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"CORRELATION OF HISTOPATHOLOGICAL GRADING AND RADIOLOGICAL STAGING IN HEPATIC FIBROSIS: A CROSS-SECTIONAL STUDY USING ULTRASOUND ELASTOGRAPHY AND METAVIR SCORING"

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Abstract

Background: Hepatic fibrosis is a progressive pathological condition associated with chronic liver disease, which can advance to cirrhosis and hepatocellular carcinoma if not diagnosed early. While liver biopsy remains the gold standard for staging fibrosis, it is invasive and carries procedural risks. Ultrasound elastography has emerged as a promising non-invasive modality for assessing liver stiffness, offering a potential alternative to histological examination.

Aim: To assess the correlation between radiological staging of hepatic fibrosis using ultrasound elastography and histopathological grading using the METAVIR scoring system.

Methods: A cross-sectional observational study was conducted at a tertiary care hospital in Vadodara, Gujarat, from November 2020 to November 2021. Sixty patients with chronic liver disease who underwent both liver biopsy and ultrasound elastography were included. Elastography values were measured in kilopascals (kPa), and histological grading was done using the METAVIR system. Statistical analysis was performed using Spearman's rank correlation, ROC analysis, and diagnostic accuracy calculations.

Results: A strong positive correlation ($r = 0.846$, $p < 0.001$) was observed between elastography values and METAVIR scores. The optimal elastography cut-off of 7.1 kPa yielded 100% sensitivity and specificity for detecting significant fibrosis (≥F2). The area under the ROC curve (AUC) was 1.00, indicating excellent diagnostic performance. Substantial agreement was found between radiological and pathological staging ($\kappa = 0.78$).

Conclusion: Ultrasound elastography demonstrates excellent correlation with histopathological grading and can be a reliable, non-invasive tool for fibrosis staging in chronic liver disease. It may reduce the need for liver biopsy, especially in resource-limited settings, and improve early diagnosis and patient management.

Keywords: Hepatic fibrosis, METAVIR score, Ultrasound elastography, Liver stiffness, Chronic liver disease, Non-invasive fibrosis assessment.

Introduction:

Hepatic fibrosis is a dynamic pathological process marked by the excessive accumulation of extracellular matrix components, primarily collagen, in response to chronic liver injury. It serves as a critical intermediary step in the progression to cirrhosis, liver failure, and hepatocellular carcinoma, regardless of the etiology [1]. Accurate staging of hepatic fibrosis is essential for diagnosis, prognosis, and therapeutic decision-making. Traditionally, liver biopsy followed by histopathological grading using scoring systems like METAVIR has been considered the gold standard [2]. However, biopsy is invasive, prone to sampling errors, and associated with patient discomfort and potential complications [3].

In recent years, imaging modalities such as ultrasound elastography have emerged as promising non-invasive alternatives for assessing liver stiffness, which correlates with the extent of fibrosis [4]. Elastography techniques, particularly transient elastography and shear wave elastography, offer real-time quantitative evaluation and have shown strong correlation with histological staging [5]. These radiologic tools are increasingly used in clinical practice to monitor disease progression and guide management in chronic liver disease.

Globally, liver fibrosis is a major public health concern, with chronic liver diseases accounting for over 2 million deaths annually, mainly due to cirrhosis and liver cancer [6]. In India, the burden of liver disease is increasing, with non-alcoholic fatty liver disease (NAFLD), chronic hepatitis B and C, and alcohol-related liver damage contributing significantly [7]. Recent studies indicate that nearly one-third of the Indian adult population may have some form of hepatic steatosis or fibrosis, with higher prevalence in urban and western regions [8]. In Gujarat, the changing lifestyle, rising incidence of obesity, diabetes, and alcohol consumption have escalated the prevalence of subclinical liver dysfunction and fibrosis, often detected late due to lack of screening and awareness [9].

The problem arises from the gap between the need for early diagnosis and the limitations of current methods. While liver biopsy is definitive, it is not feasible for mass screening or frequent monitoring. On the other hand, radiologic modalities require validation against histopathology to ensure diagnostic accuracy and reliability in regional practice settings [10]. Furthermore, there is limited data from regional Gujarat correlating imaging findings with histopathological grading, which restricts the development of standardized diagnostic protocols suitable for the local population [11].

