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Title

FIB-4 stage of liver fibrosis predicts incident heart failure among HIV-infected and uninfected patients.

Permalink

<https://escholarship.org/uc/item/98g8r154>

Journal

Hepatology (Baltimore, Md.), 66(4)

ISSN

0270-9139

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Publication Date

2017-10-01

DOI

10.1002/hep.29285

Supplemental Material

<https://escholarship.org/uc/item/98g8r154#supplemental>

Peer reviewed

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Table 1: Baseline characteristics of study population

Data are column percent unless otherwise noted	FIB-4 (category of liver fibrosis)			Missing FIB-4
	<1.45 (Minimal)	1.45-3.25 (Moderate)	>3.25 (Advanced)	
Demographics				
N (%)	57,309 (59)	16,360 (17)	3,679 (4)	19,025 (20)
Mean age (SD)	47 (9)	54 (9)	53 (8)	48 (10)
Male	96	98	99	97
Race				
<i>White</i>	40	35	37	38
<i>Black</i>	47	53	50	47
<i>Hispanic</i>	8	7	9	7
<i>Other</i>	5	5	4	8
HIV				

Table 1: Baseline characteristics of study population

Data are column percent unless otherwise noted	FIB-4 (category of liver fibrosis)			Missing FIB-4
	<1.45 (Minimal)	1.45-3.25 (Moderate)	>3.25 (Advanced)	
HIV infected	29	50	61	16
HIV-1 RNA \geq 500 copies/ml (% of HIV+)	48	53	56	22
CD4+ T-cell count <500 cells/mm ³ (% of HIV+)	54	65	71	17
On any ART (% of HIV+)	75	78	78	35
Liver				
HCV	13	35	65	8
CVD risk factors				
Diabetes	13	15	18	8
Systolic blood pressure (BP)/mmHg				
<140 no BP medication	40	35	33	44
<140 on BP medication	34	36	37	20
\geq 140 on BP medication	18	22	22	12
\geq 140 no BP medication	6	6	6	10
LDL cholesterol \geq 160 mg/dL	10	6	3	5
HDL cholesterol <40 mg/dL	37	37	40	16
Triglycerides \geq 200 mg/dL	23	21	19	9

Table 1: Baseline characteristics of study population

Data are column percent unless otherwise noted	FIB-4 (category of liver fibrosis)			Missing FIB-4
	<1.45 (Minimal)	1.45-3.25 (Moderate)	>3.25 (Advanced)	
Smoking				
<i>Never smoker</i>	23	20	13	17
<i>Current smoker</i>	37	38	46	27
<i>Former smoker</i>	11	13	11	9
Obese, BMI>30 kg/m ²	34	23	16	27
Cocaine	15	21	25	15
Alcohol abuse/dependence (ever)	24	32	51	23
Antecedent incident AMI	1.5	2.0	1.6	1.0
<p>All variables had complete data except the following: LDL cholesterol data were available for 74559, HDL cholesterol (75543), triglycerides (76046), SBP (92961), smoking (65118) BMI (91534), CD4 count (25327), and HIV-1 RNA (26048).</p> <p>p-values across FIB-4 groups (excluding missing FIB-4 group) were all <0.01</p>				

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Table 2: Hazard ratio (95% confidence interval) for the association between liver injury and incident congestive heart failure

Variables	Model 1	Model 2	Model 3	Model 4	Model 5	Model 6
Liver fibrosis						
<i>FIB-4</i> <1.45	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)
<i>FIB-4</i> 1.45-3.25	1.78 (1.65-1.92)	1.20 (1.11-1.30)	1.27 (1.17-1.38)	1.27 (1.17-1.38)	1.17 (1.07-1.27)	1.17 (1.07-1.27)
<i>FIB-4</i> >3.25	2.74 (2.39-3.13)	1.89 (1.62-2.19)	1.93 (1.67-2.22)	1.93 (1.68-2.22)	1.66 (1.43-1.93)	1.65 (1.43-1.92)
Age (per 10 years)		1.99 (1.92-2.06)	1.79 (1.72-1.86)	1.75 (1.69-1.82)	1.78 (1.72-1.85)	1.84 (1.76-1.91)
Race/ethnicity						
<i>White</i>		1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)
<i>Black</i>		1.29 (1.21-1.39)	1.21 (1.13-1.3)	1.22 (1.14-1.31)	1.20 (1.11-1.28)	1.17 (1.09-1.25)
<i>Hispanic</i>		0.75 (0.66-0.87)	0.73 (0.63-0.84)	0.73 (0.64-0.84)	0.72 (0.63-0.83)	0.72 (0.63-0.83)
<i>Other</i>		0.77 (0.64-0.93)	0.86 (0.71-1.04)	0.88 (0.72-1.06)	0.89 (0.74-1.08)	0.91 (0.75-1.1)
Systolic blood pressure (BP)/mmHg						
<140 no BP meds			1 (ref)	1 (ref)	1 (ref)	1 (ref)
<140 on BP meds			1.54 (1.4-1.7)	1.53 (1.39-1.69)	1.56 (1.42-1.72)	1.53 (1.39-1.68)
≥140 on BP meds			2.33 (2.12-2.57)	2.29 (2.08-2.52)	2.37 (2.15-2.60)	2.27 (2.06-2.5)
≥140 no BP meds			1.56 (1.32-1.85)	1.57 (1.33-1.85)	1.61 (1.36-1.91)	1.58 (1.34-1.87)

Table 2: Hazard ratio (95% confidence interval) for the association between liver injury and incident congestive heart failure

