

Running head: HOSPICE CRITERIA FOR CIRRHOSIS PATIENTS

A Retrospective Analysis of the Current Hospice Criteria for Decompensated Cirrhosis Patients
Compared to the MELD-Na Score

by

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Abstract

A recent concern is that many patients with end-stage liver disease (ESLD) do not meet the eligibility requirements to receive adequate and timely hospice care referral. Accurately predicting 6-month mortality in this population is a barrier that many physicians face. The model for end-stage liver disease + serum sodium (MELD-Na) score has been established to predict 6-month mortality in patients with ESLD and may be a useful tool to help refer these patients to hospice care. A retrospective analysis was conducted on 402 patients with decompensated cirrhosis to determine how well hospice criteria are at predicting death. The MELD-Na score was then analyzed and compared to the current hospice criteria to see which method was more accurate at predicting death. Area under the receiver operating characteristic (AUROC) curve for the prediction of 6-month mortality of the current hospice eligibility criteria for decompensated cirrhosis patients: 0.5007; ($p =$ not significant) and AUROC for MELD-Na score: 0.7141; ($p < 0.001$). The current hospice eligibility criteria are poor predictors of 6-month mortality among patients with ESLD. The MELD-Na score is more accurate at 6-month mortality than the current hospice eligibility criteria and may be a useful guide to help physicians refer end-stage liver disease patients to hospice care.

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Introduction

Since its establishment in 1982, the Medicare Hospice Benefit has been providing comfort and support services to terminally ill patients and their families. The fundamental goal of hospice care is the abatement of psychological, physical, and spiritual suffering in patients who are terminally ill. A beneficiary is eligible to receive hospice care when they are certified as having a life expectancy prognosis of 6 months or less, as predicted by a physician and a hospice director. In addition, patients must also choose to forgo life sustaining treatment for their terminal illness (Social Security Act).

In comparison to standard medical care, hospice services yield greater satisfaction in care and better fulfill needs for patients and families in the last months of life (Moore & von Gunten, 2010; Teno et al., 2004). However, even with substantial benefits of hospice care for patients with terminal illnesses many patients do not meet the eligibility requirements. This may cause patients to be referred late, near the last days of their lives. Unfortunately, barriers exist that prevent patients from receiving adequate hospice care and late entry is most predominant among non-cancer patients (Johnson, 1998).

One group of patients in particular that face hindrances from receiving adequate and timely hospice care referral are end-stage liver disease (ESLD) patients. ESLD is the twelfth leading cause of death in the United States; responsible for more than 30,000 deaths each year (Kochanek, Xu, Murphy, Minino, & Kung, 2011). While the number of deaths attributable to ESLD has been increasing in recent years, less than 2% of all patients admitted to hospice care were classified with liver disease as their primary diagnosis (NHPCO's Facts & Figures: Hospice Care in America, 2011). A recent concern is that identifying hospice eligibility for many patients with ESLD is not forthright and may result in continued poor referral rates (Antaki & Lukowski,

2007; Fox et al., 1999). A better method for determining hospice eligibility for patients with ESLD needs to be found.

Background

Liver cirrhosis is the end-stage for many chronic liver diseases. Common causes of cirrhosis include but are not limited to hepatitis B or C, excessive alcohol consumption, inherited genetic disorders, and environmental factors. Cirrhosis is characterized by the histological presence of necrosis and regenerative nodules surrounded by fibrosis throughout the liver which is caused by chronic injury (Anthony et al., 1978; Garcia-Tsao, Friedman, Iredale, & Pinzani, 2010). This scarring prohibits blood from flowing through the liver, and pressure accumulates in the portal vein, known as portal hypertension. Complications of portal hypertension include symptoms of ascites (fluid accumulation in the abdominal cavity), bleeding varices (blood vessels in the esophagus), hepatic encephalopathy (confusion), or jaundice (yellowing of the eyes or skin); all of which are indicative of decompensated cirrhosis (Sanyal, Bosch, Blei, & Arroyo, 2008). Liver transplantation is the only chance for survival for all patients with ESLD, yet the demand for livers significantly surmounts supply.

