

INTRODUCTION

Fibrosis in NASH is the only histological finding that correlates with liver related outcomes, and its improvement is a key outcome measure in assessing therapeutic trials in the disease. Fibrosis on histology is scored according to the Kleiner-Brunt system, or the Steatosis-Activity-Fibrosis (SAF) system. However, these scoring systems are limited by their categorical nature, with challenges differentiating patients at the junction between stages. NIT's developed based on these "categorical bins" are only tested for categorical outcomes (eg. Advanced fibrosis). We aimed to correlate common NIT's with a validated novel continuous histological fibrosis score (qFibrosis), to determine the performance of the NIT's as continuous variables.

METHODS

Patients with biopsy-proven NAFLD were enrolled from National University Health System, Singapore. Patients with any other causes for their liver disease were excluded. Their biopsy specimens underwent an artificial intelligence-based quantitative evaluation for fibrosis (qFIBS by HistoIndex®, Singapore). Fibrosis-4 index (FIB-4), AST to Platelet Ratio Index (APRI), NAFLD Fibrosis Score (NFS), as well as vibration-controlled transient elastography (VCTE), AGILE 3+ and FibroScan-AST (FAST) score were measured. The relationship between histological scoring for fibrosis and qFib, as well as the relationship between NITs and qFib was evaluated by simple linear regression analysis.

RESULTS

248 patients with biopsy-proven NAFLD were recruited to undergo qFIBS and non-invasive tests from 2014 to 2021.

qFibrosis and histological score for fibrosis had a linear relationship with an R2 of 0.39 (p < 0.001).

qFibrosis was significantly correlated with all evaluated NITs (all p-values < 0.001), with respective R2 values of 0.12, 0.12, 0.14, 0.44, 0.27 and 0.18 for FIB-4, APRI, NFS, VCTE, AGILE 3+ and FAST.

On scatterplots, confidence intervals for the regression lines appear narrow in the qFibrosis range of 1-3.

