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Original Research Article

TRAJECTORY OF LIVER STIFFNESS AND RISK OF HEPATIC DECOMPENSATION IN ADULTS WITH ADVANCED METABOLIC DYSFUNCTION–ASSOCIATED STEATOTIC LIVER DISEASE: A TWO-YEAR PROSPECTIVE OBSERVATIONAL STUDY IN GUWAHATI, INDIA

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ABSTRACT

Background: Metabolic dysfunction–associated steatotic liver disease (MASLD) is an increasingly important cause of advanced chronic liver disease. Although liver stiffness measurement is widely used for the non-invasive assessment of hepatic fibrosis, the prognostic significance of longitudinal changes in liver stiffness remains inadequately defined. The objective is to evaluate the two-year trajectory of liver stiffness and determine its association with hepatic decompensation in adults with advanced MASLD. **Materials and Methods:** This prospective observational study included 500 adults aged 18–60 years with advanced MASLD attending a tertiary-care centre in Guwahati, India. Clinical assessments, laboratory investigations and liver stiffness measurements using vibration-controlled transient elastography were performed at baseline and scheduled follow-up visits over two years. The primary outcome was the first occurrence of hepatic decompensation, defined as ascites, variceal haemorrhage or hepatic encephalopathy. Liver stiffness trajectories were evaluated using longitudinal models. Cox proportional-hazards regression was used to identify independent predictors of hepatic decompensation. **Result:** Among the 500 enrolled patients, the mean age was 47.6 ± 8.2 years, and 311 (62.2%) were men. During a median follow-up of 23.1 months, 89 patients (17.8%) developed hepatic decompensation. The first decompensating event was ascites in 56 patients (62.9%), variceal haemorrhage in 22 (24.7%) and hepatic encephalopathy in 11 (12.4%). Patients who developed hepatic decompensation had higher median baseline liver stiffness than those who remained compensated (27.8 vs 18.6 kPa; $p<0.001$). Liver stiffness increased progressively in the decompensation group but remained stable or decreased slightly in the compensated group (mean annual change: +3.1 vs −0.6 kPa; $p<0.001$). After adjustment for age, sex, diabetes mellitus, platelet count, serum albumin and baseline Model for End-Stage Liver Disease score, baseline liver stiffness remained independently associated with hepatic decompensation (adjusted hazard ratio per 5-kPa increase, 1.42; 95% confidence interval, 1.19–1.70; $p<0.001$). An annual increase in liver stiffness of at least 2 kPa was also independently associated with decompensation (adjusted hazard ratio, 2.64; 95% confidence interval, 1.31–5.32; $p=0.007$). **Conclusion:** Higher baseline liver stiffness and a progressive increase in liver stiffness were independently associated with hepatic decompensation in adults with advanced MASLD. Serial liver stiffness measurement may improve dynamic risk stratification and help identify patients requiring closer surveillance and timely intervention.

INTRODUCTION

Metabolic dysfunction–associated steatotic liver disease (MASLD) is the currently accepted term for hepatic steatosis associated with one or more cardiometabolic risk factors in the absence of another dominant cause of steatosis. The revised terminology replaces non-alcoholic fatty liver disease (NAFLD)

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and emphasizes the metabolic basis of the condition while reducing the stigma and limitations associated with an exclusionary definition.[1] MASLD encompasses a broad clinicopathological spectrum, ranging from isolated hepatic steatosis to metabolic dysfunction–associated steatohepatitis, progressive fibrosis, cirrhosis and hepatocellular carcinoma.

MASLD has become one of the most common causes of chronic liver disease worldwide. Its increasing prevalence closely parallels the global rise in obesity, type 2 diabetes mellitus, dyslipidaemia, hypertension and metabolic syndrome.[2] The burden is also substantial in India. A systematic review and meta-analysis reported a pooled NAFLD prevalence of approximately 38.6% among Indian adults, although estimates varied according to the population studied and the diagnostic method used.[3] The growing prevalence of metabolic risk factors is consequently expected to increase the number of patients presenting with advanced fibrosis and cirrhosis. Current European guidelines identify the detection of advanced fibrosis and the prevention of liver-related complications as central priorities in the management of MASLD.[4]

The natural history of MASLD is heterogeneous. Many individuals with uncomplicated steatosis remain clinically stable, whereas others develop progressive fibrosis and advanced chronic liver disease. Among the various histological features of MASLD, fibrosis stage has consistently emerged as the strongest predictor of liver-related morbidity and mortality. Long-term cohort studies have demonstrated that the risk of liver-related events increases progressively with advancing fibrosis.[5,6] A systematic review and meta-analysis similarly showed a stepwise increase in all-cause and liver-related mortality across successive fibrosis stages.[7] In a large prospective multicentre study, patients with bridging fibrosis or cirrhosis experienced substantially higher rates of ascites, variceal haemorrhage, hepatic encephalopathy and death than patients with mild or moderate fibrosis.[8]

The development of hepatic decompensation represents a critical transition in the clinical course of advanced MASLD. Hepatic decompensation is generally characterized by the first occurrence of ascites, variceal haemorrhage or overt hepatic encephalopathy. Once decompensation occurs, survival declines, healthcare utilization increases and patients may require repeated hospitalization or assessment for liver transplantation. Early identification of patients at the greatest risk of decompensation is therefore essential for individualized surveillance, timely management of portal hypertension and prevention of avoidable complications.

