

The Effectiveness of Shear-wave Elastography in Childhood Hepatosteatosi Grading and Comparison with Sonographic Grading

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ABSTRACT

Objective: To assess acoustic radiation force impulse (ARFI) elastography-measured liver stiffness with respect to its relationships with hepatic steatosi presence and severity in pediatric non-alcoholic fatty liver disease (NAFLD), while identifying clinical factors associated with altered liver elasticity.

Methods: This cross-sectional observational study included 31 children with ultrasonographically diagnosed NAFLD and 12 healthy controls aged 7-16 years. Clinical, anthropometric, laboratory, and imaging data were obtained from hospital records. Laboratory parameters included alanine aminotransferase, aspartate aminotransferase, fasting glucose, insulin, lipid profile, and homeostasis model assessment of insulin resistance. Liver stiffness was assessed using ARFI elastography by a single operator, with shear wave velocity (SWV) measurements acquired from segments 5-8 of the liver, excluding the left lobe.

Results: Mean age was 12.94 ± 3.20 years in the hepatosteatosi group and 11.00 ± 2.73 years in the control group ($p=0.072$); females comprised 35.5% and 58.3% of each group, respectively ($p=0.309$). The hepatosteatosi group had significantly higher body mass index (BMI) ($p=0.001$), height ($p=0.001$), and liver craniocaudal length ($p=0.002$) than controls. Among hepatosteatosi patients, those with grade 2 steatosi had significantly higher BMI ($p=0.001$) and liver size ($p=0.004$) than those with grade 1. ARFI SWV values were similar between groups and steatosi grades, and SWV values did not correlate with anthropometric or laboratory parameters.

Conclusion: ARFI elastography measurements are unaffected by hepatic steatosi severity in pediatric NAFLD and values do not correlate with clinical or laboratory parameters. As such, ARFI is a reliable non-invasive tool for fibrosis assessment, irrespective of other patient characteristics.

Keywords: Non-alcoholic fatty liver disease, elasticity imaging techniques, ultrasonography, pediatrics, biomarkers

INTRODUCTION

Non-alcoholic fatty liver disease (NAFLD), which causes steatosi and inflammatory fibrosis, is a prevalent condition that has the potential to progress into end-stage liver disease (1). It is also closely associated with obesity and insulin resistance (2,3). With rising childhood obesity rates, NAFLD has become the most common pediatric liver disorder, affecting 5-10% of children in Western countries and up to 30% in obese populations (4-6).

Ultrasonography (US) is widely used for NAFLD screening because of its accessibility and affordability, with a sensitivity of 60-94% and specificity of 66-95% for detecting hepatic steatosi (7,8). However, US relies on subjective echogenicity assessments with significant inter-observer variability (7,9). Liver biopsy is the gold

standard but is invasive, costly, and carries risks (e.g., bleeding, pain), with up to 3% of pediatric cases requiring hospitalization due to complications (10). Moreover, histological grading systems lack universal standardization, making biopsy impractical for routine follow-up (10). These limitations of different methods warrant the study of other non-invasive alternatives that can be used for diagnostic and prognostic purposes in NAFLD.

Elastography techniques have revolutionized hepatic assessment by quantifying tissue stiffness as a surrogate marker of disease severity. Among these, acoustic radiation force impulse (ARFI) elastography has had considerable success in pediatric applications (11). This modality employs conventional US devices and does not require external compression or specialized probes

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(11). The technology measures shear wave velocity (SWV) in meters/second, with values increasing proportionally to hepatic fibrosis stage (12). Emerging pediatric data suggest ARFI may also detect early changes associated with steatosis before US-detectable signs appear (13,14). However, it is unclear if the presence of steatosis could independently elevate ARFI values without the presence of actual fibrosis, potentially leading to overestimation of fibrosis (13,14). Addressing potential confounders impacting ARFI measurement reveal if the results are reliably utilized for the assessment of steatosis and fibrosis (early or overt). The sensitivity of ARFI may also be useful for assessing treatment response, as US findings are often delayed. At present, pediatric ARFI applications remain limited by unresolved steatosis-stiffness interactions, lack of standardized cut-offs, and segmental measurement variability (13).

This study aims to investigate the relationship between both ARFI-measured liver stiffness and the presence and severity (grade) of hepatic steatosis in pediatric NAFLD, and to identify potential factors associated with altered liver elasticity. By establishing these relationships, we seek to validate ARFI elastography as a reliable non-invasive tool for pediatric steatosis assessment while elucidating clinical and metabolic determinants of liver stiffness in this population.

