Multivariate regression analysis on early mortality after orthotopic liver transplantation

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Abstract
AIM: To identify the risk factors relating to early mortality after orthotopic liver transplantation.

METHODS: Clinical data of 37 adult patients undergoing liver transplantation were retrospectively collected and divided into two groups: the survived group (survival time ≥30 d) and the death group (survival time<30 d). The relationship between multivariate risk factors and early mortality after orthotopic liver transplantation were analyzed by stepwise logistic regression.

RESULTS: The survival rate was 73%. Early mortality rate was 27%. APACHE [1], preoperative serum creatinine level and interoperative bleeding quantity had a significant independent association with early mortality. (R=0.1841, 0.2056 and 0.3738).

CONCLUSION: APACHE [1], preoperative serum creatinine level and interoperative bleeding quantity are significant risk factors relating to early mortality after orthotopic liver transplantation. To improve the recipient’s preoperative critical condition and renal function and to reduce interoperative bleeding quantity could lower the early mortality after orthotopic liver transplantation.


INTRODUCTION
In recent years, the success rates of orthotopic liver transplantation (OLT) have improved markedly as a result of rapid advances in immunosuppressions, surgical and preservation techniques. One-year survival rate after liver transplantation exceeds 80%. Orthotopic liver transplantation, as an accepted treatment for end-stage liver disease, has been widely performed in the world[6-9]. In our country, the early mortality after OLT remains relatively high and current studies have focused on the improvement of survival rate after liver transplantation[6,7]. Clinical data of 37 adult patients undergoing liver transplantation were retrospectively collected in our study. The significant risk factors relating to early mortality after OLT were analyzed and determined, which may contribute to the selection of candidate and improvement of survival in patients with liver transplantation.

MATERIALS AND METHODS

Materials
Thirty-seven adult patients undergoing OLT procedures at our transplantation center from September 1993 to January 2000 were studied. The study population consisted of 32 men and 5 women with a mean age of 39.8(range 17-64) years. The grafts were obtained from donors. Indications for liver transplantation were end-stage liver cirrhosis (n=9), fulminant hepatic failure (n=8), primary liver cancer (n=14), primary sclerosing cholangitis (n=2), Willson’s disease (n=1), polycystic liver and kidney (n=1), hepatangioma (n=1), and cholangiocarcinoma (n=1).

Multiple risk factors
Thirty-seven patients were divided into two groups: survival group (survival time ≥30 d) and death group (Survival time <30 d). There were different possible risk factors relating to early mortality after liver transplantation including preoperative, interoperative and postoperative ones. Preoperative information consisted of age, APACHE[1] I, hepatoencephalopathy, previous abdominal surgery, serum albumin, prothrombin time (PT), serum creatinine level (Cr), serum Aspartate transaminase (AST), white blood cells counts (WBC), platelet counts (PLC) and mismatch (CR-PT)

Statistical methods
Experimental data were presented as x±s and frequency. For continuous data, independent 2-tailed t tests were used to determine whether there were significant differences between the two groups. Pearson’s Chi-square statistics were used to test differences in all frequencies. Data with significant difference were entered into a stepwise logistic regression analysis. And all of the statistical calculations were performed using the SPSS (version: 9.0, Chicago,USA).

RESULTS
Twenty-seven of the 37 adult patients survived more than one months after liver transplantation. Early survival rate was 73% while early mortality was 27%. The other 10 patients died postoperatively within 30 d and the major cause for their death were disseminated intravascular coagulation (DIC n=2), myocardial infarction (n= 2), acute renal failure (n=2), hepatic artery thrombosis (n=1), cerebral bleeding (n=1) and adult respiratory distress syndrome (ARDS) (n=1).

Comparison between the survival group and the death group showed significant differences only in terms of age, APACHE III, serum creatinine level, PT, was PLC and interoperative bleeding quantity, (P<0.05, Table 1). The stepwise logistic regression were used to create the best statistical model relating to early mortality after transplantation. The factors that had significant independent significance were age, APACHE III, serum creatinine level, PT, was PLC and interoperative bleeding quantity.
orthopedic bleeding quantity, with regression coefficients of 0.1841, 0.2056 and 0.3738, respectively (Table 2).