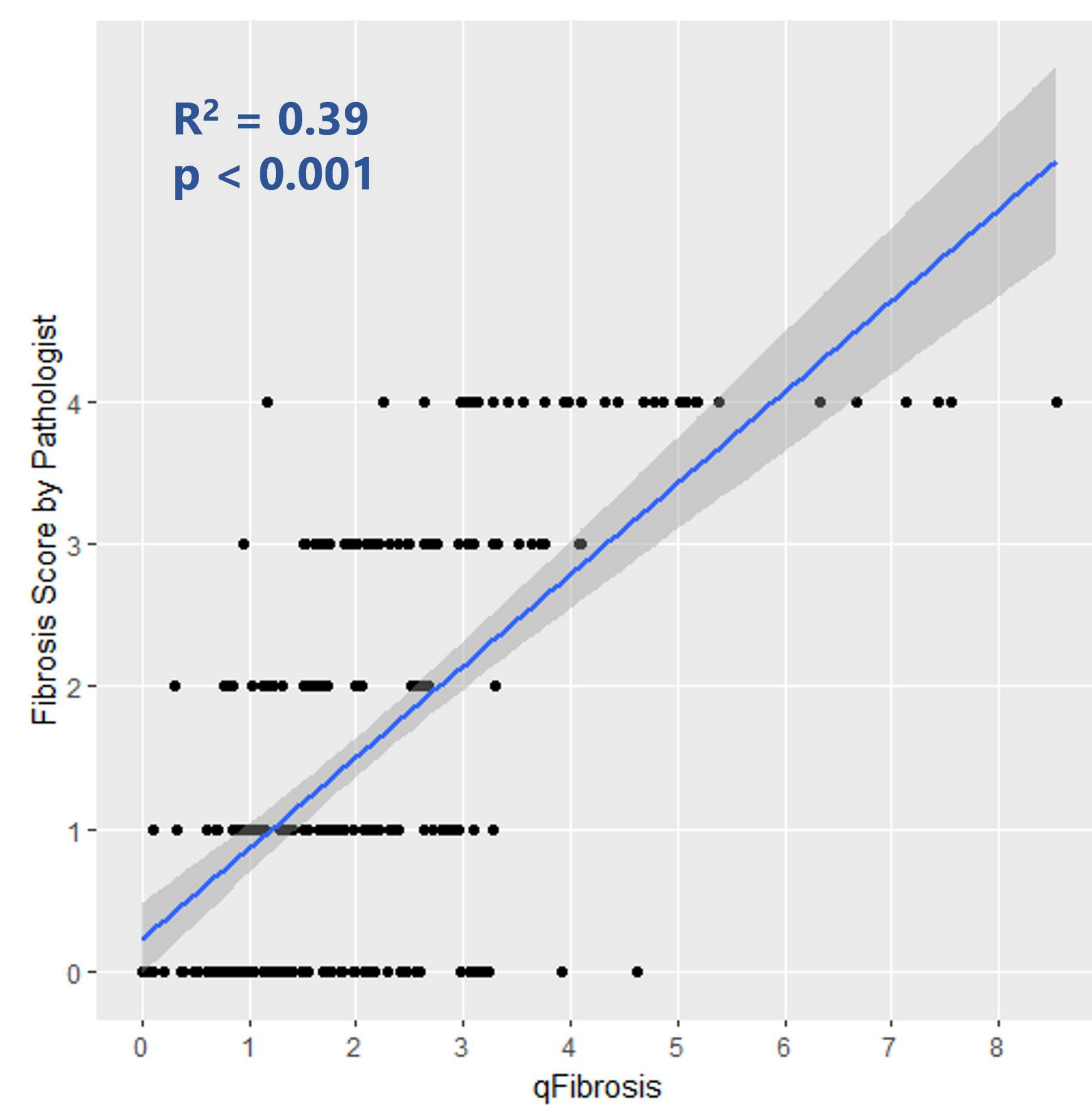
DISCUSSION

qFibrosis correlates well with pathologist-reported fibrosis scores.

