

Supplementary Information Impact of high body mass index on hepatocellular carcinoma risk in chronic liver disease: population-based prospective cohort study

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Supplementary Table S1. Baseline demographic and clinical characteristics of patients with liver cirrhosis (n = 31,260)

Characteristic	HBV-LC n = 6,403	HCV-LC n = 863	ALD-LC n = 3,073	NAFLD-LC n = 654	Unspecified LC n = 20,267
HCC	1,925	280	496	59	3,746
Sex					
Men	4,467 (69.8)	460 (53.3)	2,874 (93.5)	470 (71.9)	14,045 (69.3)
Women	1,936 (30.2)	403 (46.7)	199 (6.5)	184 (28.1)	6,222 (30.7)
BMI, kg/m ²					
<18.5	125 (2.0)	17 (2.0)	140 (4.6)	14 (2.1)	637 (3.1)
18.5–20.9	811 (12.7)	94 (10.9)	562 (18.3)	56 (8.6)	2,861 (14.1)
21–22.9	1,462 (22.8)	193 (22.4)	750 (24.4)	121 (18.5)	4,607 (22.7)
23–24.9	1,774 (27.7)	268 (31.1)	706 (23.0)	168 (25.7)	5,268 (26.0)
25–27.4	1,507 (23.5)	203 (23.5)	596 (19.4)	166 (25.4)	4,515 (22.3)
27.5–29.9	549 (8.6)	63 (7.3)	240 (7.8)	94 (14.4)	1,722 (8.5)
≥30	175 (2.7)	25 (2.9)	79 (2.6)	35 (5.4)	657 (3.2)
Glycaemic status					
Normoglycemia	4,297 (67.1)	489 (56.7)	1,374 (44.7)	377 (57.6)	11,912 (58.8)
IFG	1,258 (19.6)	177 (20.5)	808 (26.3)	140 (21.4)	4,472 (22.1)
Diabetes	848 (13.2)	197 (22.8)	891 (29.0)	137 (20.9)	3,883 (19.2)
Smoking, pack/day					
Never	4,267 (66.6)	641 (74.3)	1,196 (38.9)	400 (61.2)	12,509 (61.7)
Former	720 (11.2)	74 (8.6)	394 (12.8)	71 (10.9)	2,171 (10.7)
<0.5	445 (6.9)	53 (6.1)	471 (15.3)	52 (8.0)	1,744 (8.6)
0.5–0.9	645 (10.1)	50 (5.8)	669 (21.8)	93 (14.2)	2,400 (11.8)
1–1.9	171 (2.7)	15 (1.7)	275 (8.9)	22 (3.4)	911 (4.5)
≥2	143 (2.2)	28 (3.2)	62 (2.0)	14 (2.1)	490 (2.4)
Unknown	12 (0.2)	2 (0.2)	6 (0.2)	2 (0.3)	42 (0.2)
Alcohol, ethanol (g)/day					
None	4,736 (74.0)	685 (79.4)	1,443 (47.0)	380 (58.1)	12,763 (63.0)
<10	960 (15.0)	71 (8.2)	429 (14.0)	123 (18.8)	3,180 (15.7)
10–19	338 (5.3)	35 (4.1)	342 (11.1)	74 (11.3)	1,772 (8.7)
20–39	97 (1.5)	17 (2.0)	221 (7.2)	32 (4.9)	711 (3.5)
≥40	116 (1.8)	13 (1.5)	566 (18.4)	29 (4.4)	1,315 (6.5)
Unknown	156 (2.4)	42 (4.9)	72 (2.3)	16 (2.4)	526 (2.6)
Physical activity, times/week					
None	3,279 (51.2)	477 (55.3)	2,068 (67.3)	356 (54.4)	11,864 (58.5)
1–2	1,809 (28.3)	182 (21.1)	525 (17.1)	164 (25.1)	4,457 (22.0)

≥3	1,315 (20.5)	204 (23.6)	480 (15.6)	134 (20.5)	3,946 (19.5)
Income status, quartile					
Q1 (low)	1,033 (16.1)	170 (19.7)	701 (22.8)	106 (16.2)	4,066 (20.1)
Q2	1,024 (16.0)	146 (16.9)	772 (25.1)	110 (16.8)	3,862 (19.1)
Q3	1,591 (24.8)	200 (23.2)	828 (26.9)	174 (26.6)	5,097 (25.1)
Q4	2,755 (43.0)	347 (40.2)	772 (25.1)	264 (40.4)	7,242 (35.7)
Age groups, years					
<65	5,944 (92.8)	559 (64.8)	2414 (78.6)	538 (82.3)	16,231 (80.1)
≥65	459 (7.2)	304 (35.2)	659 (21.4)	116 (17.7)	4,036 (19.9)
Total cholesterol, mg/dL					
<200	4,987 (77.9)	732 (84.8)	2471 (80.4)	379 (58.0)	14,779 (72.9)
200–239	1,152 (18.0)	107 (12.4)	446 (14.5)	198 (30.3)	4,072 (20.1)
≥240	264 (4.1)	24 (2.8)	156 (5.1)	77 (11.8)	1,416 (7.0)

Data are expressed as numbers and percentages.

