

Background and aims

Blood fibrosis tests are generally constructed for a binary diagnostic target like significant fibrosis.

However, in clinical practice, they are interpreted by using test-specific classifications into fibrosis stages derived from Metavir fibrosis (F) stages, especially with patented tests such as Fibrotest (FT: 8 stages) and FibroMeter (FM: 6 stages) (figure 1).

Fibroscan (FS) is also classified (3/4 stages).

However, accuracy of these classifications has never been evaluated.

We aimed to evaluate and compare these different test classifications.

Methods

1991 patients were enrolled.

Population 1 included 955 chronic hepatitis C patients with FM and FT.

Populations 2 and 3 included respectively 343 and 458 chronic hepatitis C patients with FM, FT and FS.

Population 4 included 235 NAFLD patients with FM.

For FS, the following classification was used: \leq F1, F2/3, F4 (Friedrich-Rust, Gastro 2008).

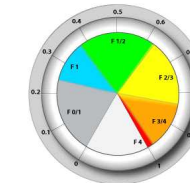
The reference was histological Metavir F staging.

All reported diagnostic accuracies are respectively for significant fibrosis (binary diagnosis) and test classification, unless otherwise indicated.

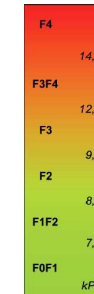
Classification into fibrosis stages

FibroTest	METAVIR Fibrosis stage estimate	Knodell Fibrosis stage estimate	Ishak Fibrosis stage estimate
0.75-1.00	F4	F4	F6
0.73-0.74	F3-F4	F3-F4	F5
0.59-0.72	F3	F3	F4
0.49-0.58	F2	F1-F3	F3
0.32-0.48	F1-F2	F1-F3	F2-F3
0.28-0.31	F1	F1	F2
0.22-0.27	F0-F1	F0-F1	F1
0.00-0.21	F0	F0	F0

Fibrotest



FibroMeter



Liver biopsy (Metavir staging)



Fibroscan

Figure 1: Different classification into fibrosis stages according to diagnostic means.

Results (1)

Population 1 (HCV):

Diagnostic accuracy was (respectively significant fibrosis and fibrosis classification): FT: 72.8% and 38.4%, FM: 77.5% ($p=0.001$ vs FT) and 74.7% ($p<10^{-4}$ vs FT).

A new FM classification, using 4 stages based on 3 cut-offs for significant fibrosis (diagnosis and 90% predictive values, Liv Inter 2008) increased the diagnostic accuracy from 74.7% to 87.5% ($p<10^{-4}$) (figure 2).

Cirrhosis diagnosis by test classification cut-off could be evaluated through the positive predictive value and the rate of cirrhosis detected (sensitivity): FT: 37.1% and 61.8% respectively, FM: 68.5% and 32.2% with $p<10^{-3}$ for difference in sensitivity.

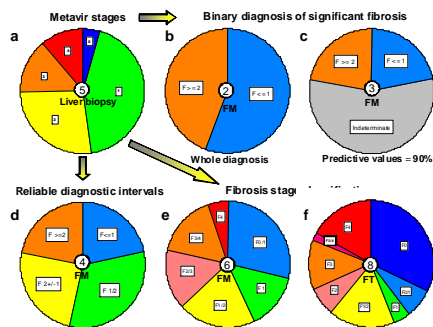


Figure 2. Summary of different available fibrosis classifications in population #1: Metavir stages by liver biopsy (a), significant fibrosis by FibroMeter (FM) (b), 90% predictive values by FM (c), reliable diagnosis intervals by FM (d), fibrosis stages classification by FM (e) or by Fibrotest (FT) (f). The central figure within the pie indicates the number of fibrosis classes.

Results (2)

Population 2 (HCV):

Diagnostic accuracy was (respectively significant fibrosis and fibrosis classification): FT: 70.0% and 33.2%, FM: 77.6% and 68.2%, FS: 65.9% and 54.8%. The comparison between the three tests were: significant fibrosis: $p < 0.002$, test classification: $p < 10^{-4}$.

Population 3 (HCV):

Diagnostic accuracy was: FT: 71.3% and 42.5%, FM: 75.2% and 68.7%, FS: 73.7% and 64.9%.

The discrepancy grade significantly varied among tests (**figure 3**).

Population 4 (NAFLD):

FM diagnostic accuracy was (respectively significant fibrosis and fibrosis classification): 91.0% and 88.5%.

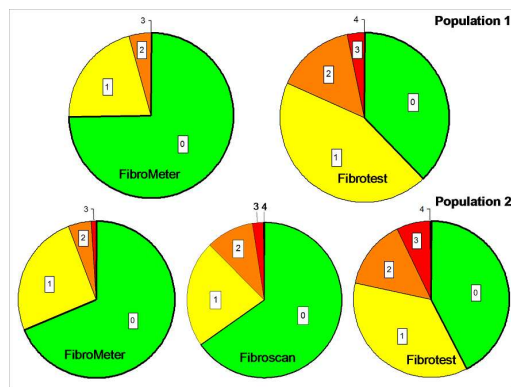


Figure 3. Discrepancy rate of fibrosis stage classification by diagnostic tests in populations #1 (top) or #3 (bottom). The figure indicates the difference in number of fibrosis stage(s) between blood test and liver biopsy. Thus, the grade 0 (green pie sector) indicates agreement with liver biopsy.

Conclusion

The diagnostic accuracy of test classifications is much lower than that of binary diagnosis for significant fibrosis with FibroScan and Fibrotest.

The diagnostic accuracy of test classifications is very significantly different between tests: FibroMeter > FibroScan > Fibrotest.

The diagnostic accuracy of a new FibroMeter classification (based on 3 cut-offs for a binary diagnosis) was significantly greater (87.5%) compared to a binary staging for significant fibrosis (77.5%) or a fibrosis classification (74.7%).

