The Nutritional Index ‘CONUT’ Is Useful for Predicting Long-Term Prognosis of Patients with End-Stage Liver Diseases

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Organ allocation in Japan remains difficult due to the shortage of deceased-donor livers. The screening tool for controlling nutritional status (CONUT) has been considered to be an established assessment model for evaluating nutritional aspects in surgical patients. However, the application of this CONUT for evaluating the prognosis of patients with end-stage liver diseases has not been evaluated. We assessed the predictability of the prognoses of 58 patients with end-stage liver disease using various prognostic models. The patients registered at the transplantation center of Tohoku University Hospital for the waiting list of Japan Organ Transplant Network for liver transplantation were retrospectively analyzed. The prognoses of the patients were evaluated using the following 5 models: CONUT, the model for ELD with incorporation of sodium (MELD-Na), Child-Turcotte-Pugh score (CTP), prognostic nutritional indices (Onodera: PNI-O), and the Japan Medical Urgency criteria of the liver (JMU). Cox’s proportional hazard model, log-rank test and concordance(c)-static were used for the statistics. The indices were 17.74 ± 5.80 for MELD-Na, 9.21 ± 2.19 for CTP, 33.92 ± 11.16 for PNI-O, and 7.57 ± 3.09 for CONUT. Univariate analysis revealed the significance of CONUT (p = 0.017, Odds: 1.325) but not MELD-Na, CTP, JMU or PNI-O for prediction. The cumulative survival rate was clearly discriminated at CONUT point 7. The c-static was 0.081 for the 6-month (M) survival rate, 0.172 for 12M, 0.517 for 36M, 0.821 for 48M, and 0.938 for 60M for CONUT. In conclusion, CONUT shows best predictability for the distant prognoses of patients with ELD.

Keywords: CONUT; MELD; nutrition; prognosis; transplantation

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The model for end-stage liver diseases (MELD) score (Kamath et al. 2001) is used world-wide as a basis for the allocation of deceased-donor (DD) livers. In Japan, Japan Medical Urgency (JMU) criteria of the liver, which defines the severity of the individual disease by specific criteria and ABO blood type matching, have been used for the organ allocation. The MELD scale is a reliable parameter of the mortality risk in patients with end-stage liver diseases (ELD) and is suitable for use as a disease severity index to determine organ allocation priorities (Wiesner et al. 2003; Kogure et al. 2006). More recently, MELD plus sodium scoring (MELD-Na) was developed for its superiority to MELD for the prediction of 3-month mortality (Ruf et al. 2005). Thus, Child-Turcotte-Pugh (CTP) scoring, MELD and MELD-Na have been comparable for predicting the 6-month mortality of patients with ELD (Boursier et al. 2009). Apart from these established models, protein-energy malnutrition is commonly observed in patients with ELD (Moriwaki 2006). The nutrition status (Alberino et al. 2001), including energy metabolism (Tajika et al. 2002), handgrip strength, subjective global assessment, and prognostic nutritional index (PNI) are well-known tools to predict the survival of liver disease patients (Alvares-da-Silva and Reverbel da Silveira 2005) and the quality of life of such patients (Kawamura et al. 2004). The preoperative nutritional status of liver transplantation (LT) recipients is also implicated in the surgical outcome (Stephenson et al. 2001). These suggest the potential significance of a nutritional scoring system for predicting the survival of ELD patients. Thus, in the current study, we tested the applicability of the CONUT score for the prediction of the progno-
sis of end stage patients with liver diseases who were listed as transplantation recipients in comparison with other indices.