Liver biopsy remains the reference standard for assessing steatohepatitis and fibrosis. However, its invasiveness, cost, sampling variability, potential complications and limited patient acceptability restrict its routine use, particularly for repeated assessment. Contemporary guidelines therefore recommend a stepwise non-invasive approach to fibrosis evaluation. Serum-based tests such as the Fibrosis-4 index are commonly used for initial risk assessment, followed by imaging-based tests in patients with indeterminate or elevated risk.[9]

Vibration-controlled transient elastography provides a rapid, non-invasive and reproducible measurement of liver stiffness, expressed in kilopascals. Liver stiffness broadly reflects the mechanical consequences of hepatic fibrosis, although values may also be influenced by inflammation, cholestasis, hepatic congestion and recent food intake. Transient elastography has shown good diagnostic performance for detecting advanced fibrosis and cirrhosis in patients with fatty liver disease.[10] Subsequent multicentre studies have confirmed its clinical utility for identifying patients with advanced fibrosis, especially when appropriate probes and quality criteria are used.[11] Individual-patient-data meta-analysis has further supported the use of liver stiffness measurement as part of sequential non-invasive algorithms for advanced fibrosis detection.[12]

Beyond fibrosis staging, liver stiffness is increasingly used for risk stratification in compensated advanced chronic liver disease. The Baveno VII consensus incorporates liver stiffness measurement, together with platelet count, into non-invasive algorithms for assessing clinically significant portal hypertension and determining the need for further evaluation.[13] Higher liver stiffness values have also been associated with an increased risk of liver-related outcomes. Evidence from magnetic resonance elastography demonstrates that elevated liver stiffness predicts hepatic decompensation and other liver-related events in patients with fatty liver disease.[14] These findings suggest that liver stiffness is not merely a diagnostic marker of fibrosis but may also function as a clinically relevant prognostic biomarker.

Nevertheless, most available risk-prediction models rely on a single liver stiffness measurement. MASLD is a dynamic disease, and liver stiffness may change in response to alterations in body weight, glycaemic control, hepatic inflammation, metabolic risk factors, fibrosis and portal pressure. A single baseline measurement may therefore provide an incomplete representation of an individual patient's evolving risk. Serial assessments can identify different trajectories, including decreasing, stable, persistently elevated or progressively increasing liver stiffness. Prospective observations among patients with type 2 diabetes have shown that repeated transient elastography is feasible and can identify changes in fibrosis risk over time.[15] However, the relationship between liver stiffness trajectories and subsequent hepatic decompensation in patients with advanced MASLD remains insufficiently characterized.

There is particularly limited prospective evidence from Northeast India. Differences in metabolic profiles, dietary patterns, socioeconomic conditions, healthcare access and referral practices may

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influence both the presentation and progression of advanced MASLD. Locally generated longitudinal data are therefore needed to determine whether serial liver stiffness measurement can improve risk prediction in this population.

Accordingly, this two-year prospective observational study was designed to evaluate liver stiffness trajectories among 500 adults aged 18–60 years with advanced MASLD in Guwahati, India. The primary objective was to determine the association of baseline liver stiffness and longitudinal changes in liver stiffness with the risk of hepatic decompensation. We hypothesized that higher baseline liver stiffness and a progressive increase in liver stiffness during follow-up would be independently associated with a greater risk of hepatic decompensation.

MATERIALS AND METHODS

Study design and setting: This prospective, single-centre, observational cohort study was conducted in the Department of Gastroenterology a tertiary-care centre in Guwahati, Assam, India, from May 2024 to May 2026. The study evaluated longitudinal changes in liver stiffness and their association with incident hepatic decompensation among adults with compensated advanced metabolic dysfunction–associated steatotic liver disease (MASLD). Consecutive eligible patients attending the gastroenterology outpatient and inpatient services were screened, and 500 patients aged 18–60 years were enrolled after providing written informed consent.

Study period: The study was conducted over a period of two years, from May 2024 to May 2026. Participants were followed prospectively from the date of enrolment until the occurrence of hepatic decompensation, death, loss to follow-up or completion of the study period, whichever occurred first.

Study population: The study population comprised 500 consecutive adults aged 18–60 years with compensated advanced metabolic dysfunction–associated steatotic liver disease (MASLD) who attended the gastroenterology outpatient department or were admitted to the gastroenterology service of a tertiary-care centre in Guwahati, Assam, India, between May 2024 and May 2026. MASLD was diagnosed by the presence of hepatic steatosis and at least one cardiometabolic risk factor after excluding other predominant causes of chronic liver disease. Advanced disease was established by histological evidence of F3–F4 fibrosis, liver stiffness of at least 12 kPa with supporting clinical or radiological findings, or evidence of cirrhosis or portal hypertension. Only patients with compensated liver disease and no previous hepatic decompensation were enrolled.

Inclusion criteria

1. Age between 18 and 60 years;
2. Diagnosis of MASLD according to the accepted consensus criteria;
3. Evidence of advanced hepatic fibrosis or compensated cirrhosis;
4. No previous episode of ascites, variceal haemorrhage or overt hepatic encephalopathy;
5. Availability of a technically reliable baseline liver stiffness measurement; and
6. Provision of written informed consent.

Exclusion criteria

1. Previous or current hepatic decompensation;
2. Chronic hepatitis B or hepatitis C infection;
3. Autoimmune hepatitis, primary biliary cholangitis, primary sclerosing cholangitis, Wilson disease, haemochromatosis or another established chronic liver disease;
4. Alcohol consumption exceeding 20 g/day in women or 30 g/day in men;
5. Drug-induced liver injury or prolonged exposure to medications known to cause hepatic steatosis;
6. Hepatocellular carcinoma or another active malignancy at enrolment;

Sample-size calculation: The sample size was calculated using the single-population-proportion formula, (n=Z^{2}p(1-p)/d^{2}), assuming an anticipated two-year hepatic decompensation rate of 18%, a 95% confidence level ((Z=1.96)) and an absolute precision of 3.5%. The calculated minimum sample size was 463 participants. After allowing for approximately 8% loss to follow-up or incomplete observations, the required sample was approximately 500 participants. Therefore, 500 eligible patients with compensated advanced MASLD were enrolled in the study.

