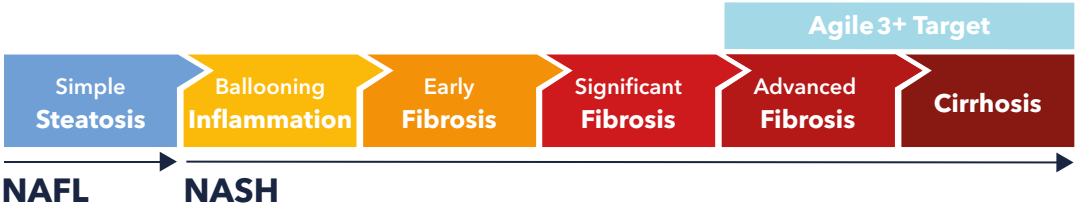
Scores
by echosens

Agile 3+

Identification of advanced fibrosis in NAFLD patients

NAFLD is the most common chronic liver disease worldwide. Early intervention can reverse liver damage and improve patient outcomes. Identifying patients with advanced fibrosis is key for the management of patients with NALFD since they are at increased risk of developping liver-related complications.

Target



Construction

Performance

- Excellent performance in suspected NAFLD patients in large derivation and validation cohorts from different geographical origins
- Optimized PPV* by combining FibroScan® and routine blood markers
- Reduce the number of unnecessary liver biopsies

Formula is public with a free calculator available on myFibroScan app

myFibroScan

Google Play App Store

Free app

References:

A.J. Sanyal, J. Foucquier, Z.M. Younossi, S.A. Harrison, P.N. Newsome, W.K. Chan, Y. Yilmaz, V. De Ledinghen, C. Costentin, M.H. Zheng, V.W.S. Wong, M. Elkhashab, R.S. Huss, R.P. Myers, A. Labourdette, M. Destro, C. Fournier-Poizat, V. Miette, L. Sandrin, J. Boursier, Enhanced diagnosis of advanced fibrosis and cirrhosis in non-alcoholic fatty liver disease patients with FibroScan-based Agile scores, paper under submission

*PPV Positive Predictive Value
NAFLD : Non-Alcoholic Fatty Liver Disease / NASH : Non-Alcoholic Steatohepatitis / AST: Aspartate Aminotransferase / ALT: Alanine Aminotransferase
LSM: Liver Stiffness Measurement /

CE

Clinical validation ILC 2021

	Derivation cohort	Internal validation cohort	Muticentric US external validation cohort	Multicentric French external validation cohort
N patients	**1434**	**700**	**585**	**1042**
AUROC [95% CI]	0.90	0.91	0.86	0.87
Rule out cut-off	<0.45			
% patients	44%	42%	54%	53%
Se/Sp	0.85/0.78	0.87/0.76	0.82/0.75	0.83/0.75
NPV	0.90	0.91	0.88	0.87
Indeterminate zone	≥0.45 - <0.68			
% patients	13%	17%	16%	18%
Rule in cut-off	≥0.68			
% patients	17%	16%	10%	8%
Se/Sp	0.71/0.90	0.69/0.91	0.61/0.87	0.61/0.90
PPV	0.81	0.81	0.73	0.79

Se Sensitivity/Sp Specificity/NPV Negative Predictive Value/PPV Positive Predictive Value

Development and validation of Agile 3+: Novel FibroScan based score for the diagnosis of advanced fibrosis in patients with non-alcoholic fatty liver disease

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BACKGROUND AND AIMS: Currently available noninvasive tests, including FIB-4 and liver stiffness measurement (LSM) by Vibration Controlled Transient Elastography (VCTE), are highly effective in excluding advanced fibrosis (F >= 3) yet their ability to rule it in is moderate. Our objective was to develop and validate a new score (Agile 3+), combining LSM with routine clinical parameters to identify advanced fibrosis in NAFLD patients, with optimized positive predictive value (PPV) and reduced number of cases with indeterminate results.