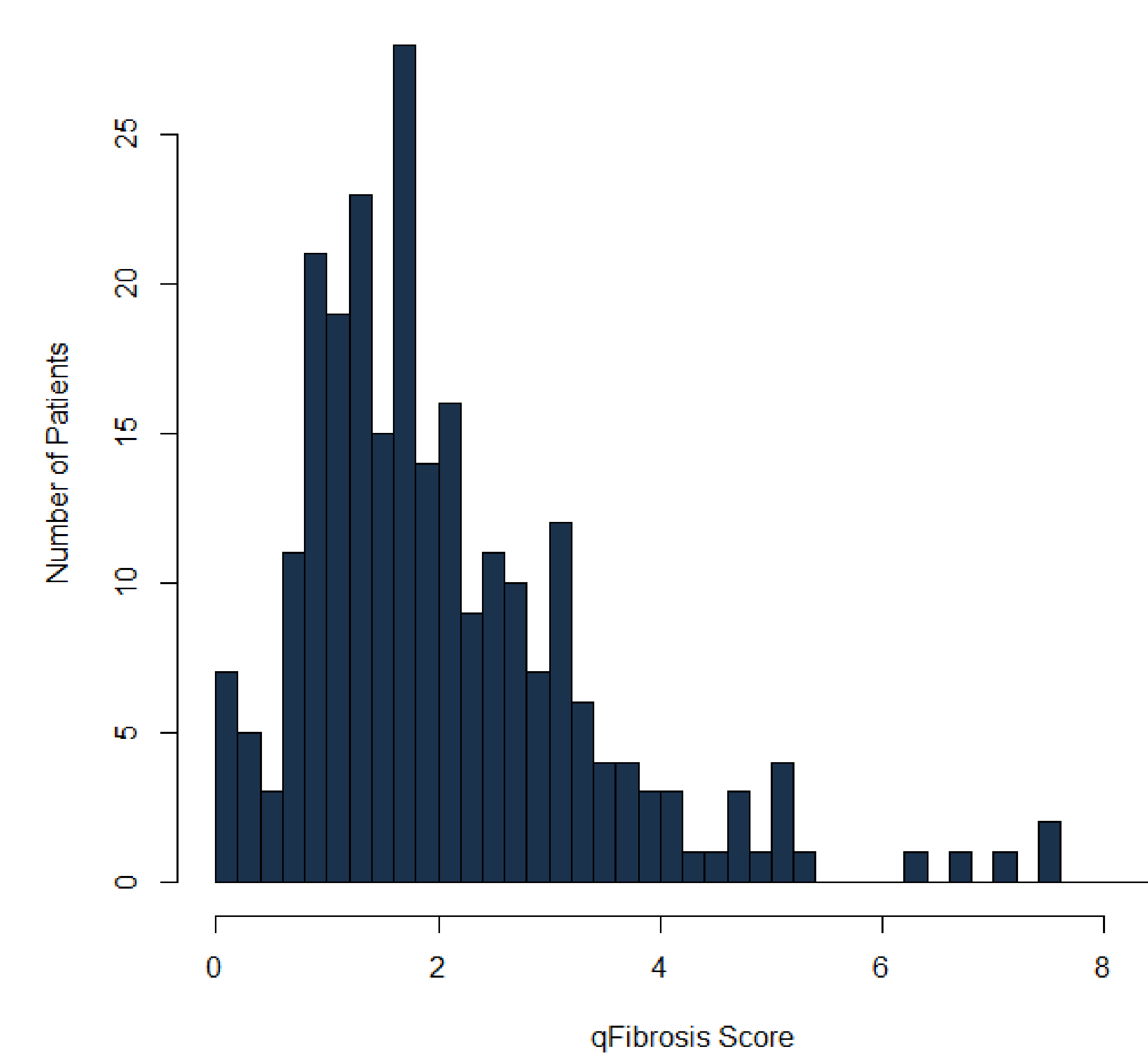
NITs may have a role as continuous measures of fibrosis in NAFLD, which may be used as more sensitive indicators of fibrosis progression or regression, or to evaluate response to therapy.

Given the narrow confidence intervals at low to intermediate levels of fibrosis, NITs may perform well in such settings, where early intervention has greatest yield. However, serum NITs are limited in assessing stage differences due to their narrow dynamic range. VCTE is moderately correlated and with the highest dynamic range, and may potentially be the most useful NIT for evaluating degree of fibrosis as a continuous variable.