Abbreviations: HBV, hepatitis B virus; LC, liver cirrhosis; HCV, hepatitis C virus; ALD, alcoholic liver disease; NAFLD, non-alcoholic fatty liver disease; HCC, hepatocellular carcinoma; BMI, body mass index; IFG, impaired fasting glucose

Supplementary Table S2. Categorical analysis of the association between body mass index and the risk of hepatocellular carcinoma according to liver disease

Subgroup	Parameter	HR (95% CI)	P
HBV	<18.5	1.02 (0.87–1.19)	0.823
	18.5–20.9	0.99 (0.92–1.06)	0.763
	21–22.9	1.04 (0.98–1.10)	0.231
	23–24.9	1.00 (reference)	
	25–27.4	0.99 (0.94–1.05)	0.747
	27.5–29.9	1.09 (1.01–1.18)	0.028
	≥30	1.20 (1.06–1.36)	0.004
HCV	<18.5	0.69 (0.49–0.98)	0.036
	18.5–20.9	0.83 (0.70–0.99)	0.037
	21–22.9	0.90 (0.78–1.03)	0.121
	23–24.9	1.00 (reference)	
	25–27.4	0.99 (0.86–1.13)	0.837
	27.5–29.9	1.09 (0.91–1.31)	0.365
	≥30	1.00 (0.73–1.36)	0.975
ALD	<18.5	1.14 (0.91–1.43)	0.246
	18.5–20.9	1.19 (1.05–1.35)	0.007
	21–22.9	1.28 (1.14–1.43)	<0.001
	23–24.9	1.00 (Reference)	
	25–27.4	1.00 (0.89–1.12)	0.988
	27.5–29.9	1.22 (1.06–1.42)	0.007
	≥30	1.38 (1.10–1.74)	0.006
NAFLD	<18.5	1.38 (0.72–2.61)	0.329
	18.5–20.9	1.11 (0.81–1.53)	0.516
	21–22.9	1.05 (0.82–1.34)	0.694
	23–24.9	1.00 (Reference)	
	25–27.4	0.99 (0.80–1.22)	0.921
	27.5–29.9	1.36 (1.06–1.74)	0.014
	≥30	1.42 (1.00–2.01)	0.051
LC	<18.5	0.69 (0.57–0.82)	<0.001
	18.5–20.9	0.83 (0.76–0.90)	<0.001
	21–22.9	0.94 (0.88–1.01)	0.078
	23–24.9	1.00 (Reference)	
	25–27.4	1.00 (0.93–1.07)	0.992
	27.5–29.9	1.11 (1.02–1.22)	0.020
	≥30	1.07 (0.93–1.24)	0.362

Abbreviations: HR, hazard ratio; CI, confidence interval; HBV, hepatitis B virus; HCV, hepatitis C virus; ALD, alcoholic liver disease; NAFLD, non-alcoholic fatty liver disease; LC, liver cirrhosis

Supplementary Table S3. Linear analysis of the association between body mass index and the risk of hepatocellular carcinoma according to the aetiology of liver disease, for each 5-kg/m² BMI increase (BMI $\geq$ 25 kg/m²)

Subgroup	LC	Participants/HCC, n	HR (95% CI)	<i>P</i>
HBV	with LC	2,231/739	1.19 (0.98–1.45)	0.075
	without LC	37,024/2,539	1.15 (1.03–1.27)	0.011
HCV	with LC	291/90	1.38 (0.75–2.51)	0.297
	without LC	4,979/493	1.09 (0.86–1.37)	0.486
ALD	with LC	915/162	1.36 (0.92–2.02)	0.125
	without LC	41,959/739	1.32 (1.10–1.58)	0.003
NAFLD	with LC	295/25	1.59 (0.53–4.76)	0.410
	without LC	42,581/296	1.52 (1.17–1.97)	0.002

Abbreviations: BMI, body mass index; LC, liver cirrhosis; HCC, hepatocellular carcinoma; HR, hazard ratio; CI, confidence interval; HBV, hepatitis B virus; HCV, hepatitis C virus; ALD, alcoholic liver disease; NAFLD, non-alcoholic fatty liver disease

Supplementary Table S4. Cox regression analysis of hepatocellular carcinoma risk according to liver cirrhosis aetiology, for each 5-kg/m² BMI increase (BMI ≥25 kg/m²)

Subgroup	Participants/HCC, n	Parameter	HR (95% CI)	<i>P</i>	<i>P</i> for interaction
HBV-LC	2,231/739	overall	1.19 (0.98–1.45)	0.075	
		male	0.95 (0.74–1.22)	0.698	0.003 ^a
		female	1.73 (1.28–2.32)	<0.001	
		<65 years	1.17 (0.95–1.43)	0.131	0.734 ^b
		≥65 years	1.30 (0.72–2.35)	0.378	
HCV-LC	291/90	overall	1.38 (0.75–2.51)	0.297	
		male	0.76 (0.26–2.19)	0.612	0.127 ^a
		female	2.16 (0.95–4.95)	0.067	
		<65 years	1.41 (0.66–3.01)	0.381	0.247 ^b
		≥65 years	0.60 (0.18–2.04)	0.414	
ALD-LC	915/162	overall	1.36 (0.92–2.02)	0.125	
		male	1.43 (0.95–2.15)	0.087	0.957 ^a
		female	1.35 (0.20–9.20)	0.758	
		<65 years	1.31 (0.84–2.05)	0.234	0.822 ^b
		≥65 years	1.48 (0.57–3.87)	0.424	
NAFLD-LC	295/25	overall	1.59 (0.53–4.76)	0.410	
		male	0.82 (0.13–5.18)	0.831	0.408 ^a
		female	2.11 (0.59–7.58)	0.253	
		<65 years	0.76 (0.19–3.05)	0.699	0.036 ^b
		≥65 years	11.08 (1.38–89.24)	0.024	

Abbreviations: BMI, body mass index; HCC, hepatocellular carcinoma; HR, hazard ratio; CI, confidence interval; HBV, hepatitis B virus; LC, liver cirrhosis; HCV, hepatitis C virus; ALD, alcoholic liver disease; NAFLD, non-alcoholic fatty liver disease

^a *P* for interaction between sexes

^b *P* for interaction between age groups