

Risk of hepatocellular carcinoma in patients with immune-tolerant chronic hepatitis B

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INTRODUCTION

Recent studies have suggested that patients with immune-tolerant chronic hepatitis B (CHB), characterized by hepatitis B e antigen (HBeAg) positive patients with high serum hepatitis B virus (HBV) DNA but normal alanine aminotransferase (ALT), may develop hepatocellular carcinoma (HCC). However, it is unclear how to stratify HCC risk in these patients.

AIM

In this study, we assessed long-term HCC risk among non-cirrhotic patients presumed in immune tolerant phase defined by HBeAg positivity, very high HBV DNA levels and normal ALT levels. In addition, whether age and FIB-4 index could be used to stratify HCC risk in these patients was assessed.

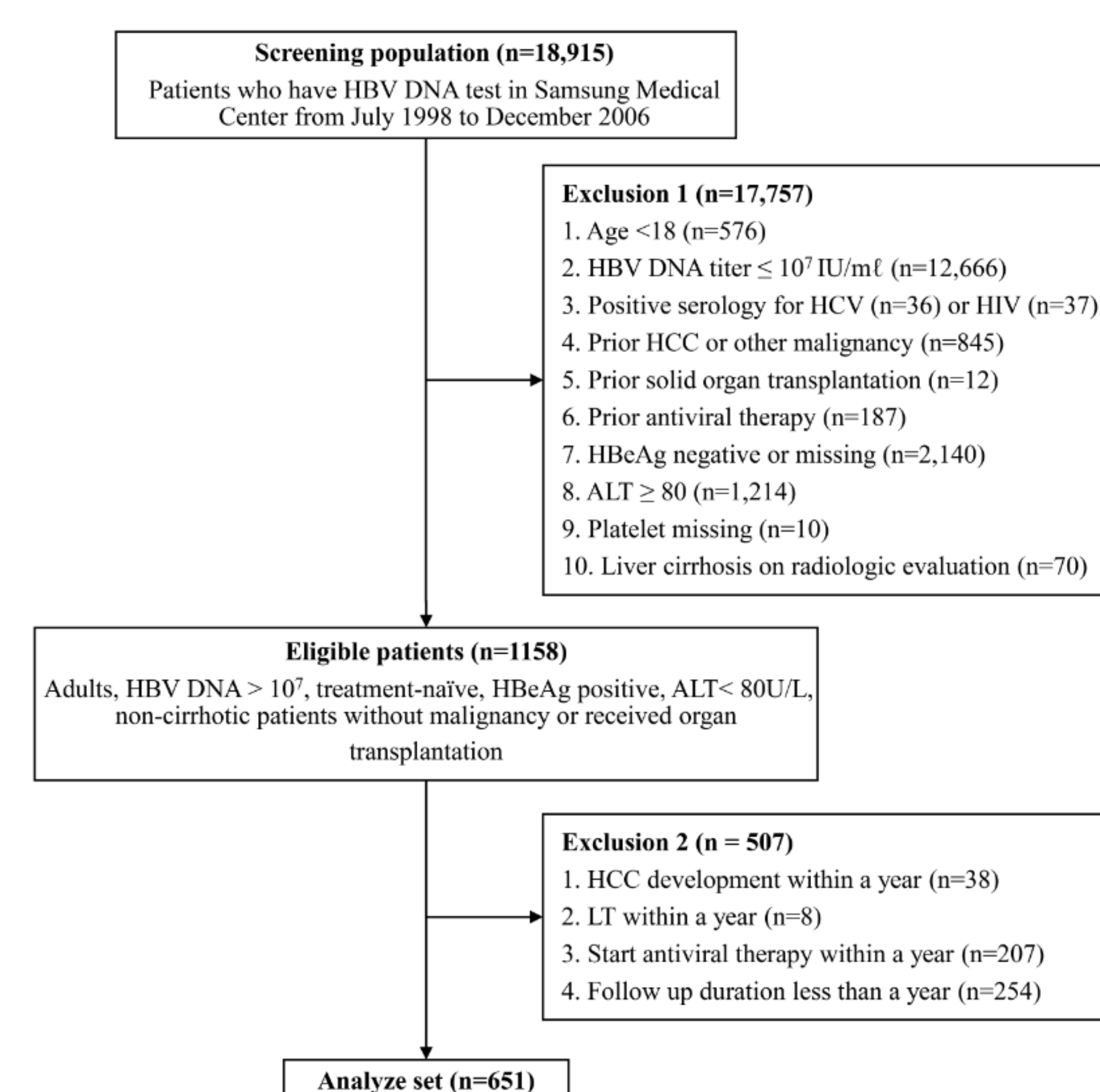
METHOD

A retrospective cohort of 651 HBeAg positive, adult patients with high serum HBV DNA levels (>7 log IU/mL) but normal or mildly elevated ALT levels (<80 U/L) were analyzed. Age and FIB-4 index were used to categorize patients, and assessed actual HCC incidence rate in each subgroups. Normal ALT was defined as <35 U/L for males and <25 U/L for females.

RESULTS

During a median 5.2 years of follow-up (range: 1.0-17.8 years), 24 (3.7%) patients developed HCC. Age and FIB-4 index were independent factors associated with HCC development. When stratified, 5 and 10-year cumulative HCC incidence rates were 0% and 2.0% for patients aged <40 years plus FIB-4 index <1.45, and were 5.9% and 32.7% for patients aged ≥40 years plus FIB-4 index ≥1.45, respectively ($p < 0.001$). When analysis was limited to patients with normal ALT levels ($n = 301$), 10-year HCC incidence rate was 0% for patients aged <40 years plus FIB-4 index <1.45, while 5 and 10-years HCC incidence rate was 4.5% and 27.1% for patients aged ≥40 years plus FIB-4 index ≥1.45, respectively ($p < 0.001$).

