Consensus scoring systems for nonalcoholic fatty liver disease: an unmet clinical need

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Noninvasive diagnosis of nonalcoholic fatty liver disease (NAFLD) has received increasing attention (1,2). Nowadays, when we search the item 'scoring system and fatty liver' in PubMed, we can see a sharp increase in the number of related papers in the past few years. In fact, an era of 'information explosion' of noninvasive tests (NITs) for NAFLD is coming. For one thing, these newly identified biomarkers or noninvasive panels allow clinicians to detect nonalcoholic steatohepatitis (NASH) and liver fibrosis without the need for liver biopsy; for another, there are too many NITs for clinicians to choose from. Clinicians may be at a loss as to which NIT to use in different clinical contexts.

NITs for NAFLD can be classified according to the target of interest, namely steatosis, NASH, significant/advanced fibrosis, and more recently the so-called 'fibrotic NASH' (3,4), based on either serum-based tests or imaging (such as ultrasound scan, vibration-controlled transient elastography or magnetic resonance elastography) (5,6). NITs based on widely-available imaging techniques, such as Hamaguchi score and the ultrasonographic fatty liver indicator (US-FLI), are derived from ultrasonographic findings (7,8). Serum-based NITs incorporate readily accessible clinical parameters or novel biomarkers, both of which have merits and demerits. NITs based on routine clinical parameters (such as the fatty liver index, NAFLD fibrosis score, Fibrosis-4 index, Hepamet fibrosis score (9), and aspartate aminotransferase-to-platelet ratio index) are simple and easy to use but have modest accuracies. They can be easily confounded by several factors like liver enzymes and age (10); also, NITs with dual-cutoffs often leave a significant proportion of patients in the gray zone. Some of these scores were originally derived in patients with other liver diseases (11). NITs based on novel biomarkers, on the other hand, have more reproducible results with definite biological meanings, particularly those novel markers for liver fibrosis; however, these biomarkers may be expensive and not widely available, and we need to figure out how to integrate some of these novel indicators into clinical practice. The reliability and feasibility of some 'omics' markers of gene loci and metabolites remain to be validated in the future.

NAFLD biomarkers and surrogate scores, can target the following domains: (I) diagnostic markers reflecting the stage of fibrosis or NASH; (II) prognostic markers, stratifying the fibrosis progression risk; (III) monitoring biomarkers that may be used to track the disease progression and/or the treatment response (12,13). In the last two decades, some progress has been made in detection of new biomarkers and subsequently new NITs in hepatology. However, for many of them further independent validations are need. In reality, only a few
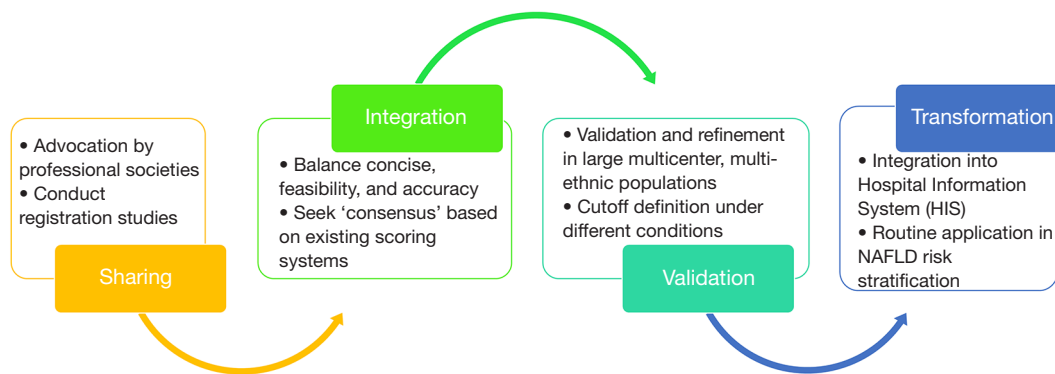
Figure 1 A diagram to illustrate procedures to generate 'consensus scoring systems' for clinical management of NAFLD. NAFLD, nonalcoholic fatty liver disease.

NITs have been well validated in more than three cohorts. Many scoring systems work well in the original reports but have much lower accuracies when tested in NAFLD cohorts of different clinical and ethnic compositions, limiting their value for wider clinical application. In some way, these endless newly-published panels without sufficient clinical validation can cause the reader to feel 'esthetic fatigue'. As a saying goes: 'less is more', it is high time that we streamline these existing NITs to facilitate clinical usage (*Figure 1*).

Firstly, professional societies [European Association for the Study of the Liver (EASL), American Association for the Study of Liver Diseases (AASLD), and Asian Pacific Association for the Study of the Liver (APASL)] can advocate for data sharing to integrate resources (raw data from randomized clinical trials (RCTs), prospectively collected clinical cohorts, etc.), in order to conduct registration studies and establish a high-quality global database based on pathological diagnosis [such as Liver Investigation: Testing Marker Utility in Steatohepatitis (LITMUS) (14)]. Secondly, by integration of existing resources, we can compare and identify the common elements in the existing scoring systems, and develop a more accurate, more pragmatic 'consensus scoring system', taking into account both clinical availability and novelty/accuracy. Thirdly, the 'consensus scoring system' needs to be prospectively validated and refined in large multicenter, multi-ethnic populations with diverse background (e.g., ongoing RCT) and determine optimal cutoff values under different contexts. Lastly, the 'consensus scoring system' can finally be transformed into daily clinical application in NAFLD risk stratification

and prognosis evaluation (such as integration into the hospital information system), in order to better guide the clinical diagnosis and treatment of NAFLD.

Footnote

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