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Liver fibrosis assessed by transient elastography is significantly associated with chronic kidney disease progression

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Objectives: Liver fibrosis and fatty liver has been related to incident chronic kidney disease. However, association of liver stiffness and steatosis assessed with transient elastography with renal function decline was uncertain.

Methods: This study retrospectively included 498 patients who underwent transient elastography between March 2012 and December 2013. Baseline estimated glomerular filtration rate of patients was 30 or more but less than 90 mL/min/1.73m². The study outcome was a composite renal outcome of a \geq 50% decrease in estimated glomerular filtration rate or the incident end-stage renal disease.

Results: During the follow up period (median 5.96 years), the composite renal outcome event occurred in 24 (4.82%) patients. There were 142 (28.51%) patients with significant liver fibrosis (>8.0 kPa) and 222 (44.58%) patients with fatty liver (>250 dB/m). Liver stiffness (per 1kPa) was associated with renal function deterioration (hazard ratio[HR] 1.058, 95% CI 1.031-1.085, $p < 0.001$). In multivariable Cox analysis, significant liver fibrosis was independently associated with increased risk of renal function decline (hazard ratio 6.70, 95% CI 2.22-20.22, $p < 0.001$). However fatty liver was not associated with worsening of renal function.

Conclusions: In this study, significant liver fibrosis, but not fatty liver, was significantly associated with increased risk of renal function deterioration.

Table 1. Baseline characteristics of patients

Table 1. Baseline characteristics of patients by liver fibrosis or fatty liver

Variables	Total (n=498)	Liver fibrosis			P	Fatty liver		P
		no (n=235)	minimal (n=121)	significant (n=142)		no (n=276)	yes (n=222)	
Age, years	64.4 ± 10.5	64.5 ± 10.8	64.1 ± 10.6	64.6 ± 9.9	0.922	64.9 ± 10.2	63.8 ± 10.8	0.233
Female, n (%)	169 (33.9)	80 (34.0)	37 (31.6)	52 (36.6)	0.591	93 (33.7)	76 (34.2)	0.924
HTN, n (%)	195 (39.2)	98 (41.7)	47 (38.8)	50 (35.2)	0.457	97 (35.1)	98 (44.1)	0.043
DM, n (%)	124 (24.9)	52 (22.1)	31 (25.6)	41 (28.9)	0.339	58 (21)	66 (29.7)	0.025
BMI, kg/m ²	24.4 ± 2.6	24.2 ± 2.5	24.6 ± 2.6	24.5 ± 3.0	0.470	23.5 ± 2.2	25.5 ± 2.7	<0.001
Hemoglobin, g/dl	14.0 (12.6-15.0)	14.2 (13.1-15.2)	13.8 (12.4-14.8)	13.9 (12.0-14.9)	0.021	13.8 (12.2-14.8)	14.3 (13.2-15.2)	<0.001
PLT, x10 ³ /mm ³	196.0 (155.0-233.0)	212.0 (179.0-247.0)	199.0 (171.0-233.0)	147.0 (107.8-191.5)	0.03	188.0 (147.3-222.8)	208.0 (168.3-244.3)	<0.001
AST, U/L	29 (22-42)	24 (20-34)	29 (22-43)	37 (28-57)	<0.001	29 (22-40)	29 (22-43)	0.742
ALT, U/L	27 (18-42)	22 (16-34)	29 (21-48)	32 (20-51)	<0.001	25 (17-37)	29 (20-48)	0.001
GGT, U/L	31 (21-61)	24 (17-40)	37 (24-66)	50 (26-85)	<0.001	29 (19-61)	36 (23-61)	0.014
Albumin, g/dl	4.2 (3.8-4.4)	4.2 (3.9-4.4)	4.2 (3.8-4.4)	4.1 (3.7-4.3)	0.011	4.1 (3.7-4.3)	4.2 (3.9-4.4)	0.001
Triglyceride, mg/dl	114 (79-123)	109 (75-131)	114 (88-129)	114 (79-114)	0.202	111 (72-114)	114 (87-151)	<0.001
LDL cholesterol, mg/dl	98.0 ± 22.4	98.8 ± 26.6	95.3 ± 20.9	98.9 ± 14.9	0.135	96.0 ± 21.3	100.5 ± 23.6	0.059
HDL cholesterol, mg/dl	44.0 ± 8.6	45.1 ± 10.2	42.8 ± 6.6	43.3 ± 7.0	0.203	44.5 ± 9.1	43.4 ± 7.9	0.035
Creatinine, mg/dl	0.98 ± 0.26	0.98 ± 0.28	0.98 ± 0.21	0.99 ± 0.25	0.549	1.00 ± 0.30	0.96 ± 0.19	0.665
eGFR, mL/min/1.73m ²	76.4 ± 13.1	76.8 ± 12.9	76.5 ± 12.5	75.5 ± 14.0	0.882	75.7 ± 14.4	77.2 ± 11.3	0.808
Liver stiffness, kPa	5.9 (4.4-8.8)	4.3 (3.7-4.8)	6.6 (6.1-7.3)	12.6 (10.1-21.3)	<0.001	5.9 (4.3-9.5)	5.9 (4.4-8.3)	0.854
CAP, dB/m	242 (212-277)	243 (212-274)	246 (215-299)	240 (213-274)	0.33	215 (198-231)	284 (265-312)	<0.001
Fatty liver >250.0 dB/m	222 (44.6)	104 (44.3)	58 (47.9)	60 (42.3)	0.647			

Values are presented as number (%), mean ± SD, or median (interquartile range)
 HTN, hypertension; DM, diabetes mellitus; BMI, body mass index; PLT, platelet; AST, aspartate aminotransferase; ALT, alanine aminotransferase; GGT, gamma-glutamyltransferase;
 LDL, low-density lipoprotein; HDL, high-density lipoprotein; eGFR, estimated glomerular filtration rate; kPa, kilopascal; CAP, Controlled attenuation parameter

Table 2. Multivariable proportional hazard models

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	Model 1		Model 2		Model 3	
	HR (95% CI)	P value	HR (95% CI)	P value	HR (95% CI)	P value
Values as continuous variables						
Liver fibrosis, per 1kPa	1.057 (1.039-1.077)	<0.001	1.061 (1.040-1.081)	<0.001	1.058 (1.031-1.085)	<0.001
Liver steatosis, per 1dB/m	1.001 (0.994-1.009)	0.691	1.000 (0.991-1.009)	0.968	1.004 (0.994-1.014)	<0.001
Values as categorical variables						
No fibrosis <5.6kPa	1		1		1	
Mild fibrosis 5.6-8.0kPa	2.478 (0.665-9.239)	0.177	2.268 (0.603-8.529)	0.226	1.952 (0.495-7.692)	0.339
Significant fibrosis >8.0kPa	6.701 (2.221-20.220)	0.001	6.467 (2.126-19.674)	0.001	5.493 (1.523-19.818)	0.009
Fatty liver >250.0dB/m	1.334 (0.596-2.983)	0.483	1.179 (0.480-2.898)	0.718	1.629 (0.629-4.223)	0.315

Model 1: adjusting for age and gender

Model 2: adjusting for age, gender, hypertension, diabetes mellitus, body mass index

Model 3: adjusting for age, gender, hypertension, diabetes mellitus, body mass index, and all laboratory results

Abbreviations: HR, hazard ratio; kPa, kilopascal