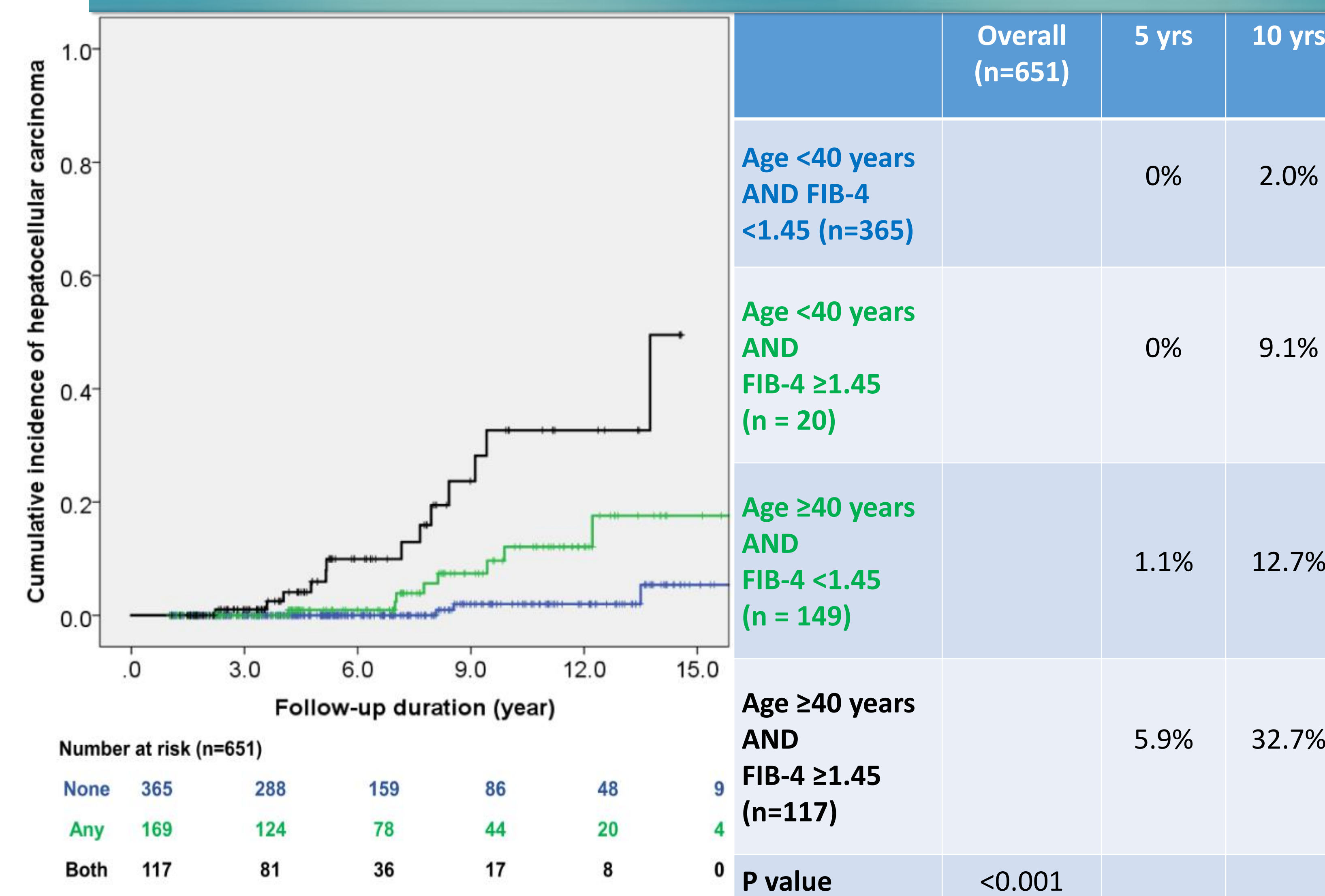
Patients flow chart



Factors associated with HCC development

	HCC incidence rate at 5 years	HCC incidence rate at 10 years	p	Multivariable model	p
Age			<0.001		
<40	0%	2.6%		Reference	
≥40	3.1%	20.4%		5.21 (1.61-16.7)	0.006
Sex			0.005		
Female	0%	3.9%		Reference	
Male	1.7%	14.0%		3.84 (1.29-11.3)	0.015
HBV DNA			0.052		
7-8	2.2%	14.9%		Reference	
>8	0.4%	5.8%		0.71 (0.30-1.65)	0.429
ALT			0.003		
Normal ALT	0.5%	4.3%		Reference	
Mildly Elevated ALT	1.9%	15.7%		2.42 (0.93-6.31)	0.069
FIB-4			<0.001		
<1.45	0.3%	5.3%		Reference	
≥1.45	4.9%	27.1%		2.93 (1.19-7.19)	0.019

Cumulative incidence of HCC



CONCLUSIONS

In patients with immune-tolerant CHB, HCC risk was considerably high for aged patients with elevated FIB-4 index while HCC risk was very low for young patients with low FIB-4 index. These two factors could effectively stratify HCC risk, indicating that they may guide management plan for this population.

REFERENCES

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