish Srivastava

Department of Surgical Gastroenterology and Liver Transplantation. Sir Ganga Ram Hospital. New Delhi, India

Received: 5/12/2019
Accepted: 28/4/2020

Correspondence: Vinayak Nikam. Institute of Liver Diseases. HPB Surgery and Transplantation. Global Hospital. Room no. 202, 2nd floor. 35 Dr. E Borges Road, Opp. Shirodkar High School. Parel, Mumbai. 40001 Maharashtra, India

E-mail: vinayaknikam7183@gmail.com

ABSTRACT

Background: spontaneous bacterial peritonitis (SBP) is a common complication in patients with cirrhosis and is associated with a high mortality rate. Only a few reports have analyzed the impact of treated SBP that occurs in the immediate pre-operative period on outcome after a living donor liver transplantation (LDLT). The results of whether post-transplant patients are dependent on pre-transplant infections are still debatable and unclear. Therefore, this study examined the outcomes of LDLT recipients with recent episodes of SBP and LDLT recipients without prior episodes of SBP.

Patients: the records of 62 LDLT recipients who underwent LDLT were retrospectively reviewed. Twenty-four (36%) recipients had at least one episode of SBP before LDLT. However, active SBP was not present in any of the recipients at the time of LDLT. Both recipient groups were compared in terms of demographic profile, perioperative and postoperative variables and outcomes.

Results: higher pre-operative Child-Turcotte-Pugh (CTP) score (mean [SD] 11.77 [1.37] vs 10.5 [1.22], p < 0.001) and prior history of renal dysfunction (mean serum creatinine [SD]
1.715 [1.08] vs 1.02 [0.479] mg/dl, p = 0.002) were more commonly associated with the SBP group as compared to the non-SBP group. However, there was no statistically significant difference between the two groups in terms of the following variables: previous diabetes mellitus (3 [12.5 %] vs 6 [15.8 %]), pre-operative model for end-stage liver disease (MELD) score (median [IQR] 21 [10-37] vs 22 [9-39]), operative time (mean [SD] 789.57 [153.49] vs 800.86 [138.69] min), total number of blood transfusion (median [IQR] 10 [2-19] vs 8 [1-18]), hospital stay (median 21 vs 20 days), re-exploration (4 [16.6 %] vs 2 [5.3 %]), postoperative sepsis (8 [33 %] vs 5 [13 %]) and 30-day mortality (3 [12.5 %] vs 2 [5.3 %]).

**Conclusions:** the presence of previous episodes of pre-operative SBP in LDLT recipients does not result in adverse post-operative short-term outcomes.

**Keywords:** End-stage liver disease. Spontaneous bacterial peritonitis. Living donor liver transplantation.

**INTRODUCTION**

The survival of liver transplant recipients has improved tremendously with the new and advanced surgical techniques (1). Patients with end-stage liver disease liver (ESLD) are more vulnerable to bacterial infection and have high death rates due to sepsis (2). These patients have a low immunological capacity to fight high-risk infection and therefore, have reduced bactericidal cells activity, deficiency of complement level, altered gut microbiota, intestinal barrier disruption, abnormal inflammatory response and hemodynamic instability (3). One of the most common infections is spontaneous bacterial peritonitis (SBP), which is followed by urinary tract infection and pneumonia (4). Spontaneous bacterial peritonitis is defined as a positive ascitic fluid culture and/or high ascitic fluid absolute polymorphonuclear cell count (PMN cells > 250 cells/mm³) in the absence of an intra-abdominal surgically correctable cause of infection.

The death rate of the patient suffering from SBP has reduced to 15-20 % from 90 % with an early diagnosis and the appropriate use of antibiotics. However, prognosis is poor with end-stage liver disease and a previous episode of SBP, where the mortality rate is 60-70 % at one-year follow-up (5). Whether post-transplant patients are dependent on pre-transplant infections is still debatable and unclear. Hence, we studied the effect of pre-transplant SBP
on post-transplant morbidity and mortality.

MATERIALS AND METHODS
The prospective records of 60 consecutive recipients who underwent LDLT at Sir Ganga Ram Hospital (New Delhi, India) between 2014 and 2016 were retrospectively reviewed from the institutional database. Liver disease patients with SBP were defined as those having positive ascitic fluid monomicrobial cultures and/or an ascitic fluid polymorphonuclear (PMN) neutrophil count > 250/mm³. The PMN neutrophil count was corrected (one PMN neutrophil cell reduced for every 250 red blood cells) when the ascitic fluid tapping was hemorrhagic (red blood cells > 10,000/ml) (6).

