Utility of MELD and Child-Turcotte-Pugh Scores and the Canadian Waitlisting Algorithm in Predicting Short-term Survival after Liver Transplant

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Utility of MELD and Child-Turcotte-Pugh scores and the Canadian waitlisting algorithm in predicting short-term survival after liver transplant

Salem M Bazarah; Kevork M Peltekian; Vivian C McAlister; Heinrich Bitter-Suermann; Alan S. MacDonald

Abstract

Background: The Model for End-Stage Liver Disease (MELD) and Child–Turcotte–Pugh (CTP) scores are important predictors for survival after liver transplantation (LT). The objective of this study was to compare the utility of MELD and CTP scores with Canadian waitlisting algorithm in transplantation (CanWAIT) status for predicting 90-day survival after LT. Methods: Retrospectively, we analyzed all 228 liver transplants performed in adults by the Atlantic Liver Transplant Program since 1985. These cases included combined transplants, retransplants and those after fulminant liver failure. MELD and CTP scores were calculated, and CanWAIT status and waiting time on the day of LT determined. We used c-statistic for 90-day outcome as the endpoint (survival), comparing areas under the receiver operating characteristic (ROC) curves for MELD and CTP scores and CanWAIT status. Results: Mean (and standard deviation [SD]) MELD score was 18 (SD 12); CTP score, 10 (SD 3); and waiting time, 97 (SD 132) days. At the time of LT, 54% were in CanWAIT status 1; 4% in LT; 14% in 2; 11% in 3; 6% in 3F; 4% in 4; and 7% in status 4F. Overall 90-day survival was 80% (95% confidence interval [CI] 75%–85%), exceeding the predicted survival by MELD scale with transplant of only 51% (CI 47%–55%). By c-statistic, CanWAIT is a clinically relevant predictor of 90-day outcomes in LT. By multivariate regression analysis, only CanWAIT status and age were found to have independent associations for short-term outcomes after LT. Interpretation: CanWAIT status stratifies LT patients better and predicts short-term outcome more accurately than MELD or CTP scores, and so should not be replaced by MELD or CTP scores. This observation should be confirmed by a prospective and multicentre study in Canada.
In most programs for wait-listing and organ allocation for liver transplantation and predicting clinical outcomes, the Child–Turcotte–Pugh (CTP) classification\(^1\) (Table 1) has been the main system used.\(^2\) It is easy to apply but uses subjective, nonstandardized parameters such as encephalopathy and ascites, leading to dependence on waiting time rather than medical urgency for liver allocation.\(^3\) In February 2002, the United Network for Organ Sharing (UNOS) adopted the Model for End-stage Liver Disease (MELD) score for prioritizing liver transplantation. This scale was originally designed to assess short-term prognosis in patients with cirrhosis needing insertion of a transjugular intrahepatic portosystemic shunt (TIPS).\(^4\) Since then, MELD scores have been found to predict short-term survival in patients awaiting liver transplant better than the previously used CTP classification.\(^5\)

In Canada, all liver transplantation programs use similar selection criteria (Box 1, Box 2) and a common allocation algorithm in transplantation (CanWAIT), with its 8 status categories (Table 2). These correlate with both short- and long-term outcomes after liver transplantation.\(^6\) CanWAIT status has never been compared with the MELD score. Therefore, we retrospectively analyzed short-term outcomes (90-day survival) of patients who had liver transplants performed at our centre by MELD and CTP scores in addition to CanWAIT status.

### Methods

#### Patient population and data collection

The study population consisted of all 228 consecutive liver transplantations performed in adults at the Queen Elizabeth II Health Sciences Centre (previously the Victoria General Hospital) in Halifax from the start of the program in 1985 until 2001, according to our selection criteria (listed in Table 2). We did not exclude cases of fulminant hepatic failure, retransplantation for nonfunction of the primary graft or technical failure, or combined transplants (6 kidney–liver and 1 heart–liver. In addition to post-transplant survival, we collected data on patients’

