



# The Evolution of the MELD Score and Its Implications in Liver Transplant Allocation: A Beginner's Guide for Trainees

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## INTRODUCTION

Liver transplant allocation policies have undergone significant evolution over the past several years with the goal of increasing equity, reducing disparities, and optimizing outcomes. The United Network of Organ Sharing (UNOS) regulates organ transplantation in the United States. Understanding the key changes in transplant allocation policies is critical for trainees to understand liver transplantation, its implications, and existing pitfalls. This editorial aims to concisely review the history of the model for end-stage liver disease (MELD) score and its evolution because it relates to liver transplant allocation.

## PRE-MELD TRANSPLANT PRIORITIZATION

Understanding the evolution of MELD is key to learning transplant allocation policy. Before the inception of the MELD score, priority on the liver transplant waiting list was based on hospitalization status, time on the waitlist, and eventually the Child-Turcotte-Pugh (CTP) score and its iterations. However, these methods of prioritization allowed for manipulation of the system through loopholes, which led to unfair prioritization of patients on the waiting list. For example, it allowed for patients to be admitted into the hospital to increase their priority on the waiting list even without a true indication for admission. In addition, the subjective components of the CTP score, namely, the presence and degree of ascites or encephalopathy, allowed for inappropriately scoring the severity of a patient's condition to benefit his or her position on the waitlist.

In 2000, the Final Rule, which was devised by the United States Department of Health and Human Services, sought to ensure justice by allocating organs equitably across geographic regions and prioritizing transplantation based on medical urgency defined by objective standardized criteria.<sup>1</sup> The Final Rule prompted the need for a validated objective score for liver transplant prioritization with the aims of eliminating subjective bias.

## MELD SCORE IN TRANSPLANT ALLOCATION

The MELD score was first developed in 2001 to predict survival in cirrhotic patients undergoing transjugular intrahepatic portosystemic shunt.<sup>2</sup> Its use was broadened to predict severity of disease and survival in cirrhosis even more accurately than the CTP score.<sup>3</sup> Its objectivity and increased accuracy prompted UNOS to approve the use of MELD for transplant allocation and prioritization in 2002.<sup>4</sup> MELD increased rates of transplantation for patients with more severe illness and reduced waitlist mortality while maintaining posttransplant survival.<sup>5</sup> Soon after, the sodium (Na) level was found to be an independent predictor of mortality in cirrhosis<sup>6</sup> and was then incorporated into the MELD score, further enhancing its ability to predict mortality.<sup>7</sup> Although the MELD-Na score is the most widely adopted prediction model in the field of liver transplantation, it carries inherent limitations.

## LIMITATIONS TO MELD-NA SCORE

Despite its improved predictive ability of mortality in cirrhosis, MELD-Na still has limitations. It is a dynamic score that changes over time. Recent studies demonstrate a reducing predictive ability of the MELD-Na score with the changing epidemiology of liver diseases. The MELD-Na score was developed when hepatitis C was the most common indication for transplantation. As the prevalence of hepatitis C declines and the incidence of nonalcoholic fatty liver disease and alcohol-associated liver disease increases, the discriminative ability of MELD-Na to predict mortality has diminished.<sup>8</sup>

The MELD-Na score also disadvantages certain populations. The inclusion of serum creatinine into the score imprecisely reflects true renal function.<sup>9,10</sup> Individuals with lower muscle mass (ie, sarcopenia) may have lower serum creatinine levels inaccurately reflecting their true renal function.<sup>11</sup> Similarly, women have less muscle mass compared with male counterparts and, therefore, have reduced creatinine levels disadvantaging their MELD-Na score prioritization on the waitlist.<sup>12</sup> In fact, 1 study of over 90,000 participants demonstrated that women were 20% less likely to be transplanted than men despite having a higher mortality.<sup>13</sup> In addition, the cutoff of serum creatinine level in the MELD-Na score has been called into question because it caps at 4 mg/dL implying similar mortality among those with higher creatinine values and regardless of whether they are on dialysis.<sup>14</sup>

The MELD-Na score was developed to predict mortality in decompensated cirrhosis but does not accurately predict risk in those with acute-on-chronic liver failure (ACLF). ACLF is a distinct entity characterized by systemic inflammation and the development of organ failures leading to increased mortality without liver transplantation.<sup>15-17</sup> In fact, ACLF grade 3 has been shown to have higher mortality compared with patients listed as status 1a, independent of their MELD score.<sup>18</sup> Despite this, those with ACLF grade 3 are less likely to get transplanted. Unfortunately, as its prevalence rises in the United States, there is increasing concern with MELD's ability to capture mortality risk in patients with ACLF, which may continue to disadvantage ACLF grade 3 patients who carry a 1-year mortality of 90%.<sup>19</sup> Improved prognostic models for predicting outcomes of ACLF are needed.

## IMPROVING THE MELD SCORE WITH MELD 3.0

Many investigators have aimed to improve the prediction of the MELD-Na score because of its existing limitations. Models, including but not limited to MELD-lactate and MELD-Na with transient elastography (TE), were devised to improve prediction of mortality with the shifting landscape of liver disease.<sup>20-22</sup> One iteration of the MELD-Na score has particularly stood out.

In 2021, Kim et al developed the MELD 3.0 score with the goal to optimize the prediction of the MELD-Na score using contemporary data.<sup>23</sup> The final model, which included variables for female sex and serum albumin, demonstrated improved discrimination (C-statistic of 0.869 vs 0.862,  $P < 0.01$ ), correctly reclassified 8.8% of patients to a higher MELD score improving their chances of transplantation, particularly in women, and decreased waitlist death compared with MELD-Na. The MELD 3.0 reliably addresses sex disparity of the current MELD-Na score. To this date, discussions by UNOS to implement the MELD 3.0 for prioritization of liver transplantation are underway.

The advent of the MELD score has revolutionized liver transplant allocation. The MELD score accurately predicts 90-day mortality risk in patients with cirrhosis and provides the first objective criteria to equitably prioritize patients on the liver transplant waiting list. However, as the epidemiology of liver disease shifts, the MELD score is losing its predictive ability. In addition, the current score disadvantages certain populations, particularly women, further limiting its use.

Although the development of MELD and MELD-Na serves as a robust scientific discovery, improved iterations of the score are needed. The MELD 3.0 may in fact serve as the future score that helps us more reliably predict mortality in cirrhosis in the contemporary era while also providing fair and equitable liver transplant allocation across different populations. Understanding the implications of key liver transplant allocation policies is imperative to the trainee's education.

## DISCLOSURES

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