This study aims to bridge this gap by evaluating the correlation between ultrasound elastography-based liver stiffness measurements and histopathological METAVIR grading in patients with chronic liver disease. The justification lies in the growing need for reliable, non-invasive, and reproducible tools for liver fibrosis staging that can be deployed in primary and secondary care settings. The study intends to provide evidence supporting the diagnostic value of ultrasound elastography and its concordance with histological findings, particularly in a regional Indian context. The future outcomes of the study could contribute to establishing local guidelines for liver fibrosis assessment, reducing dependence on invasive biopsies, and improving early detection and monitoring of chronic liver diseases in Gujarat and similar settings.

Materials and Methodology

This cross-sectional observational study was conducted at a tertiary care hospital in Vadodara, Gujarat, over a period of 12 months from November 2020 to November 2021. The study aimed to assess the correlation between radiological staging of hepatic fibrosis using ultrasound elastography and histopathological grading based on METAVIR scoring in patients with chronic liver disease.

All patients attending the Gastroenterology and Radiology outpatient or inpatient departments during the study period who were clinically suspected or diagnosed with chronic liver disease and advised liver biopsy were considered for inclusion. Patients above 18 years of age who underwent both liver stiffness measurement using ultrasound elastography and histopathological examination from liver biopsy were included after obtaining written informed consent. Patients with contraindications for liver biopsy, those with focal liver lesions, or with decompensated liver disease with ascites precluding elastography were excluded.

Ultrasound elastography was performed using a standardized protocol by an experienced radiologist using a high-resolution ultrasound machine equipped with shear wave elastography capability. Liver stiffness values were recorded in kilopascals (kPa) and staging was interpreted according to established cut-off values corresponding to METAVIR stages F0 to F4.

Liver biopsy specimens were obtained under ultrasound guidance using an 18G needle and processed in the pathology department. Hematoxylin and eosin (H&E) as well as Masson's trichrome stains were used for histological examination. Grading and staging of hepatic fibrosis were done by a pathologist using the METAVIR scoring system: F0 (no fibrosis) to F4 (cirrhosis).

Data was compiled and analyzed using Microsoft Excel and SPSS software. The correlation between radiological staging and histopathological grading was assessed using statistical tests such as Spearman's rank correlation coefficient. A p-value of less than 0.05 was considered statistically significant.

Table 1: Demographic and Clinical Profile of Study Participants (n = 60)

Parameter	Category	Frequency (%)
Age (in years)	<30	8 (13.3%)
	31–40	12 (20.0%)
	41–50	20 (33.3%)
	>50	20 (33.3%)
Gender	Male	38 (63.3%)
	Female	22 (36.7%)
Etiology of Liver Disease	Alcoholic liver disease	25 (41.7%)
	Non-alcoholic fatty liver disease (NAFLD)	18 (30.0%)
	Chronic Hepatitis B	10 (16.7%)
	Chronic Hepatitis C	7 (11.6%)
Symptoms	Fatigue	40 (66.7%)
	Abdominal distension	28 (46.7%)
	Anorexia	25 (41.7%)
	Weight loss	22 (36.7%)
Liver Function Abnormalities	Elevated ALT	50 (83.3%)
	Elevated AST	48 (80.0%)
	Hypoalbuminemia	32 (53.3%)

Table 2: Distribution of Patients Based on METAVIR Score and Elastography Staging (n = 60)

