



Model for End-stage Liver Disease (MELD) score and liver transplant: benefits and concerns

Florencia I. Aiello, Magdalena Bajo, Fernanda Marti, Adrian Gadano, Carlos G. Musso

Human Physiology Department, Instituto Universitario del Hospital Italiano de Buenos Aires, Argentina

Correspondence to: Carlos Guido Musso, MD, PhD. Human Physiology Department, Instituto Universitario del Hospital Italiano de Buenos Aires, Argentina. Email: carlos.musso@hospitalitaliano.org.ar.

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The Model for End-stage Liver Disease (MELD) score was developed as a simple, and more objective hepatic score compared to Child-Pugh. It accurately predicts short-term mortality on the liver transplant waiting list, and its three variables: serum bilirubin, creatinemia, and international normalized ratio, highlight the prognostic significance of the interactions between liver and renal functional variables in cirrhotic patients. Recently, MELD alternative forms (sodium MELD, and corrected creatinine MELD), and its combination with estimated glomerular filtration rate (eGFR), have been proposed as more reliable markers. The MELD score has been widely validated in different populations of cirrhotic patients, but it has been suggested that creatinine weighs too heavily on this score. Conclusion: despite some concerns, MELD score is currently useful for guiding liver transplant allocation.

For many decades the Child-Pugh score has been the main prognostic tool for cirrhotic patients. This score is based on five variables: ascites, encephalopathy, serum bilirubin, serum albumin and prothrombin time, which was empirically selected, and has been proved to be a reliable prognostic tool in many clinical situations (1,2). However, the Child-Pugh score has the limitations of the subjective interpretation of ascites and encephalopathy. Thus, the Model for End-stage Liver Disease (MELD) score was developed as a simple, and more objective hepatic score compared to Child-Pugh score (*Table 1*) (1-3). The MELD score accurately predicts short-term mortality on the liver transplant waiting list. The three variables included by this score, which are two hepatic (serum bilirubin and

one international normalized ratio) and one renal (serum creatinine), highlight the prognostic significance of the interactions between liver and renal functions in cirrhotic patients (*Table 1*) (1-5). It is worth mentioning that since MELD score was introduced, increased utilization of combined kidney and liver transplants without a significant change in post-transplant survival has been reported (3-6).

Recently, MELD-Na has been proposed as an alternative to MELD for liver transplant allocation due to the inverse association between serum sodium and short-term survival on the waiting list (*Table 2*) (4,5). Even though, the MELD score is the criterion to prioritize patients for liver allocation, the presence of ascites (and its severity) is a well-known determinant of glomerular filtration rate (GFR) due to hemodynamic mechanisms. In practice, a MELD score of 15 is now considered as the limit above which a liver transplantation should be considered (except when hepatocarcinoma is present) (6-9). Even though, the MELD score has been widely validated in different populations of cirrhotic patients, and serum creatinine has a significant prognostic value in this group, even better than liver functional markers themselves (1,10,11), it has been suggested that creatinine weighs too heavily on this score, being a variable which has some concerns, such as (1,10-16):

- (I) serum creatinine is an inaccurate renal functional marker in the majority of cirrhotic patients since creatinine generation and excretion are usually modified in cirrhotic individuals. Since creatinine is synthesized in the liver, any cause of hepatic parenchymal dysfunction will reduce its production,

Table 1 MELD, MELD-Na and MELD-corrected creatinine scores

MELD = $3.8 \log_e [\text{bilirubin (mg/dL)}] + 11.2 \log_e [\text{IRN}] + 9.6 \log_e [\text{creatinemia (mg/dL)}] + 6.4$

MELD-Na = MELD + 1.59 (135 – Na) with maximum and minimum Na of 135 and 120 mmol/L, respectively

MELD-corrected creatinine = $3.8 \log_e [\text{bilirubin (mg/dL)}] + 11.2 \log_e [\text{IRN}] + 9.6 \log_e [1 + \text{creatinemia (mg/dL)}] + 6.4$

MELD, model for end-stage liver disease; IRN, international normalized ratio.

Table 2 The 3-month survival for each MELD score

3-month mortality, %	MELD score
1.9–3.7	<9
6–20	10–19
19.6–45.5	20–29
52.6–74.5	30–39
71–100	>40

MELD, model for end-stage liver disease.

leading to a markedly lower serum creatinine levels compared to general population (11,13);

- (II) the muscle mass, protein intake, age, gender and ethnicity, can also influence serum creatinine levels. Moreover, there is creatinemia fluctuation in those cirrhotic patients with refractory ascites and/or those receiving diuretics (5,12-16);
- (III) serum creatinine value depends on the assay method and calibration used. Even more, serum creatinine measurement can be altered in cirrhosis: routine creatinine assay is based on spectrophotometry, and in patients with jaundice, bilirubin interferes with creatinine dosage as a chromogen, resulting in a lower creatinine value (10).

Additionally, other serum substances which can be elevated in these patients (pyruvate, ketoacid, etc.), as well as certain drugs usually prescribed to them interfere with creatinine renal secretion or measurement (14,16).

Regarding sex-related difference in creatinine concentrations, it can partially account for gender disparities in outcomes on the waiting list in the MELD era (3-6). In this sense, it has been documented that if the renal function status is evaluated using a creatinine-based GFR equation (eGFR) or chromium 51-EDTA GFR measurement, then women would have higher MELD scores than using measured serum creatinine (7-9). This phenomenon could be explained by the fact that measured GFR or eGFR are better renal functional marker than serum creatinine, or because of Modificación of Diet in Renal Disease

(MDRD)-based eGFR could overcorrect for gender differences in serum creatinine, specifically in cirrhosis (6). Additionally, since the MELD score includes serum bilirubin and international normalized ratio in addition to creatinine, then at any given MELD category, women tend to have greater hepatic dysfunction. Though differences in bilirubin and international normalized ratio are small, both impaired hepatic and renal function may contribute to reduced survival in women compared with men, as was observed particularly in patients with MELD scores between 21 and 35, which represent nearly one-half of transplant recipients (6).

Many cirrhotic patients have baseline serum creatinine below 1 mg/dL and some of them have significant impairment in renal function. The assumption that mortality is constant for creatinine less than 1 mg/dL is false. Thus, a modified MELD score: 1 + creatinine (mg/dL), has been proposed. This modified score seems to be slightly superior the current MELD score (*Table 1*) (1).

In conclusion, it seems that the MELD score is currently useful for guiding liver transplant allocation, but its adjustment to some variables such as serum sodium, creatinine, and measured or calculated GFR, should be taken into account.

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Footnote

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