ADAPT and VCTE show comparable performance for identifying MASH patients with significant fibrosis: Implications for selecting patients eligible for therapy

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BACKGROUND

Metabolic dysfunction-associated steatotic liver disease (MASLD) is a leading cause of liver-related morbidity and mortality, with fibrosis stage being the strongest predictor of adverse outcomes. Following the recent approval of pharmacological therapies for metabolic dysfunction–associated steatohepatitis (MASH) in patients with moderate fibrosis (F2–F3) without cirrhosis (F4), there is an urgent need for reliable non-invasive tests (NITs) to identify patients eligible for therapy.

The **ADAPT algorithm**, incorporating the serum biomarker PRO-C3, along with platelets, age, and diabetes status, has recently transitioned to the Roche Cobas® e801 high throughput IVD analyzer.

Objective: We evaluated the diagnostic performance of two well-established NITs for fibrosis assessment—the PRO-C3–based ADAPT algorithm and vibration-controlled transient elastography (VCTE) for identifying F2-3, F3-4 or F4 patients in a Danish prospective outpatient cohort.

METHODS

This single-centre, prospective study included 259 patients with histologically confirmed F0–F4 MASLD from the Copenhagen Cohort of MASLD (CoCoMASLD; >1,000 participants), recruited at Hvidovre Hospital between 2017 and 2022. Among participants, 91 (35.1%) had significant fibrosis F2–F3, 88 (34%) had advanced fibrosis F3-4 and 48 (18.5%) had cirrhosis (F4). ADAPT was calculated using Elecsys® (Roche) PRO-C3, platelet count, age, and diabetes status, VCTE by FibroScan® (Echosens). FIB-4 and standard biochemical parameters were collected. Cut-offs utilized for diagnosis of F2-3 were: ≥9–<11 for ADAPT and ≥8–<15 kPa for VCTE; for F3-4 were; ADAPT≥10 and VCTE≥12kPa; F4 were >11 for ADAPT and >15 kPa for VCTE. Diagnostic performance was assessed by calculating AUROC, sensitivity, specificity, PPV, and NPV.

ADAPT Algorithm

- Age (years)
- Diabetes status (yes/no)
- PRO-C3 (ng/mL)
- Platelet count (10^9/L)

$$ADAPT = exp\left(log_{10}\left(\frac{Age \times PRO\text{-}C3}{\sqrt{Platelets}}\right)\right) + Diabetes$$

VCTE

- Vibration-controlled transient elastography
- Liver stiffness assessed in kPa at the clinic

Table 1. Baseline Characteristics of the MASLD cohort (n=259)

Variable	Statistic / Category	Value
Age (Years)	Median (Q1, Q3)	56.0 (43.0, 64.0)
BMI	Median (Q1, Q3)	33.2 (29.4, 38.1)
AST (U/L)	Median (Q1, Q3); N-missing=43	48.0 (34.0, 63.2)
ALT (U/L)	Median (Q1, Q3)	69.0 (40.0, 98.0)
Platelets (10^9/L)	Median (Q1, Q3)	225.0 (190.0, 275.5)
PRO-C3 (ng/mL)	Median (Q1, Q3)	39.4 (33.0, 51.0)
ADAPT	Median (Q1, Q3)	9.0 (7.8, 10.9)
VCTE (kPa)	Median (Q1, Q3)	10.3 (7.0, 15.4)
Sex		
	Female	113 (43.6%)
	Male	146 (56.4%)
Diabetes		
	No	152 (58.7%)
	Yes	107 (41.3%)
Fibrosis stage		
	F0	56 (21.6%)
	F1	64 (24.7%)
	F2	51 (19.7%)
	F3	40 (15.4%)
	F4	48 (18.5%)
Significant fibrosis		
	No	120 (46.3%)
	Yes	139 (53.7%)
Advanced fibrosis		
	No	171 (66.0%)
	Yes	88 (34.0%)
F2+F3		
	No	168 (64.9%)
	Yes	91 (35.1%)

ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; GGT, gamma-glutamyl transferase; SD, standard deviation