Patients and Methods

The patients who had registered as the recipients for liver transplantation through Japan Organ Transplant Network (JOTN) at the transplantation center of Tohoku University Hospital from January, 2000 to March, 2008 were enrolled in this retrospective study. The data obtained at the registration for JOTN were retrospectively analyzed. The observation period in the current study was from January 2000 to August 2009. The prognoses of the patients were evaluated using the following 5 different models for predicting survival: CONUT (Ignacio de Ulibarri et al. 2005) (Table 1), MELD-Na (= 11.2*LN(INR) + 3.78*LN(Bilirubin) + 9.57*LN(Creatinine) + 6.43 + 1.59(135-Na)), CTP, PNI-O (= 10Albumin + 0.005(total lymphocyte count)) (Onodera et al. 1984), and JMU (http://www.jotnw.or.jp/). Cox’s proportional hazard model, log-rank test and receiver operating characteristics (ROC) were applied for the analysis with SPSS software ver.17.0® (IBM Japan, Ltd. Tokyo, Japan) and Excel statistics 2010® software (Social Survey Research Information Co Ltd. Tokyo, Japan). Patients were followed up until death, liver transplantation, or the last available follow-up visits. In this study, the ‘transplantation’ has been regarded as discontinuance, while the ‘death’ has been regarded as endpoint. Statistical significance was defined as \( p < 0.05 \).

Results

Patient Characteristics

There were 58 patients in the database who were enrolled in the study. The characteristics of the patients are summarized in Table 2. The composition of the group consisted of primary biliary cirrhosis, 15; Hepatitis C related, 14; Hepatitis B related, 6; post Kasai procedure, 8; primary sclerosing cholangitis, 6; others, 9. All of the patients were Asian races.

Overall survival

The cumulative survival curve is shown in Fig. 1. At the end of the follow up, 27 (45.7%) patients had died. Two and 14 of the patients underwent DDLT and living donor liver transplantation (LDLT) during the observation periods, respectively.

Parameters, predictive scales and significance

Ascites, total bilirubin, total cholesterol and total lymphocyte count were statistically significant parameters in relation to the patients’ survival (Table 3). The prognostic scales are listed in Table 3. Among CTP \( (p = 0.493) \), MELD-Na \( (p = 0.174) \), JMU \( (p = 0.951) \), CONUT and PNI-O \( (p = 0.209) \), CONUT alone showed significant predictability for death \( (p = 0.017) \), Odds ratio 1.325 by univariate analysis. Accordingly, the CONUT scale clearly discriminated the cumulative survival at the cut-off level as CONUT 7 points (Fig. 2).

ROC curve and c-static

CONUT, PNI-O, MELD-Na and CTP were evaluated using the ROC curve (Fig. 3). PNI-O showed superiority for the prediction of death compared to the other scales at 6 months. At 4 years, the predictability was reversed and CONUT had the highest predictability according to the c-static (area under the ROC curve) (Fig. 4). C-static was 0.141 for the survival rate at 0.5 months, 0.136 for that at 3 months, 0.081 for 6 months, 0.172 for 12 months, 0.289 for 24 months, 0.517 for 36 months, 0.821 for 48 months and

| Parameter                      | Normal (score) | Mild      | Moderate | Severe
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<td>Albumin (g/dL)</td>
<td>≥ 3.5 (0)</td>
<td>3.0-3.4</td>
<td>2.5-2.9</td>
<td>&lt; 2.5</td>
</tr>
<tr>
<td>Total lymphocyte count (mL)</td>
<td>≥ 1,600 (0)</td>
<td>1,200-1599</td>
<td>800-1,199</td>
<td>&lt; 800</td>
</tr>
<tr>
<td>Total cholesterol (mg/dL)</td>
<td>≥ 180 (0)</td>
<td>140-179</td>
<td>100-139</td>
<td>&lt; 2.5</td>
</tr>
<tr>
<td>Dysnutritional states (total)</td>
<td>Normal (0-1)</td>
<td>Mild (2-4)</td>
<td>Moderate (5-8)</td>
<td>Severe (9-12)</td>
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*: (Ignacio de Ulibarri et al. 2005)

Table 1. The screening tool for controlling nutritional status (CONUT)*.
0.938 for 60 months for CONUT, 0.750, 0.750, 0.844, 0.692, 0.556, 0.622, 0.268 and 0.156 for PNI-O, 0.360, 0.329, 0.246, 0.454, 0.363, 0.491, 0.484 and 0.792 for MELD-Na, and 0.238, 0.303, 0.403, 0.416, 0.375, 0.400, 0.583 and 0.863 for CTP. Thus, in contrast to the prognosis, the CONUT scale has potential predictability for the distant prognoses of patients with ELD.

