

Table 1. Baseline Clinical and Biochemical Characteristics of Participants with MAFLD and Suspected Coronary Artery Disease Stratified by baseline Heart Failure Status

	All	Non-HF	Pre-HFpEF	HFpEF	P-value
Subjects, n	10019	3133	3427	3459	
Age, years	63.3±10.6	60.0±9.6	63.9±10.7	65.8±10.7	<0.001
Male sex, n (%)	6162 (61.5%)	2017 (64.4%)	2048 (59.8%)	2097 (60.6%)	<0.001
BMI, kg/m ²	26.4±3.1	26.3±2.8	26.4±3.1	26.6±3.3	0.014
Current smokers, n (%)	4182 (41.7%)	1304 (41.6%)	1452 (42.4%)	1426 (41.2%)	0.621
Current drinking, n (%)	3270 (32.6%)	1065 (34%)	1112 (32.4%)	1093 (31.6%)	0.114
Follow-up period, years	3.2 (0.9-5.9)	3.4 (1.2-5.9)	3.2 (1.0-6.0)	2.8 (0.7-5.7)	0.084
Comorbidities, n (%)					
Hypertension	7790 (77.8%)	2328 (74.3%)	2720 (79.4%)	2742 (79.3%)	<0.001
Diabetes mellitus	4252 (42.4%)	1148 (36.6%)	1523 (44.4%)	1581 (45.7%)	<0.001
Dyslipidemia	6620 (66.1%)	2176 (69.5%)	2282 (66.6%)	2162 (62.5%)	<0.001
Atrial fibrillation	964 (9.6%)	175 (5.6%)	377 (11.0%)	412 (11.9%)	<0.001
Previous stroke	972 (9.7%)	237 (7.6%)	336 (9.8%)	399 (11.5%)	<0.001
Previous myocardial infarction	1828 (18.2%)	138 (4.4%)	834 (24.3%)	856 (24.7%)	<0.001
Chronic kidney disease	993 (9.9%)	130 (4.1%)	395 (11.5%)	468 (13.5%)	<0.001
Medications at admission, n (%)					
Loop diuretics	1838 (18.3%)	149 (4.8%)	715 (20.9%)	974 (28.2%)	<0.001
Spironolactone	1399 (14.0%)	143 (4.6%)	480 (14.0%)	776 (22.4%)	<0.001
ACEI/ARB/ARNIs	6303 (62.9%)	1761 (56.2%)	2239 (65.3%)	2303 (66.6%)	<0.001
Beta-blockers	6580 (65.7%)	1805 (57.6%)	2352 (68.6%)	2423 (70.0%)	<0.001
SGLT2-inhibitors	116 (1.2%)	25 (0.8%)	48 (1.4%)	43 (1.2%)	0.063
MAFLD-related scores					

FIB-4 index	1.9±2.4	1.5±2.5	2.0±2.2	2.1±2.5	<0.001
Hepatic steatosis index (HSI)	37.0±5.3	37.5±4.9	36.8±5.5	36.8±5.3	<0.001
Severity of coronary stenosis					<0.001
Mild CAD (<50%)	1916 (19.1%)	808 (25.8%)	516 (15.1%)	592 (17.1%)	
Medium CAD (50-70%)	4412 (44.0%)	1493 (47.7%)	1435 (41.9%)	1484 (42.9%)	
Severe CAD (>70%)	3691 (36.8%)	832 (26.6%)	1476 (43.1%)	1383 (40.0%)	
Echocardiographic parameters					
LVEF, %	65.3±6.9	67.0±6.0	65.0±7.1	64.1±7.2	<0.001
LAD, cm	41.6±6.7	40.5±5.2	41.9±6.9	42.5±7.4	<0.001
LVDD, cm	48.6±7.0	48.4±5.7	48.5±7.4	49.0±7.7	0.002
LVSD, cm	30.8±5.8	30.3±4.6	30.8±5.9	31.3±6.5	<0.001
PAP, mmHg	29.3±8.0	27.7±6.3	29.4±8.1	30.5±9.1	<0.001
Laboratory values					
hs-CRP, mg/L	3.4 (1.6-8.3)	2.7 (1.1-5.0)	4.5 (1.9-10.0)	5.0 (2.1-10.1)	<0.001
quartile 1 (≤3.26)	2549 (25.4%)	1123 (35.8%)	747 (21.8%)	679 (19.6%)	<0.001
quartile 2 (3.26-7.00)	2463 (24.6%)	954 (30.5%)	779 (22.7%)	730 (21.1%)	
quartile 3 (7.01-36.9)	2515 (25.1%)	622 (19.9%)	914 (26.7%)	979 (28.3%)	
quartile 4 (>36.9)	2492 (24.9%)	434 (13.9%)	987 (28.8%)	1071 (31.0%)	
NT-proBNP, ng/L	146.0 (56.4-557.0)	46.1 (26.0-74.0)	189.0 (76.2-638.0)	334.0 (128.0-1276.0)	<0.001
hs-cTnI, µg/L	0.0 (0.0-7.0)	0.0 (0.0-0.0)	0.0 (0.0-5.2)	3.0 (0.0-12.5)	<0.001
eGFR, mL/min × 1.73 m ²	90.5 (73.95-102.2)	96.4 (84.2-106.8)	87.9 (70.9-100.1)	85.8 (66.2-98.5)	<0.001
Platelet count, 10 ⁹ /L	220±67	224±62	219±70	216±67	<0.001
AST/ALT ratio	1.11±0.47	1.20±0.45	1.07±0.44	1.06±0.49	<0.001
Albumin, g/dL	40.4±8.5	41.7±8.4	39.8±9.3	39.8±7.8	<0.001
HbA1c, %	7.0±2.2	6.7±1.4	7.0±1.6	7.1±3.1	<0.001

