Journal of Clinical and Translational Hepatology **2024**
DOI: 10.14218/JCTH.2024.00261

Research Letter

The Failure Rate of Liver Stiffness Measured by Vibration-controlled Transient Elastography in the United States and Relevant Factors

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Received: July 29, 2024 | **Revised:** October 11, 2024 | **Accepted:** October 23, 2024 | **Published online:** November 08, 2024

Citation of this article: Zhou R, Chen J, Huang R, Yang Y, Shi Y. The Failure Rate of Liver Stiffness Measured by Vibration-controlled Transient Elastography in the United States and Relevant Factors. J Clin Transl Hepatol 2024. doi: 10.14218/JCTH.2024.00261.

Liver cirrhosis is the 11th leading cause of death worldwide, with an estimated one million deaths annually due to complications of cirrhosis.[1] Since the progression to cirrhosis is often asymptomatic, it is critical to screen individuals at risk of progressive fibrosis to prevent the development of cirrhosis in the general population. Vibration-controlled transient elastography (VCTE), which measures liver stiffness by analyzing the speed of shear waves, is increasingly used as a non-invasive tool to screen for advanced liver fibrosis. It has demonstrated excellent performance compared to liver biopsy.[2,3] However, ensuring a high success rate for the measurements is particularly important, especially in the context of large-scale screening. While a high success rate of liver stiffness measurement (LSM) by VCTE has been reported in patients with metabolic-associated steatotic liver disease,[4] limited data is available on its application in the general population. In this study, we aimed to analyze the failure rate of LSM by VCTE and explore the factors associated with failure in a U.S. general population.

Data were derived from the 2017–2020 National Health and Nutrition Examination Survey (NHANES), including a total of 7,096 participants over the age of 20 who underwent VCTE examinations performed by experienced NHANES health technicians. Unsuccessful tests or test failures were defined as cases where participants had fewer than 10 valid measurements within the given time or had a liver stiffness interquartile range (IQR)/median (M) ratio over 30%. Participants with 10 or more valid stiffness measurements, fasting for over 3 h, and an IQR/M ratio ≤30% were considered to have successfully completed the VCTE exam. Socio-demographic characteristics and liver-related variables were collected, including age (divided into quantiles: <36, 36–52, 52–64, ≥64), sex (male, female), body mass index (BMI, normal: <25 kg/m^2, overweight: 25–30 kg/m^2, obese: ≥30 kg/m^2), race (Mexican American or other Hispanic, Non-Hispanic White, Non-Hispanic Black, Other), poverty income ratio (<1.3, 1.3–3.5, ≥3.5, missing), education level (less than high school, high school graduate, college or above), alanine transferase (U/L), aspartate transferase (U/L), total bilirubin (mg/dL), albumin (g/dL), platelet count (×10^9/L), Fibrosis-4 index (FIB-4, risk of fibrosis: low (FIB-4 < 1.3, FIB-4 < 2 for age ≥ 65 years), indeterminate risk (FIB-4 between 1.3 and 2.67, FIB-4 between 2 and 2.67 for age ≥ 65 years), and high risk (FIB-4 > 2.67)), diabetes status, and the type of probes (medium, extra-large). Statistical analysis was conducted based on the complex sampling design of NHANES, using the sampling weights from the mobile exam center visit (WTMECPRP). Participant characteristics were presented as medians (Q1, Q4) or as numbers and proportions. Comparisons were made between participants with successful and unsuccessful VCTE exams, and the prevalence of unsuccessful tests was analyzed across different subgroups. Multivariable logistic regression models were utilized to explore factors associated with test failure. To avoid multicollinearity between independent variables, the variance inflation factor (VIF) was calculated, with VIF > 5 indicating collinearity in the regression model. Detailed information about the VCTE test and methodology is provided in the Supplementary File 1.