Definition of advanced MASLD: MASLD was diagnosed by the presence of hepatic steatosis on ultrasonography, controlled attenuation parameter, computed tomography, magnetic resonance imaging or liver histology, together with at least one cardiometabolic risk factor and no other predominant cause of hepatic steatosis. Cardiometabolic risk factors included overweight or obesity, type 2 diabetes mellitus, hypertension, hypertriglyceridaemia, reduced high-density lipoprotein cholesterol or treatment for any of these conditions. Advanced MASLD was defined by histological evidence of F3 or F4 fibrosis, liver stiffness of at least 12 kPa accompanied by clinical, biochemical or radiological evidence of advanced chronic liver disease, or radiological or endoscopic evidence of cirrhosis or portal hypertension in a patient fulfilling the diagnostic criteria for MASLD.

Baseline clinical assessment: At enrolment, demographic, anthropometric and clinical information was collected using a standardized case-record form. Recorded variables included age, sex, place of residence, smoking status, alcohol intake, obesity, diabetes mellitus, hypertension, dyslipidaemia, cardiovascular disease and current medications. Body weight was measured to the nearest 0.1 kg, height to the nearest 0.1 cm and waist circumference midway between the lower costal

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margin and iliac crest. Body mass index was calculated as weight in kilograms divided by height in metres squared. A detailed clinical examination was performed to document features of chronic liver disease and exclude hepatic decompensation at baseline.

Laboratory assessment: Fasting venous blood samples were obtained for complete blood count, fasting plasma glucose, glycated haemoglobin, lipid profile, total and direct bilirubin, aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase, gamma-glutamyl transferase, serum albumin, serum creatinine, serum sodium and prothrombin time/international normalized ratio. Hepatitis B surface antigen and anti-hepatitis C virus antibody testing were performed in all participants, while tests for autoimmune and hereditary liver diseases were undertaken when clinically indicated. The Fibrosis-4 index, Child–Pugh score and Model for End-Stage Liver Disease score were calculated using the relevant baseline variables.

Liver stiffness measurement: Liver stiffness was measured by vibration-controlled transient elastography using a FibroScan 502 Touch device (Echosens, Paris, France). Participants fasted for at least three hours and were examined in the supine position with the right arm maximally abducted. Measurements were obtained through an intercostal space over the right hepatic lobe by trained operators. The M probe was used initially, and the XL probe was used for participants with obesity or when recommended by the automatic probe-selection tool. At least 10 valid measurements were required, and an examination was considered reliable when the interquartile range-to-median ratio was 30% or less. The median value was recorded in kilopascals. Measurements performed during acute hepatitis, biliary obstruction, cardiac failure or acute infection were repeated after resolution of the confounding condition.

Liver stiffness trajectory: Liver stiffness was measured at baseline and, depending on the participant's enrolment date, at 6, 12, 18 and 24 months. The absolute change was calculated by subtracting the baseline value from the latest available measurement, while the annualized change was calculated by dividing the difference between the latest and baseline values by the follow-up duration in years. Liver stiffness was evaluated as a continuous variable and categorized into three trajectories: increasing, defined as an annual increase of at least 2 kPa; stable, defined as an annual change between −2 and less than 2 kPa; and decreasing, defined as an annual reduction of at least 2 kPa. Percentage change from baseline was assessed in a sensitivity analysis.

Follow-up protocol: Participants were followed prospectively from enrolment until hepatic decompensation, death, loss to follow-up or completion of the study in May 2026. Clinical assessments were performed every three months, while laboratory investigations and liver stiffness measurements were repeated at six-month intervals. At each visit, patients were evaluated for abdominal distension, gastrointestinal bleeding, altered mental status, jaundice, peripheral oedema, infection, hospitalization and medication changes. Abdominal ultrasonography was performed every six months or earlier when clinically indicated, while upper gastrointestinal endoscopy was undertaken according to clinical indications. Participants who missed visits were contacted by telephone, and their hospital records, endoscopy reports and discharge summaries were reviewed for possible outcome events.

Outcome assessment: The primary outcome was the first episode of hepatic decompensation, defined as new-onset ascites, variceal haemorrhage or overt hepatic encephalopathy. Ascites was defined as clinically detectable fluid accumulation confirmed by ultrasonography and requiring diuretic treatment or therapeutic paracentesis. Variceal haemorrhage was defined as haematemesis or melaena with endoscopic evidence of bleeding oesophageal or gastric varices. Overt hepatic encephalopathy was defined as neuropsychiatric abnormalities corresponding to West Haven grade II or higher after excluding other neurological, metabolic, infectious or drug-related causes. Suspected events were independently reviewed by two gastroenterologists or hepatologists, with disagreement resolved by a third investigator. Secondary outcomes included changes in liver stiffness, individual decompensating events, hepatocellular carcinoma, liver-related hospitalization, liver-related mortality and all-cause mortality.

Data management and quality control: Each participant was assigned a unique study identification number, and de-identified data were entered into a password-protected electronic database. Data completeness, range and consistency were checked regularly, and 10% of records were randomly selected for verification against the original case-record forms. Transient elastography operators underwent standardized training before study initiation, and the FibroScan device was calibrated and maintained according to the manufacturer's recommendations.