The model for end-stage liver disease (MELD) was originally conceived to predict 3-month mortality in patients undergoing a procedure to treat refractory bleeding esophageal varices known as a transjugular intrahepatic portosystemic shunt (TIPS) (Rossle, Siegerstetter, Huber, & Ochs, 1998). Conversely, the MELD has been confirmed to be a valuable predictor of death in patients with ESLD without a TIPS procedure. Currently, the MELD is utilized to help predict short term mortality for patients with ESLD and prioritize organ allocation on the liver transplant waiting list (Kamath et al., 2001). The MELD is measured using total bilirubin, creatinine, and international normalized ration (INR) for prothrombin time. These laboratory values are calculated using an algorithm to produce a numeric score. Scores range from 5 to 40, with 40 being demonstrative of the most serious stage of ESLD. In a recent study, the MELD

score has been shown to correspond well to hospice survival rates in cirrhosis patients without hepatocellular carcinoma, and that the MELD score may be used to assist physicians project survival in this population (Antaki et al, 2007).

Studies have shown that in addition to the MELD specifications, serum sodium (Na) is a valuable adjoining predictor of mortality for patients on the liver transplant waiting list (Ruf et al, 2005). Low serum sodium, or hyponatremia, has been shown to be associated with severe complications of cirrhosis; such as ascites, hepatorenal syndrome, and liver-related mortality. While the MELD is used to predict 3-month mortality in ESLD patients, the MELD-Na system was established to predict 6-month mortality in cirrhosis patients awaiting liver transplantation. An advantage of the MELD-Na score is that it produces a more accurate survival rate prediction than the MELD score alone (Biggins et al., 2006). In particular, the MELD-Na score is more predictive of the risk of death in severe patients; especially those with a MELD score greater than 20 (Kim et al., 2008).

Purpose of the Study

The purpose of this research study was to ascertain the accuracy of hospice eligibility criteria at predicting death in patients with decompensated liver disease, and to determine whether the MELD-Na score would be a better instrument for qualifying this population to receive hospice care.

Justification and Significance

According to the National Hospice Organization, to be eligible for the Medicare Hospice Benefit it is required that a patient have a prognosis of 6 months or less to live (Stuart et al., 1996). In addition, for patients with ESLD, laboratory values must include both a prothrombin time elevated more than five seconds over control or an INR greater than 1.5, as well as a serum albumin that is less than 2.5 g/dL. Patients must additionally exhibit one or more of the following conditions: ascites despite diuretics, spontaneous bacterial peritonitis, hepatorenal syndrome, hepatic encephalopathy despite treatment, or reoccurring bleeding esophageal varices regardless of therapy (Stuart et al., 1996).

A plurality of patients enrolled into hospice care are enrolled somewhat late in the duration of their terminal condition (Christakis & Escarce, 1996). The median length of stay for patients in hospice care is approximately 21 days. However, almost 33% of patients are directed to hospice within the last week of life, while yet another 10% are directed to hospice within only 24 hours of death. It is recommended, though, that for patients and families to be provided with adequate physical and emotional support the patients should receive hospice services for at least 3 months (Iwashyna, & Christakis, 1998).

In order to receive hospice care, a patient's physician and director of hospice must verify that the patient has a life expectancy of 6 months or less. Unfortunately, predicting patient survival is a subjective decision based on numerous factors that may change before and after hospice enrollment. A study recently reported that the currently used clinical prediction criteria are not effective in identifying ESLD patients with a survival prognosis of 6 months or less (Fox et al., 1999). As such, one of the biggest barriers for hospice referral has been the difficulty in accurately predicting survival in these patients.

Although hospice utilization has been increasing in recent years, only approximately 20% of terminally ill patients receive hospice care services (United States General Accounting Office, 2000). Predicting this estimation can be difficult for some physicians and they may be hesitant to predict a patient's death (Brickner, Scannell, Marquet, & Ackerson, 2004). Physicians were surveyed to gather information on their perceptions of hospice utilization, referral patterns, and their observed barriers. Of the physicians, 37% reported difficulty in predicting 6-month mortality correctly as the most common obstacle for hospice referral. Deficiency of knowledge about patient hospice eligibility requirements was also reported by physicians (Brickner et al., 2004).