METHODS

Study Design and Ethical Approval

This study was designed as a cross-sectional, observational study conducted at the Department of Pediatric Radiology, İstanbul Faculty of Medicine, İstanbul University, İstanbul, Türkiye. The study was carried out between January 2014 and June 2014, with the approval of the Ethics Committee of İstanbul University (decision no:16, date: 26.09.2014). Written informed consent was obtained from all participants and their legal guardians.

Study Population

The study population consisted of two groups: a hepatosteatosi group and a control group. The hepatosteatosi group included 31 school-aged children who were followed at the general pediatric outpatient clinic due to US-diagnosed NAFLD. The control group comprised 12 healthy school-aged children without any clinical or radiological signs of hepatic steatosis. Inclusion criteria for the hepatosteatosi group were: age between 7 and 16 years, diagnosis of hepatic steatosis based on ultrasound, and absence of acute or chronic viral hepatitis, autoimmune liver disease (e.g., autoimmune hepatitis, primary biliary cirrhosis, and primary sclerosing cholangitis), drug-induced or herbal hepatotoxicity, and inherited or metabolic liver diseases (e.g., Wilson's disease, hemochromatosis, glycogen storage disorders). The control group included children aged 7-16 years with normal liver echogenicity on US and no history of metabolic syndrome or liver disease.

Data Collection and Laboratory Parameters

Clinical data of the participants were retrospectively collected from patient files and our hospital's digital database. The available data were based on records from clinical examination, laboratory analysis, and imaging studies. These included demographic and anthropometric data, biochemical parameters, liver size measurements, hepatic steatosis grading, and liver stiffness measurements obtained via ARFI elastography. Weight and height were measured using calibrated digital scales and stadiometers. Body mass index (BMI) was calculated using the standard formula (weight in kilograms divided by height in meters squared).

Venous blood samples were obtained in the morning after an 8-hour fasting period. Alanine aminotransferase (ALT), aspartate aminotransferase (AST), fasting glucose, cholesterol, and triglyceride levels were measured in the central laboratory using standard automated chemical analyzers. Serum insulin levels were measured by radioimmunoassay. Insulin resistance was evaluated by calculating the homeostasis model assessment of insulin resistance (HOMA-IR) using the formula: $\text{HOMA-IR} = (\text{glucose} \times \text{insulin}) / 405$ (15).

Ultrasound and ARFI Measurements

All imaging was performed using the Siemens ACUSON S3000™ ultrasound system (Siemens Healthcare, Erlangen, Germany) with a 4 MHz transabdominal convex probe. Scans were conducted in the morning after at least 8 hours of fasting. Initially, a routine upper abdominal US was performed to assess liver morphology and measure the craniocaudal length of the liver. Patients with space-occupying lesions or extrahepatic abnormalities identified during the scan were excluded. Hepatosteatosi was graded as described previously (16). For ARFI elastography, cases were scanned in the supine position through the intercostal space. Measurements were obtained from segments 5, 6, 7, and 8 of the liver, avoiding vascular and biliary structures (Figure 1). For each segment, two measurements were taken by placing a 5-10 mm rectangular region of interest at a depth of 2-5 cm from the capsule. Measurements taken outside the specified depth range (2-5 cm from the capsule) were excluded from analysis. Mean velocity values in meters per second (m/s; SWV) were recorded for each segment and an average liver stiffness value was calculated. The left lobe was excluded due to motion and cardiac pulsation artifacts. All measurements were performed by the same radiologist with experience in abdominal sonography.

Statistical Analysis

Analyses were performed using Number Cruncher Statistical System 2007 and Power Analysis and Sample Size 2008 statistical software (Utah, USA). Descriptive statistics, including mean, standard deviation, median, 1st quartile, 3rd quartile, frequency, and percentage, were used to summarize the data. The normality of the data distribution was assessed. For comparisons of quantitative variables between two independent groups, the

