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The prognostic role of the ELF test, compared to liver biopsy, in patients with metabolic dysfunction-associated steatotic liver disease (MASLD)

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Introduction and aim

Liver fibrosis stands out as the main prognostic risk factor in MASLD. The enhanced liver fibrosis (ELF) test is a composite of direct fibrosis biomarkers (tissue inhibitor of metalloproteinases 1, amino-terminal peptide of type 3 procollagen and hyaluronic acid) that reflect extracellular matrix turnover. While the ELF test exhibits high diagnostic accuracy for advanced liver fibrosis in MASLD patients, its role as a prognostic biomarker remains uncertain. Our aim is to compare the prognostic effectiveness of ELF, FIB4, Liver Stiffness Measurement (LSM) and liver histology in patients with MASLD.

Materials and Methods

We retrospectively enrolled 289 patients with MASLD who underwent liver biopsy between 2013 and 2023. The ELF score was automatically calculated in accordance with the manufacturer's instruction (Siemens Healthineers) using a serum sample collected at baseline. FIB4 computation, LSM with Fibroscan and liver biopsy were performed at baseline. Liver fibrosis stage was assessed according to the METAVIR classification.

The primary outcome was a composite endpoint including all-cause mortality, hepatocellular carcinoma, liver transplantation or complications related to cirrhosis (ascites, variceal bleeding, hepatic encephalopathy, MELD≥15).

Subjects were stratified based on existing literature cut-offs for ELF (<9.8, 9.8-11.2, >11.2), LSM (<10, 10-15, >15 kPa), FIB-4 (<1.3, 1.3-2.67, >2.67), and histology (F≤2, F3, F4) to assess the risk of occurrence of the primary outcome.

Table.1 Baseline patients' characteristics

		Composite outcome during follow-up		
	Total (n=289)	Yes n = 34	No n = 255	P value
Follow-up time (months)	51 (21 – 68)	22.5 (8.5 – 39.5)	49 (22 – 70)	0.06
Gender (male)	201 (69.6)	19 (55.9%)	182 (71.4%)	0.06
Age (y)	49 (39 - 58)	63.3 (60 – 68.7)	47 (37 – 55)	<0.01
Diabetes	81 (28.0)	23 (67.6%)	58 (22.7%)	<0.01
Hypertension	110 (38.1)	18 (52.9%)	92 (36.1%)	0.06
BMI (Kg/m^2)	28.7 (25.5 – 31.8)	26.7 (24.2 – 30.8)	28.7 (26.1 – 32.4)	0.09
ALT (IU/L)	52 (34 – 78)	44 (22.2 – 56.0)	53 (35 – 81.5)	0.18
AST (IU/L)	39 (27 – 54)	41.5 (28 – 58)	39 (27 – 54)	0.07
GGT (IU/L)	58 (31 – 107)	48 (30.7 – 105.2)	58 (31.5 – 110)	0.31
Tot Bilirubin (mg/dl)	0.9 (0.7 – 1.5)	1.1 (0.8 – 1.4)	0.9 (0.7 – 1.6)	0.08
Platelets (x10^9/ml)	220 (164 – 268)	105 (69 – 139)	228 (184 – 270)	<0.01
FIB-4	1.13 (0.77 – 2.15)	5.09 (3.0 – 6.35)	1.03 (0.72 – 1.67)	<0.01
Low	166 (57.4)	2 (5.9%)	164 (64.3%)	<0.01
Medium	72 (24.9)	6 (17.6%)	66 (25.9%)	
high	51 (17.6)	26 (76.5%)	25 (9.8%)	
ELF	9.11 (8.42 – 10.1)	11.71 (11.08 – 12.11)	8.98 (8.35 – 9.57)	<0.01
<9.8	187 (64.7)	1 (2.9%)	186 (73%)	<0.01
9.8-11.2	69 (23.9)	10 (29.4%)	59 (23.1%)	
>11.2	33 (11.4)	23 (67.7%)	10 (3.9%)	
LSM (kPa)	7.8 (6.1 – 11.4)	7.5 (5.8 – 9.4)	21.5 (16.4 – 29.5)	<0.01
<10	202 (69.9)	3 (8.8)	199 (78.0)	<0.01
10-15	41 (14.2)	5 (13.7)	36 (14.1)	
>15	46 (15.9)	26 (76.5)	20 (7.8)	
Histology				
F<3	207 (71.6)	4 (11.8)	203 (79.6)	<0.01
F3	46 (15.9)	7 (20.6)	39 (15.3)	
F4	36 (12.4)	23 (67.6)	13 (5.1)	

Results

We included data of 289 patients (30.4% female, median age 50y [IQR 39-58]). Over a median follow-up time of 41 months (IQR 21-68), the composite endpoint occurred in 34 (11.8%) patients. (Table 1)

The frequency of the primary outcome exhibited a stepwise increase with ELF scores <9.8 (0.5%), 9.8 to 11.2 (14.5%) and >11.2 (69.7%).