These criteria currently utilized to predict which patients with liver disease are eligible for hospice care have been shown to be ineffective and may deprive many patients full access to the benefits of hospice care (Fox et al., 1999). Indeed, current hospice eligibility criteria are most accurate in patients with incurable metastatic cancer due to the predictable deterioration in both weight and function near death (Morris, Suissa, Sherwood, Wright, & Greer, 1986). With ESLD, there is a more variable progression towards death (Lynn, Harrell, Cohn, Wagner, & Connors, 1997) and is therefore more difficult to predict utilizing current hospice criteria. More research is needed to explore the predictive value of other measures.

Research Hypothesis

The hypothesis for this study was that the MELD-Na score would be more accurate than current hospice criteria at predicting 6-month mortality among patients with decompensated cirrhosis.

Methodology

Study Design

A retrospective analysis was conducted on a pre-existing cohort of 402 patients with decompensated cirrhosis to determine how well hospice criteria are at predicting death, and was then compared to the MELD-Na. Current hospice criteria and MELD-Na were established at the time of hospital discharge, and the key follow-up interval was 6 months after hospital discharge. Duration of follow-up for each patient was determined by the outpatient medical record, and those lost to follow-up before 6 months were excluded from the analysis.

Study Type

This study type was a quantitative research utilizing statistical analysis to compare the effectiveness of hospice eligibility criteria and the MELD-Na score at predicting death in patients with cirrhosis.

Patient Population

The patient population included in this retrospective analysis was a pre-existing cohort of 402 ESKD patients. Subjects included adults 18 years of age and older, whom were discharged from the University of Michigan hospital between January 1, 2007 and July 1, 2009 following hospitalization due to cirrhosis complications. The patients were identified by their diagnoses at discharge using the International Classification of Disease-9 (ICD-9) codes or common procedure terminology codes as related to cirrhosis: alcoholic cirrhosis (571.2), ascites (789.5), biliary cirrhosis (571.6), cirrhosis not due to alcohol (571.5), esophageal varices with bleeding (456.0, 456.2), hepatic encephalopathy (572.2), hepatocellular carcinoma (155.0), hepatorenal syndrome (572.4), paracentesis (54.91), portal hypertension (572.3), spontaneous bacterial peritonitis (567.23), or other sequelae of chronic liver disease (572.8).

These patients exhibited at least one of the following complications during their hospitalization: 1) ascites requiring paracentesis, 2) hepatic encephalopathy, defined as altered mental status diagnosed as hepatic encephalopathy in the chart and improved after treatment with lactulose, 3) renal failure in the presence of ascites, defined as rise in serum creatinine by 0.5 mg/dL (to >1.5 mg/dL), with ascites documented on exam or ultrasound, or admitted on diuretics for the treatment of ascites, 4) spontaneous bacterial peritonitis, defined as >250 polymorphonuclear cell count in the ascitic fluid, or 5) variceal hemorrhage, defined as a clinically substantial gastrointestinal bleed (tachycardia, hypotension, requirement for blood transfusion, or >2g drop in hemoglobin) and varices seen on endoscopy (Volk, Tocco, Bazick, Rakoski, & Lok, 2012).

Data Gathering Procedures

Data such as patients' age, gender, discharge diagnosis, laboratory values, and MELD scores were collected from the pre-existing data set of decompensated cirrhosis patients. This was first acquired by reviewing CareWeb; one of The University of Michigan's main electronic clinical information systems for patient medical records. Patients' status (alive or deceased) was also obtained using CareWeb. The Mayo Clinic's MELD-Na calculator was utilized to calculate patients' MELD-Na score (Mayo Clinic, 2008). The equation is as follows:

$\text{MELD} + 1.59 \times (135 - \text{Na})$, with minimum and maximum Na of 120 and 135 mEq/L, respectively (Biggins et al., 2006).

Measures to Insure Safety and Confidentiality

Subjects were identified and referenced by a study identifying number with restricted access to only those who are affiliated with the research. Only the data appropriate to the research proposal was extracted and used. All data was stored on a password protected

University of Michigan server. A waiver of informed consent and HIPPA authorization were approved by the University of Michigan's Institutional Review Board, as well as the College of Health and Human Services' Human Subjects Review Committee at Eastern Michigan University.