Among the 7,096 participants who underwent exams, 279 failed LSM, accounting for 3.37% of the U.S. population. A significantly higher rate of unsuccessful tests was observed in older individuals (age ≥ 64: 4.55%), those with obesity (5.86%) or diabetes (5.33%), and individuals tested with the extra-large (XL)-probe (8.86%) (Fig. 1A). Consistent with the failure rate, those with unsuccessful tests were older (median age: 48.00 vs 55.00; p = 0.008), had a higher BMI (median BMI: 28.50 kg/m^2 vs 35.20 kg/m^2; p < 0.001), lower albumin levels (median albumin: 4.10 g/dL vs 4.00 g/dL; p = 0.004), a higher prevalence of diabetes (14.06% vs 22.66%; p = 0.008), and more frequent use of the XL-probe (26.20% vs 72.98%; p < 0.001), compared to participants with successful tests (Supplementary Table 1).

Multicollinearity was not observed in the multivariate

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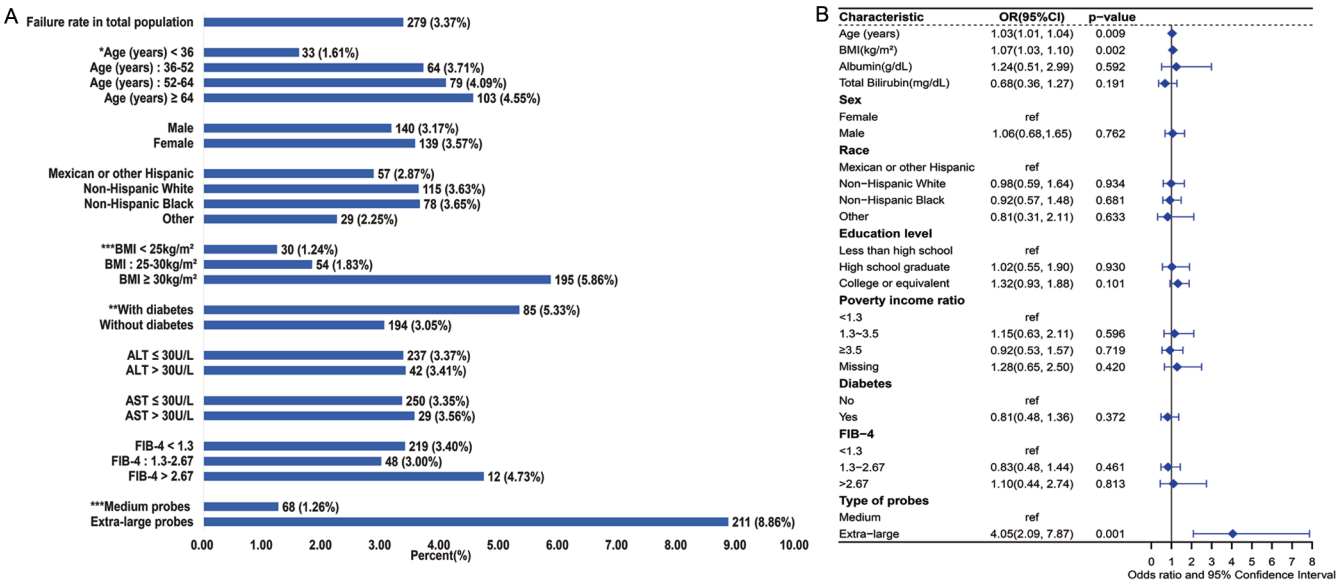