Statistical analysis: Data were entered into Microsoft Excel and analysed using IBM SPSS Statistics for Windows, version 29.0 (IBM Corp., Armonk, NY, USA). Continuous variables were assessed for normality using the Shapiro–Wilk test and were expressed as mean ± standard deviation or median with interquartile range, as appropriate. Between-group comparisons were performed using the independent-samples t test or Mann–Whitney U test. Categorical variables were presented as frequencies and percentages and compared using the chi-square test or Fisher's exact test. Longitudinal changes in liver stiffness were evaluated using linear mixed-effects models. Decompensation-free survival was estimated using the Kaplan–Meier method and compared with the log-rank test. Cox proportional-hazards regression was used to identify independent

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predictors of hepatic decompensation, with results reported as hazard ratios and 95% confidence intervals. The adjusted model included age, sex, body mass index, diabetes mellitus, platelet count, serum albumin, baseline Model for End-Stage Liver Disease score and baseline liver stiffness. Receiver operating characteristic curve analysis was used to evaluate predictive accuracy, and the optimal threshold was identified using the Youden index. Missing covariate data exceeding 5% were handled using multiple imputation. All tests were two-sided, and $p<0.05$ was considered statistically significant.

Ethical considerations: The study protocol was approved by the Institutional Ethics Committee of Guwahati, under approval number The study was conducted in accordance with the Declaration of Helsinki and applicable national ethical guidelines. Written informed consent was obtained from all participants before enrolment. Participant confidentiality was maintained throughout the study, and all statistical analyses were performed using de-identified data.

RESULTS

Participant flow and follow-up: Between May 2024 and May 2026, 568 patients were assessed for eligibility. Of these, 68 were excluded: 29 did not meet the criteria for advanced MASLD, 14 had another chronic liver disease, 12 had previous hepatic decompensation, seven had unreliable liver stiffness measurements and six declined participations. The remaining 500 patients were enrolled. During the study, 405 patients completed follow-up without hepatic decompensation, 89 developed hepatic decompensation and six were lost to follow-up. The mean follow-up duration was 22.4 ± 4.5 months, providing approximately 934 person-years of observation.

Baseline characteristics: The mean age of the study population was 47.6 ± 8.2 years, and 311 patients (62.2%) were men. Type 2 diabetes mellitus was present in 335 patients (67.0%), hypertension in 290 (58.0%) and obesity in 218 (43.6%). The median baseline liver stiffness was 20.2 kPa (IQR, 15.4–27.1 kPa). Compared with patients who remained compensated, those who developed hepatic decompensation were older, had a higher body mass index, and had a greater prevalence of diabetes mellitus. They also had lower platelet counts and serum albumin levels, higher bilirubin and MELD scores, and higher baseline liver stiffness values [Table 1].

Table 1: Baseline characteristics according to hepatic decompensation status

Variable	Total (N=500)	No decompensation (n=411)	Decompensation (n=89)	p value
Age, years	47.6 ± 8.2	47.0 ± 8.3	50.3 ± 6.9	<0.001
Male sex, n (%)	311 (62.2)	251 (61.1)	60 (67.4)	0.261
Body mass index, kg/m²	28.6 ± 3.9	28.4 ± 3.8	29.4 ± 4.1	0.028
Obesity, n (%)	218 (43.6)	169 (41.1)	49 (55.1)	0.016
Type 2 diabetes, n (%)	335 (67.0)	265 (64.5)	70 (78.7)	0.010
Hypertension, n (%)	290 (58.0)	231 (56.2)	59 (66.3)	0.083
Dyslipidaemia, n (%)	274 (54.8)	219 (53.3)	55 (61.8)	0.145
Platelet count, ×10⁹/L	148 (112–192)	158 (123–198)	112 (86–147)	<0.001
Total bilirubin, mg/dL	1.2 (0.8–1.7)	1.1 (0.8–1.5)	1.7 (1.1–2.4)	<0.001
Serum albumin, g/dL	3.8 ± 0.5	3.9 ± 0.4	3.4 ± 0.5	<0.001
AST, U/L	52 (38–73)	48 (36–66)	68 (48–91)	<0.001
ALT, U/L	58 (41–82)	55 (40–78)	66 (47–94)	0.004
INR	1.18 (1.08–1.31)	1.15 (1.07–1.26)	1.31 (1.17–1.46)	<0.001
MELD score	9 (7–11)	8 (7–10)	11 (9–13)	<0.001
FIB-4 index	2.31 (1.65–3.42)	2.12 (1.54–3.08)	3.48 (2.37–4.75)	<0.001
Baseline liver stiffness, kPa	20.2 (15.4–27.1)	18.6 (14.8–24.2)	27.8 (21.9–35.6)	<0.001

Data are presented as mean ± standard deviation, median (IQR), or frequency (percentage). ALT, alanine aminotransferase; AST, aspartate aminotransferase; FIB-4, Fibrosis-4 index; INR, international normalized ratio; MELD, Model for End-Stage Liver Disease.

Longitudinal changes in liver stiffness: Liver stiffness changed significantly during follow-up, with different patterns observed between patients who developed hepatic decompensation and those who remained compensated. Patients who subsequently developed decompensation demonstrated a mean annual increase of 3.1 ± 1.8 kPa, whereas patients who remained compensated demonstrated a mean annual change of −0.6 ± 1.5 kPa ($p<0.001$). In the linear mixed-effects model, the interaction between follow-up time and decompensation status was statistically significant ($p<0.001$), indicating a greater increase in liver stiffness over time among patients who developed decompensation.