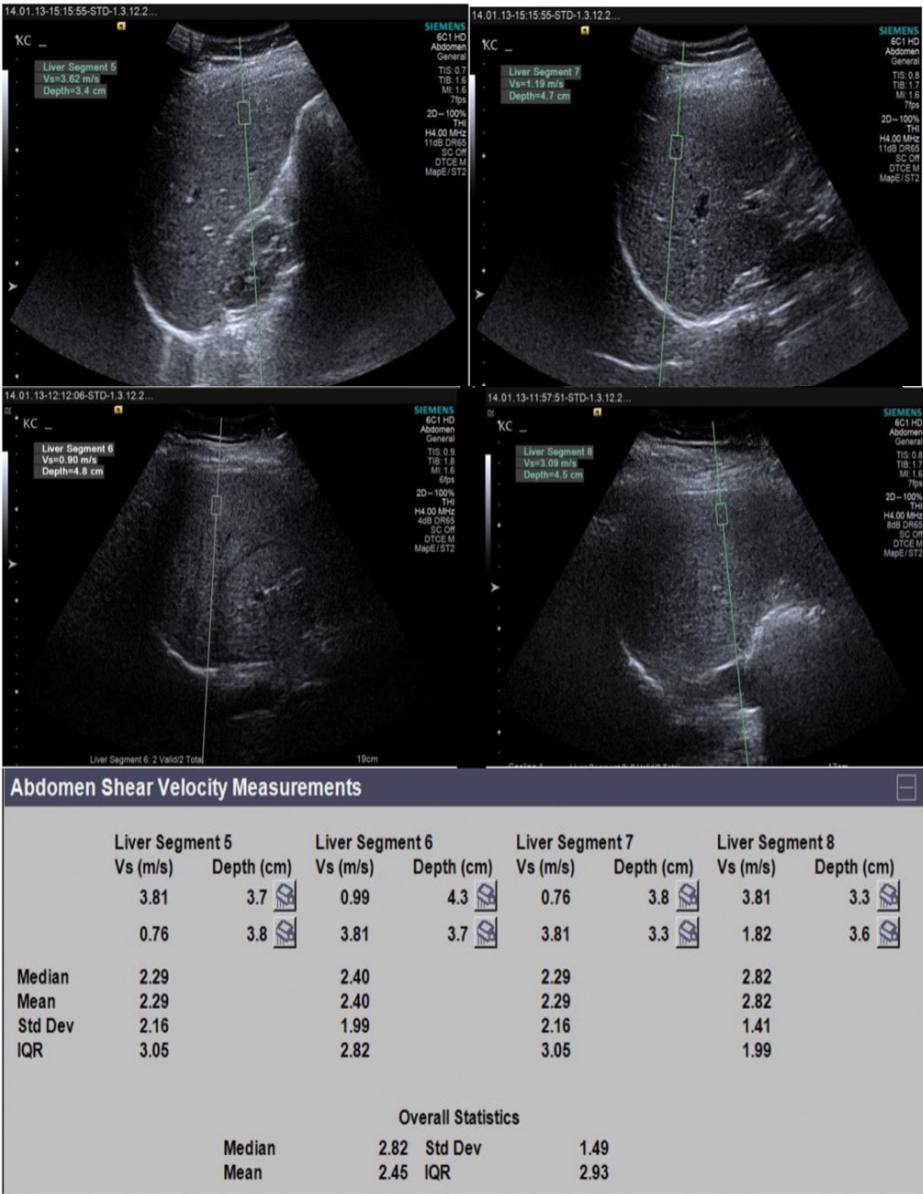


Figure 1. Measurement of shear wave velocity (SWV) using ARFI elastography. The image demonstrates the calculation of mean and median SWV values (ms) from multiple region-of-interest measurements across different liver segments
ARFI: Acoustic radiation force impulse

Mann-Whitney U test and independent t-test was used due to non-normal distribution of the data. Categorical variables were compared using the Yates’ corrected chi-square test. Correlations between continuous variables were evaluated using Spearman’s rank correlation coefficient. A p-value of less than 0.05 was considered significant.

RESULTS

The mean age of the hepatosteatois group was 12.94±3.20, while the control group’s mean age was 11.00±2.73 (p=0.072). In the hepatosteatois group, 35.5% were female, compared to 58.3% in the control group (p=0.309). The median weight and BMI of the hepatosteatois group were significantly higher than those of the control group (p=0.001). The liver craniocaudal length in

the hepatosteatois group was also significantly greater than that in the control group (p=0.002). No significant differences were observed between groups regarding any ARFI measurements (Table 1).

Among patients with grade 2 hepatosteatois, both liver craniocaudal length (p=0.004) and BMI (p=0.001) were significantly higher than in patients with grade 1 hepatosteatois (Table 2). ARFI measurement values did not differ significantly between grade 1 and grade 2 hepatosteatois groups (Table 2).

