Is Fasting Necessary for Individuals with Nonalcoholic Fatty Liver Disease to Undergo Vibration-Controlled Transient Elastography?

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Abstract

OBJECTIVES: To investigate the effect of meal intake on liver stiffness measurement (LSM) and controlled attenuation parameter (CAP) in patients with biopsy-proven nonalcoholic fatty liver disease undergoing vibration-controlled transient elastography.

METHODS: LSM and CAP were assessed at baseline and serially for 6 hours after meal intake in 24 patients.

RESULTS: A significant increase in LSM was seen up to the 2-hour time point (26 +/- 25%, P = 0.02). The CAP scores changed minimally with a maximal change of 3% (P > 0.1).

CONCLUSIONS: Three hours of fasting is necessary before evaluation with vibration-controlled transient elastography.

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INTRODUCTION

Staging of liver fibrosis by liver biopsy is integral to the evaluation and management of nonalcoholic fatty liver disease (NAFLD) (1). Because of the invasive nature of the biopsy, vibration-controlled transient elastography (VCTE) is widely in use owing to its ability to noninvasively assess liver fibrosis with liver stiffness measurement (LSM) and steatosis with controlled attenuation parameter (CAP) (2-4).

Previous studies using a medium (M+) probe and a meal challenge with commercial formulas in healthy subjects and patients with viral hepatitis showed a peak increase in LSM at 60 minutes with values returning to baseline within 120 minutes (5-7). The effect of meal intake on CAP scores is currently not well understood because 1 study (5) reported an increase, whereas the other, a decrease (8). The objectives of this study were to systematically investigate the impact of meal intake and its time course on LSM and CAP in individuals with and without advanced fibrosis from NAFLD. To examine the relationship between the calorie content and the change in LSM/CAP, the meal challenge allowed for unrestricted consumption of food from the hospital cafeteria.

MATERIALS AND METHODS

Study population

The effect of food intake on LSM and CAP was assessed in 24 patients with biopsy-proven NAFLD (12 with advanced fibrosis (stages 3 and 4) and 12 without advanced fibrosis (<=stage 2)). To assess the variability of LSM and CAP with time, 8 of the study participants were randomly selected to serve as unfed controls and underwent LSM and CAP measurements on a subsequent day, but in the fasting state. The Indiana University Institutional Review Board approved the study. All subjects provided written informed consent before participating in the current study.

Determination of LSM and CAP by VCTE

An expert operator obtained baseline measurements of LSM and CAP 5 minutes apart (the average served as the baseline) using FibroScan 502 Touch (Echosens, France) after an overnight fast. When 10 valid measurements with interquartile (IQR)/median ratio of <30% were obtained, the site was marked

with a pen for subsequent measurements of LSM/CAP. A registered dietician calculated the calorie, fat, carbohydrate, and protein content of the meal using the MyFitnessPal app (https://www.myfitnesspal.com/). The patients returned for the postprandial measurement of LSM/CAP at 30 minutes, 1, 2, 3, 4, 5, and 6 hours after completion of the meal.

Statistical analysis

For descriptive analysis, continuous variables were expressed as mean +/- s.d. and categorical variables as frequency (%). The multivariable mixed model approach was used to analyze the effect of a meal on LSM and CAP at each time point compared with the baseline (or premeal values). $P < 0.05$ was taken as statistical significance. Stata software version 14 and SAS v9.4 (SAS Institute, Cary, NC) were used to perform the statistical analyses.

RESULTS

The mean age of the study cohort was 50 +/- 11 years (54% females; body mass index (BMI): 38 +/- 6 kg/m^2) with a mean alanine aminotransferase of 47 +/- 21 U/L. Seventeen of the 24 subjects underwent VCTE with the extra-large (XL+) probe. All scans were valid (10 values) and reliable with IQR/median <30%. The median LSM was 9.6 kPa (95% confidence interval: 8.0-14.9 kPa). The median CAP score was 343 dB/m (95% confidence interval: 323-361 dB/m). The study participants consumed a mean of 894 +/- 330 kcal in 18 +/- 7 minutes.