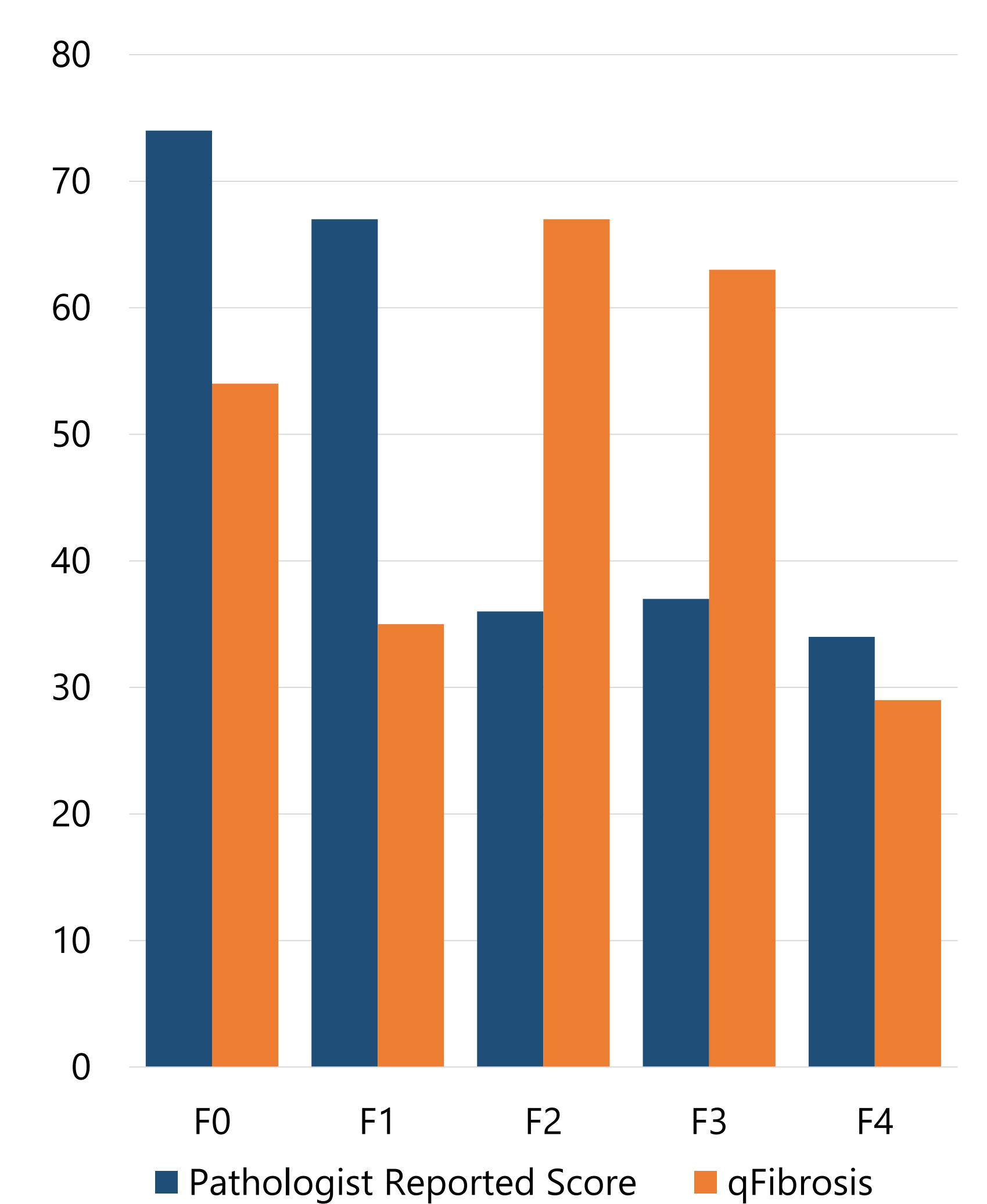
Scatterplot:
qFibrosis score against Pathologist Score for Fibrosis