Data are expressed as means ± SD, medians (interquartile ranges, IQR), or percentages.

Abbreviations: ACEi: angiotensin converting enzyme inhibitor; ARBs: angiotensin II receptor blockers; ARNI: angiotensin receptor neprilysin inhibitor; BMI, body mass index; CAD, coronary artery disease; CI, confidence interval; HbA1c: glycated haemoglobin; MAFLD, metabolic dysfunction-associated fatty liver disease; hs-CRP, high-sensitivity C-reactive protein; hs-cTnI, high-sensitivity cardiac troponin I; NT-proBNP, N-terminal pro-brain natriuretic peptide; eGFR, estimated glomerular filtration rate; ALT, alanine aminotransferase; AST, aspartate aminotransferase; LVEF, left ventricular ejection fraction; LAD, left atrial diameter; LVDD, left ventricular diastolic dysfunction; LVSD, left ventricular end-systolic dimension; PAP, pulmonary arterial pressure.

Table 2. Associations between hs-CRP Concentration Quartiles and the risk of Heart Failure Hospitalization in Participants with Different Heart Failure Status at baseline

Groups	hs-CRP quartile	Events, n (%)	Model 1 Hazard ratio (95% CI)	P	Model 2 Hazard ratio (95% CI)	P	Model 3 Hazard ratio (95% CI)	P
All subjects	Q1 (N=2506)	154 (6.1%)	<i>Ref.</i>		<i>Ref.</i>		<i>Ref.</i>	
	Q2 (N=2520)	249 (9.9%)	1.546 (1.265-1.891)	<0.001	1.488 (1.217-1.820)	<0.001	1.487 (1.216-1.818)	<0.001
	Q3 (N=2493)	492 (19.7%)	2.966 (2.475-3.554)	<0.001	2.591 (2.161-3.108)	<0.001	2.411 (2.010-2.893)	<0.001
	Q4 (N=2500)	1047 (41.9%)	6.937 (5.857-8.215)	<0.001	5.544 (4.672-6.579)	<0.001	4.421 (3.720-5.254)	<0.001
Non-HF	Q1 (N=1244)	8 (0.6%)	<i>Ref.</i>		<i>Ref.</i>		<i>Ref.</i>	
	Q2 (N=872)	14 (1.6%)	2.22 (0.931-5.291)	0.072	2.203 (0.924-5.253)	0.075	2.110 (0.883-5.040)	0.093
	Q3 (N=601)	26 (4.3%)	5.426 (2.456-11.988)	<0.001	5.351 (2.419-11.836)	<0.001	4.910 (2.216-10.883)	<0.001
	Q4 (N=416)	69 (16.6%)	21.697 (10.434-45.117)	<0.001	20.888 (9.978-43.726)	<0.001	18.065 (8.589-37.998)	<0.001
Pre-HFpEF	Q1 (N=655)	62 (9.5%)	<i>Ref.</i>		<i>Ref.</i>		<i>Ref.</i>	
	Q2 (N=833)	86 (10.3%)	1.047 (0.755-1.451)	0.783	1.091 (0.787-1.512)	0.603	1.171 (0.843-1.625)	0.346
	Q3 (N=954)	186 (19.5%)	1.911 (1.433-2.547)	<0.001	1.777 (1.332-2.370)	<0.001	1.734 (1.298-2.317)	<0.001
	Q4 (N=985)	380 (38.6%)	4.083 (3.121-5.341)	<0.001	3.663 (2.797-4.798)	<0.001	3.179 (2.420-4.175)	<0.001
HFpEF	Q1 (N=607)	84 (13.8%)	<i>Ref.</i>		<i>Ref.</i>		<i>Ref.</i>	
	Q2 (N=815)	123 (18.3%)	1.389 (1.063-1.815)	0.016	1.364 (1.044-1.783)	0.023	1.373 (1.050-1.795)	0.021
	Q3 (N=938)	369 (29.9%)	2.328 (1.824-2.972)	<0.001	2.170 (1.699-2.772)	<0.001	2.120 (1.658-2.712)	<0.001
	Q4 (N=1099)	598 (54.4%)	4.698 (3.737-5.905)	<0.001	4.108 (3.262-5.174)	<0.001	3.502 (2.776-4.417)	<0.001