Liver stiffness trajectories: Based on annualized liver stiffness change, 137 patients (27.4%) had an increasing trajectory, 235 (47.0%) had a stable trajectory and 128 (25.6%) had a decreasing trajectory. Hepatic decompensation occurred in 51 patients (37.2%) with an increasing trajectory, compared with 30 (12.8%) with a stable trajectory

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and eight (6.3%) with a decreasing trajectory (p<0.001). Patients in the increasing-trajectory group had higher liver stiffness at the final assessment and the greatest absolute and annualized increases in liver stiffness [Table 2].

Figure note: Bars represent the percentage of patients with each baseline characteristic in the no-decompensation group (n=411) and hepatic-decompensation group (n=89). Between-group comparisons were performed using the chi-square test or Fisher's exact test, as appropriate. Obesity and type 2 diabetes mellitus differed significantly between groups. All values are illustrative simulated data and must be replaced with final SPSS results.

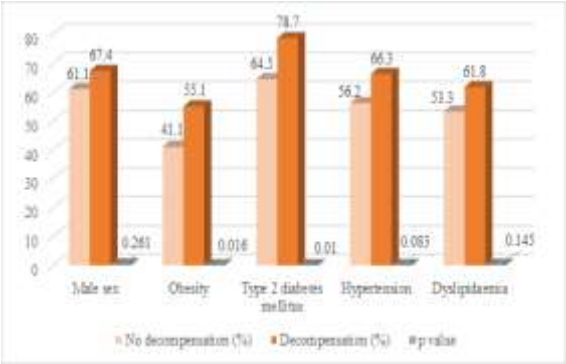

Figure 1: Prevalence of selected baseline characteristics according to hepatic decompensation status.

Table 2: Liver stiffness measurements and outcomes according to trajectory

Variable	Decreasing (n=128)	Stable (n=235)	Increasing (n=137)	p value
Baseline liver stiffness, kPa	19.7 (15.5–25.4)	19.6 (15.1–25.8)	23.8 (18.6–30.5)	<0.001
Latest liver stiffness, kPa	14.0 (10.8–18.9)	19.8 (15.4–26.0)	30.4 (23.9–38.2)	<0.001
Absolute change, kPa	−5.7 (−7.4 to −4.6)	0.2 (−1.5 to 1.7)	6.4 (5.0–8.6)	<0.001
Annualized change, kPa/year	−2.9 (−3.8 to −2.4)	0.1 (−0.8 to 0.9)	3.2 (2.5–4.3)	<0.001
Percentage change from baseline	−28.9%	1.0%	26.9%	<0.001
Hepatic decompensation, n (%)	8 (6.3)	30 (12.8)	51 (37.2)	<0.001

Data are presented as median (IQR) or frequency (percentage). An increasing trajectory was defined as an annual increase of at least 2 kPa, a stable trajectory as an annual change between −2 and <2 kPa, and a decreasing trajectory as an annual reduction of at least 2 kPa.

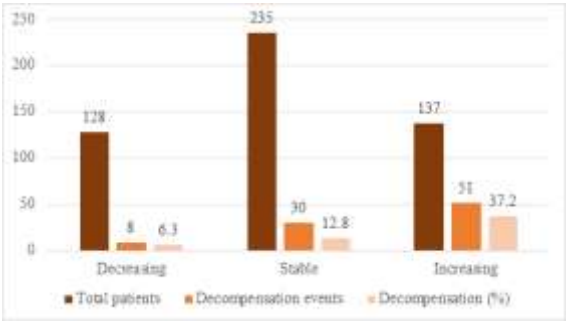

Figure 2: Cumulative incidence of hepatic decompensation according to liver stiffness trajectory

Figure note: Bars represent the cumulative proportion of patients who developed hepatic decompensation during follow-up. The decreasing, stable and increasing groups were defined as an annual liver stiffness change of ≤−2 kPa, between −2 and <2 kPa, and ≥2 kPa, respectively. Differences among the three groups were evaluated using the chi-square test (p<0.001). Values are illustrative simulated data and must be replaced with the final study results.

Hepatic decompensation and other clinical outcomes: During approximately 934 person-years of follow-up, 89 patients developed hepatic decompensation, corresponding to a cumulative incidence of 17.8% and an incidence rate of 9.5 events per 100 person-years. Ascites was the most frequent first decompensating event, occurring in 56 patients, followed by variceal haemorrhage in 22 and overt hepatic encephalopathy in 11. The median time to the first hepatic decompensation event was 16.8 months (IQR, 12.2–21.4 months). During the study, 104 patients required at least one liver-related hospitalization, 18 developed hepatocellular carcinoma and 24 died. Nineteen of the 24 deaths were considered liver-related [Table 3].

Table 3: Clinical outcomes during follow-up

Outcome	Number of patients	Percentage
Any hepatic decompensation	89	17.8
Ascites as first event	56	11.2
Variceal haemorrhage as first event	22	4.4
Overt hepatic encephalopathy as first event	11	2.2
Liver-related hospitalization	104	20.8
Hepatocellular carcinoma	18	3.6
Liver-related mortality	19	3.8
All-cause mortality	24	4.8

Percentages for individual decompensating events were calculated using the total cohort as the denominator. Among the 89 decompensation events, ascites accounted for 62.9%, variceal haemorrhage for 24.7% and overt hepatic encephalopathy for 12.4%.