There were no significant correlations between mean SWV and liver craniocaudal length (r=0.009, p=0.961), ALT levels (r=-0.173, p=0.325), AST levels (r=-0.186, p=0.283), HOMA-IR (r=-0.179, p=0.361), cholesterol levels (r=-0.103, p=0.633), or triglyceride levels (r=-0.273, p=0.056) (Table 3).

Table 1. Demographic, clinical, and ARFI elastography characteristics of study participants

	Hepatosteatosi group (n=31)	Control group (n=12)	p-value
Age, years	12.94±3.20	11.00±2.73	0.072
Sex			
Female	11 (35.5%)	7 (58.3%)	0.309
Male	20 (64.5%)	5 (41.7%)	
Height, cm	157.74±17.32 (162)	146.25±16.15 (144)	0.054
Weight, kg	(54-89)	(32-49)	0.001
BMI, kg/m ²	30 (26-33)	19 (15-21)	0.001
ALT, U/L	26 (34-82)		
AST, U/L	31 (24-44)		
Insulin, µIU/mL	52 (39-112)		
Glucose, mg/dL	92 (86-109)		
HOMA-IR	16 (12-41)		
Cholesterol, mg/dL	169 (146-201)		
Triglyceride, mg/dL	56-302 (136.59±63.35)		
Hepatosteatosi grade			
Grade 1	26 (83.9%)		
Grade 2	5 (16.1%)		
Liver craniocaudal Length, mm	138.16±18.87	118.08±12.75	0.002
ARFI measurements			
Mean liver velocity, m/s	1.5(0.9-2.1)	1.3 (0.7-1.9)	0.163
Segment 5 mean velocity, m/s	1.4 (0.6-2.2)	1.2 (1.0-1.4)	0.056
Segment 6 mean velocity, m/s	1.4 (0.8-2.3)	1.3 (0.9-2.6)	0.350
Segment 7 mean velocity, m/s	1.3 (0.9-2.0)	1.3 (0.8-2.3)	0.323
Segment 8 mean velocity, m/s	1.3 (1.1-1.6)	1.3 (1.0-1.6)	0.498

Data are presented as mean ± standard deviation or median (1st - 3rd quartile) for continuous variables depending on their distribution and n (%) for categorical variables. P-values were obtained from independent t-tests (normal distribution) or Mann-Whitney U tests (non-normal distribution) for continuous variables and chi-square tests for sex comparison. Bolded p-values indicate statistical significance (p<0.05). ARFI: Acoustic radiation force impulse, BMI: Body mass index, ALT: Alanine aminotransferase, AST: Aspartate aminotransferase, HOMA-IR: Homeostatic model assessment of insulin resistance

DISCUSSION

The current study investigated the impact of hepatic steatosis on ARFI elastography measurements in pediatric NAFLD. Our results demonstrated that children with NAFLD exhibited significantly higher BMI and liver craniocaudal length compared to healthy controls, confirming the association between obesity and hepatomegaly in this population. However, ARFI-derived SWV measurements showed no significant differences between NAFLD patients and controls, nor between grade 1 and grade 2 steatosis subgroups. Furthermore, SWV values did not correlate with liver size, aminotransferase levels (ALT/AST), insulin resistance (HOMA-IR), or lipid profiles (cholesterol/triglycerides).

The increasing prevalence of pediatric NAFLD necessitates reliable non-invasive tools for fibrosis assessment, since this can

improve the prediction of cirrhosis risk (17). ARFI elastography has proved considerable efficacy for this purpose, with SWV measurements acting as a surrogate for fibrosis severity (18). Hanquinet et al. (19) 32 demonstrated significantly higher SWV in chronic liver disease (1.99 m/s) versus controls (1.12 m/s), with 100% sensitivity for severe fibrosis at a cut-off <2 m/s. Noruegas et al. (20) validated the utility in different fibrosis stages, while Marginean and Marginean (21) noted elevated SWV in pediatric NAFLD and correlations with AST and inflammation. Despite this level of evidence, it is still unclear whether hepatic steatosis alone (regardless of fibrosis) influences ARFI results. Our study addresses this gap, revealing no significant SWV differences between NAFLD patients and healthy controls, indicating that steatosis presence alone does not intrinsically alter ARFI-derived stiffness measurements in pediatric NAFLD. Our results are supported

Table 2. Comparison of clinical and ARFI elastography parameters between Grade 1 and Grade 2 hepatosteatosi patients