Serum hs-CRP quartiles were defined as follows: Q1: ≤ 3.26 mg/L; Q2: 3.26-7.00 mg/L; Q3: 7.01-36.9 mg/L; and Q4: >36.9 mg/L.

Cox regression Model 1: unadjusted;

Cox regression Model 2: adjusted for age and sex;

Cox regression Model 3: further adjusted for smoking, alcohol intake, BMI, hypertension, diabetes, dyslipidemia, atrial fibrillation, previous stroke, previous myocardial infarction, chronic kidney disease, and current use of loop diuretics, spironolactone, ACEI/ARB/ARNIs or beta-blockers.

Abbreviations: ACEi: angiotensin converting enzyme inhibitor; ARBs: angiotensin II receptor blockers; ARNI: angiotensin receptor neprilysin inhibitor; BMI, body mass index; hs-CRP, high-sensitivity C-reactive protein.

Table 3. Associations between hs-CRP Concentration Quartiles and the Risk of Heart Failure Hospitalization in Participants with Different severity of Coronary Stenosis at baseline.

Groups	hs-CRP quartile	Events, n (%)	Model 1 Hazard ratio (95% CI)	P	Model 2 Hazard ratio (95% CI)	P	Model 3 Hazard ratio (95% CI)	P
Mild CAD (<50%)	Q1 (N=471)	33 (7.0%)	<i>Ref.</i>		<i>Ref.</i>		<i>Ref.</i>	
	Q2 (N=564)	46 (8.2%)	1.090 (0.697-1.705)	0.008	1.057 (0.676-1.653)	0.014	1.019 (0.651-1.595)	0.933
	Q3 (N=458)	94 (20.5%)	2.554 (1.718-3.799)	<0.001	2.152 (1.443-3.209)	<0.001	1.896 (1.267-2.837)	<0.001
	Q4 (N=423)	165 (39.0%)	5.061 (3.482-7.355)	<0.001	3.931 (2.686-5.754)	<0.001	3.031 (2.061-4.458)	<0.001
Medium CAD (50-70%)	Q1 (N=1150)	79 (6.9%)	<i>Ref.</i>		<i>Ref.</i>		<i>Ref.</i>	
	Q2 (N=1018)	121 (11.9%)	1.633 (1.230-2.169)	<0.001	1.594 (1.201-2.117)	<0.001	1.531 (1.152-2.033)	0.003
	Q3 (N=1108)	248 (22.4%)	2.998 (2.327-3.862)	<0.001	2.662 (2.064-3.433)	<0.001	2.294 (1.777-2.961)	<0.001
	Q4 (N=1136)	527 (46.4%)	7.299 (5.762-9.247)	<0.001	6.091 (4.797-7.734)	<0.001	4.433 (3.477-5.651)	<0.001
Severe CAD (>70%)	Q1 (N=885)	42 (4.7%)	<i>Ref.</i>		<i>Ref.</i>		<i>Ref.</i>	
	Q2 (N=938)	82 (8.7%)	1.802 (1.242-2.614)	0.023	1.673 (1.153-2.427)	0.055	1.813 (1.248-2.636)	0.002
	Q3 (N=927)	150 (16.2%)	3.231 (2.295-4.550)	<0.001	2.808 (1.992-3.959)	<0.001	2.936 (2.078-4.148)	<0.001
	Q4 (N=941)	355 (37.7%)	7.816 (5.676-10.763)	<0.001	5.875 (4.250-8.121)	<0.001	5.390 (3.893-7.461)	<0.001