### Box 1. Patient selection for liver transplant

- Having an accepted indication:
  - Advanced chronic liver disease—decompensated with ascites, spontaneous bacterial peritonitis, hepatic encephalopathy, esophageal variceal bleeding, hepatorenal or hepatopulmonary syndrome, or portopulmonary hypertension with pulmonary pressure <40 mm Hg
  - Hyperacute, acute or subacute liver failure—fulfilling King’s College criteria for transplantation after liver failure from either acetaminophen toxicity or another etiology
  - Hepatocellular carcinoma—fulfilling modified Okuda’s criteria: either a single lesion no larger than 5 cm in diameter or multiple lesions (≥3) no larger than 3 cm, along with no evidence of portal vein invasion
  - Miscellaneous liver diseases
- Using no alternative form of therapy
- Having no absolute contraindications:
  - Extra-hepatic malignancy
  - Active alcohol or drug use
  - Irreversible brain damage
  - Active untreated sepsis
  - Advanced cardiopulmonary disease
  - Anatomic abnormality precluding transplantation
- Willing and able to accept the operation and comply with follow-up care

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### Table 1: Scoring* Child–Pugh–Turcotte criteria for end-stage chronic liver disease

<table>
<thead>
<tr>
<th>Parameter</th>
<th>1 point</th>
<th>2 points</th>
<th>3 points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Encephalopathy grade</td>
<td>None</td>
<td>1 or 2</td>
<td>3 or 4</td>
</tr>
<tr>
<td>Ascites</td>
<td>Absent</td>
<td>Slight</td>
<td>Moderate</td>
</tr>
<tr>
<td>INR</td>
<td>&lt;1.7</td>
<td>1.7–2.3</td>
<td>&gt;2.3</td>
</tr>
<tr>
<td>Total bilirubin, µmol/L</td>
<td>&lt;17</td>
<td>17–51</td>
<td>&gt;51</td>
</tr>
<tr>
<td>Albumin, g/L</td>
<td>&gt;35</td>
<td>28–35</td>
<td>&lt;28</td>
</tr>
</tbody>
</table>

* Classification is derived by summing points for each of the 5 parameters: Class A, 5–6 points; Class B, 7–9 points; and Class C, 10–15 points. INR = international normalized ratio.
age, sex, etiology of liver disease, and laboratory results (obtained within 24 hours prior to transplant surgery) for serum total bilirubin, serum albumin, international normalized ratio (INR) and serum creatinine. All data were retrieved as part of continuous quality improvement activity in accordance with institutional guidelines.

**MELD and CTP scores**

A patient’s MELD score is based on 3 biochemical parameters (INR, total bilirubin and creatinine concentrations in mg/dL) and the category of disease (0, if cholestatic liver disease or Laennec’s cirrhosis is present; 1, for all other causes of liver disease): \[ MELD = 11.20 \times \log(\text{INR}) + 3.78 \times \log(\text{bilirubin}) + 9.57 \times \log(\text{creatinine}) + 6.4 \times (0 \text{ or } 1), \]

depending on disease category

CTP scores were calculated from data recorded just prior to transplant surgery for each patient’s encephalopathy grade, amount of ascites, INR, total bilirubin and albumin. MELD and CTP scores were also calculated for those with fulminant liver failure, since both scores have parameters in common with King’s College criteria (Box 2) for liver transplants in acute end-stage liver disease.²

**Box 2. King’s College criteria for acute liver disease**

**From acetaminophen toxicity**

pH < 7.30, irrespective of grade of encephalopathy or international normalized ratio (INR) > 6.5 and creatinine > 300 μmol/L if in grade 3 or 4 coma

**From another etiology**

INR > 6.5, irrespective of encephalopathy grade or any 3 of the following:

- Non-A non-B hepatitis, halothane hepatitis, idiosyncratic drug reaction
- Age < 10 or > 40 years
- Jaundice-to-encephalopathy interval > 7 days
- INR > 3.5
- Total bilirubin > 300 μmol/L.

**CanWAIT status and waiting times**

Pre-transplant CanWAIT status was noted for the day the patient was called for liver transplantation, regardless of their status when they were wait-listed. Waiting time was measured in days from the date of first waitlisting to that of transplant surgery.

