

Non-invasive measures of liver fibrosis in NAFLD is associated with cardiovascular risk

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Background and Aims: Many patients with non-alcoholic fatty liver disease (NAFLD) simultaneously suffer from cardiovascular diseases and often carry multiple cardiovascular risk factors.¹⁻² Several cardiovascular risk factors are known to drive the progression of fibrosis in NAFLD.³⁻⁴ It was the aim of this study to investigate whether established cardiovascular risk scores such as the Framingham risk score (FRS) and the Heart Score of the European Society of Cardiology (HS) are associated with the degree of fibrosis in NAFLD.

Methods: We screened 2138 asymptomatic subjects (59.6 ± 10.2 years, 50% males, BMI 27.2 ± 4.6 kg/m²). The diagnosis of NAFLD was labeled if 1. (Areas of significant increased echogenicity in relation to the renal parenchyma present in right upper quadrant ultrasound) and 2. (Exclusion of viral, autoimmune, hereditary liver disease and excess alcohol consumption evaluated by a questionnaire) were fulfilled. The FRS (estimates the ten-year risk of developing coronary heart disease) and HS (estimates ten-year risk of fatal cardiovascular disease) were calculated for each subject, as were NAFLD Fibrosis Score (NFS) and Fibrosis 4 Score (Fib4). Subsequently, NFS, Fib4, FRS and HS were correlated.

Results: Of 2138 subjects, 829 (38.7%) had NAFLD, **Figure 1**. Patients with NAFLD had a significantly higher cardiovascular risk: FRS: no NAFLD: $5.5 \pm 5.2\%$; NAFLD: $8.8 \pm 6.5\%$ ($p < 0.001$); HS: no NAFLD: $2.9 \pm 3.8\%$; NAFLD: $3.7 \pm 4.1\%$ ($p = 0.002$), **Table 1**. Patients with NAFLD were grouped into three groups according their NFS: F0-F2 ($n = 663$); indifferent ($n = 155$); F3-F4 ($n = 11$). In patients with F0-F2 according to NFS, FRS was $8.0 \pm 6.1\%$; with indifferent NFS, $10.8 \pm 6.4\%$; and in F3-F4 (NFS): $11.5 \pm 5.2\%$, respectively. HS showed a similar pattern: F0-F2 (NFS): $3.0 \pm 3.4\%$; with indifferent NFS, $5.4 \pm 4.5\%$, and in F3-F4 (NFS): $7.0 \pm 5.7\%$, respectively, **Table 2**. NFS correlated significantly with FRS ($r = 0.18$, $p < 0.001$) and HS ($r = 0.27$, $p < 0.001$). Likewise, patients with NAFLD were grouped into three groups according to their Fib4: F0-F1 ($n = 589$); indifferent Fib4 ($n = 411$); F3-F4 ($n = 58$). In patients with F0-F1 according to Fib4, FRS was $7.3 \pm 5.8\%$; with indifferent Fib4, $11.1 \pm 6.7\%$; and in F3-F4 (Fib4): $11.1 \pm 6.9\%$ respectively. HS did not change with respect to Fib4 estimated degree of fibrosis: F0-F1 (Fib4), $3.2 \pm 3.6\%$; with indifferent Fib4, $3.3 \pm 3.8\%$, and in F3-F4 (Fib4): $2.9 \pm 3.9\%$, respectively. Fib4 correlated with FRS ($r = 0.25$, $p < 0.001$), but not with HS ($r = 0.02$, $p = 0.55$).

Conclusion: In this large asymptomatic screening cohort, subjects with non-invasive indicators of advanced stages of NAFLD had an increased risk of coronary heart disease and cardiovascular outcomes. A multidisciplinary approach including hepatologists and cardiologists is important to ensure optimal care for these patients at high risk of CVD and liver-related endpoints.