Effect of meal intake on LSM

The increase in the LSM was seen up to the 2-hour time point with a mean increase of 1.6 +/- 3.8 kPa (26% +/- 25%) ($P = 0.02$). The mean increase in LSM at 3, 4, 5, and 6 hours was less than 1.2 kPa (10%). The increase in LSM was seen in both early (1.34 +/- 1.85 kPa or 31% +/- 29%) and advanced fibrosis groups (2.0 +/- 5.3 kPa or 21% +/- 21%), and reached statistical significance ($P = 0.027$) (Figure 1). Compared with the unfed state, LSM was significantly increased at 30 minutes ($P = 0.0024$), 1 ($P = 0.0013$), and 2 h ($P <= 0.0001$) with a maximal % increase of 26% +/- 19% (Figure 2). This difference remained significant even after adjusting for age, sex, and BMI. Subjects who underwent VCTE using M+ probe did not differ from those who underwent study with XL + probe in either the absolute (2 +/- 4.5 vs 0.7 +/- 1.4 kPa, $P = 0.1$) or the relative increase in LSM (28 +/- 27 vs 20% +/- 20%, $P = 0.4$) at the 2-hour time point.

The maximal increase in the LSM in the initial 2 hours was significantly correlated with the number of calories in the meal in the entire group (r = 0.4, P = 0.03). We then examined the relationship between meal contents in individuals (n = 8) who developed >= 2 kPa (arbitrary but clinically meaningful) increase in LSM at the 2-hour time point. These individuals consumed significantly higher protein (42 +/- 10 vs 31 +/- 10 g, P = 0.019), but not fat (45 +/- 14 vs 38 +/- 15 g, P = 0.2) or carbohydrates (125 +/- 65 vs 84 +/- 37 g, P = 0.1).

Effect of food intake on CAP

In the fed state, the CAP score was numerically lower with a maximal change of -3% +/- 13% throughout the study and was not statistically significant from the baseline when adjusted for age, BMI, sex, and baseline CAP values. The absolute change at 2 hours after meal ingestion was -13 +/- 36 dB/m (P = 0.11).

DISCUSSION

In the current study, the maximal increase in LSM occurred at the 2-hour time point with a return to the values close to the baseline by 3 hours. This finding is in contrast to previously reported studies, implying that LSM values returned to baseline by 2 hours (6,7). The additional hour required for the return of LSM to near-baseline values is possibly because of the number of calories consumed, content of the meal, or underlying liver disease. The current study suggests that patients with NAFLD with early fibrosis are more susceptible to a meal-related increase in LSM. The increase in the LSM does not appear to be related to the probe size. Finally, the meal intake did not affect the CAP values in a significant way. In summary, at least 3 hours of fasting is necessary to minimize the false increase in LSM and its effect on diagnostic accuracy. The meal intake does not influence the CAP scores.

CONFLICTS OF INTEREST

Guarantor of the article: Naga Chalasani, MD.

Specific author contributions: N.C. is the corresponding and senior author. R.V., N.C., S.W., and N.S.: writing of the manuscript and approving the final version. R.W., L.H., and S.R.: data collection. R.V. and J.S.: analysis.

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Figure 1

Percent change in LSM (kPa) as compared to baseline after meal challenge in patients with NAFLD with no/early fibrosis, i.e., F0-F2 (n = 12), and with advanced fibrosis, i.e., F3-F4 (n = 12). At baseline, the median LSM in no/early fibrosis group was 6.9 kPa (95% CI: 6.0–9.9 kPa) and in advanced fibrosis group, was 11.8 kPa (95% CI: 8.6–21.5 kPa). CI, confidence interval; LSM, liver stiffness measurement, NAFLD, nonalcoholic fatty liver disease.