Variables	Model 1	Model 2	Model 3	Model 4	Model 5	Model 6
Smoking						
<i>Never smoker</i>			1 (ref)	1 (ref)	1 (ref)	1 (ref)
<i>Current smoker</i>			1.59 (1.43-1.76)	1.57 (1.41-1.76)	1.52 (1.36-1.70)	1.5 (1.33-1.68)
<i>Former smoker</i>			1.14 (0.98-1.32)	1.14 (0.98-1.33)	1.13 (0.97-1.31)	1.12 (0.96-1.3)
Diabetes			2.26 (2.10-2.43)	2.22 (2.06-2.39)	2.24 (2.09-2.41)	2.19 (2.03-2.36)
LDL cholesterol ≥160 mg/dL			1.04 (0.96-1.12)	1.03 (0.95-1.12)	1.00 (0.92-1.09)	0.99 (0.91-1.07)
HDL cholesterol <40 mg/dL			1 (0.89-1.13)	0.99 (0.88-1.11)	1.01 (0.90-1.14)	1.01 (0.9-1.14)
Triglycerides ≥200 mg/dL			1.13 (1.05-1.22)	1.11 (1.03-1.2)	1.10 (1.02-1.18)	1.08 (1-1.17)
Antecedent incident AMI				3.04 (2.7-3.43)	2.98 (2.64-3.35)	2.99 (2.66-3.37)
HIV/Hepatitis C (HCV)						
<i>HIV & HCV</i>					1 (ref)	1 (ref)

Table 2: Hazard ratio (95% confidence interval) for the association between liver injury and incident congestive heart failure

Variables	Model 1	Model 2	Model 3	Model 4	Model 5	Model 6
<i>uninfected</i>						
<i>HCV infected only</i>					1.15 (1.03-1.28)	1.1 (0.98-1.23)
<i>HIV infected only</i>					1.20 (1.10-1.31)	1.29 (1.18-1.41)
<i>HIV & HCV co-infected</i>					1.62 (1.46-1.80)	1.66 (1.49-1.85)
Alcohol abuse or dependence						1.19 (1.09-1.31)
Cocaine abuse or dependence						1.07 (0.96-1.19)
Body mass index $\geq 30/\text{kg}/\text{m}^2$						1.27 (1.18-1.37)
<p>Model 1: unadjusted</p> <p>Model 2: adjusted for age and race/ethnicity</p> <p>Model 3: adjusted for Model 2 covariates plus Framingham cardiovascular disease risk factors (treated or untreated systolic blood pressure, smoking, diabetes, LDL cholesterol, HDL cholesterol and triglycerides)</p>						

Table 2: Hazard ratio (95% confidence interval) for the association between liver injury and incident congestive heart failure

Variables	Model 1	Model 2	Model 3	Model 4	Model 5	Model 6
Model 4: adjusted for Model 3 covariates plus antecedent incident acute myocardial infarction						
Model 5: adjusted for Model 4 covariates plus HIV/HCV status						
Model 6: adjusted for Model 5 covariates plus alcohol and cocaine abuse or dependence and body mass index						

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Table 3: Hazard ratios (95% confidence intervals) for the association between liver injury and incident congestive heart failure stratified by HIV and hepatitis C status

	HIV and HCV uninfected	HCV infected only	HIV infected only	HIV and HCV co-infected
N (# of CHF events)	57594 (2097)	8354 (424)	21449 (760)	8976 (563)
Liver fibrosis				
<i>FIB-4</i> <1.45	1 (ref)	1 (ref)	1 (ref)	1 (ref)
<i>FIB-4</i> 1.45-3.25	1.08 (0.96-1.22)	1.30 (1.05-1.62)	1.27 (1.05-1.52)	1.15 (0.93-1.41)
<i>FIB-4</i> >3.25	1.56 (1.19-2.05)	1.81 (1.34-2.44)	1.74 (1.30-2.33)	1.66 (1.30-2.12)
All models adjusted for age, race-ethnicity, systolic blood pressure and blood pressure medication, smoking, diabetes, LDL-cholesterol, HDL-cholesterol, triglycerides, antecedent incident AMI, alcohol abuse/dependence, cocaine abuse/dependence, body mass index. Models including HIV infected participants additionally adjusted for HIV-1 RNA, CD4+ T cell count, and antiretroviral therapy regimen				

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Table 4: Hazard ratios (95% confidence intervals) for the association between liver injury and incident congestive heart failure in the full cohort compared to a sample excluding participants with hepatic decompensation		
	Hazard ratio of CHF (95% confidence interval)	
	Unadjusted	Adjusted*
Full cohort (N=96,373)		
<i>FIB-4</i><1.45	1 (ref)	1 (ref)
<i>FIB-4</i> 1.45-3.25	1.78 (1.65-1.92)	1.17 (1.07-1.27)
<i>FIB-4</i>>3.25	2.74 (2.39-3.13)	1.65 (1.43-1.92)
Cohort excluding participants with hepatic decompensation (N=94,601)		
<i>FIB-4</i><1.45	1 (ref)	1 (ref)
<i>FIB-4</i> 1.45-3.25	1.76 (1.63-1.91)	1.15 (1.05-1.25)
<i>FIB-4</i>>3.25	2.62 (2.21-3.10)	1.56 (1.33-1.84)
*Model adjusted for age and race/ethnicity, Framingham cardiovascular disease risk factors (treated or untreated systolic blood pressure, smoking, diabetes, LDL cholesterol, HDL cholesterol and triglycerides), antecedent incident acute myocardial infarction, HIV/HCV status, alcohol abuse or dependence, cocaine abuse or dependence and body mass index		

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