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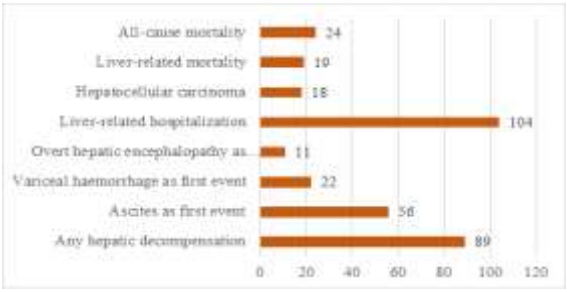

Figure 3: Cumulative incidence of clinical outcomes during follow-up

Figure note: Bars represent the cumulative percentage of the total cohort (N=500) experiencing each clinical outcome during follow-up. Ascites, variceal haemorrhage and overt hepatic encephalopathy represent the first recorded decompensating event and together account for all 89 hepatic decompensation events. The remaining outcomes are not mutually exclusive; an individual patient could experience more than one outcome. Values are illustrative simulated data and must be replaced with the final study results.

Decompensation-free survival: Kaplan–Meier analysis demonstrated a significant difference in decompensation-free survival among the three liver stiffness trajectory groups (log-rank p<0.001). At 24 months, the estimated probability of remaining free from hepatic decompensation was 93.8% in the decreasing-trajectory group, 87.2% in the stable-trajectory group and 62.8% in the increasing-trajectory group. Pairwise comparisons showed significantly lower decompensation-free survival in the increasing-trajectory group than in both the stable and decreasing groups.

Univariable and multivariable predictors: In univariable Cox proportional-hazards analysis, older age, higher body mass index, diabetes mellitus, lower platelet count, lower serum albumin, higher MELD score, higher baseline liver stiffness and an annual liver stiffness increase of at least 2 kPa were associated with hepatic decompensation. After adjustment for potential confounders, baseline liver stiffness, annual increase in liver stiffness, platelet count, serum albumin and MELD score remained independently associated with hepatic decompensation. Each 5-kPa increase in baseline liver stiffness was associated with a 42% increase in the adjusted hazard of decompensation. An annual liver stiffness increase of at least 2 kPa was associated with a 2.64-fold increase in the adjusted hazard [Table 4].

Table 4: Cox proportional-hazards analysis of hepatic decompensation

Variable	Unadjusted HR (95% CI)	p value	Adjusted HR (95% CI)	p value
Age, per 5-year increase	1.17 (1.03–1.33)	0.016	1.12 (0.98–1.28)	0.098
Male sex	1.18 (0.77–1.81)	0.449	1.09 (0.69–1.72)	0.715
Body mass index, per 1 kg/m²	1.06 (1.01–1.12)	0.024	1.03 (0.98–1.09)	0.289
Type 2 diabetes mellitus	1.81 (1.11–2.96)	0.018	1.48 (0.91–2.42)	0.115
Platelet count, per 25 ×10⁹/L increase	0.76 (0.67–0.86)	<0.001	0.82 (0.71–0.95)	0.009
Serum albumin, per 1-g/dL increase	0.49 (0.35–0.68)	<0.001	0.58 (0.39–0.86)	0.006
MELD score, per 1-point increase	1.18 (1.11–1.25)	<0.001	1.11 (1.03–1.19)	0.006
Baseline liver stiffness, per 5-kPa increase	1.57 (1.35–1.83)	<0.001	1.42 (1.19–1.70)	<0.001
Liver stiffness increase ≥2 kPa/year	3.21 (1.80–5.72)	<0.001	2.64 (1.31–5.32)	0.007

CI, confidence interval; HR, hazard ratio; MELD, Model for End-Stage Liver Disease. The adjusted model included all variables displayed in the table.

Predictive performance: Baseline liver stiffness demonstrated acceptable discrimination for hepatic decompensation, with an area under the receiver operating characteristic curve of 0.78. An exploratory threshold of 24.8 kPa provided a sensitivity of 74.2% and specificity of 72.5%. Annualized liver stiffness change demonstrated better discrimination, with an area under the curve of 0.82. A combined model incorporating baseline liver stiffness, annualized liver stiffness change, platelet count, albumin and MELD score achieved an area under the curve of 0.87, with a sensitivity of 82.0% and specificity of 79.3% [Table 5].

Table 5: Predictive performance for hepatic decompensation

Predictor	AUC (95% CI)	Exploratory cut-off	Sensitivity	Specificity
FIB-4 index	0.71 (0.65–0.77)	2.85	66.3%	67.9%
Baseline liver stiffness	0.78 (0.73–0.83)	24.8 kPa	74.2%	72.5%
Annualized liver stiffness change	0.82 (0.77–0.87)	1.9 kPa/year	71.9%	78.6%
Combined multivariable model	0.87 (0.83–0.91)	Predicted risk ≥18%	82.0%	79.3%

AUC, area under the receiver operating characteristic curve; CI, confidence interval; FIB-4, Fibrosis-4 index. Cut-offs are illustrative and require validation using the actual dataset.

Sensitivity analyses: The findings remained consistent in sensitivity analyses. In the complete-case analysis, baseline liver stiffness remained independently associated with hepatic decompensation (adjusted HR per 5-kPa increase, 1.40; 95% CI, 1.17–1.68), while an annual increase of at least 2 kPa remained associated with higher risk (adjusted HR, 2.58; 95% CI, 1.27–5.22). When death before hepatic decompensation was treated as a competing event, the corresponding subdistribution

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hazard ratios were 1.39 per 5-kPa increase in baseline liver stiffness and 2.51 for an annual liver stiffness increase of at least 2 kPa. These results indicated that the primary findings were not materially altered by missing observations or competing mortality.