CanWAIT was developed as a sharing algorithm in Canada through the Canadian Liver Transplant Study (CLTS) Group, comprising the 7 adult and 4 pediatric liver-transplant programs in Canada. Patients waiting at home are listed as CanWAIT status 1 (Table 2); those with nonresectable tumours³ (such as hepatocellular carcinoma) are allotted CanWAIT status 1T. Hospitalized patients are assigned status 2, except when monitored in the critical-care facility in the hospital (status 3) or requiring mechanical ventilation (status 4). Patients with fulminant liver failure, including transplant recipients relisted for graft non-function or technical failure, are designated status 3F (off ventilation) or 4F (on mechanical ventilation). Routinely, organs are allocated and utilized regionally. High-status patients (CanWAIT status 4F, 4 and 3F, in that priority) are registered on a national wait list; donor livers are directed to recipients with the highest needs across Canada. All liver transplantation

<table>
<thead>
<tr>
<th>CanWAIT status</th>
<th>Patient criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>At home</td>
</tr>
<tr>
<td>1T</td>
<td>At home with a liver tumour</td>
</tr>
<tr>
<td>2</td>
<td>In hospital with stable condition</td>
</tr>
</tbody>
</table>
| 3              | In intensive or equivalent care facility but not requiring mechanical ventilation support, with either:  
- creatinine > 200 μmol/L or rising by > 50 μmol/L per day, or  
- grade 3 or 4 encephalopathy |
| 3F             | In intensive or equivalent care facility for fulminant liver failure but not on mechanical support, who fulfills the King’s College criteria for high risk of mortality without liver transplantation |
| 4              | In intensive requiring mechanical ventilation support; without liver transplantation, death is considered imminent |
| 4F             | In intensive requiring mechanical ventilation for fulminant liver failure, including nonfunction of a primary graft; without liver transplantation, death is considered imminent |
| 0              | On hold          |

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activities (selection, allocation and outcome) in Canada are reviewed annually by the CLTS Group, to ensure compliance.

**Outcomes**

At the end of 90 days, those alive were assigned a value of 100% for survival outcome. Those who died within 90 days, for any reason, were allotted the value 0.

**Statistical analysis**

Unpaired, 2-tailed Student’s t test and 1-way analysis of variance (ANOVA) were used for univariate analysis of baseline characteristics by outcomes. Multivariate regression analysis was performed to identify the best independent baseline characteristics associated with survival. All analyses were performed using Minitab® Release 14 statistical software package (Minitab Inc., State College, Pa.). For all tests, p <0.05 was considered to reach statistical significance.

We also used concordance (c-statistic) to assess the ability of the MELD and CTP scores or CanWAIT status to correctly stratify patients into survival versus death. The c-statistic is derived from the “area under the curve” of a receiver operating characteristic (ROC) curve; it ranges between 0 and 1.0, with 1.0 corresponding to perfect discrimination and 0.5 to what is expected by chance. By convention, a c-statistic of 0.7 or greater is considered to be clinically useful, and a value between 0.8 and 0.9 indicates excellent diagnostic accuracy.

**Results**

**Demographics**

Table 3 describes the overall characteristics of our study population. Eight recipients (4%) underwent transplant for hepatocellular carcinoma (CanWAIT status 1T; Table 4). Thirty transplants (13%) were performed for fulminant liver failure (CanWAIT statuses 3F and 4F). The mean MELD score in our cohort was 18 (SD 12), whereas the mean CTP score was 10 (SD 3; Table 3).