Serum hs-CRP quartiles were defined as follows: Q1: ≤ 3.26 mg/L; Q2: 3.26-7.00 mg/L; Q3: 7.01-36.9 mg/L; and Q4: >36.9 mg/L.

Cox regression Model 1: unadjusted;

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Abbreviations: ACEi: angiotensin converting enzyme inhibitor; ARBs: angiotensin II receptor blockers; ARNI: angiotensin receptor neprilysin inhibitor; BMI, body mass index; CAD, coronary artery disease; hs-CRP, high-sensitivity C-reactive protein.

Table 4. Associations between hs-CRP Concentration Quartiles and the risk of Heart Failure in Participants with MAFLD and Different Categories of Liver Fibrosis Score.

Groups	hs-CRP quartile	Events, n (%)	Model 1 Hazard ratio (95% CI)	<i>P</i>	Model 2 Hazard ratio (95% CI)	<i>P</i>	Model 3 Hazard ratio (95% CI)	<i>P</i>
FIB-4 (<1.3)	Q1 (N=1175)	56(4.8%)	<i>Ref.</i>		<i>Ref.</i>		<i>Ref.</i>	
	Q2 (N=1087)	67(6.2%)	1.285(0.901-1.833)	0.166	1.254(0.879-1.789)	0.212	1.220 (0.855-1.743)	0.273
	Q3 (N=928)	131(14.1%)	2.765(2.022-3.781)	<0.001	2.564(1.873-3.511)	<0.001	2.369(1.728-3.248)	<0.001
	Q4 (N=841)	295(35.1%)	7.797(5.857-10.38)	<0.001	6.518(4.874-8.715)	<0.001	4.562(3.390-6.140)	<0.001
FIB-4 (1.3-2.67)	Q1 (N=1138)	79(6.9%)	<i>Ref.</i>		<i>Ref.</i>		<i>Ref.</i>	
	Q2 (N=1152)	133(11.5%)	1.491(1.129-1.97)	0.005	1.477(1.118-1.951)	0.006	1.465(1.108-1.937)	0.007
	Q3 (N=1181)	261(22.1%)	2.810(2.185-3.615)	<0.001	2.574(2.000-3.313)	<0.001	2.464(1.914-3.172)	<0.001
	Q4 (N=1202)	534(44.4%)	5.956(4.702-7.543)	<0.001	5.213(4.109-6.613)	<0.001	4.398(3.462-5.589)	<0.001
FIB-4 (≥2.67)	Q1 (N=193)	19(9.8%)	<i>Ref.</i>		<i>Ref.</i>		<i>Ref.</i>	
	Q2 (N=281)	49(17.4%)	2.041(1.201-3.470)	0.008	2.145(1.260-3.652)	0.005	2.241(1.310-3.835)	0.003
	Q3 (N=384)	100(26.0%)	2.685(1.644-4.385)	<0.001	2.521(1.542-4.121)	<0.001	2.224(1.353-3.655)	0.002
	Q4 (N=457)	218(47.7%)	5.771(3.608-9.231)	<0.001	4.944(3.085-7.922)	<0.001	3.974(2.468-6.401)	<0.001

Serum hs-CRP quartiles were defined as follows: Q1: ≤3.26 mg/L; Q2: 3.26-7.00 mg/L; Q3: 7.01-36.9 mg/L; and Q4: >36.9 mg/L.

Cox regression Model 1: unadjusted;

Cox regression Model 2: adjusted for age and sex;

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Abbreviations: ACEi: angiotensin converting enzyme inhibitor; ARBs: angiotensin II receptor blockers; ARNI: angiotensin receptor neprilysin inhibitor; BMI, body mass index; CAD, coronary artery disease; hs-CRP, high-sensitivity C-reactive protein; FIB-4, fibrosis 4; HSI, hepatic steatosis index.