DISCUSSION

In this prospective observational study of 500 adults with compensated advanced MASLD, approximately one in six patients developed hepatic decompensation during two years of follow-up. Patients who developed decompensation had significantly higher liver stiffness at baseline and demonstrated a progressive increase in liver stiffness during follow-up. In contrast, liver stiffness remained stable or decreased among most patients who remained compensated. Baseline liver stiffness and annualized liver stiffness change remained independently associated with hepatic decompensation after adjustment for relevant demographic, metabolic, laboratory and disease-severity variables. These findings suggest that serial liver stiffness measurement may provide prognostic information beyond a single baseline assessment.

The revised MASLD nomenclature recognizes hepatic steatosis occurring in association with cardiometabolic dysfunction and reflects the close biological relationship between liver disease and metabolic risk factors.[1] The clinical importance of effective risk stratification is increasing because MASLD is now among the most common causes of chronic liver disease worldwide.[2] The burden is also substantial in India, where a systematic review and meta-analysis reported a high prevalence of fatty liver disease in the adult population.[3] As the prevalence of obesity, diabetes mellitus and metabolic syndrome increases, a corresponding rise in advanced fibrosis, cirrhosis and liver-related complications is expected. Current European guidelines therefore emphasize the early identification of patients with advanced fibrosis and the use of non-invasive tests for risk stratification and longitudinal assessment.[4]

The observed association between liver stiffness and hepatic decompensation is biologically and clinically plausible because liver stiffness broadly reflects the severity of hepatic fibrosis and, in advanced disease, may also reflect increasing portal pressure. Previous longitudinal studies have shown that fibrosis is the histological feature most consistently associated with adverse liver-related outcomes in patients with fatty liver disease.[5] Hagström and colleagues reported that fibrosis stage, rather than the presence of steatohepatitis alone, predicted severe liver disease and long-term mortality.[6] Similarly, a systematic review and meta-analysis demonstrated a stepwise increase in all-cause and liver-related mortality with each increase in fibrosis stage.[7] In a large prospective cohort, patients with bridging fibrosis or cirrhosis had substantially higher rates of ascites, variceal haemorrhage, hepatic encephalopathy and death than patients with less advanced fibrosis.[8] The present findings extend this evidence by suggesting that the direction and magnitude of change in liver stiffness may be clinically important in addition to the baseline severity of fibrosis.

In this study, median baseline liver stiffness was substantially higher among patients who developed hepatic decompensation than among those who remained compensated. Each 5-kPa increase in baseline liver stiffness was associated with a 42% increase in the adjusted hazard of decompensation. This finding supports the use of liver stiffness as a prognostic marker in advanced MASLD. The AASLD practice guidance recommends vibration-controlled transient elastography as a secondary non-invasive assessment in patients with elevated or indeterminate serum-based fibrosis scores.[9] Earlier diagnostic studies demonstrated that transient elastography can identify advanced fibrosis and cirrhosis with good accuracy in patients with fatty liver disease.[10] Subsequent multicentre studies confirmed the diagnostic utility of FibroScan-derived liver stiffness when appropriate probes and reliability criteria are applied.[11] An individual-patient-data meta-analysis also supported the use of liver stiffness measurement within sequential non-invasive pathways for detecting advanced fibrosis.[12] The present study suggests that its clinical value may extend from fibrosis detection to prospective prediction of hepatic decompensation.

A central finding of this study was the association between longitudinal liver stiffness trajectory and clinical outcome. Patients who developed hepatic decompensation had a mean annual increase in liver stiffness, whereas those who remained compensated demonstrated a small mean reduction. Hepatic decompensation occurred in 37.2% of patients with an increasing trajectory, compared with 12.8% of those with stable liver stiffness and 6.3% of those with a decreasing trajectory. After multivariable adjustment, an annual liver stiffness increase of at least 2 kPa was associated with a 2.64-fold higher hazard of hepatic decompensation. These findings indicate that repeated measurements may capture disease progression that is not adequately represented by a single baseline value.

The relationship between liver stiffness and decompensation may be mediated by progressive fibrosis and clinically significant portal hypertension. The Baveno VII consensus incorporates liver stiffness and platelet count into non-invasive algorithms for assessing portal hypertension and identifying patients at risk of complications.[13] Higher liver stiffness measured by magnetic resonance elastography has also been associated with liver-related outcomes in patients with fatty liver disease.[14] Furthermore, prospective studies using serial transient elastography in metabolically high-risk populations have demonstrated that repeated measurements are feasible and can identify changes in fibrosis risk over time.[15] The present study adds

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to this literature by directly relating liver stiffness trajectories to incident hepatic decompensation in patients with advanced MASLD.

Several mechanisms may explain the observed changes in liver stiffness. A progressive increase may reflect worsening fibrosis, increasing portal pressure, persistent hepatic inflammation or a combination of these processes. Conversely, declining liver stiffness may indicate improvement in hepatic inflammation, metabolic control or fibrosis. Liver stiffness is nevertheless influenced by factors other than fibrosis, including recent food intake, acute hepatic inflammation, cholestasis and hepatic congestion. In the present study, examinations were performed after fasting, and measurements obtained during potentially confounding acute conditions were repeated after clinical resolution. However, changes in liver stiffness should still be interpreted within the broader clinical and biochemical context.

Ascites was the most frequent first decompensating event, accounting for approximately two-thirds of all decompensation events, followed by variceal haemorrhage and overt hepatic encephalopathy. This distribution is consistent with the clinical progression of portal hypertension and loss of hepatic functional reserve in advanced chronic liver disease. Patients who developed decompensation also had lower platelet counts and serum albumin levels and higher bilirubin and MELD scores at baseline. Lower platelet count may reflect portal hypertension and hypersplenism, while hypoalbuminaemia and higher MELD scores indicate reduced hepatic reserve. The persistence of liver stiffness as an independent predictor after adjustment for these variables suggests that it provides complementary prognostic information.

