Accuracy of FibroScan in Assessing Liver Fibrosis in Patients with Nonalcoholic Fatty Liver Disease (NAFLD) in a Community Clinic Setting

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Purpose

- To evaluate the accuracy of FibroScan compared to liver biopsy in assessing liver fibrosis in patients with nonalcoholic fatty liver disease (NAFLD) in a community setting
- To evaluate the concordance of the liver stiffness measure (LSM) and the Metavir fibrosis on liver biopsy with a difference of 1 or less in staging

Study Background

- Nonalcoholic fatty liver disease (NAFLD) is the most common cause of liver disease with a global prevalence of 25%. In the United States, NAFLD has a prevalence of 30% and nonalcoholic steatohepatitis (NASH) has a prevalence of 5%.
- NAFLD is associated with increased morbidity and mortality including liver cirrhosis in addition to increased risk of cardiovascular disease, extra-hepatic cancers, Type 2 diabetes and chronic kidney disease.
- Liver fibrosis is part of the healing process from liver injury. Continuous injury can lead to progressive fibrosis and liver cirrhosis. Liver fibrosis may be reversible if the liver condition is treated. Accurate evaluation of fibrosis is a good indicator for response to therapy, fibrosis progression and prognosis.
- Evaluating these patients involves blood testing, imaging and liver biopsy. Modalities available for imaging include ultrasound, CT scan or MRI which evaluate the presence of steatosis or advanced cirrhosis. The new non-invasive methods are either 'biological' (biochemical markers) or 'physical (FibroScan, MR elastography) modalities.
- Accuracy of transient elastography (FibroScan) has been compared to liver biopsy with a sensitivity and specificity of 0.95 and 0.71. Several studies have concluded that transient elastography could be a reliable method as an alternative to liver biopsy in different liver conditions. Several factors have been reported to potentially affect the liver stiffness measure (LSM) obtained by FibroScan including inflammation, hepatic congestion, cholestasis and fibrosis.
- FibroScan has gained wide availability since it is non-invasive, less costly and performed in physician's offices. Data from clinical trials show excellent sensitivity and specificity and physicians are relying on it to provide the patient with prognostic information and advice on need for therapy.

Methods

- Charts of 90 consecutive NAFLD patients seen at a community clinic in Arlington, Texas were reviewed.
- Data were collected on age, gender, race, liver biopsy date, BMI, waist circumference, NAS score, fibrosis stage on liver biopsy, FibroScan date, probe side used, liver stiffness measure (LSM in kPa), ALT, AST and HbA1c.
- Data were entered into Excel. Analysis included Chi-square test for comparative analysis and Spearman rank test for correlational analysis. Receiver operating characteristic (ROC) curves were utilized to analyze the diagnostic performance of the FibroScan LSM using the recommended cut-off points for NAFLD.

Study Population

- **Inclusion Criteria**:
  - NAFLD patients being seen at this community clinic
  - Patients seen between 2019 to 2021
  - FibroScan report and liver biopsy pathology completed within 2 month timespan
  - FibroScan reports needed to have LSM with IQR/Med value <30% showing consistence in the measurements
  - Only 1 set of readings for each patient were used
- **Study Population**:
  - Patients seen in an adult gastroenterology practice
  - All patients were evaluated for NAFLD including laboratory, imaging, anthropometic measurements

Characteristics of the NASH and Non-NASH Groups

	Total Sample (n=90)	NASH Group (n=54)	Non-NASH Group (n=36)	P Value
Age	62.6 ± 10.7	61.3 ± 10.8	64.0 ± 10.5	0.70
Waist (cm)	114.7 ± 14.7	116.0 ± 14.8	111.1 ± 14.0	0.26
BMI	34.3 ± 6.9	35.1 ± 7.4	33.1 ± 6.2	0.31
ALT	45.0 ± 30.4	53.5 ± 33.9	32.3 ± 18.4	0.75
AST	40.4 ± 27.3	47.6 ± 31.6	29.5 ± 13.3	0.25
HbA1c	6.3 ± 1.0	6.4 ± 1.1	6.2 ± 0.9	0.84
LSM	11.8 ± 8.4	13.6 ± 8.4	9.1 ± 7.7	0.53

Characteristics of the NASH and Non-Nash Groups

	Total Sample (n=90)	NASH Group (n=54)	Non-NASH Group (n=36)	P Value
Fibrosis				0.005
F-0-F1	22% (n=20)	11% (n=6)	39% (n=14)	
F1.5-F2	23% (n=21)	28% (n=15)	17% (n=6)	
F2.5-F3	22% (n=20)	28% (n=15)	14% (n=5)	
F3.5-F4	32% (n=29)	33% (n=18)	31% (n=11)	
ALT group				0.057
<40	60% (n=54)	54% (n=27)	75% (n=27)	
40-<80	28% (n=25)	31% (n=17)	22% (n=8)	
80 -<120	8% (n=7)	11% (N=6)	3% (n=1)	
≥120	4% (n=4)	7% (n=4)	0% (n=0)	
AST Group				0.033
<40	67% (n=60)	56% (n=30)	83% (n=30)	
40-<80	27% (n=24)	33% (n=18)	17% (n=6)	
80-<120	3% (n=3)	6% (n=3)	0% (n=0)	
≥120	3% (n=3)	6% (n=3)	0% (n=0)	

