Reduced hepatic steatosis is associated with higher risk of hepatocellular carcinoma in chronic hepatitis B infection

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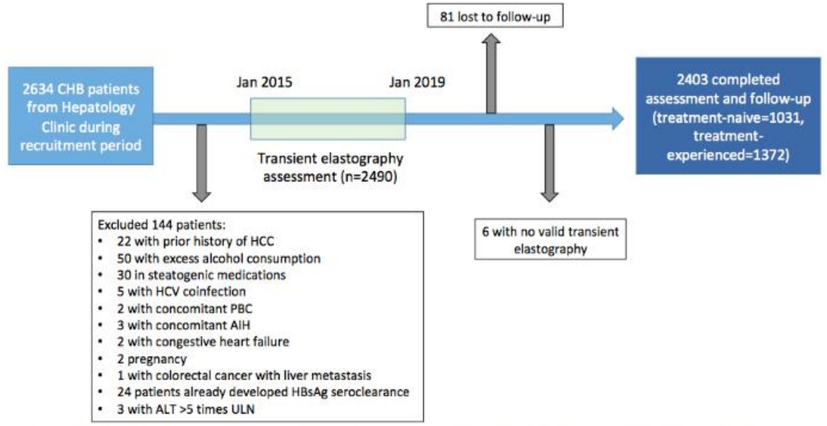
Introduction

Concomitant chronic hepatitis B infection (CHB) and non-alcoholic fatty liver disease (NAFLD) is common, but the implications of NAFLD on clinical outcomes of CHB, including hepatocellular carcinoma (HCC), are not well-investigated.

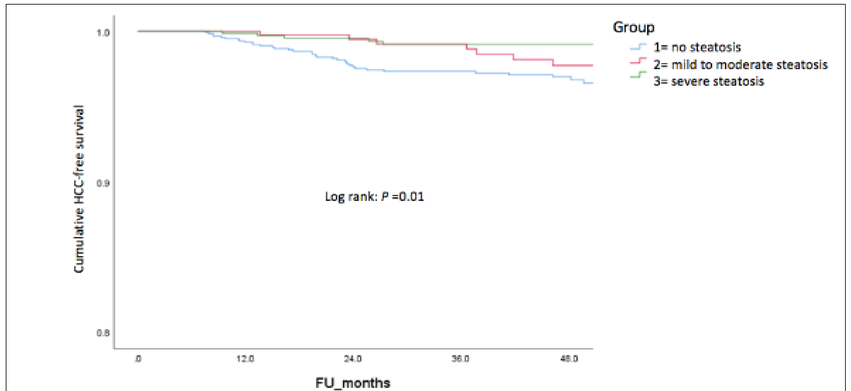
Methodology

CHB patients [both treatment-naïve and treated with nucleos(t)ide analogues (NA)] were recruited for transient elastography assessment for liver stiffness, and controlled attenuation parameter (CAP), a non-invasive quantification of hepatic steatosis, and were prospectively followed up for development of HCC. Steatosis and severe steatosis were diagnosed by CAP ≥248 dB/m and ≥280 dB/m respectively, and advanced fibrosis/ cirrhosis was diagnosed by liver stiffness ≥9 kPa

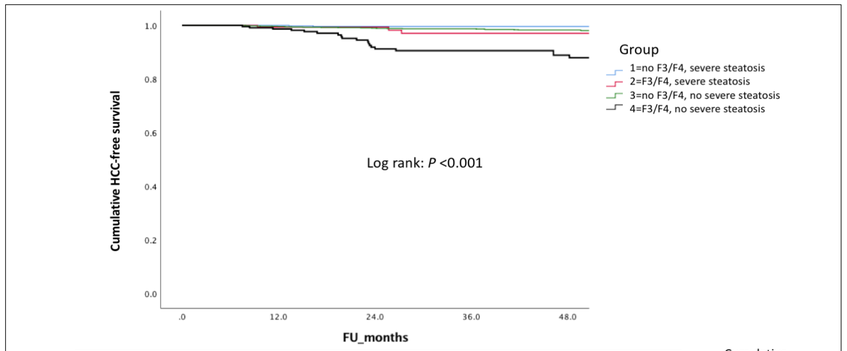
	Median/ frequency	Interquartile range
Age (years)	55.6	46.7 – 62.9
Gender (male)	1336 (55.6%)	-
Follow-up duration (months)	46.4	24.4 – 51.1
Body height (cm)	163	157 – 170
Body weight (kg)	64.7	56.2 – 73
Body mass index (kg/m²)	24.0	21.7 – 26.9
Waist circumference (cm)	87	79 – 94
Systolic blood pressure (mmHg)	133	121 – 147
Diastolic blood pressure (mmHg)	79	72 – 87
Presence of diabetes mellitus (yes)	657/2277 (28.9%)	-
Glycated hemoglobin (%)	5.7	5.3 – 6.4
Presence of dyslipidaemia (yes)	1275/2393 (53.3%)	-
Platelet count (x100/L)	208	165 – 248
Albumin (gram/L)	45	43 – 47
Bilirubin (umol/L)	10	7 – 13
Alanine aminotransferase (U/L)	26	19 – 36
Aspartate aminotransferase (U/L)	26	21 – 32
HBV DNA (log IU/mL)	1.3	1.3 – 2.7
HBeAg positivity (yes)	230 (9.6%)	-
On NA therapy (yes)	1372 (57.1%)	-
CAP (dB/m)	246	206 – 290
Proportion of severe steatosis	706 (29.4%)	-
Liver stiffness (kPa)	5.6	4.0 – 7.8
Proportion of F3/F4	371 (15.4%)	-



AIH: autoimmune hepatitis, ALT: alanine aminotransferase, CHB: chronic hepatitis B, HBsAg: hepatitis B surface antigen, HCC: hepatocellular carcinoma, HCV: hepatitis C virus, PBC: primary biliary cholangitis, ULN: upper limit of normal



Number at risk	0 months	12 months	24 months	36 months	48 months	Cumulative probability of HCC
Group 1	1248	1217	1019	952	519	2.88%
Group 2	450	445	328	299	161	1.56%
Group 3	705	700	490	417	222	0.71%



Number at risk	0 months	12 months	24 months	36 months	48 months	Cumulative probability of HCC
Group 1	560	555	401	338	169	0.35%
Group 2	146	143	87	77	51	2.05%
Group 3	1472	1445	1208	1130	585	1.56%
Group 4	225	217	139	121	94	8.89%

F3/F4: advanced fibrosis/cirrhosis, HCC: hepatocellular carcinoma

Results

- Among 2403 CHB patients (55.6% male, median age 55.6 years, 57.1% NA-treated, median ALT 26 U/L), 48 patients developed HCC during a median follow-up of 46.4 months.
- Multivariate analysis showed increased CAP to be inversely associated with HCC development (OR 0.994, 95%CI 0.988-0.999).
- The cumulative probability of HCC was 2.88%, 1.56% and 0.71%, respectively for patients with no steatosis, mild-to-moderate steatosis, and severe steatosis, respectively (p=0.01).
- Subgroup analysis among patients without advanced fibrosis/cirrhosis and NA-treated patients showed increased CAP remaining to be inversely associated with HCC (OR 0.991, 95%CI 0.983-0.999; and OR 0.993, 95%CI 0.987-0.999 respectively).
- The risk of HCC increased from 1.56% to 8.89% in patients without severe steatosis if advanced fibrosis/cirrhosis were present (p<0.001).

Conclusion

Reduced hepatic steatosis was significantly associated with a higher risk of incident HCC in CHB patients. Routine CAP and liver stiffness measurements can be important for risk stratification.

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