■ Sat-075 ■

Risk of hepatocellular carcinoma in chronic hepatitis B patients presumed as immune tolerant phase

성균관의대 삼성서울병원

*성결, 신동현, 강원석, 곽금연, 최문석, 이준혁, 고광철, 백승운, 백용한

Background/Aims: Recent studies suggested minor but significant proportion of patients presumed in immune-tolerant phase, defined by hepatitis e antigen (HBeAg) positive, high serum hepatitis B virus (HBV) DNA, and normal alanine aminotransferase (ALT) levels, develop complication. International HBV guidelines recommended age and non-invasive biomarkers (e.g., FIB-4) to stratify future complication risk, but evidence to support this approach is limited. **Methods:** A retrospective cohort of 651 HBeAg positive, adult patients with high serum HBV DNA levels (> 7 logIU/mL) but normal or mildly elevated ALT levels (<80 U/L) were analyzed. We tested whether age and FIB-4 are independent risk factors for hepatocellular carcinoma (HCC) development. Actual HCC incidence rate in patient subgroups divided by age and FIB-4 was assessed. Normal ALT was defined as <35U/L for males and <25U/L for females. **Results:** During a median 5.2 years of follow-up (range: 1.0-17.8 years), 24 patients (3.7%) developed HCC. Age and FIB-4 levels were independent factors associated with HCC development. When stratified, 5 and 10-years HCC incidence rate was 0% and 2.0% for patients aged <40 years plus FIB-4 <1.45, while 5 and 10-years HCC incidence rate was 5.9% and 32.7% for patients aged ≥40 years plus FIB-4 ≥1.45, respectively, (p<0.001). When analysis was limited to patients with normal ALT levels (n=301), 5 and 10-years HCC incidence rate was 0% and 0% for patients aged <40 years plus FIB-4 <1.45, while 5 and 10-years HCC incidence rate was 4.5% and 27.1% for patients aged ≥40 years plus FIB-4 ≥1.45, respectively, (p<0.001). **Conclusions:** Among patients presumed in immune tolerant phase, HCC risk was considerably high for aged patients with elevated FIB-4 index, while the risk was minimum for young patients with low FIB-4 index. These two factors could effectively stratify HCC risk, thus may guide management plan, among patients presumed in immune tolerant phase.

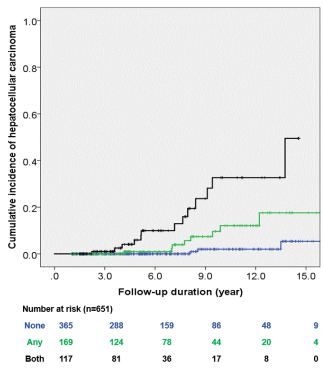

Table 3 Hepatocellular carcinoma incidence rate according to age and FIB-4 levels

	Age <40 years AND FIB-4 <1.45 (n=365)	Age ≥40 years OR FIB-4 ≥1.45 (n=169)	Age ≥40 years AND FIB-4 ≥1.45 (n=117)	P value
Overall (n=651)				<0.001
5 years	0%	0.1%	5.9%	
10 years	2.0%	12.1%	32.7%	
Men (n=404)				<0.001
5 years	0%	1.7%	8.0%	
10 years	1.9%	19.3%	46.4%	
Women (n=247)				0.079
5 years	0%	0%	2.9%	
10 years	2.2%	4.5%	7.6%	
Normal ALT by AASLD cutoff (n=301)				<0.001
5 years	0%	0%	4.3%	
10 years	0%	4.5%	27.1%	
Normal ALT by EASL cutoff (n=388)				<0.001
5 years	0%	0%	3.6%	
10 years	0%	3.8%	22.9%	
Mildly elevated ALT (n=350)				<0.001
5 years	0%	2.1%	6.7%	
10 years	5.1%	20.0%	38.4%	
HBV DNA 7-8 log$_{10}$U/L (n=285)				<0.001
5 years	0%	2.7%	7.7%	
10 years	2.6%	21.8%	38.1%	
HBV DNA >8 log$_{10}$U/L (n=366)				<0.001
5 years	0%	0%	3.6%	
10 years	1.7%	6.3%	28.6%	