In this study, SBP was compared with non-SBP patients, who underwent LDLT between 2014 and 2016. Recipient demographic characteristics and clinical, biochemical and surgical parameters were collected and analyzed. The model for end-stage liver disease (MELD) and the Child-Turcotte-Pugh (CTP) score were used to calculate the liver disease severity of recipients. Intra-operative and postoperative parameters such as surgery duration, blood loss, hospital stay, re-exploration, postoperative sepsis and mortality were compared between both groups. All SBP patients were treated with intravenous (IV) antibiotics for five days, to which the organism is highly susceptible (e.g., injection of cefotaxime 2 g IV every 8 h empirically followed by more specific treatment after susceptible results were available).

Subsequently, these patients were kept on prophylaxis antibiotics (tab Norfloxacin 400 mg once a day) until the time of LDLT. The SBP group patients were more prone to renal dysfunction. Thus, the majority of patients were prescribed with intravenous albumin as renal protective effects.

Statistical analysis was performed using the SPSS Software version 17.0. The Student’s t-test and Chi-squared test were used to compare continuous and categorical variables respectively. A p-value < 0.05 was considered as significant. The study was approved by the Institutional Review Board.

RESULTS
In our study, 62 adult patients underwent a living donor liver transplantation (LDLT). Twenty-four patients (38.7%) had an SBP within 30 days before liver transplantation,
whereas there were 38 patients (61.3%) in the non-SBP group. Of the 24 of SBP patients, nine (37.5%) had a monomicrobial positive culture and 15 (62.5%) had a culture-negative SBP (PMN neutrophils > 250 mm$^3$). The organisms isolated from ascitic fluid cultures were: a) E. coli (67%); b) Klebsiella spp. (22%); and c) coagulase-negative staphylococci (11%). All SBP patients had completed antibiotic treatment (empirical or as per antibiotics culture and sensitivity) and were declared infection-free before transplantation in repeat ascites fluid tapping and culture and sensitivity.

The demographic characteristics of the recipients are shown in table 1. Patients with SBP before liver transplantation had significantly more severe liver disease, which was calculated using the CTP score. In addition, the SBP group had a high incidence of renal dysfunction.

Post-LDLT outcome parameters are shown in table 1. There was no difference between both groups in term of intraoperative parameters such as total blood transfusion (median [IQR] 10 [2-19] vs 8 [1-18]) (p = 0.07) and surgery duration (mean [SD] 789.57 [153.49] vs 800.86 [138.69] min) (p = 0.77).

The percentage of patients with postoperative septic complications was 33% for patients with SBP before transplantation versus 13% for patients with no SBP (p = 0.10). Post-liver transplant sepsis was caused by different pathogens, at different body locations as compared to pre-transplant infections. The postoperative re-exploration was not significantly different between the groups for various reasons (4 [16.6%] vs 2 [5.3%]) (p = 0.19). The overall 90-day mortality rate in the SBP group was 12.5% (3 of 24) and was not significantly different when compared to the non-SBP group 5.3% (2 of 38) (p = 0.37). The 90-day Kaplan-Meier analysis showed no difference in survival between the two groups (Fig. 1).

**DISCUSSION**

In the present study, the post-transplant mortality rate was unaffected by SBP, even if such a patient had a higher severity of liver disease (CTP score) and renal dysfunction. The intraoperative events, such as higher blood transfusion and total surgery duration, were not statistically different between the two groups. Appropriate antibiotic treatment of SBP before LDLT did not adversely affect outcomes, including the risk of post-transplant sepsis, hospital stay and re-exploration after liver transplantation. Spontaneous bacterial peritonitis
is one of the most common infectious complications in patients with ESLD and is associated with a serious outcome, occurring in 3.5 % of OPD the patient and 25-35 % of hospitalized patients. The recurrence incidence of SBP within one year from the first episode was 34-70 % (7,8).

The mortality rate within 30 days of an SBP episode was 26-48.7 %. Hence, the previous history of a single episode of SBP is an indication for early referral and liver transplantation (9). There are only a few articles that analyze the impact of treated SBP occurring in the immediate pre-operative period on outcomes after LDLT. Therefore, we examined the outcomes of LDLT recipients with prior episodes of SBP with LDLT recipients without prior episodes of SBP.