Diagnostic performance for identifying F0-2 vs F3-4

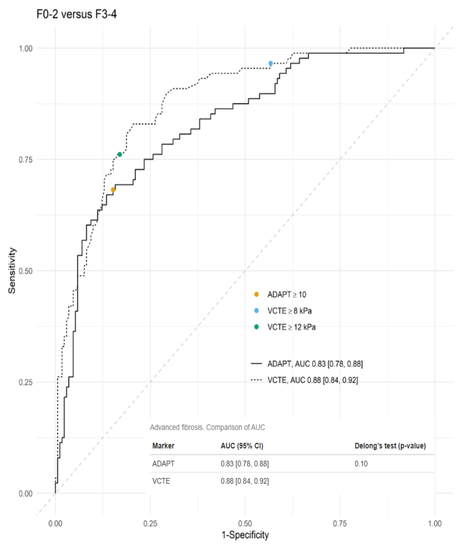

Figure 1. ROC curve for ADAPT and VCTE for identification of advanced fibrosis at indicated cut-offs. ADAPT and VCTE perform similar. Long dashed line: line of no discrimination. AUC, area under the curve; ROC, receiver operating curve.

Diagnostic performance for identifying F0-3 vs F4

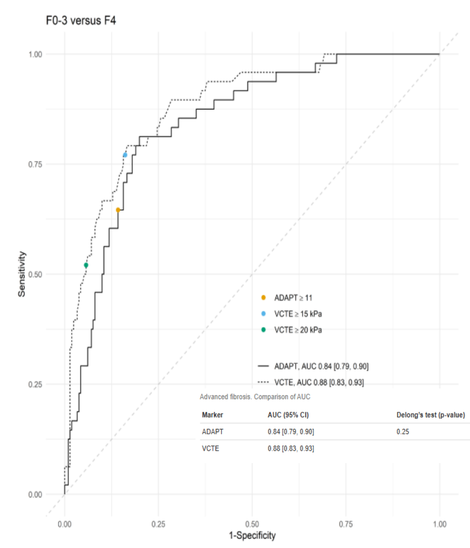

Figure 2. ROC curve for ADAPT and VCTE for identification of cirrhosis at indicated cut-offs. ADAPT and VCTE perform similar. Long dashed line: line of no discrimination. AUC, area under the curve; ROC, receiver operating curve.

RESULTS

The cohort had a median age of 56 years (Q1–Q3: 43–64), 56.4% male, BMI 33.2 (29.4–38.1), and 41.3% had diabetes. Median AST was 48 U/L (34–63.2), ALT 69 U/L (40–98), PRO-C3 39.4 ng/mL (33–51), ADAPT 9 (7.8–10.9), and VCTE 10.3 kPa (7–15.4). For F4 fibrosis, both ADAPT and VCTE demonstrated strong diagnostic accuracy: AUROC 84% (95% CI: 79–90%) for ADAPT (sens 0.65, spec 0.86, PPV 51%, NPV 91%) and 88% (95% CI: 83–93%) for VCTE (sens 0.77, spec 0.84, PPV 52%, NPV 94%), with no statistically significant differences between tests (AUROC p=0.25; sens/spec p=0.18/0.64). While PPV was modest, limiting the ability to rule in cirrhosis (~50%), NPV was high (~91%). For F2–F3 fibrosis, diagnostic performance was lower: ADAPT sens/spec 0.31/0.78, PPV 43%, NPV 68%; VCTE 0.61/0.67, PPV 50%, NPV 75%. Sensitivity was higher for VCTE (p<0.001), whereas specificity was higher for ADAPT (p=0.017). Both tests demonstrated modest rule-in capability, but some capability of ruling out F2–F3 patients (NPV 68-77%). F0-3 vs F3-4 demonstrated similar performance with no statistical differnces on sens/spec (p=0.23/0.75) using VCTE ≥12 and ADAPT ≥10.