Data Analysis

The primary dichotomous outcome variable was whether the patient was alive or dead at 6 months after hospital discharge. The statistical analysis involved calculating specificity and sensitivity as well as positive and negative likelihood ratios for the current hospice criteria. Since MELD-Na is a continuous variable, analysis of the receiver operating characteristics (ROC) curve was performed to determine the optimal cutoff which maximized sensitivity and specificity for predicting 6-month mortality. The accuracy of the current hospice criteria and the MELD-Na score was compared to the concordance statistic from logistic regression.

Results

Demographics of the Study Cohort

The original study cohort comprised of 402 decompensated cirrhosis patients. Due to lack of follow-up in the medical charts, 40 patients were excluded from the analysis because living status at 6 months after discharge could not be ascertained. Thus, in total, the analysis was conducted on 362 patients. Demographic and clinical characteristics of this patient cohort are summarized in Table 1. Of these 362 patients included in the analysis, 255 were alive, 107 were deceased, and 47 underwent a liver transplantation during the course of the 6 months. The data was analyzed with and without the transplant patients and no significant differences were observed and therefore these 47 patients were included in the final results.

Table 1. Demographic and clinical characteristics of decompensated cirrhosis patients

Median age, years	54 (range 19-88)
Gender (%)	57 female
Race/ethnicity (%)	
White	83
Black	4
Hispanic	8
Other	5
Etiology of liver disease (%)	
Alcohol	30
Viral hepatitis	36
Cryptogenic/fatty liver	17
Other	17
Median MELD-Na score	19 (range 6-40)
Cirrhosis complications during hospitalization (%)	
Ascites requiring paracentesis	52
Hepatic encephalopathy	35
Variceal hemorrhage	20
Spontaneous bacterial peritonitis	14
Renal failure with ascites	25

Note: MELD-Na = Model for End-Stage Liver Disease + serum sodium.
N=362

Current Hospice Eligibility Criteria Analysis

Patients in the study cohort were subdivided into four groups in order to calculate the sensitivity and specificity for current hospice eligibility criteria. The sensitivity yields a value called the true positive rate. For this analysis, the sensitivity shows the percentage of all patients who died and were determined to be eligible for hospice care utilizing the current hospice criteria. The specificity, on the other hand, provides a value called the true negative rate. In this analysis the specificity represents the percentage of all patients who lived and were not eligible for hospice care based on current hospice criteria. Table 2 depicts the number of patients in each category used to calculate both the sensitivity and specificity.

Table 2. Hospice Eligibility Categories

True Positive	Patients who died and were eligible for hospice	14
False Positive	Patients who lived and were eligible for hospice	33
False Negative	Patients who died and were not eligible for hospice	93
True Negative	Patients who lived and were not eligible for hospice	222

To calculate the sensitivity and specificity, Equation 1 and Equation 2 were used, respectively.

Equation 1. Sensitivity for current hospice eligibility

$$\text{Sensitivity} = \frac{\text{True Positive}}{\text{True Positive} + \text{False Negative}} = \frac{14}{14 + 93} = 0.13$$

Equation 2. Specificity for current hospice eligibility

$$\text{Specificity} = \frac{\text{True Negative}}{\text{True Negative} + \text{False Positive}} = \frac{222}{222 + 33} = 0.87$$

A sensitivity of 0.13 indicates that only 13% of patients who died were correctly identified as having a life expectancy of 6 months or less. A specificity of 0.87 indicates that 87% of patients who lived were correctly identified as having a life expectancy of more than 6 months.

In addition, both the positive and negative likelihood ratios were calculated employing Equation 3 and Equation 4, respectively.