	Grade 1 (n=26)	Grade 2 (n=5)	p-value
Liver craniocaudal length, mm	133.46±15.79	162.60±14.84	0.004
ARFI measurements			
Mean velocity for overall liver, m/s	1.4 (0.8-2.0)	1.9 (1.3-2.8)	0.361
Segment 5 mean velocity, m/s	1.4 (0.5-2.2)	1.6 (0.8-2.0)	0.788
Segment 6 mean velocity, m/s	1.4 (0.7-1.8)	1.7 (1.5-2.0)	0.747
Segment 7 mean velocity, m/s	1.3 (0.6-2.2)	1.7 (0.8-1.9)	0.227
Segment 8 mean velocity, m/s	1.3 (0.6-2.3)	1.7 (1.0-2.0)	0.347
BMI (kg/m²)	29 (21-32)	42 (32-47)	0.001
ALT, U/L	18 (14-38)	32 (19-49)	0.085
AST, U/L	22 (15-39)	26 (18-51)	0.893
Cholesterol, mg/dL	175 (151-192)	154 (146-174)	0.065
Triglyceride, mg/dL	(79-151)	(101-132)	0.977
HOMA-IR	5 (3-12)	8 (7-22)	0.085

Data are presented as mean ± standard deviation or median (1st - 3rd quartile), and independent t-tests (normal) and Mann-Whitney U (non-normal) were performed accordingly. Bold p-values significant (p<0.05)
ARFI: Acoustic radiation force impulse, BMI: Body mass index, ALT: Alanine aminotransferase, AST: Aspartate aminotransferase, HOMA-IR: Homeostatic model assessment for insulin resistance

Table 3. Correlation analysis between mean liver ARFI velocity and clinical parameters

Mean liver velocity, m/s		
	r	p
Liver craniocaudal length, mm	0.009	0.961
ALT, U/L	-0.173	0.325
AST, U/L	-0.186	0.283
HOMA-IR	-0.179	0.361
Cholesterol, mg/dL	-0.103	0.633
Triglyceride, mg/dL	-0.273	0.056

ALT: Alanine aminotransferase, AST: Aspartate aminotransferase, HOMA-IR: Homeostatic model assessment of insulin resistance, r: Spearman correlation coefficients

by data from several studies. Motosugi et al. (22) showed no differences in SWV values between adults with fatty liver (SWV: 1.02±0.12 m/s) and those without (1.03±0.12 m/s). Similarly, Rifai et al. (23) found no association between steatosis and SWV in biopsy-proven cases. Taken together, these studies indicate that fibrosis is the primary factor altering SWV, particularly in human steatosis, as animal studies appear to show varying findings (24). It is also crucial to note that tissue-specific and methodological factors may alter the results. This alteration includes the varying impact of inflammation and lipids on the microenvironment (25), as well as the differences in results based on the site of SWV measurement in the liver (13). These variations might be unavoidable given the technical limitations of US-based analyses versus magnetic resonance imaging (MRI) (14). Nonetheless, while steatosis may indirectly influence stiffness via altering inflammation

or fibrosis, our evidence suggests it does not systematically bias ARFI measurements. Despite this reliability for fibrosis screening in pediatric NAFLD, combining it with biomarkers like AST/ALT ratios could optimize diagnostic precision (26).

The relationship between hepatic steatosis severity and ARFI-derived liver stiffness remains controversial, with conflicting evidence regarding whether fat accumulation grade independently influences SWV measurements (27). In our study, we observed no significant differences in SWV values between children with Grade 1 and Grade 2 steatosis, suggesting that steatosis severity alone may not directly alter ARFI-based stiffness assessments. The literature on this topic reveals contrasting results. Yoneda et al. (28) reported an inverse relationship between steatosis grade and SWV, with decreasing velocities in higher grades (Grade 1: 1.38 m/s; Grade 2: 1.14 m/s; Grade 3: 1.08 m/s). This is an unexpected decline, and it raises questions regarding the application of ARFI; however, such an intriguing finding could also be demonstrating the technical limitations of SWV in different disease states and progression. Oana et al. (13) documented elevated SWV in the right lobe (segment 8: 1.982±0.85 m/s) compared to segment 1 (1.325±0.27 m/s) in obese children, implying regional stiffness variations driven by uneven fat distribution rather than global grading. This is partially supported by data from pediatric patients showing higher SWV in obese children with steatosis (1.746±0.49 m/s) versus controls (1.080±0.27 m/s), despite the absence of correlations between SWV and BMI (13). Animal models further complicate interpretation: Guzmán et al. (24) demonstrated that diet-induced steatosis markedly increases SWV, with strong histological correlation. However, species-specific metabolic responses limit extrapolation to humans. Crucially, Rifai et al. (23)