### Table 1: Risk factors relating to early mortality after liver transplantation

<table>
<thead>
<tr>
<th>Risk factors</th>
<th>Survival group</th>
<th>Death group</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>38.3±2.5</td>
<td>47.8±2.2</td>
<td>0.0000</td>
</tr>
<tr>
<td>Previous abdominal surgery</td>
<td>11% (27/247)</td>
<td>30% (3/10)</td>
<td>0.3130</td>
</tr>
<tr>
<td>APACHE III (score)</td>
<td>40.3±6.7</td>
<td>63.4±12.9</td>
<td>0.0000</td>
</tr>
<tr>
<td>Hepatomegaly</td>
<td>15% (4/27)</td>
<td>40% (4/10)</td>
<td>0.1712</td>
</tr>
<tr>
<td>Serum creatinine level (mmol L⁻¹)</td>
<td>82.2±10.8</td>
<td>132.8±33.2</td>
<td>0.0000</td>
</tr>
<tr>
<td>AST (IU L⁻¹)</td>
<td>97.5±18.5</td>
<td>125.8±80.5</td>
<td>0.0951</td>
</tr>
<tr>
<td>Albumin (g L⁻¹)</td>
<td>36.9±1.7</td>
<td>32.7±2.9</td>
<td>0.0000</td>
</tr>
<tr>
<td>TB (ml L⁻¹)</td>
<td>298.3±67.9</td>
<td>314.9±87.1</td>
<td>0.5447</td>
</tr>
<tr>
<td>PT /s</td>
<td>22.5±3.2</td>
<td>25.5±3.7</td>
<td>0.0175</td>
</tr>
<tr>
<td>WBC/ (×10⁹·l⁻¹)</td>
<td>7.3±1.2</td>
<td>6.8±1.1</td>
<td>0.2351</td>
</tr>
<tr>
<td>PLC / (×10¹³)</td>
<td>129.9±17.5</td>
<td>53.6±12.3</td>
<td>0.0000</td>
</tr>
<tr>
<td>Dismissal ABO group</td>
<td>7.3% (2/27)</td>
<td>30% (3/10)</td>
<td>0.1102</td>
</tr>
<tr>
<td>Heat ischemic time /min</td>
<td>3.8±0.1</td>
<td>3.9±0.3</td>
<td>0.1478</td>
</tr>
<tr>
<td>Cold ischemic time /s</td>
<td>44.9±26.9</td>
<td>471.2±46.3</td>
<td>0.6104</td>
</tr>
<tr>
<td>Anasthetic time /s</td>
<td>87.5±4.9</td>
<td>90.3±10.5</td>
<td>0.2704</td>
</tr>
<tr>
<td>Interoperative bleeding quantity /ml</td>
<td>5615.1±1033.7</td>
<td>12263.6±3606.1</td>
<td>0.0000</td>
</tr>
<tr>
<td>Rate of acute rejection</td>
<td>18% (5/27)</td>
<td>20% (2/10)</td>
<td>1.0000</td>
</tr>
<tr>
<td>Rate of postoperative complications</td>
<td>9% (16/27)</td>
<td>70% (7/10)</td>
<td>0.709</td>
</tr>
</tbody>
</table>

### DISCUSSION

Orthotopic liver transplantation is a treatment for end-stage liver disease. Early mortality was below 10%[10,19], which remains high in our country. The serious preoperative condition of recipient and the late timing for operation may account for this result[10,11]. A number of investigators have examined the factors associated with outcome after liver transplantation including PT, APACHE III and so on[10-16]. In our study, 10 of 37 patients died postoperatively, with an early mortality of 27%. After analyzed with stepwise logistic regression, APACHE III, preoperative serum creatinine level (Cr) and interoperative bleeding quantity showed significant associations with early mortality after liver transplantation.