Fig. 1. Prevalence of unsuccessful LSM tests and relevant factors. (A) Prevalence of unsuccessful LSM tests in the total population and subgroups. The bar plot presents the percentage of unsuccessful LSM tests in the total population and subgroups. The number of unsuccessful tests and the percentage are listed on the right side of the columns. The number is unweighted, while the percentage is weighted according to the analytic guidance of the National Health and Nutrition Examination Survey. Significant differences in the prevalence of unsuccessful tests were observed among subgroups based on age, BMI, diabetes, and type of exam probes. *p < 0.05; **p < 0.01; ***p < 0.001. (B) Factors associated with VCTE failure. The multivariable logistic model was adjusted for age, sex, BMI, race, poverty income ratio, education level, diabetes, total bilirubin, albumin, FIB-4, and type of probes. ALT, alanine transferase; AST, aspartate transferase; BMI, body mass index; CI, confidence interval; FIB-4, Fibrosis-4 index; OR, odds ratio; LSM, liver stiffness measurement.

model, with VIF < 5 for all variables. Age (odds ratio [OR] [per 1-year increase] = 1.03, 95% confidence interval [CI]: 1.01–1.04, p = 0.009) and BMI (OR [per 1 kg/m^2 increase] = 1.07, 95% CI: 1.03–1.10, p = 0.002) were identified as independent factors associated with unsuccessful tests (Fig. 1B). Additionally, the use of the XL-probe was significantly associated with an increased likelihood of test failure in the total population (OR = 4.05, 95% CI: 2.09–7.87, p = 0.001) and across BMI categories. No interactions were observed between probe type and subgroups of age (p for interaction = 0.572) or BMI (p for interaction = 0.166) (Supplementary Table 2).

In a nationally representative cohort of the U.S. population, the rate of unsuccessful LSM measured by VCTE was generally low (3.37%). A previous study reported a higher failure rate of 15.8%, primarily due to an IQR/LSM ratio greater than 30%.[5] However, that study was conducted in a population with a high likelihood of chronic liver diseases, potentially overestimating the failure rate for the general population. Notably, the FibroScan device has been updated since its initial implementation, and the latest machine was used in this study, which facilitated faster and more successful testing.[6]

Our study observed a higher likelihood of test failure in obese individuals. Obesity is widely recognized as a confounder of LSM tests, as adipose tissue interferes with FibroScan waves, though the utilization of the XL-probe has improved LSM accuracy in obese individuals.[7,8] We found a significantly higher failure rate (8.86%) in the XL-probe group. However, this finding should be interpreted with caution, as there was no direct comparison between the M and XL probes. The XL-probe is often used as a rescue test when the M-probe fails to produce a valid measurement.[9] In a study comparing the M and XL probes in patients suspected of having chronic liver diseases, the XL-probe resulted in approximately 15% unsuccessful LSM tests, slightly higher than the 11.9% with the M-probe. However, the XL-probe rescue test resulted in 11 successful measurements out of 24 tests that failed with the M-probe.[9] Although diabetes was not identified as an independent factor related to test failure in our study, a higher failure rate of LSM was observed in participants with diabetes, which warrants further investigation. Additionally, operator expertise should be considered, as it has been independently associated with test failure in previous studies.[5]

VCTE for estimating LSM has a low failure rate when deployed in the U.S. general population, though special attention should be given to elderly and obese individuals.

Funding

The work was supported by the National Key Research and Development Program of China (No. 2022YFC2304501 and No. 2021YFC2301800), the Fundamental Research Funds for the Central Universities (2023QZJH50), the Medical Health Science and Technology Project of the Zhejiang Provincial Health Commission (No. 2022RC141), and the Chinese National Natural Science Foundation (No. 81870425).

Conflict of interest

YS has been an Editorial Board Member of *Journal of Clinical and Translational Hepatology* since 2022. The other authors have no conflict of interests related to this publication.

Author contributions

Methodology (JC, RH, YS, YY), investigation, formal analysis, writing - original draft (RZ), conceptualization, writing - review & editing, supervision (YS), and conceptualization (YY). All authors have approved the final version and publication of the manuscript.

Ethical statement

This study was conducted according to NHANES protocols. Participants were de-identified and sourced from a public database. All NHANES participants provided informed consent.

Data sharing statement

Data will be available upon request and approval from the corresponding author.

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