Equation 3. Positive likelihood ratio for current hospice eligibility

$$\text{Positive Likelihood Ratio} = \frac{\text{Sensitivity}}{1 - \text{Specificity}} = \frac{0.13}{1 - 0.87} = 1$$

Equation 4. Negative likelihood ratio for current hospice eligibility

$$\text{Negative Likelihood Ratio} = \frac{1 - \text{Sensitivity}}{\text{Specificity}} = \frac{1 - 0.13}{0.87} = 1$$

Both likelihood ratios are equal to one, suggesting that the current hospice eligibility criteria have little practical diagnostic significance. Also, the area under the receiver operating characteristic (AUROC) curve for current hospice eligibility was calculated using logistic regression and was found to be 0.5007; a value near the area under the line of no discrimination, indicative of a mere guess. This AUROC calculation had a p-value of 0.97. From statistics, this p-value is not below the significance level of 0.05 and therefore it can be said that the current hospice eligibility criteria is a poor predictor of death.

MELD-Na Analysis of AUROC

Sensitivity and 1-Specificity were calculated for the MELD-Na eligibility data series and plotted as a ROC curve (Figure 1). In statistics, the ROC curve graph is a method to help visualize and select classifiers based on their performance. The point in the ROC space that represents 100% sensitivity and 100% specificity would be in the upper left corner at coordinate (0,1). The AUROC for MELD-Na eligibility was found to be 0.7141, a value greater than the AUROC for current hospice eligibility indicating that it is a better method for predicting death in ESLD patients. In addition, with a p-value less than 0.001, the MELD-Na scores are a statistically significant predictor of death.

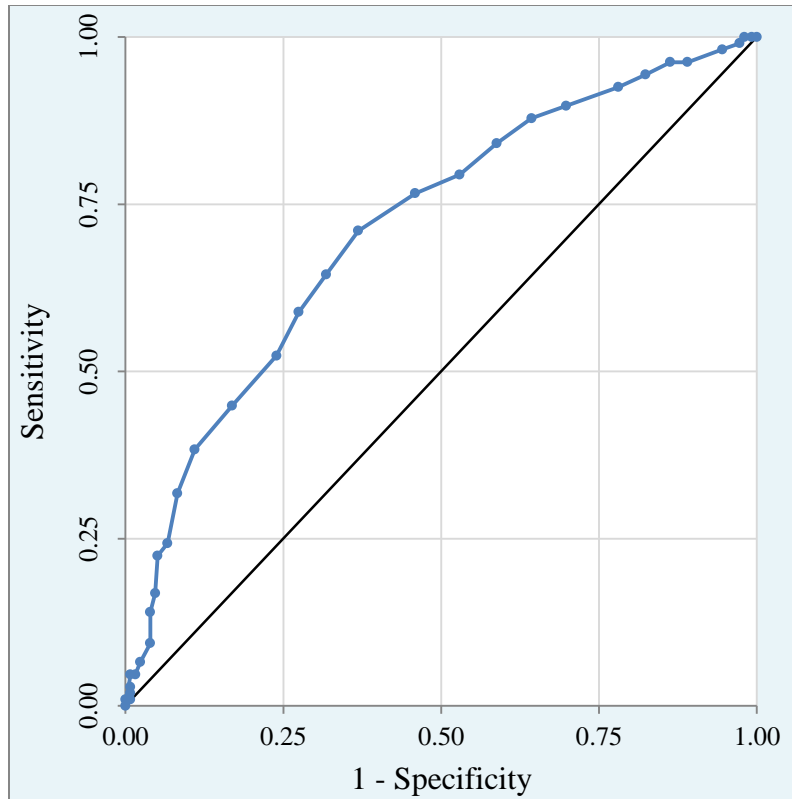


Figure 1. Receiver operating characteristic curve for MELD-Na scores to predict 6-month mortality in decompensated cirrhosis patients

MELD-Na Optimal Sensitivity Cut-offs

In addition to generating the ROC curve, three sensitivity cutoffs were selected to represent different true positive rates for hospice eligibility. These cutoffs were chosen to be at 90%, 75%, and 50% sensitivity. From the data, the nearest to each of these sensitivities were 90%, 77%, and 52%. In Table 3 the sensitivities and their corresponding MELD-Na scores are shown, as well as the specificities, positive likelihood ratios, and negative likelihood ratios.

Table 3. MELD-Na sensitivity cutoffs for hospice eligibility

Sensitivity (%)	MELD-Na (and greater)	Specificity (%)	Positive Likelihood Ratio	Negative Likelihood Ratio
90	15	30	1.29	0.34
77	19	54	1.67	0.43
52	23	76	2.19	0.63

Note: MELD-Na = Model for End-Stage Liver Disease + serum sodium.