**Discussion**

Several prognostic models have been developed for predicting the prognosis of ELD in order to ensure optimal organ allocation. The Japanese government altered the rule
K. Fukushima et al. for the DDLT as effective in 2010. The qualification as DD was made possible on the agreement of the families of potential donors under the condition of brain death, even if he or she had never shown a living-will for the donation of organs. Therefore, the number of DDLT cases is expected to grow larger. In the current study, we evaluated the prediction models with the data at a single transplant center. It should be noted that the nutrition index CONUT is likely to have potential predictability for the prognoses. Moreover, the scale shows its superiority especially for the prediction of distant prognosis. MELD or MELD-Na was developed for predicting the short-term (3 month or 6 month) survival. Thus, other scales such as CONUT could be used in combination with such short-term prediction scales. However, differing from previous reports, MELD-Na did not show significant predictability for death in the current study. Even more, MELD-Na showed an increase of c-static in the later period. To account for this discrepancy, we speculate that there might be differences in the patients’ backgrounds compared to other studies. In our study, a significant pro-

![Figure 3](image1.png)  
Fig. 3. The predictability of each scale has a characteristic pattern. The ROC curve at 6 months (upper left), 12 months (upper right), 4 years (lower left) and 5 years (lower right) were demonstrated. TPF: true positive fraction; FPF: false positive fraction.

![Figure 4](image2.png)  
Fig. 4. The time-dependent changes in c-static values. C-static reveals the superiority of 1) PNI-O for the prediction of early death, and 2) CONUT for the distant prognosis over the other scales. X-axis: months; Y-axis for c-static value.
portion of the patients with a history of undergoing the Kasai procedure (Kasai 1974) for biliary atresia was enrolled. Another possible explanation is that a substantial number of the patients had opportunities for undergoing LDLT during the observation period in the current study. These factors might be the reason for such discrepancies. Also, due to the small size of each subgroup of patients, we could not find significant differences regarding gender, etiology, and ages. These factors should be evaluated in future large-scale studies.

The CONUT was proposed primarily as a tool for the early detection of low nutrition status in hospitalized patients (Ignacio de Ulibarri et al. 2005). The validation was performed in comparison with other nutritional assessments such as subjective global assessment or full nutritional assessment by the authors. However, as a nutritional index, there should be more information with CONUT in terms of the predictive scale for the life-span. Therefore, the potential predictability of a prognostic nutritional score such as CONUT should be validated in a multi-centered study. The essential properties of the scale for the prediction are considered to be simple, convenient and objective. However, for the purpose of organ allocation, the predictability of early death is essential. In this context, CONUT seems to be unsuitable for urgent organ allocation. Respiratory quotient, serum albumin, INR, total bilirubin, creatinine, sodium, ascites and encephalopathy are major factors that determine the prognosis of end-stage liver patients (Miwa et al. 2000). As an allocation model, MELD is definitely reliable for the prediction, and has been regarded as a global standard. However, there is a concern with this scale, which is the lack of nutritional or immunological factors such as albumin or total lymphocyte count. Instead, MELD contains INR, creatinine and total bilirubin in its formula. The resource for these factors would be derived originally from the large database in the US. Accordingly, these factors are considered adequate for the prediction of the early death. However, the addition of other factors including nutritional indices might improve the predictability of the distant prognosis of liver disease patients. Moreover, from the nutritional aspect, nutritional intervention such as the administration of branched chain amino acids with or without a late-evening snack increases the albumin (Plauth et al. 2006), which could improve the nutritional status and potentially improve the CONUT scale. In conclusion, CONUT seems to be a beneficial index for predicting the long term prognosis for patients with ELD.

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Conflict of Interest

The authors do not have any potential conflict of interest regarding this study.

References


