

# Quantifying the Eyeball Test: Sarcopenia, Analytic Morphomics, and Liver Transplantation

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The physiological implications of end-stage liver disease (ESLD) are so pervasive that measuring the severity of the disease is challenging and imperfect. Although the Model for End-Stage Liver Disease (MELD) score is convenient and reliable, clinicians appreciate the broad range of disease severity among patients with any given MELD score. Within this context, most MELD-based allocation systems allow exception points for patients whose risk of wait-list mortality is poorly reflected by their calculated MELD scores. In the United States, the majority of MELD exceptions are granted for objective diagnoses such as hepatocellular carcinoma and hepatopulmonary syndrome, and patients who are subjectively assessed to be "sicker than their MELD score" likely have increased wait-list mortality. Importantly, allocation policy and treatment algorithms work best with objective clinical assessments (eg, the MELD score), which are well suited for standardization and the rigorous modeling of predicted risk. In all, better objective measures of disease severity in patients with liver disease are needed.

One such objective measure of disease severity, sarcopenia, is described by Tandon et al.<sup>1</sup> in this issue of *Liver Transplantation*. This good work has several key take-home points. First, the authors demonstrate that sarcopenia is a strong and independent predictor of mortality among patients waiting for liver transplanta-

tion and especially among patients with low MELD scores. This is an important and clinically relevant observation. Moreover, all liver transplant clinicians deal in their clinics with patients with low MELD scores who are doing poorly. Many of these individuals will likely be too sick by the time that their MELD score progresses and deceased donor transplantation is a reality. Potentially objective measures of mortality such as sarcopenia (as described in this article) may help clinicians optimally care for these patients. Most experienced clinicians likely feel that they can identify these high-risk individuals with the eyeball test. A second important observation in this article calls this into question. More specifically, the subjective global assessment, which is a validated assessment similar to the informal eyeball test, was not effective in identifying patients at high risk for wait-list mortality. Unfortunately, this assessment was performed by dietitians, and transplant clinicians potentially would be better at this assessment. Nonetheless, this underscores the need for better objective measures of risk for patients with ESLD.

A broader view of Tandon et al.'s article<sup>1</sup> yields a very exciting concept: the use of cross-sectional imaging for risk stratification. Most patients with severe illnesses such as ESLD will undergo an extensive evaluation including advanced imaging. As radiologists and clinicians review these images, they focus on the area of the pathology (eg, an evaluation of the liver for hepatocellular carcinoma). This focus is too narrow. Cross-sectional images contain vast amounts of

Abbreviations: ESLD, end-stage liver disease; MELD, Model for End-Stage Liver Disease.

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additional data specific to that patient that are never assessed by clinicians. This work by Tandon et al. adds to the growing literature of analytic morphomics.<sup>2-5</sup> This novel field uses clinical cross-sectional images for a more global assessment of patients. Although the focus of this work is trunk muscle size, novel measures clinically relevant to the care of complex liver disease patients may include fat distribution, vascular calcification, bone mineral density, muscle density and size, and solid organ imaging characteristics. We can even envision an automated clinical risk assessment performed completely with imaging. The use of cross-sectional imaging at least may provide objective measures of the physiological changes associated with end organ disease. These observations may inform both our understanding of the mechanisms of liver disease and clinical decision making.

Although a focus on muscle size is convenient and generalizable, it may be too narrow as a measure of global health status. The measurement of muscle size and the ways in which it relates to a patient's strength, body composition, muscle characteristics (edema and fat infiltration), and functional status are complex and not well understood. More work is needed to better understand these important issues before trunk muscle size measurements are likely to become clinically relevant. Some investigators have taken a broader view of objective measures of global health and have focused on frailty. Sarcopenia is a component of frailty, but frailty describes a broader "biologic syndrome of decreased reserve and resistance to stressors, resulting from cumulative declines across multiple physiologic systems, and causing vulnerability to adverse outcomes."<sup>6</sup> In other disciplines, frailty has been identified as a measure of such functional deficits and has been found to be a more powerful predictor of functional status in the elderly than age or comorbidity, with increases in an individual's frailty greatly increasing the risk of death and poor surgical outcomes.<sup>6-9</sup> Frailty is also applicable to the diminished homeostatic reserve seen in patients with chronic illness and organ failure.<sup>10</sup> As such, frailty may be an ideal characteristic for studying health outcomes in the ESLD population.

Among the hardest jobs of the liver transplant clinician is the determination of who is clinically suitable for transplantation. Underlying many of these decisions is a subjective assessment of the patient's function, nutritional status, and global health status. As we continue to expand the margins of liver transplantation and specifically perform transplantation for

older and sicker recipients, better tools for risk stratification will clearly be needed for both wait-list and posttransplant survival. Future work should focus on developing intuitive and objective measures of patient risk. Such measures may both inform liver allocation policies and clarify the pathophysiology of ESLD. Whether understanding these concepts will lead to specific therapeutic approaches such as nutrition, exercise or a better understanding of transplant benefit remains to be seen. Nonetheless, momentum continues to build for global health assessments such as frailty and sarcopenia. Undoubtedly, these concepts will be an important part of the care of the patient with ESLD in the future.

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