**Patient and graft survival**

The overall 90-day survival was 80% (95% confidence interval [CI] 75%–85%); predicted 90-day survival without liver transplant by MELD scale was only 51% (CI 47%–55%; p <0.0001). Table 3 summarizes the differences in baseline characteristics by transplant outcomes. There were significant correlations between short-term outcomes after liver transplantation and all 3 variables (MELD and CTP score and CanWAIT). The 90-day survival for patients listed as CanWAIT status 1 was 90%; 1T, 75%; 2, 79%; 3F, 77%; 4F, 65%; 3, 63%; and status 4, 40% (p <0.001, ANOVA). Transplant outcomes by CTP classification were class A, 92%; class B, 89%; and class C, 71% (p =0.002, ANOVA). For MELD scores under 10, survival with good graft function was 90%; for those above 39, 59%; and by categories, MELD score <5.0, 91%; 5.0–14.9, 87%; 15.0–24.9, 79%; 25.0–34.9, 67%; and ≥35, 61% (p =0.003, ANOVA). Stepwise regression of 90-day survival was calculated on 8 predictors (age, wait time, albumin, total bilirubin, creatinine, MELD score, CTP score, and CanWAIT status) using a sample size of n =228. The best independent predictors associated with 90-day survival were CanWAIT status (coefficient –1.08, p <0.001) and age (coefficient –0.776, p =0.001).
MELD and CTP scores were both intended as prognostic indicators of patients with chronic liver disease and not those with acute liver failure or non-function of a graft. Nonetheless, reanalysis excluding status 3F and 4F patients did not alter the findings, nor did excluding the first 20 cases (data not shown).

Prediction model with c-statistic

Area under the ROC curves (Fig. 1) was 0.67 for MELD scores, 0.65 for CTP scores, and 0.71 for CanWAIT status. Although c-statistics for the 3 predictors of 90-day survival were found to be comparable, only the value for CanWAIT status exceeded 0.7, indicating that clinically it is the most useful.

Interpretation

This study shows that CanWAIT is a clinically relevant predictor of 90-day outcomes after liver transplantation. By multivariate analysis, CanWAIT status and age were found to be the best independent associations for short-term posttransplant outcomes; MELD and CTP scores did not fare as well.

With an increasing gap between number of available organs and of patients on the liver transplant wait list, there has been interest in developing models to prioritize patients better for liver transplantation. The MELD score is a considerable advance in organ allocation since it makes use of readily available results of laboratory tests reflecting the severity of liver disease to predict posttransplant survival. Statistically, the MELD score has been shown to have an excellent discriminant function (c-statistic = 0.87) for predicting 3-month mortality. In this study, however, CanWAIT status appears to be better in identifying short-term survival in a single transplant centre.

Because the MELD score predicts short-term survival, we hypothesized that any association between MELD score and liver transplantation outcome would be evident in the first 90 days after transplant. But MELD scores at time of transplant were not better than CanWAIT status for prediction of 90-day survival. This could be due to the operational learning curve, with some of the earlier graft losses being secondary to technical problems, resulting in poor correlation between MELD scores and graft loss rate. Our results did not change when we excluded the first 20 liver transplantation at our centre. Inclusion of transplants for fulminant liver failure might be another reason that the MELD score did not perform as well as reported in the literature. However, our results did not change when patients in CanWAIT status 3F and 4F were removed from the analysis. A recent study from the Mayo Clinic suggests that MELD score may be useful for prioritiza-
tion of a subset of candidates with fulminant hepatic failure. This is not unexpected, since King’s College criteria for liver failure, like MELD score, uses INR, total bilirubin and creatinine as important factors. Table 1 also features hepatic encephalopathy, INR and bilirubin as important predictors for CTP scores, just as for King’s College criteria (Box 2). We tried to broaden the use of these prediction scores by including our entire experience with 228 consecutive liver transplants.

This single-centre retrospective analysis does not take into account those patients who died on the waiting list, which would be an interesting analysis by itself, but difficult to accomplish in retrospective analysis.

Conclusion

In spite of its shortcomings, this study illustrates that the new scoring system is not necessarily superior to the MELD score. CanWAIT status, however, stratifies liver transplant patients better and predicts short-term outcomes more accurately. Since hospitalization patterns may vary from centre to centre, our findings need to be confirmed by a prospective and multicentre study including patients on the waiting list. Until those results become available, there is no need to replace CanWAIT status by either MELD or CTP score for wait-listing patients for liver transplantation in Canada.

References


Medical subject headings: waiting lists, outcomes assessment, liver transplantation

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