Malik S et al. published a retrospective study in an abstract form that showed that patients with pre-transplant SBP did not have a higher post-transplant mortality rate at 30 days in comparison with those without pre-transplant SBP. Recipients with SBP were more likely to have higher MELD and CTP scores, pre-transplant renal dysfunction, longer hospital stays and mortality from sepsis post-transplant (10).

Rawad M et al. analyzed the records of 1,491 adult patients who underwent LT and stated that 80 (5.4 %) had at least one episode of SBP before LT. Patients with SBP had a higher severity of liver disease at the time of liver transplantation compared with the non-SBP group. However, there was no statistical difference in long-term mortality between these two groups. In contrast to our study, the re-exploration rate and septic complications in the SBP group within one year of LT were significantly higher (11).

Van Thiel DH et al. studied 100 liver transplant recipients retrospectively for an episode of SBP within 30 days of their transplant and compared the outcome between SBP and non-SBP group in terms of sepsis within 30 days of transplant. Post-transplant sepsis occurred in 8.8 % and 10 % in SBP and non-SBP groups, respectively. In conclusion, they stated that pre-transplant SBP does not increase the rate of postoperative infection if appropriate antibiotic treatment for SBP is administered before transplantation (12).

There are many other studies that have analyzed the influence of pre-transplant infection on clinical outcome after liver transplant and they have collectively concluded that adequately treated pre-transplant infection does not have a significant risk of an adverse outcome, including post-transplant mortality. However, contrary to the current study, these
studies included all types of infective pathogens such as fungal infection as well as other sites of infections (13-15).

Two potential limitations of the current study should be highlighted. Firstly, the retrospective study design, which has a potential inherent bias. Another limitation was the small sample size.

CONCLUSIONS
In conclusion, recipients with pre-transplant SBP had higher CTP scores and are more prone to renal dysfunction than those without SBP. The presence of previous episodes of pre-operative SBP in LDLT recipients does not result in adverse post-operative short term outcomes if it was adequately treated with antibiotics before undergoing LDLT.

ACKNOWLEDGMENTS
The authors would like to thank Dr. Yasmin Shaikh and Miss Anusha Nikam for language editing help and technical support. We have permission from them to use their full names in this section.

REFERENCES


Table 1. Demographic and postoperative variables of LDLT recipients

<table>
<thead>
<tr>
<th>Variables</th>
<th>Preoperatively treated SBP (n = 24)</th>
<th>No preoperative SBP (n = 38)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>45</td>
<td>45</td>
<td>0.89</td>
</tr>
<tr>
<td>Gender (male)</td>
<td>23 (95.8 %)</td>
<td>30 (78.9 %)</td>
<td>0.14</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>3 (12.5 %)</td>
<td>6 (15.8 %)</td>
<td>1.0</td>
</tr>
<tr>
<td>Median MELD score</td>
<td>21 (IQR = 8)</td>
<td>23 (IQR = 10.5)</td>
<td>0.75</td>
</tr>
<tr>
<td>Median CTP score</td>
<td>11.77 (IQR = 1.37)</td>
<td>10.7 (IQR = 1.25)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Serum creatinine</td>
<td>1.7</td>
<td>0.86</td>
<td>0.002</td>
</tr>
<tr>
<td>Intraoperative blood products</td>
<td>10 (IQR = 4)</td>
<td>8 (IQR = 6.5)</td>
<td>0.07</td>
</tr>
<tr>
<td>Duration of surgery (min)</td>
<td>789</td>
<td>800</td>
<td>0.77</td>
</tr>
<tr>
<td>Hospital stay (days)</td>
<td>21 (IQR = 17.5)</td>
<td>20 (IQR = 6)</td>
<td>0.376</td>
</tr>
<tr>
<td>Re-exploration (%)</td>
<td>4 (16.6 %)</td>
<td>2 (5.2 %)</td>
<td>0.19</td>
</tr>
<tr>
<td>Postoperative sepsis (%)</td>
<td>8 (33 %)</td>
<td>5 (13 %)</td>
<td>0.10</td>
</tr>
<tr>
<td>Mortality</td>
<td>3 (12.5 %)</td>
<td>2 (5.3 %)</td>
<td>0.37</td>
</tr>
</tbody>
</table>

IQR: interquartile range.
Fig. 1. Kaplan-Meier survival analysis.