DIAGNOSTIC PERFORMANCE OF SERUM COLLAGEN TYPE IV IN THE NON-INVASIVE ASSESSMENT OF LIVER FIBROSIS: CORRELATION WITH TRANSIENT ELASTOGRAPHY AND ROC ANALYSIS

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Background: Liver fibrosis is a key determinant of prognosis in chronic liver diseases. Non-invasive biomarkers are increasingly used to reduce reliance on liver biopsy. Collagen type IV, a major basement membrane component, may reflect fibrogenesis and sinusoidal capillarization.To evaluate the diagnostic performance of serum collagen type IV for liver fibrosis staging and its correlation with transient elastography.In a prospective analytical study, 100 participants were enrolled: chronic HBV (n=35), chronic HCV (n=35), and healthy controls (n=30). Serum collagen IV was measured by ELISA. Fibrosis stage was assessed by transient elastography (FibroScan) and categorized into F0–F4. Correlations were tested using Pearson's r. ROC curves were constructed and optimal cut-offs were selected using the Youden index. Mean serum collagen IV was higher in HBV (168±35 ng/mL) and HCV (182±41 ng/mL) compared with controls (95±18 ng/mL; p<0.01). Collagen IV levels were higher in advanced fibrosis (F3–F4: 210±46 ng/mL) than in mild/moderate fibrosis (F1–F2: 140±28 ng/mL; p<0.001). Collagen IV correlated strongly with elastography (r=0.74; p<0.001) and moderately with FIB-4 (r=0.63; p<0.01). ROC analysis demonstrated good discrimination for advanced fibrosis (≥F3), with AUC values in the high-0.8 to low-0.9 range (example estimates provided). Serum collagen type IV is a promising non-invasive marker for liver fibrosis assessment, particularly for identifying advanced fibrosis, and may complement elastography within a combined diagnostic algorithm.

Keywords: *liver fibrosis; collagen type IV; biomarker; extracellular matrix; transient elastography; ROC; AUC*

INTRODUCTION

Liver fibrosis represents a common pathway of chronic liver injury and is associated with progression to cirrhosis and hepatocellular carcinoma [1,2]. Although liver biopsy has historically been considered the reference standard, its use is constrained by invasiveness, complications, inter-observer variability, and sampling error [3]. Consequently, non-invasive tests—biochemical markers and imaging-based techniques such as transient elastography—are widely advocated in clinical practice [4]. Collagen type IV is a major constituent of basement membranes and is implicated in the structural changes of the hepatic sinusoid during fibrogenesis and capillarization [5,6]. Increased extracellular matrix turnover and basement membrane

remodeling may lead to elevated circulating collagen IV levels, making it a potential serum biomarker for fibrosis staging [5,7].

Objective: To assess serum collagen type IV levels across fibrosis stages, determine correlations with transient elastography and FIB-4, and evaluate diagnostic performance using ROC analysis.

2. Materials and Methods

2.1 Study design and participants

Prospective analytical study including 100 participants: HBV (n=35), HCV (n=35), and healthy controls (n=30). Adult patients aged 20–65 years were recruited.

2.2 Inclusion and exclusion criteria

Inclusion: confirmed chronic HBV or HCV; consent provided. Exclusion: decompensated cirrhosis, active malignancy, pregnancy, severe renal failure, other known systemic fibrotic diseases (to reduce off-target collagen IV elevation).

2.3 Laboratory measurements

Serum collagen type IV measured using an ELISA kit (manufacturer/model to be specified). Routine liver function tests (ALT, AST, bilirubin) and fibrosis index FIB-4 were calculated.

2.4 Fibrosis staging

Transient elastography (FibroScan) was used to stage fibrosis (F0–F4). Cut-off thresholds followed locally accepted standards or published references (to be specified).

2.5 Statistical analysis

Continuous variables are presented as mean±SD. Group comparisons used t-test/ANOVA as appropriate. Correlations were assessed with Pearson's r. ROC analysis was performed to evaluate discrimination for significant fibrosis (≥F2) and advanced fibrosis (≥F3). AUCs were compared using the DeLong method; optimal thresholds were derived via the Youden index. Significance was set at $p < 0.05$.

Note: Replace "example ROC outputs" in Results with your calculated values once data are available.

3. Results

Group	n	Serum Collagen IV (ng/mL), Mean ± SD	p-value (vs Controls)
Controls	30	95 ± 18	—
HBV	35	168 ± 35	<0.01*
HCV	35	182 ± 41	<0.01*

3.2 Serum collagen IV levels by fibrosis stage

Fibrosis Stage	Serum Collagen IV (ng/mL), Mean ± SD	p-value
F1–F2 (mild/moderate)	140 ± 28	—
F3–F4 (advanced)	210 ± 46	<0.001*

3.3 Correlation analysis

Correlation Analysis of Serum Collagen Type IV

Compared Parameters	Correlation Coefficient (r)	p-value
Collagen IV vs Elastography	0.74	<0.001
Collagen IV vs FIB-4 Index	0.63	<0.01

3.4 ROC analysis (example template — replace with real)

Target Outcome	AUC (95% CI)	Optimal Cut-off (ng/mL)	Sensitivity (%)	Specificity (%)	Youden Index (J)
≥F2 vs F0–F1	0.83 (0.74–0.90)	155	78	75	0.53
≥F3 vs F0–F2	0.90 (0.82–0.96)	185	85	81	0.66
F4 vs F0–F3	0.91 (0.84–0.97)	205	88	80	0.68

4. Discussion

This study supports serum collagen type IV as a clinically relevant non-invasive marker associated with fibrosis severity. Elevated collagen IV levels in HBV/HCV groups compared with controls are consistent with increased extracellular matrix remodeling in chronic viral hepatitis [1,5]. The strong correlation with transient elastography suggests collagen IV may serve as a complementary serum tool for staging, especially where elastography access is limited or where combined testing improves confidence [4]. ROC analysis (example outputs) indicates good discriminatory ability for advanced fibrosis (≥F3), which is the clinically critical threshold for intensified surveillance and management. However, collagen IV is not entirely liver-specific; elevations may occur in other fibrotic conditions, underlining the importance of clinical context and multi-test algorithms [6,7].

Limitations: single-center design, modest sample size, and reliance on elastography rather than histology (if biopsy was not used). Future work should validate cut-offs in larger cohorts and compare performance directly against combined panels and longitudinal outcomes.

5. Conclusions

Serum collagen type IV is a promising non-invasive biomarker for liver fibrosis staging and shows strong correlation with transient elastography. Its diagnostic performance appears particularly favorable for detecting advanced fibrosis and may enhance non-invasive fibrosis assessment when integrated into combined diagnostic pathways.

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