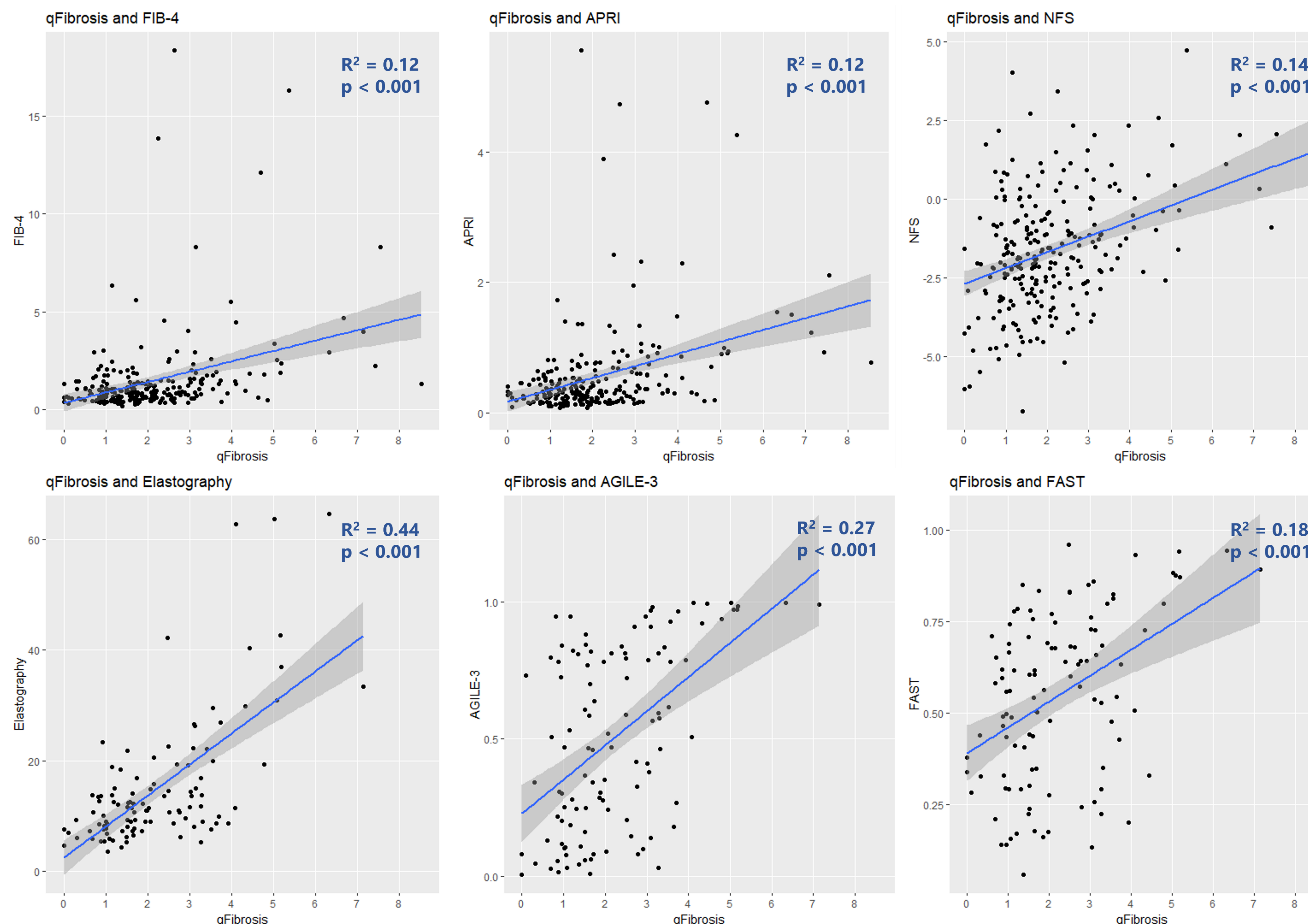
Histogram showing distribution of qFibrosis scores



qFibrosis 'stage' and Pathologist Score for Fibrosis



Correlation between qFibrosis and Various NITs



Baseline characteristics

Age, mean (SD)	45.3 (12.7)
Male Gender, n (%)	129 (52.0%)
Ethnicity, n (%)	
Chinese	149 (60.0%)
Malay	52 (21.0%)
Indian	34 (13.7%)
Others	13 (5.24%)
BMI, mean (SD)	32.2 (8.93)
Overweight (25-29.9)	76 (30.6%)
Obese (≥ 30)	121 (48.8%)
Hypertension, n (%)	114 (46.0%)
Diabetic, n (%)	108 (43.5%)
Glycated Haemoglobin A1c (%)	6.45 (1.42)
HDL-Cholesterol (mmol/L)	1.25 (0.322)
LDL-Cholesterol (mmol/L)	2.91 (0.843)
Triglyceride (mmol/L)	1.56 (1.17)
Platelet (x 10⁹ / L)	268 (83.8)
Albumin (g/L)	41.7 (4.22)
Total Bilirubin (umol/L)	18.7 (40.3)
AST (U/L)	45.7 (39.0)
ALT (U/L)	61.1 (55.0)
AST / ALT Ratio	0.930 (0.443)
Steatosis (S0/1/2/3)	52 / 116 / 39 / 41
Fibrosis (F0/1/2/3/4)	74 / 67 / 36 / 37 / 34
NAFLD Activity Score (0/1/2/3/4/5/6/7/8)	45 / 35 / 28 / 32 / 40 / 38 / 20 / 9 / 1