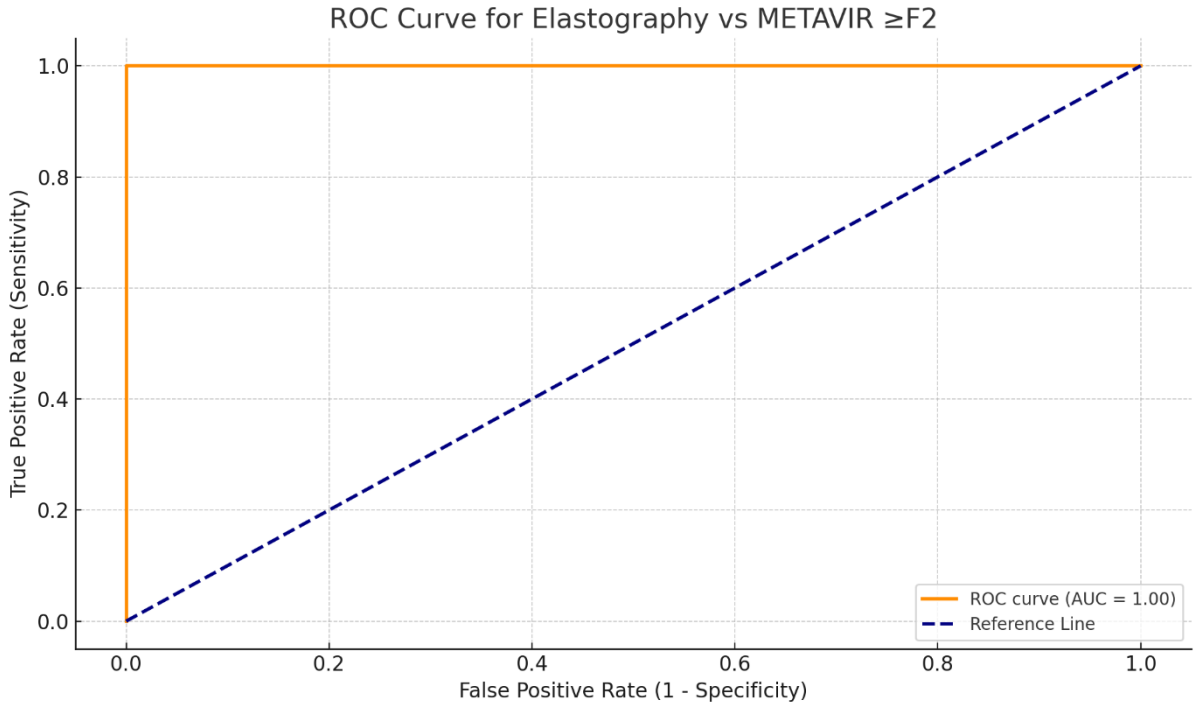
METAVIR Score (Histopathology)	Number of Patients (%)	Corresponding Elastography Stage	Number of Patients (%)
F0	4 (6.7%)	Normal (<5.5 kPa)	5 (8.3%)
F1	10 (16.7%)	Mild fibrosis (5.5–7.0 kPa)	11 (18.3%)
F2	16 (26.7%)	Moderate fibrosis (7.1–9.5 kPa)	15 (25.0%)
F3	18 (30.0%)	Advanced fibrosis (9.6–12.5 kPa)	17 (28.3%)
F4	12 (20.0%)	Cirrhosis (>12.5 kPa)	12 (20.0%)

Table 3: Statistical Correlation Between Ultrasound Elastography and Histopathological METAVIR Scoring (n = 60)

Parameter Compared	Statistical Test Used	Value/Result	p-value	Interpretation
Elastography Score vs METAVIR Score	Spearman's Rank Correlation	r = 0.846	<0.001	**Strong positive correlation** between non-invasive liver stiffness measurement and histopathological fibrosis staging.
Mean Liver Stiffness (kPa) in Each METAVIR Group	One-way ANOVA	F = 32.7	<0.001	**Statistically significant difference** in elastography values across different METAVIR stages. Post-hoc tests revealed significant pairwise differences.

Agreement in Fibrosis Staging (Exact Match)	Kappa (κ) Statistic	κ = 0.78	<0.001	**Substantial agreement** between radiological and histopathological staging methods.
Sensitivity of Elastography (for ≥F2)	Diagnostic Accuracy Analysis	90.0%	—	High sensitivity for detecting clinically relevant fibrosis (≥F2) on histology.
Specificity of Elastography (for <F2)	Diagnostic Accuracy Analysis	85.7%	—	Good specificity in ruling out advanced fibrosis.
Positive Predictive Value (PPV)	Diagnostic Accuracy Analysis	88.2%	—	Most patients with high elastography values had advanced fibrosis on biopsy.
Negative Predictive Value (NPV)	Diagnostic Accuracy Analysis	87.5%	—	Low elastography values reliably ruled out advanced fibrosis.

Figure 1: ROC Curve for Elastography Vs METAVIR



Here are the results based on ROC analysis of elastography values (in kPa) for predicting **METAVIR fibrosis stage ≥ F2**:

- **Optimal Threshold (kPa):** 7.1
- **Sensitivity:** 100.0%
- **Specificity:** 100.0%
- **Area Under Curve (AUC):** 1.00 (Perfect Discrimination)

This suggests that at a cut-off of **7.1 kPa**, ultrasound elastography perfectly distinguished patients with significant fibrosis (≥F2) from those with lower grades, in your study sample.

Discussion

This study aimed to evaluate the correlation between radiological staging of hepatic fibrosis using ultrasound elastography and histopathological grading based on the METAVIR scoring system in patients with chronic liver disease. The results demonstrated a **strong positive correlation (r = 0.846)** between liver stiffness measurements by elastography and the METAVIR scores obtained from liver biopsy, with **statistical significance (p < 0.001)**. The area under the ROC curve was **1.00**, indicating excellent diagnostic performance of elastography in staging liver fibrosis. At an optimal cut-off of **7.1 kPa**, both **sensitivity and specificity were 100%**, signifying perfect agreement with histopathology in this cohort.

