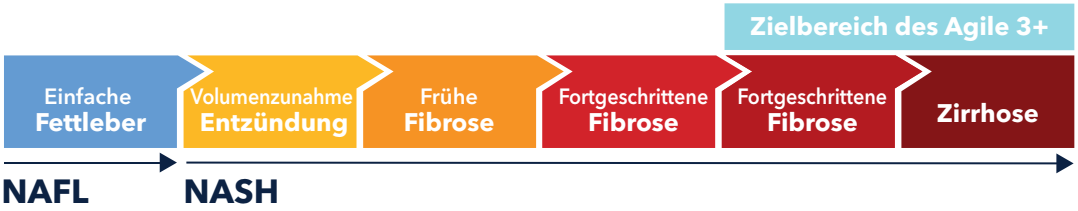
Scores
by echosens

# Agile 3+

## Identifizierung von fortgeschrittener Fibrose bei NAFLD-Patienten

NAFLD ist die weltweit häufigste chronische Lebererkrankung. Ein frühzeitiges Eingreifen kann die Leberschädigung rückgängig machen und Patientenergebnisse verbessern. Die Identifizierung von Patienten mit fortgeschrittener Fibrose ist entscheidend für die Behandlung von Patienten mit NALFD, da sie ein erhöhtes Risiko haben, leberbezogene Komplikationen zu entwickeln.

## Zielgruppe




## Funktionsweise


## Leistungsfähigkeit

- Ausgezeichnete Leistung bei Patienten mit Verdacht auf NAFLD in großen Ableitungs- und Validierungskohorten unterschiedlicher geografischer Herkunft
- Optimierter PPV* durch Kombination von FibroScan® und routinemäßigen Blutmarkern
- Verringerte Anzahl unnötiger Leberbiopsien


Die Formel ist öffentlich mit einem kostenlosen Rechner in der myFibroScan-App erhältlich.

myFibroScan

GET IT ON Google Play · Download on the App Store

**Kostenlose App**

**Referenzen:**

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", Artikel in Einreichung

*PPV = positiver Vorhersagewert
NAFLD: Nichtalkoholische Fettlebererkrankung / NASH: Nichtalkoholische Steatohepatitis / AST: Aspartataminotransferase / ALT: Alanin-Aminotransferase
LSM: Lebersteifigkeitsmessung /

CE

# Klinische Validierung 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 Sensitivität / Sp Spezifität / NPV negativer Vorhersagewert / PPV positiver Vorhersagewert

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

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*on behalf of the NASH Clinical Research Network, NIDDK, NIH

**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

J. Boursier, C. Canivet, M. Roux, A. Lannes, I. Fouchard Hubert, F. Oberti

**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.