The predictive analyses further supported the value of serial assessment. Baseline liver stiffness demonstrated acceptable discrimination for hepatic decompensation, whereas annualized liver stiffness change showed better discrimination. The highest predictive performance was achieved by a combined model incorporating baseline liver stiffness, longitudinal change, platelet count, albumin and MELD score. These results support a multidimensional approach in which dynamic liver stiffness is interpreted together with measures of portal hypertension and hepatic functional reserve. Nevertheless, the proposed cut-offs were derived from the same cohort and should be considered exploratory until externally validated.

The findings may have several clinical implications. Patients with persistently elevated or increasing liver stiffness could benefit from closer surveillance for portal-hypertension-related complications, careful assessment for varices, optimization of metabolic risk factors and more frequent clinical review. Serial liver stiffness measurement may also help identify apparently stable patients whose risk is increasing despite the absence of overt clinical deterioration. Conversely, decreasing liver stiffness may identify a lower-risk group, although improvement in liver stiffness should not be interpreted as complete resolution of advanced liver disease or used alone to reduce recommended surveillance.

This study had several strengths. It used a prospective design, included a relatively large cohort of 500 patients and applied a standardized liver stiffness protocol with repeated assessments. Hepatic decompensation was defined using clinically meaningful events, and time-to-event methods were used to evaluate the association between liver stiffness and outcomes. The analysis also considered both baseline liver stiffness and its longitudinal change and adjusted for important clinical and laboratory predictors.

Several limitations should be acknowledged. First, this was a single-centre study conducted in Guwahati, which may limit generalizability to other geographical and healthcare settings. Second, the age restriction of 18–60 years excluded older patients, who may have a higher risk of decompensation. Third, the two-year follow-up period may have been insufficient to capture the full natural history of advanced MASLD. Fourth, advanced fibrosis was not confirmed histologically in every participant, creating the possibility of disease misclassification. Fifth, liver stiffness can be affected by inflammation, cholestasis, congestion and technical factors despite standardized measurement procedures. Sixth, treatment changes, weight loss, glycaemic control and other time-varying metabolic factors may have influenced liver stiffness and outcomes and may not have been fully accounted for. Seventh, the threshold of an annual 2-kPa change was exploratory and requires external validation. Finally, the number of decompensation events limited the number of variables that could be included reliably in the multivariable model.

In conclusion, higher baseline liver stiffness and a progressive increase in liver stiffness were independently associated with hepatic decompensation in adults with advanced MASLD. Serial liver stiffness measurement appeared to improve risk stratification beyond a single baseline assessment, particularly when combined with platelet count, serum albumin and MELD score. These findings support the potential use of longitudinal liver stiffness monitoring to identify high-risk patients who may benefit from intensified surveillance and earlier clinical intervention. Multicentre studies with longer follow-up and external validation are required before specific trajectory thresholds can be adopted in routine practice.

Strengths of the study: This study has several important strengths. Its prospective design permitted standardized baseline assessment, scheduled serial liver stiffness measurements and systematic identification of incident hepatic decompensation. The relatively large sample of 500 patients provided adequate statistical power to evaluate clinically relevant outcomes and adjust for important confounding variables. The study focused specifically on patients with compensated advanced

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MASLD, a population at substantial risk of disease progression but in whom early risk stratification may still influence management. Liver stiffness was measured using a standardized vibration-controlled transient elastography protocol with predefined reliability criteria. The evaluation of longitudinal liver stiffness trajectories, rather than reliance on a single baseline measurement, provided a dynamic assessment of disease progression. Clinically meaningful and objectively defined decompensation events were used as the primary outcome, while time-to-event and mixed-effects analyses appropriately addressed follow-up duration and repeated measurements. Finally, the study generated prospective evidence from Northeast India, a region from which longitudinal data on advanced MASLD remain limited.

Limitations of the study: Several limitations should be considered when interpreting the findings. First, this was a single-centre study conducted at a tertiary-care hospital in Guwahati, which may introduce referral bias and limit the generalizability of the results to community populations or other geographical regions. Second, the inclusion of patients aged 18–60 years excluded older adults, who may have a greater burden of fibrosis and a higher risk of hepatic decompensation. Third, the two-year follow-up period may have been insufficient to capture the complete natural history of advanced MASLD and less frequent liver-related outcomes. Fourth, advanced fibrosis was not confirmed by liver biopsy in every participant, creating the possibility of disease misclassification. Fifth, liver stiffness may be influenced by hepatic inflammation, cholestasis, congestion, food intake and technical factors in addition to fibrosis. Sixth, changes in body weight, glycaemic control, medications and other metabolic factors during follow-up may have affected liver stiffness and were not fully incorporated as time-varying covariates. Seventh, the annual 2-kPa threshold used to define liver stiffness trajectories was exploratory and requires external validation. Finally, the predictive model was developed and assessed in the same cohort without external validation; therefore, its cut-offs and performance estimates should not be applied directly to routine clinical practice until confirmed in independent, multicentre studies.

CONCLUSION

In this two-year prospective observational study of adults with advanced metabolic dysfunction-associated steatotic liver disease, higher baseline liver stiffness and a progressive increase in liver stiffness over time were independently associated with an increased risk of hepatic decompensation. Serial vibration-controlled transient elastography may therefore complement routine clinical and laboratory assessments by providing dynamic risk stratification and identifying patients who require closer surveillance and earlier management. However, the proposed liver-stiffness trajectory threshold is exploratory and requires validation in larger, multicentre cohorts with longer follow-up before routine clinical application.

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