Diagnostic performance of ADAPT and VCTE for staging F2-3, F3-4 or F4 patients

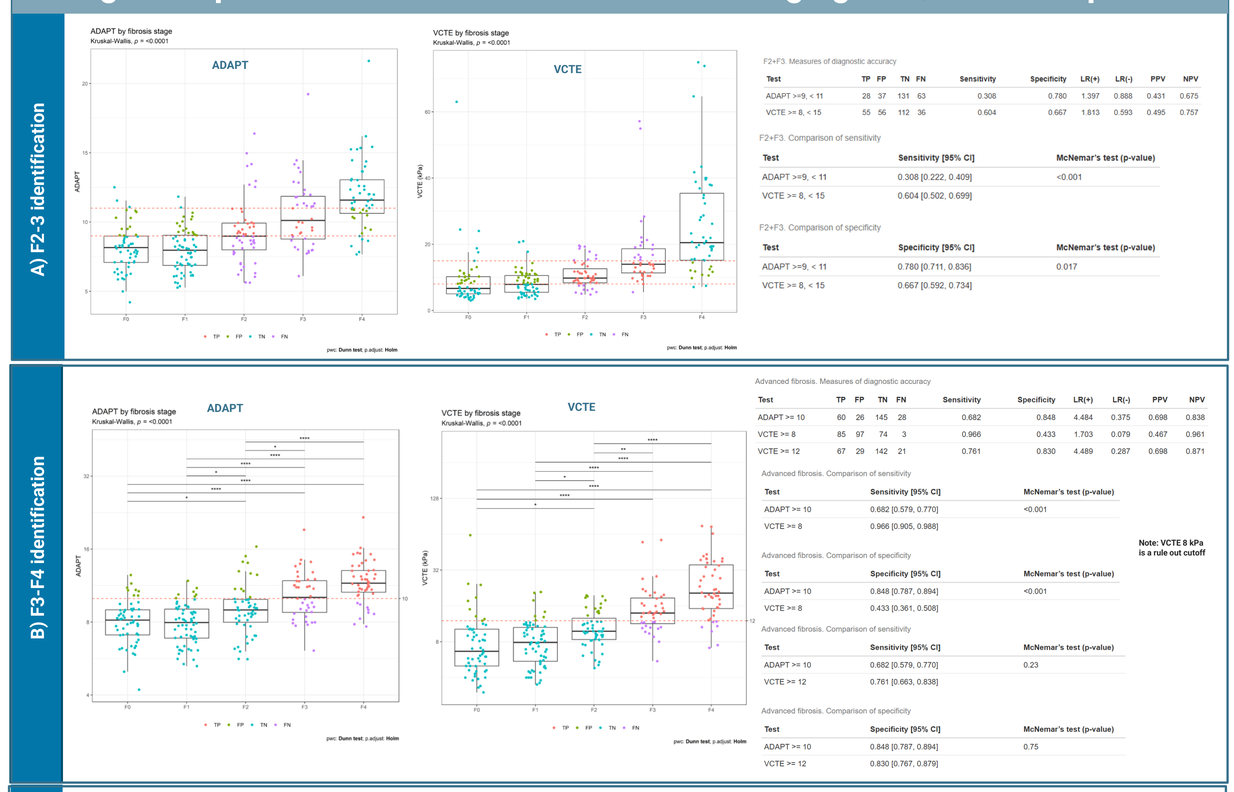

Figure 3. Boxplots illustrate the median, interquartile range, and whiskers (extending to 1.5 times the interquartile range) for the ADAPT score and VCTE stratified according to liver fibrosis stage. Cut-offs are indicated by A) red dashed lines for ADAPT (9-11) and for VCTE (8-15 kPa) for F2/3; B) red dashed line for ADAPT (10) and VCTE (12 kPa) and C) grey dashed lines for ADAPT (11) and VCTE (15 kPa) for F4 identification. True positives (TP), False positives (FP), True negatives (TN), False negatives (FN), NPV= Negative Predictive value, PPV= Positive Predictive value, LR(+) =Positive Likelihood ratio, LR(-)= negative Likelihood Ratio reflects identification of A) F2/F3 or B) F4 patients as cases.

Key Take Home Messages

- ADAPT and VCTE performed similarly in detecting F2-F3, F3-4 fibrosis or F4 cirrhosis, one being blood-based and the other imaging-based.
- Many F2-F3 cases are missed thus indicates a large number of patients may be left untreated using only one test
- These findings support further investigation of NITs for non-invasive fibrosis assessment and for identifying patients eligible for MASH therapy

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