Of the three, the 90% sensitivity MELD-Na score would maximize the number of patients eligible for hospice that may need it. However, it also has a high false positive rate, resulting in more patients that may not need hospice being classified as eligible. Both the positive and negative likelihood ratios were calculated for these three cutoffs as well and are shown in Table 3. The data illustrates, as expected, that as the MELD-Na score for hospice eligibility increases, so too does the likelihood that a patient will die if they are deemed eligible for hospice.

From the ROC curve, it was concluded that the optimal cutoff for hospice eligibility is a MELD-Na of 20, as this is the point located furthest away from the line of no discrimination. This cutoff has the greatest balance between having a higher number of true positives while also having a lower quantity of false positives. At this MELD-Na score, the sensitivity is 71% while the specificity is 63%.

Discussion

The data shows that the existing hospice eligibility criteria for end-stage liver disease patients in this study cohort are not adequate at predicting death. With a sensitivity of only 13%, 87% of people that could have benefitted from the services of hospice were not eligible to receive them. However, with a specificity of 87%, only 13% of people that did not need hospice services were eligible for them. This shows that the current hospice eligibility criteria are very stringent, and may overlook many patients that could have benefitted from the services. In addition, the AUROC of 0.5007 indicates that current hospice eligibility is merely a random guess at whether a patient will be alive at 6 months.

The current hospice eligibility is overlooking a large proportion of patients in need of hospice care due to its stringent criteria. This shows the importance of having a new set of criteria that can better predict death in ESLD patients.

The MELD score was first reported by Medici et al. (2008) as a potential tool in helping to guide hospice referrals. They found a significant association between the MELD score and length of stay in hospice care. More recently, adding serum sodium level to the MELD score has been shown to improve mortality prediction. The MELD-Na is an objective and reliable metric for estimating 6 month mortality in decompensated cirrhosis. The bivariate regression analysis shows that the MELD-Na scores are more accurate than current hospice eligibility criteria at predicting death for decompensated cirrhosis patients in this study cohort. As indicated by the AUROC, the MELD-Na scores have a fair/moderate discriminatory ability, superior to that of the current hospice criteria. Utilizing MELD-Na scores to determine hospice eligibility could grant more patients access to hospice care.

An additional benefit in using the MELD-Na score for hospice referral is that it is dependent on objective variables, whereas the current hospice eligibility criteria are based on subjective measures such as survival predictions from physicians. Physicians experience difficulty with providing their best judgment in estimating life expectancy of less than 6 months. Using a more objective metric such as the MELD-Na score, physicians may be able to make better prognostic judgments about mortality which may contribute to better and timely referral rates.

However, this study suggests that no specific MELD-Na cutoff should be used for hospice referral. Indeed, while the results show that certain MELD-Na scores are a good predictor of death, it is still important to take into account other factors that the MELD-Na does not consider. By utilizing any specific cutoff, patients that could benefit from hospice benefits may not be considered eligible due to not having a high enough MELD-Na score. It is in this regard that physician subjectivity still plays an important role in referring patients to hospice. It is suggested, though, that the MELD-Na scores be used as a guide to assist physicians in the hospice referral process.

Limitations

By virtue of the study's retrospective analysis and single center characteristics various limitations are present. First, the sample included only patients who were hospitalized at the time of entry. However, relatively few patients die of liver disease without experiencing hospitalization, so this is a minor limitation. Secondly, 40 patients were excluded from the final analysis because their living status could not be determined at 6 months. Also, most patients included were white, so further studies should include a more diverse racial and socioeconomic mix.

In addition, this study does not recommend a specific cutoff for a MELD-Na score at which point patients should be referred to hospice care. It is instead argued that, while the MELD-Na score can be a good predictor of death, it should be used in conjunction with other health indicators to determine hospice eligibility. Perhaps future studies could take into account additional variables such as laboratory values indicating declining health common in ESLD patients or recent episodes of decompensation in order to develop a range of MELD-Na scores that could be utilized to determine hospice eligibility.

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