METHODS: This multi-national, retrospective study included 7 cohorts of adults with suspected NAFLD who underwent liver biopsy (LB), LSM by VCTE, and blood sampling in either routine clinical practice or during screening for clinical trials. The population was randomly divided into a training set (TS; n = 1434), on which the best fitting logistic regression model was built, and an internal validation set (VS; n = 700), on which performance and goodness of fit of the model were assessed. Furthermore, Agile 3+ was externally validated on 2 large cohorts: NASH CRN cohort (8 US centers, n = 585) and French NAFLD cohort (3 centers, n = 1042). Cut-offs for at least 85% sensitivity and 90% specificity in the TS were derived to rule-out and rule-in advanced fibrosis, respectively for FIB-4, LSM and Agile 3+ and then tested in the VS.

RESULTS: Agile 3+ combined LSM, AST/ALT ratio, platelets, gender, age and presence of diabetes mellitus. Calibration plots of Agile 3+ indicated excellent goodness of fit. The area under the receiver operating characteristic curves (AUROC) of Agile 3+ ranged from 0.86 to 0.90. In all datasets, Agile 3+ outperformed LSM and FIB-4 in terms of AUROC, percentage of patients with indeterminate results and that of patients with advanced fibrosis with a score above the high cut-off. Moreover, in the TS and internal VS, the rate of patients with F<3 with a score below the low cut-off and the PPV for patients above the high cut-off were higher with Agile 3+ compared to FIB-4 and LSM (Figure).

CONCLUSION: A novel noninvasive score including LSM by VCTE and routine clinical parameters improves the identification of advanced fibrosis among patients with NAFLD and may reduce the necessity of liver biopsy in this patient population. In addition, external validation on primary and secondary care centers could assess its potential as a new tool to refer patients to liver specialists.

Prognostic value of Agile scores in patients with non-alcoholic fatty liver disease

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BACKGROUND AND AIMS: Recently, Agile 4 and Agile 3+, two scores combining liver stiffness measurement (LSM) by vibration-controlled transient elastography (VCTE) with routine clinical parameters were proposed to diagnose cirrhosis and advanced fibrosis in NAFLD patients, respectively. The objective of the present work was to assess the prognostic accuracy of Agile 4 and Agile 3+ for the prediction of liver-related events (LRE) and to compare them to LSM alone.

METHOD: This retrospective study included adults with NAFLD from a French tertiary care center who underwent LSM and blood sampling as part of routine clinical practice. The main study outcome was LRE, a composite endpoint combining cirrhosis complication or hepatocellular carcinoma LRE were ascertained by chart review. Cut-off values of Agile 4 and Agile 3+ previously determined (1) and Baveno cut-off values for LSM (10kPa - 15kPa) were used to define the rule-out, indeterminate and rule-in zones at baseline. Kaplan-Meier curves were compared using the Log-rank test.

RESULTS: 341 NAFLD patients were included in the study (median age: 58 years, male sex: 65%, diabetes: 36%). LRE occurred in 27 (7.9%) patients after a median follow-up of 5.2 years (1st and 3rd quartiles: 2.9-7.2). The rate of patients included in the rule-out / indeterminate / rule-in zones of the Agile 3+ and Agile 4 were respectively 56%/15%/29% and 83%/9%/8%. Kaplan-Meier curves (Figure) for Agile 4 and Agile 3+ showed significant differences between the rule-out and the rule-in zones (p<0.001 for both) and between indeterminate and rule-in zones (p≤0.002 for both), while the difference between indeterminate and rule-out zones was not significant. By comparison, the rates of patients included in the rule-out / indeterminate / rule-in zones with LSM were 57%/23%/20%.Using LSM, patients experiencing a LRE were initially either in the indeterminate or the rule-in zones and consequently, a significant difference (p<0.001) between the rule-out and the indeterminate zone was observed while the difference between the indeterminate and rule-in was less significant (p=0.03).

CONCLUSION: Agile 4 and Agile 3+ well predict the occurrence of liver-related events in patients with NAFLD. Particularly, rule-in cut-offs of both scores better identify at-risk patients than LSM alone. These results demonstrate the interest of those scores in the identification of patients requiring hepatocellular carcinoma and esophageal varices screening.