Characteristics of the Concordant and Discordant Groups

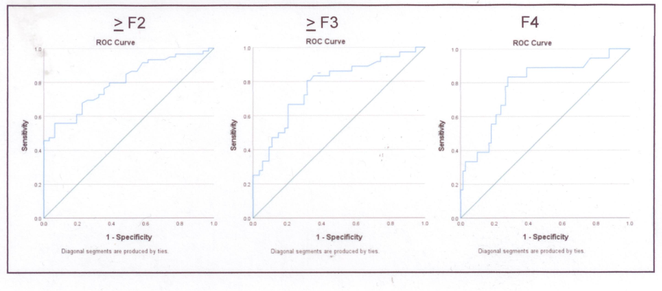
	Total Sample (n=90)	Concordant Group (n=59)	Discordant Group (n=31)	P Value
Age	62.6 ± 10.7	62.6 ± 11.4	62.5 ± 9.4	0.49
Waist (cm)	114.7 ± 14.7	113.0 ± 14.5	117.9 ± 14.7	0.08
BMI	34.3 ± 6.9	33.7 ± 7.5	35.4 ± 5.7	0.07
ALT	45.0 ± 30.4	42.5 ± 29.0	29.8 ± 32.8	0.44
AST	40.4 ± 27.3	40.1 ± 29.0	40.9 ± 25.1	0.56
HbA1c	6.3 ± 1.0	6.4 ± 1.1	6.2 ± 0.8	0.64
LSM	11.8 ± 8.4	12.3 ± 9.6	10.8 ± 5.5	0.30

Concordant = ≤1 stage difference between LSM and Metavir fibrosis
LSM = Liver stiffness measure

Accuracy of LSM Values in Diagnosing ≥F2, ≥F3 and F4 As Measured by AUROC

Fibrosis	AUROC (95% CI)	Sensitivity	Specificity	PPV	NPV	Cut Off
≥F2	0.799 (0.71-0.89)	0.73	0.65	0.80	0.56	7.5
≥F3	0.74 (0.67-0.88)	0.69	0.70	0.61	0.78	10.0
F4	0.78 (0.66-0.90)	0.61	0.74	0.39	0.89	14.0

Graph 1: ROC Curves for ≥ F2, ≥ F3 and for F4



Codes: LSM = liver stiffness measure
Concordant = ≤1 stage difference between LSM and Metavir fibrosis
NASH = having ≥1 point in each of steatosis, inflammation and ballooning
AUROC = area under the receiver operating characteristic curve

Sample Description

- Total number of subjects were 90 (61 females; 29 males)
- Race was 74 White (82%), 3 Black (3%), and 12 Hispanic (15%).
- Age range was 33 to 82 years with median age of 63
- There were 54 subjects (60%) with a liver biopsy showing NASH (NASH diagnosis meaning ≥1 point in each of steatosis, inflammation and ballooning)
- There were 59 subjects (66%) with concordance between the FibroScan LSM and Metavir fibrosis (≤1 stage difference).

Results

- A significant association was seen with NASH subjects having more advanced fibrosis (Chi-square =10.57, p<0.01) and higher AST levels (Chi-square =8.75, p <0.03). There was also a trend toward higher ALT levels in NASH subjects (Chi-square =7.51, p <0.057). Although not indicative of a strong association, the Spearman rank correlation between LSM and liver biopsy, waist circumference and BMI category were positive (r=0.56, p <0.001; r-0.25, p <0.02; r=0.38, p<0.001, respectively)
- Accuracy of the LSM was defined as concordance with the Metavir fibrosis on liver biopsy with a difference of ≤1 in staging. Concordant LSM was identified in 59 (66%) subjects with 31 (34%) having discordant LSM. Under staging happened in 14 subjects (45%) and over staging in 17 subjects (55%). No significant associations were identified related to the concordance of the LSM measurements.
- Accuracy of the LSM values in diagnosing ≥F2, ≥F3, and F4, using the currently recommended cut-off points, was evaluated by area under the curve (AUC) as well as sensitivity and specificity testing. The interpretation of usefulness of the LSM values based upon AUC and sensitivity /specificity are in the sufficient to good level (0.6 – 0.7 and 0.7 to 0.8, respectively).

Conclusions

- Our data in this sample indicate that the accuracy of the FibroScan measurements compared to liver biopsy is low. The clinic population has a significant number of subjects with morbid obesity, advanced fibrosis, as well as elevated NAS and liver enzyme levels. The potential for bias in LSM related to increased liver inflammation has ben reported. This may indicate that different cut-off scores are needed in subjects with these confounders.
- Multiple methods are needed to accurately evaluate liver fibrosis and these methods should be used in conjunction. The current non-invasive methods should be used to decrease the frequently of a liver biopsy but not to replace it. Our current standard histologic evaluation is the best method available, but has several limitations including its semi-quantitative nature.
- Our data show that even in an experienced high volume community clinic, the reliance on one modality to evaluate liver fibrosis may be misleading. A complete evaluation of a patient presenting to a clinic for an initial evaluation of NAFLD should include biochemical markers, radiologic evaluation in addition to a possible liver biopsy.
- Potential limitations of our study include sample size, a higher percentage of morbidly obese patients, higher NAS scores, and elevated ALT/AST levels which are potential confounders. Further studies are needed to evaluate the role of FibroScan as a fibrosis measurement tool and development of specific guidelines for use in patients.