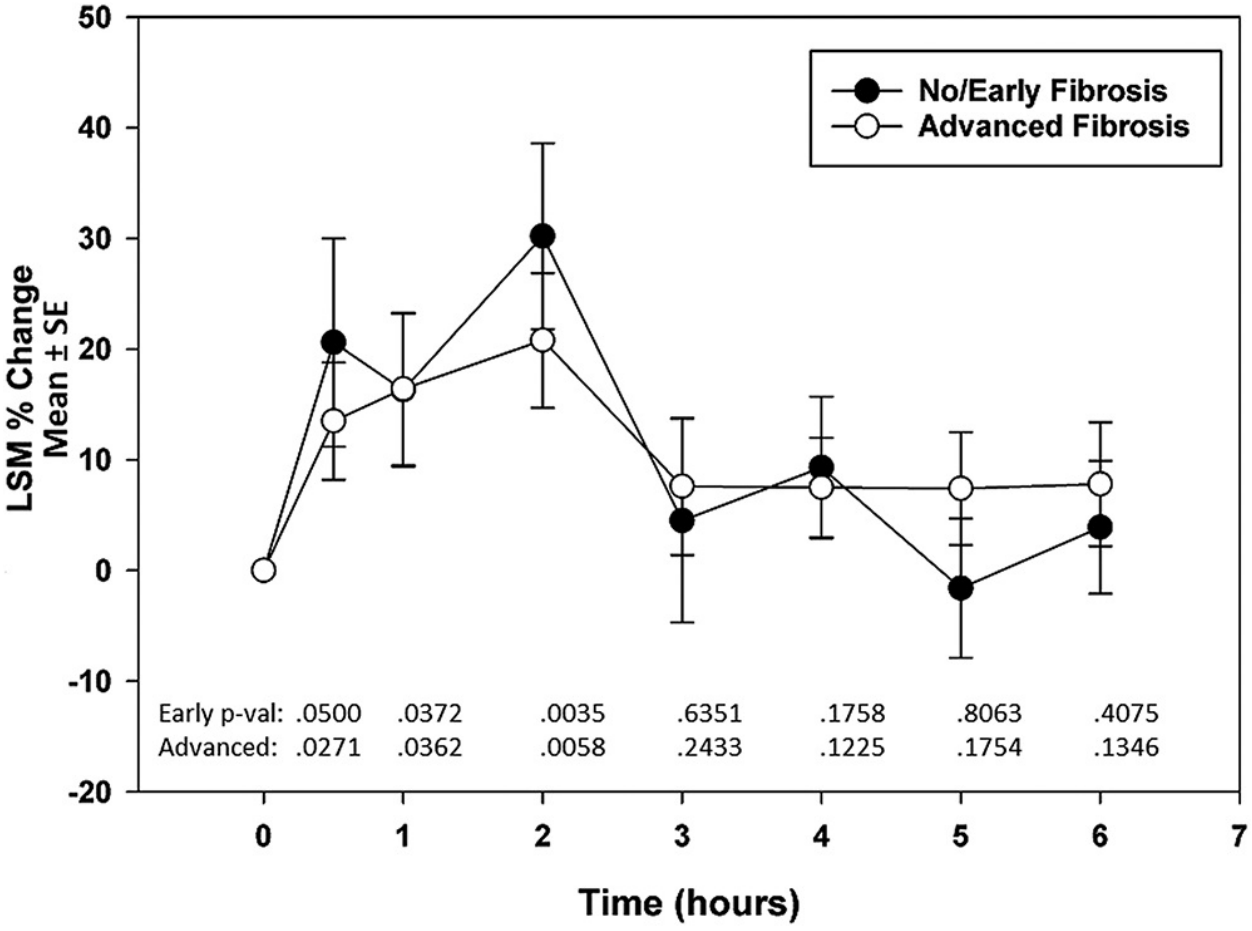

Figure 2

Percent change from baseline in LSM (%) with and without meal challenge during the study period, 0–6 hours (n = 8). Each participant underwent LSM/CAP measurement with and without meal challenge on different days. CAP, controlled attenuation parameter; LSM, liver stiffness measurement.