Survival curves for comparisons between groups revealed significant differences for all index tests based on pre-defined histological and non-invasive test stratification (Log Rank test p <0.05). (Figure 1)

At multivariate Cox regression analysis, ELF and liver histology were significant predictors of the primary outcome after adjusting for gender, diabetes, age and BMI. (ELF > 11.2 vs < 9.8 HR 132.7 [95%CI 15.6-1127.4 p<0.01], 9.8-11.2 vs <9.8 HR 22.5 [95%CI 2.8-184.3 p=0.04]) (F4 vs F≤2 HR 92.0 [95%CI 20.1-421.9 p<0.01], F3 vs F≤2 HR 10.2 [95%CI 2.3-45.5 p=0.05]). (Table 2)

Figure 1. Kaplan Meier survival curves for comparisons between groups

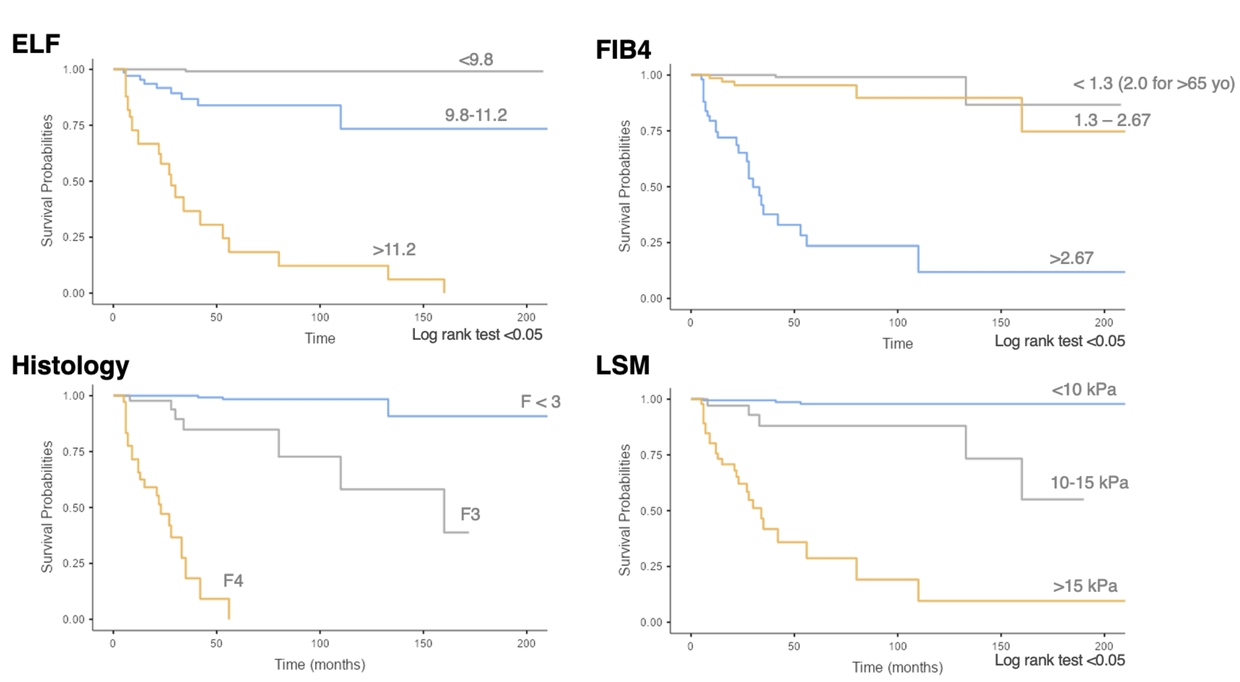

Table 2. Risk of composite endpoint for 3 risk groups defined by test-specific cut-offs.

	Events/patients in group (%)	Unadjusted Hazard Ratio	P value	Adjusted* Hazard Ratio	P value
ELF					
<9.8	1/187 (0.5%)	1 (Reference)		1 (Reference)	
9.8-11.2	10/69 (14.5%)	29.14 (3.69 – 230.30)	<0.01	22.56 (2.76 - 184.32)	0.04
>11.2	23/33 (69.7%)	227.43 (30.49 – 1696.68)	<0.01	132.76 (15.63 – 1127.44)	<0.01
LSM					
<10	3/202 (1.5%)	1 (Reference)		1 (Reference)	
10-15	5/41 (12.2%)	9.33 (2.20 – 39.58)	<0.01	5.51 (1.25 – 24.18)	0.02
>15	26/46 (56.5%)	67.71 (20.13 – 227.78)	<0.01	22.89 (6.17 – 84.94)	<0.01
Histology					
F<3	4/207 (1.9%)	1 (Reference)		1 (Reference)	
F3	7/46 (15.2%)	13.29 (3.37 – 52.40)	<0.01	10.20 (2.29 – 45.51)	0.02
F4	23/36 (63.9%)	217.09 (57.89 – 814.15)	<0.01	92.05 (20.13 – 421.91)	<0.01
FIB-4					
Low	2/166 (1.2%)	1 (Reference)		1 (Reference)	
Medium	6/72 (8.3%)	5.34 (1.03 – 27.68)	0.04	2.87 (0.53 – 15.55)	0.22
high	26/51 (51.0%)	83.32 (19.58 – 354.56)	<0.01	26.93 (5.49-132.4)	<0.01

**covariates: diabetes, age, gender, BMI*

Conclusion

The ELF test demonstrated comparable performance to histologically evaluated fibrosis in forecasting clinical outcomes. It should be regarded as a viable alternative to liver biopsy for conducting prognostic assessments in patients with MASLD.

Poster P29 – Antonio Liguori MD