While APACHE III score is a best predictor of mortality[17,18,19], APACHE III that results from the addition of 3 groups of variables (acute physiology, age and chronic health) consists of multiple organ function evolution, including heart, lung, liver, kidney, brain, etc. It is more accurate than APACHE III. And now it has been widely used to evaluate the severely ill in patients’ condition and to predict the mortality of patient[20,21]. In our study, the APACHE III score was 40.5±6.7 and 63.4±12.9 in the survival group and the death group respectively. There was a statistical difference between the two groups in APACHE III score, P<0.001. The stepwise logistic regression analysis showed a significant independent association with early mortality after transplantation, with a regression coefficient of 0.1841. As one of the main risk factors, it can act as a reference index of the selection of recipient and timing for operation. However because it is not specific to liver function, it needs combination with other indexes when used to predict outcome of OLT.

Renal dysfunction is a common dangerous complication in patients with end-stage liver disease. It results from acute tubular necrosis and caused by hepatorenal syndrome[22,23]. Gunning[20] reported a significant decrease of 43% in glomerular filtration rate (GFR) during transplantation in patients with normal renal function. Both high preoperative serum creatinine level and interoperative venovenous bypass can lead to renal hemodynamic unstablity during operation[24,25,29]. The postoperative nephrotic immunosuppressions can also contribute to the irreversible renal insufficiency, leading to renal failure after liver transplantation[30,31]. In our study, 2 of 10 patientsdied of renal failure, who were all along with high preoperative serum creatinine level and hepatorenal syndrome before transplantation. A significant differencewas found between the survival group and the death group was shown in serum creatinine level (P<0.001), with a mean of 82±11 and 133±33, respectively. The stepwise logistic regression analysis, it also showed a statistical independent association with early mortality after liver transplantation, with a regression coefficient of 0.2056. It is also a main risk factor which predicts early mortality after OLT. It is very important to correct renal malfunction before transplantation. How to prevent and treat renal failure Kuse[23] reported that Uroditin can treat acute renal failure following OLT. Gowan and the other investigators[33,34] reported that renal failure need dialysis. Our principles were to avoid using nephrotoxic treatments and drugs, to maintain stable hemodynamically and monitor central venous pressure, to use small dose of Dopamine (2-5µg·kg⁻¹·min⁻¹) and Procraine to dilate renal artery and protect renal function, to use diuretics appropriately, to perform hemodialysis properly performed if needed, and not to use Alprostadil(PGE1).

Interoperative bleeding quantity is the third important risk factor relating to early mortality after liver transplantation[98]. If it exceeded 10000ml, mortality was very high. The interoperative bleeding quantity of the death group was more than that of the survival group statistically (P<0.05), with a mean of 12264±3606mL and 5615±1040mL respectively. Logistic regression analysis showed a significant relationship between interoperative bleeding quantity and early mortality after transplantation, with a regression coefficient of 0.3738. Severe bleeding and a large amount of transfusion during operation may lead to hemodynamic unstablity and DIC. And long-term hypopiasy may accelerate preoperative renal insufficiency, leading to irreversible renal failure, and increasing the early mortality after operation[99,100]. Interoperative severe bleeding may due to previous upper abdominal surgery, abdominal extensive adhesions, portal hypertension, splenic hyperfunction, severe coagulation disorders, etc.[101-104]. In our study, there was no significant difference between the two groups with previous surgical histories. But it should be emphasized that some of our findings might be accidental because of insufficient cases involved in the study. We should pay attention to these patients with previous surgical histories. In these patients, severe bleeding and coagulation disorders may occur during operation because of abdominal extensive adhesions and difficulties in sequestration and ligation, consequently DIC and acute renal failure may follow. In our centre, 2 patients developed DIC.

The other risk factors showed no significant associations with early mortality after liver transplantation. But some of the factors did influence the outcome of the recipients and should be considered carefully, including mismatch ABO group, heat ischemic time, cold ischemic time, rate of acute rejection, rate of postoperative complications, etc[105-109]. Except emergent cases, the recipients and the donors were matched in ABO group at our center. Heat ischemic time and cold ischemic time were also limited strictly within 5 min and 12 h respectively during operation. After transplantation, ultrasonography B, chest X-ray examination, CMV detection and liver biopsy were performed periodically. Acute rejection and other postoperative complications were diagnosed and treated earlier. In patients diagnosed as having acute rejection, a large dose of methylprednisolone and FK506 were administrated with a treatment rate of 100%. Therefore, these risk factors showed no significant value in statistical analysis in our study.

### REFERENCES