Bibliography:

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n = 2138	Framingham Risk Score	Heart Score ESC
no NAFLD (n = 1309)	$5.5 \pm 5.2\%$	$2.9 \pm 3.8\%$
NAFLD (n = 829)	$8.8 \pm 6.5\%$	$3.7 \pm 4.1\%$
	p < 0.001	p = 0.002

Table 1. Influence of presence of NAFLD on cardiovascular risk

NAFLD Fibrosis Score	Framingham Risk Score	Heart Score ESC
F0 - F2 (n = 663)	$8.0 \pm 6.1\%$	$3.0 \pm 3.4\%$
indifferent (n = 155)	$10.8 \pm 6.4\%$	$5.4 \pm 4.5\%$
F3 - F4 (n = 11)	$11.5 \pm 5.2\%$	$7.0 \pm 5.7\%$
	r = 0.18, p < 0.001	r = 0.27, p < 0.001

Table 2. Influence of degree of fibrosis on cardiovascular risk

NAFLD in screened subjects (n = 2138)

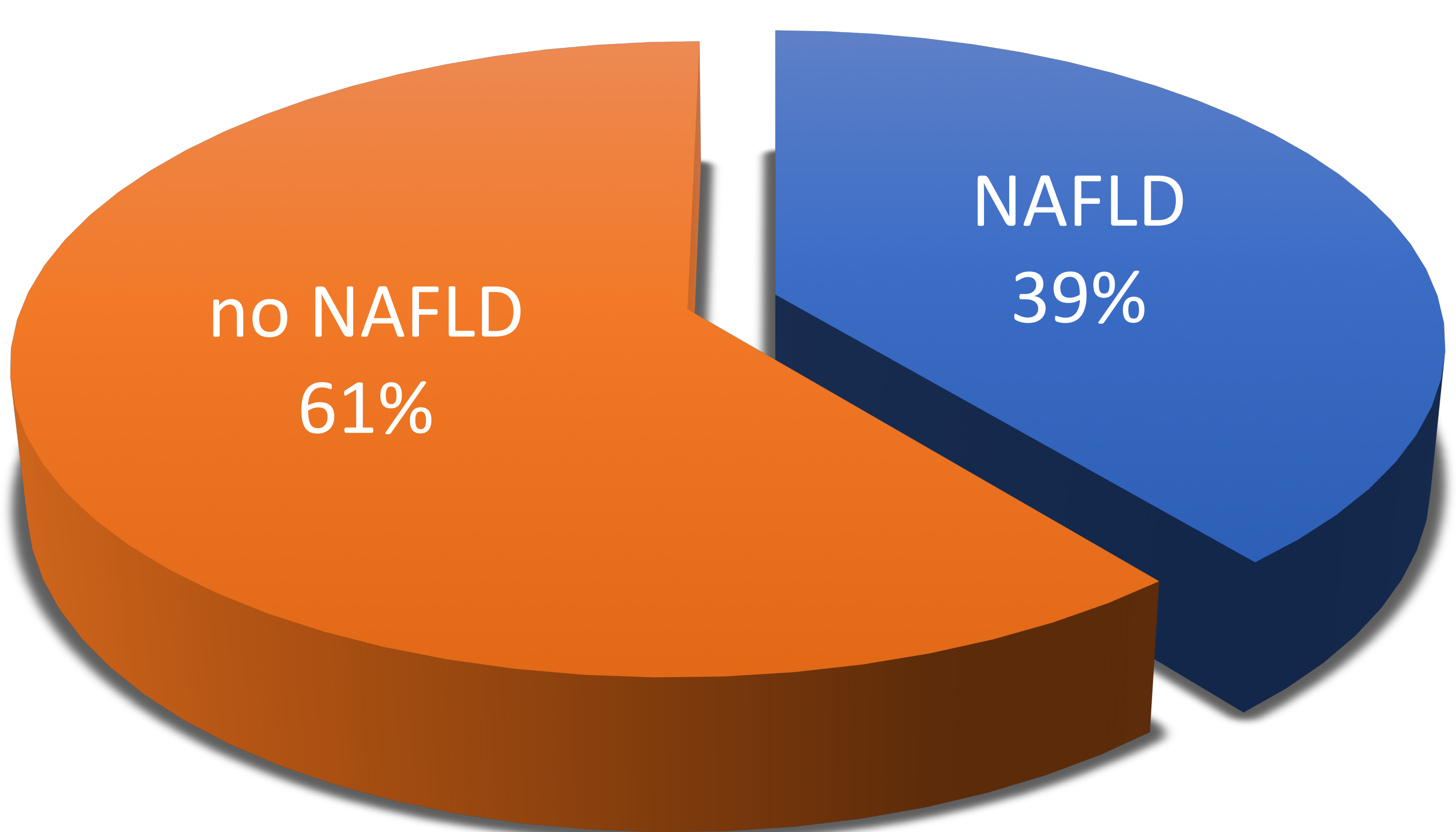


Figure 1. Percentage of NAFLD in screened subjects