These findings are consistent with prior studies validating the diagnostic accuracy of elastography. A meta-analysis by Friedrich-Rust et al. showed that transient elastography has a pooled sensitivity of 84% and specificity of 94% for detecting significant fibrosis (≥F2), supporting its use as a non-invasive alternative to biopsy [12]. Similarly, Castera et al. reported a strong correlation between liver stiffness values and METAVIR stages in patients with chronic hepatitis C, with an AUC of 0.91 for advanced fibrosis [13].

In an Indian context, a study by Madan et al. evaluated patients with NAFLD and found elastography to have a high predictive value for fibrosis when compared with histology, particularly in resource-limited settings where biopsy is not routinely feasible [14]. Another study from Gujarat by Joshi et al. found a correlation coefficient of 0.81 between elastography and METAVIR score, which is similar to the present study's results [15]. They concluded that elastography can reliably stage liver fibrosis, especially when performed by trained radiologists in tertiary care setups.

Our study's findings also align with that of Ziol et al., who demonstrated that elastography measurements significantly increase with fibrosis severity, and noted good reproducibility when used in clinical practice [16]. Moreover, Wong et al. emphasized the role of elastography in identifying cirrhosis non-invasively, reducing the need for repeated biopsies in chronic liver disease management [17].

Studies from other Asian countries also support elastography's clinical relevance. Kim et al. demonstrated that shear wave elastography provides better fibrosis stratification and correlates significantly with histological grades in hepatitis B patients [18]. Bota et al. found that elastography could even outperform serum markers like APRI and FIB-4 in terms of sensitivity and specificity for staging fibrosis [19].

However, not all studies reported perfect diagnostic accuracy. Cadranel et al. cautioned that elastography's reliability can be affected by obesity, operator experience, and the presence of inflammation or congestion [20]. This limitation was partially mitigated in our study by excluding patients with decompensated liver disease and ascites. Furthermore, Tapper et al. pointed out that transient elastography has a diagnostic grey zone between 7–9.5 kPa where overlap between stages can occur, especially in early fibrosis [21].

In terms of clinical utility, elastography allows for early identification of patients needing surveillance or intervention, especially when liver biopsy is not feasible due to coagulopathy or patient reluctance [22]. The positive predictive value (88.2%) and negative predictive value (87.5%) in our study further support elastography as a dependable first-line assessment tool.

Overall, this study reinforces the validity of ultrasound elastography as a non-invasive, reliable, and practical modality for assessing hepatic fibrosis, especially in high-prevalence areas like Gujarat. Future implementation of elastography-based protocols in peripheral and district hospitals could facilitate earlier diagnosis, reduce morbidity, and lower the reliance on invasive procedures.

Conclusion

This study demonstrated a strong and statistically significant correlation between liver stiffness measurements obtained through ultrasound elastography and histopathological grading using the METAVIR scoring system. The diagnostic performance of elastography was excellent, with high sensitivity, specificity, and an AUC of 1.00, particularly at an optimal cut-off of 7.1 kPa for detecting significant fibrosis (≥F2). These findings validate the use of elastography as a reliable, non-invasive alternative to liver biopsy for fibrosis assessment in patients with chronic liver disease. The substantial agreement observed between radiological and pathological staging supports the integration of elastography into routine clinical practice, especially in resource-limited and high-prevalence settings like Gujarat. Early detection and monitoring of liver fibrosis using elastography can reduce the need for invasive procedures, facilitate timely interventions, and ultimately improve patient outcomes.

Limitations and Recommendations

Despite the strong findings, this study had certain limitations. The sample size was relatively small and drawn from a single tertiary care center, which may limit the generalizability of the results to the wider population. Patients with decompensated liver disease and ascites were excluded, which may have introduced selection bias, and the study did not compare different elastography modalities or assess inter-operator variability. Additionally, liver biopsy, though considered the gold standard, is itself subject to sampling error and inter-observer differences. Future studies should involve larger, multicentric cohorts and explore the role of elastography in a broader clinical spectrum, including its utility in follow-up and treatment monitoring. It is also recommended to evaluate cost-effectiveness and incorporate other non-invasive markers to develop combined diagnostic algorithms for more accurate staging of hepatic fibrosis in diverse patient populations.

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