■ Sat-076 ■

Predictors of HCC development at sustained virological response among chronic hepatitis C patients

연세대학교 의과대학 내과학교실 소화기내과

*전호수, 김범경, 박준용, 김도영, 안상훈, 한광협, 김승업

Background/Aims: Liver fibrosis is associated with an increased risk of hepatocellular carcinoma (HCC) development. We investigated the predictors of HCC development at the time of sustained virological response (SVR) among chronic hepatitis C (CHC) patients. **Methods:** Between 2003 and 2016, 669 CHC patients achieved SVR through interferon-based regimens. The predictors of HCC development was assessed using Cox proportional hazards regression model. **Results:** After SVR achievement, HCC developed in 19 (2.8%) patients. Patients with HCC had older age (mean 67.7 vs. 59.4 years), higher proportion of male gender (89.5 vs. 42.3%), liver cirrhosis (57.9 vs. 15.5%), hypertension (52.6 vs. 23.1%), and diabetes (36.8 vs. 16.5%), lower platelet count (mean 120 vs. 182 109/L), higher alpha-fetoprotein (mean 8.5 vs. 3.4 ng/mL), higher aspartate and alanine aminotransferase (mean 42.7 vs. 23.6 IU/L and mean 33.1 vs. 19.8 IU/L), lower total cholesterol (mean 161.8 vs. 182.7 mg/dL), and higher FIB-4 level (mean 7.0 vs. 2.2) (all P<0.05). On multivariate analysis, FIB-4 independently predicted HCC development (hazard ration=1.072; 95% confidence interval, 1.027-1.120, P=0.002), together with male gender, hypertension, and alpha-fetoprotein (all P<0.05). When the study population was stratified into three groups with different risk of significant fibrosis according to FIB-4 level (<1.45 with low-risk, 1.45–3.25 with intermediate-risk, ≥3.25 with high-risk), the cumulative incidence rate of HCC significantly different between the groups (all P<0.05 by log-rank tests). **Conclusions:** FIB-4 independently predicted HCC development, together with male gender, hypertension and alpha-fetoprotein. The cumulative incidence rate of HCC was significantly different between three groups according to FIB-4 level. The assessment of fibrotic burden using FIB-4 at the time of SVR might be useful for the risk stratification of HCC development in CHC patients.

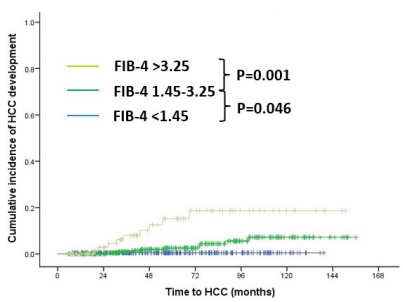

Figure. The cumulative incidence of HCC development according to FIB-4 category

Table. Independent predictors of HCC development after SVR

Variables	Univariate	Multivariate using liver cirrhosis			Multivariate using FIB-4		
	P value	HR	95% CI	*P* value	HR	95% CI	*P* value
Demographic variables							
Age	0.009	1.026	0.973-1.083	0.342	-	-	-
Male gender	0.001	9.192	2.023-41.767	0.004	7.390	1.636-33.380	0.009
Liver cirrhosis	<0.001	2.508	0.721-8.723	0.148	-	-	-
Hypertension	0.025	2.989	0.903-9.896	0.073	3.141	1.058-9.329	0.039
Diabetes	0.061	-	-	-	-	-	-
Genotype 1 (vs. others)	0.743	-	-	-	-	-	-
Laboratory variables							
PLT, 10^9/L	<0.001	0.985	0.973-0.997	0.019	-	-	-
AFP, ng/mL	<0.001	1.002	0.943-1.066	0.939	1.054	1.010-1.101	0.016
AST, IU/L	<0.001	0.996	0.973-1.018	0.697	-	-	-
ALT, IU/L	0.001	1.021	0.977-1.066	0.352	-	-	-
Serum Cr, mg/dL	0.976	-	-	-	-	-	-
FIB-4	<0.001	-	-	-	1.072	1.027-1.120	0.002

Age, PLT, AST, ALT were excluded from the multivariate analysis using FIB-4.