found no statistical impact of steatosis grade on ARFI in clinical cohorts. This latter result aligns with our findings and suggests steatosis grade does not confound elastography measurements. There are several possible explanations the inconsistent results in the literature. Regional heterogeneity in fat distribution can significantly influence localized SWV readings, as fat accumulation can alter tissue mechanics (13). Inflammation and its differing impacts on tissues and lesion microenvironments could also confound interpretations, as different histological outcomes in different sites (e.g., ballooning hepatocytes, lobular inflammation) may alter stiffness and SWV outputs (21,23). Finally, technical limitations of US-based steatosis grading, which lacks the precision of MRI or histology, may obscure subtle fat-stiffness relationships due to inconsistent fat quantification and threshold definitions (14). While severe steatosis appears to have the potential to influence ARFI results, current evidence does not support a consistent, grade-dependent effect on SWV measurements in pediatric NAFLD.

The robustness of ARFI elastography in pediatric NAFLD is reported to be influenced by several other clinical and biochemical variables (29); however, we did not find any significant correlations between SWV and liver size, aminotransferase levels, insulin resistance (HOMA-IR), or lipid profiles. Indeed, available literature largely suggests that ARFI results are unassociated with age, sex, and BMI (12,30-32). However, Rifai et al. (23) reported positive correlations between ARFI values and hepatomegaly/splenomegaly, suggesting that portal hypertension or volumetric changes in advanced disease may influence liver stiffness. Similarly, Takahashi et al. (32) observed that SWV data correlated with AST/ALT levels in patients with chronic liver disease; however, again, these relationships might easily be attributed to concurrent inflammation rather than NAFLD pathophysiology, which is supported by another study demonstrating that SWV results correlated with AST (but not ALT) in patients with malignancy, as well as those with NAFLD (21). This could indicate that AST elevation is a result of excessive inflammation-induced hepatocellular injury rather than being directly associated with NAFLD. Metabolic factors like BMI have been shown to influence ARFI measurements in otherwise-healthy children with obesity (21), but this relationship does not exist in patients with established NAFLD. Considering available evidence and our results, it is evident that ARFI-measured SWV results are not strongly altered by metabolic fluctuations. Nevertheless, interpretation of results might necessitate awareness of disease stage, progression, treatment characteristics and response, and tissue-level or systemic complications.

Study Limitations

The present study focuses on ultrasound-measured results and does not utilize gold standard methodology (biopsy) in the determination of steatosis and fibrosis. This is an important limitation as US-based grading remains inferior to biopsy or MRI. Second, our small sample size may be considered limited in terms

of the comparison of groups with regard to steatosis grades (in fact, grade 3 was entirely absent). Further, the single-center design may limit the generalizability of our findings to other pediatric populations with varying ethnic, geographic, or comorbidity profiles. Furthermore, all ARFI measurements were performed by a single radiologist. Although this prevented possible biases due to inter-observer variability, it must be noted that all ultrasound-based outputs have some level of subjectivity.

CONCLUSION

This study demonstrates that ARFI elastography measurements are unaffected by the presence or severity of hepatic steatosis in pediatric NAFLD and show no significant correlations with anthropometric, biochemical, or metabolic parameters. ARFI-based measurements appear to be a crucial tool for allowing non-invasive fibrosis assessment in children without steatosis-related confounding. However, further large-scale studies performing analyses with respect to histopathological data are needed. Based on present findings and prior literature, integrating ARFI with clinical and biomarker data could optimize the utility of this tool in the diagnosis and follow-up of children with NAFLD.

Ethics

Ethics Committee Approval: This study was approved by the Ethics Committee of İstanbul University (decision no: 16, date: 26.09.2014), and ethical permission was obtained prior to its initiation.

Informed Consent: Written informed consent was obtained from all participants and their legal guardians.

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Footnotes

Author Contributions: Surgical and Medical Practices - M.S.Ç.; Concept - M.S.Ç., B.A.; Design - M.S.Ç., B.A.; Data Collection and/or Processing - M.S.Ç.; Analysis and/or Interpretation - M.S.Ç.; Literature Search - M.S.Ç.; Writing - M.S.Ç., B.A.

Conflict of Interest: The authors have no conflict of interest to declare.

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