CRITERIA FOR DISTINGUISHING AND TARGETING RISK GROUPS IN THE EARLY DETECTION OF STEATOHEPATITIS

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Abstract. Early detection of steatohepatitis in metabolically at-risk populations is less about finding “fatty liver” and more about identifying the smaller subgroup with clinically significant fibrosis, because fibrosis stage best predicts liver-related outcomes and determines who needs specialist management and closer surveillance. Liver biopsy remains the reference standard for defining steatohepatitis and staging fibrosis, but it is invasive and impractical for large-scale case finding. Therefore, modern strategies rely on targeted entry criteria to select high-yield risk groups and on stepwise non-invasive testing pathways to efficiently rule out advanced fibrosis in low-risk individuals while prioritizing confirmatory testing and referral for those at higher risk.

Keywords: steatohepatitis, metabolic dysfunction–associated steatotic liver disease, risk stratification, case finding, advanced fibrosis, non-invasive tests, elastography, early detection.

INTRODUCTION

Steatohepatitis linked to metabolic dysfunction has become a routine reality in contemporary healthcare because obesity, type 2 diabetes, and related cardiometabolic risk factors are highly prevalent and persistent over the life course. Yet the clinical burden is unevenly distributed: while many individuals have hepatic steatosis, a smaller proportion develop progressive fibrotic liver disease that drives cirrhosis, portal hypertension, and hepatocellular carcinoma. For early detection programs, this creates

a practical dilemma: if we test everyone, false positives overwhelm services and do little to improve outcomes; if we test no one, we miss advanced fibrosis until late complications appear. Modern professional guidance therefore emphasizes targeted case finding in clearly defined high-risk groups rather than population-wide screening, and it recommends non-invasive tests as the backbone of triage [1].

MATERIALS AND METHODS

In practice, early detection pathways are most useful when they define "risk" in outcome-oriented terms. The goal is not merely to detect steatosis or even to label steatohepatitis, but to detect those at heightened risk of near- to medium-term liver-related events, which correlates most strongly with advanced fibrosis. In low-prevalence settings such as primary care, non-invasive tests are far more reliable for ruling out advanced fibrosis than for definitively ruling it in, which is why tiered strategies are recommended. This principle directly shapes risk group design: you want entry criteria that raise the pre-test probability enough to make testing efficient, but not so narrow that you miss clinically important disease.

Accordingly, major guidelines converge on a pragmatic entry definition for case finding: adults with cardiometabolic risk factors, abnormal liver enzymes, and or radiological evidence of steatosis, especially those with type 2 diabetes or obesity plus additional metabolic risk factors. This approach recognizes that steatohepatitis itself is difficult to diagnose non-invasively with high certainty, but advanced fibrosis risk can be stratified with acceptable performance using sequential testing [2].

RESULTS AND DISCUSSION

A high-yield risk group is one that combines common exposure with demonstrably higher probability of clinically significant fibrosis. Guidance-supported "first-priority" groups for early detection include individuals with type 2 diabetes and individuals with obesity who also have at least one cardiometabolic risk factor, as well as those with persistently elevated liver enzymes. These criteria are not arbitrary:

diabetes and obesity represent sustained metabolic pressure on hepatic lipid handling, inflammation, and fibrogenesis, and they are consistently associated with higher rates of progressive liver disease in clinical cohorts [3].

Risk grouping should also integrate incidental findings. Many patients enter the pathway because steatosis is detected on ultrasound or other imaging performed for unrelated reasons. Professional guidance recommends that such patients, when steatosis is identified in the absence of alternative etiologies, undergo a structured primary risk assessment rather than being reassured solely on the basis of mild symptoms or normal aminotransferases. This is crucial because aminotransferase levels may be normal even in patients with advanced fibrosis, and therefore "normal ALT" should not be used as an exclusion criterion when metabolic risk is high.

Finally, a realistic early detection model acknowledges that "metabolic-related steatohepatitis" can coexist with alcohol intake above traditional cutoffs or with other causes of liver disease. New nomenclature explicitly provides categories for mixed metabolic and alcohol-related disease, reinforcing the need to quantify alcohol intake and review medications and comorbidities as part of risk-group entry and interpretation. A risk group is therefore defined not only by metabolic burden but also by the absence of a better primary explanation for liver injury, or by the recognition that multiple explanations may be contributing and should be managed in parallel [4].

Once a patient is inside the pathway, the first decision point is triage, and the most scalable tool is a simple blood-based fibrosis score derived from routine labs. Both European and American guidance highlight the fibrosis-4 index as a practical first-line assessment in low-prevalence settings. When the fibrosis-4 index is below a low-risk threshold, patients can usually remain in primary care with periodic reassessment; when it is above the threshold or indeterminate, second-line testing is recommended.

Thresholds and context matter. European guidance presents a stepwise pathway in which the lower fibrosis-4 threshold is 1.3 for adults up to age 65, with an age-

adjusted lower cutoff of 2.0 in those older than 65, and a higher threshold of 2.67 used to identify patients who warrant hepatology referral and more intensive evaluation. American guidance aligns with this logic and adds operational safeguards: the fibrosis-4 index has low accuracy in younger adults under 35 and should not be used in acutely ill patients, because transient inflammatory changes can distort results. It also provides pragmatic follow-up intervals: individuals with fewer metabolic risks may be reassessed every two to three years, whereas those with prediabetes, type 2 diabetes, or multiple metabolic risk factors should be monitored more frequently, around every one to two years [5].

Importantly, these first-line criteria should be used as gatekeeping rather than labeling. EASL guidance explicitly warns against “blind” use of simple scores as singular decision tools and encourages repeat measurement and escalation when clinical suspicion remains despite a low score. This is where risk group design and clinician judgment meet: a low score in a patient with very high metabolic risk and persistent enzyme elevation should not end the diagnostic process, but it can structure the next step.

Second-line testing exists to reduce false positives and to better classify patients with indeterminate or elevated first-line scores. European non-invasive testing guidance recommends transient elastography as a key second-tier modality and provides a widely used threshold pattern for metabolic steatotic liver disease: liver stiffness below about 8 kilopascals is recommended to rule out advanced fibrosis, while higher values indicate intermediate to high risk and justify referral or additional assessment.

CONCLUSION

Operationally, the strongest pathway uses sequential non-invasive testing: first-line fibrosis-4 with age-aware thresholds and appropriate follow-up intervals, followed by elastography or specialized biomarker panels for indeterminate or elevated results, and referral for high-risk or discordant cases. Because non-invasive tools are generally

better for ruling out than ruling in advanced fibrosis in low-prevalence settings, tiered strategies are essential to avoid over-referral and to preserve diagnostic precision. When implemented with systematic reporting and clear responsibilities across primary care and metabolic clinics, these criteria enable earlier recognition of high-risk disease while minimizing unnecessary invasive procedures and optimizing use of specialist resources.

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