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External validation of the non-alcoholic fatty liver disease fibrosis score for assessing advanced fibrosis in Korean patients

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Abstract

Background: The degree of liver fibrosis in non-alcoholic fatty liver disease (NAFLD) is a critical predictive factor for patient prognosis. This study was intended to perform external validation of the various fibrosis prediction models for assessing advanced fibrosis in Korean NAFLD patients.

Methods: A retrospective study of 412 patients with NAFLD confirmed by liver biopsy in hospitals affiliated with the Koran NAFLD study group was conducted and the predictive ability of existing liver fibrosis prediction models including NAFLD fibrosis score (NFS), BARD, and fibrosis-4 were compared.

Results: Among 412 samples, 328 liver slides were suitable for evaluation. Advanced fibrosis was present in 60 (18.3%) of the patient samples. Univariate analysis found that the group with advanced fibrosis showed low alanine aminotransferase values and high aspartate aminotransferase/alanine aminotransferase ratios as well as a high incidence of diabetes. However, multivariate analysis showed that only the presence of diabetes and triglycerides was independent risk factors. The receiver operating characteristic was 0.64 in NFS, 0.58 in fibrosis-4, and 0.594 in the BARD model. The NFS was found to be the best at predicting advanced fibrosis among the three prediction models. The negative predictive value which predicts advanced fibrosis using the low cutoff (<-1.455) was high (86.6%). However, the positive predictive value which predicts advanced fibrosis using the high cutoff (>0.676) was 50.0% when we applied the NFS.

Conclusion: Negative predictive value using the low cutoff value was high, but positive predictive value using the high cutoff value was low in a Korean NAFLD cohort using NFS.

Introduction

The prevalence of nonalcoholic fatty liver disease (NAFLD) is on the rise not only across the world but also in Korea because of an increasingly westernized lifestyle. In the Korean population, the prevalence of NAFLD is reported to be around 27.3%.[1] NAFLD has already become the main cause of chronic liver disease in many countries. NAFLD represents the simple steatosis as well as steatohepatitis which can later progress to fibrosis. The clinical prognosis of fatty liver disease without fibrosis is satisfactory.[2] However, when it comes with fibrosis, it may associate with poor clinical outcome.[3–5] However, because of its invasiveness, liver biopsy can lead to complications such as bleeding and is very hard to repeat. A variety of noninvasive models have been developed to predict the progression of liver fibrosis in fatty liver disease patients. Among these models, the NAFLD fibrosis score (NFS) is the most extensively used to predict the progression of liver fibrosis in NAFLD patients.[6] The area under receiver operating

characteristic (AUROC) of NFS is 0.85 as much to predict advanced fibrosis (≥F3) using the low cutoff (<−1.455) and the high cutoff (>0.676). When using the high cutoff (>0.676) to diagnose advanced fibrosis, sensitivity and specificity were 67% and 97%, respectively.[6] Until now, the NFS has been validated externally in three Asian cohorts.[7–9] The negative predictive value (NPV) to predict advanced fibrosis (≥F3) using a low cut off of NFS was high, yet the positive predictive value (PPV) using high cut-off were relatively low as compared to original study.[6–9] The notable disparity between Asian cohorts and Western cohort is that the prevalence of non-obese NAFLD in Asian cohort was high, and prevalence of advanced fibrosis (≥F3) was low.[6,10–12]

Accordingly, the current liver fibrosis predicting models need further evaluation in a Korean NAFLD cohort with a high percentage of non-obese NAFLD and a low prevalence of advanced fibrosis (≥F3) patients. This study aimed to validate various NAFLD fibrosis prediction models in Asian patients.

Methods

Study subjects. The study was designed retrospectively using a biopsy-proven NAFLD cohort. Consecutive patients who underwent liver biopsy between January 2000 and December 2010 at nine tertiary hospitals affiliated with the "Korean NAFLD study group" were selected. Included subjects were negative for HBsAg and hepatitis C virus antibody. They were also negative for antinuclear antibody, anti-mitochondria antibody, and anti-smooth muscle antibody. The levels of immunoglobulin G, immunoglobulin M, and thyroid function tests were normal. Patients who took herbal medicine, steroids, amiodarone, and received hepatotoxic drug treatment within 3 months were excluded. Patients who consumed an average of 140 g of alcohol for men and 70 g for women were also excluded.

Serological testing. All biochemical parameters were evaluated at the time of hospital admission for liver biopsy. A blood test was conducted after 8 h of fasting. NFS was calculated as follows: $-1.675 + 0.037 \times$ age (year) $+ 0.094 \times$ body mass index (BMI) (kg/m^2) $+ 1.13 \times$ impaired fasting glucose (IFG)/diabetes (yes =1, no =0) $+ 0.99 \times$ aspartate aminotransferase (AST)/alanine aminotransferase (ALT) ratio $- 0.013 \times$ platelet ($\times 10^9$/L) $- 0.66 \times$ albumin (g/dL).[6] The BARD score was calculated as follows: AST/ALT ratio ≥0.8: 2 points; a BMI ≥28: 1 point; and the presence of diabetes; 1 point.[13] Fibrosis-4 (FIB-4) was calculated as follows: (age (year) × AST (IU/L))/(platelets (10^9/L × (sqr (ALT (IU/L))).[14]

Biopsy interpretation. Eighty-four biopsy samples were excluded because of the following reasons: biopsy size that was less than 15 mm, biopsy containing less than 11 portal tracks, or wedge biopsy cases or bariatric biopsy samples, because all those samples took as wedge biopsy. Degree of hepatic fibrosis is frequently overestimated in wedge biopsy sample. Finally, 328 liver slides were suitable for evaluation among 412 samples. To avoid inter-observer variation, one pathologist reviewed all tissue specimens. The pathologist had more than 20 years of experience and interpreted biopsy sections without any clinical information. We used Brunt's criteria to diagnose non-alcoholic steatohepatitis (NASH; steatosis plus lobular inflammation and ballooning) and that the severity of NAFLD was also assessed according to NAFLD Activity Score (NAS) system.[10] The NAS is the sum of the scores for steatosis (0–3), lobular inflammation (0–2), and hepatocellular ballooning (0–2). Fibrosis was evaluated on trichrome stain. The process began from zone 3 in adult liver and deposition of collagen fiber in the perisinusoidal space of Disse resulted in "chicken wire" pattern of fibrosis. The stage of fibrosis was analyzed as NASH Clinical Research Network Scoring System in 2005.[10] No fibrosis was F0. Perisinusoidal or periportal fibrosis was regarded as F1; it was subdivided as 1A, mild thin zone 3 perisinusoidal fibrosis, 1B, moderate dense prominent zone 3 perisinusoidal fibrosis, and 1C, portal or periportal fibrosis. If perisinuoidal and portal to periportal fibrsosis occurred together, it was regarded as F2. The bridging fibrosis and cirrhosis were regarded as F3 and F4, respectively. Advanced liver fibrosis indicates F3 and F4.

Analysis. Chi-squared tests and student's *t*-tests were conducted to determine the relevance of clinical factors. Multivariate logistic regression was also performed including variables with $P < 0.2$ as well as clinically relevant variables such as age and BMI in order to find predictive factors used to predict the progression of liver fibrosis.

External validation was conducted for the previously reported models (NFS, BARD, and FIB-4 index) for advanced liver fibrosis in NAFLD using the collected data and AUROC, sensitivity, specificity, PPV, and NPV were obtained. All statistical analyses were performed with SAS version 9.4 (SAS Institute, Carey, NC) and R version 3.2.3 (http://cran.r-project.org/), and statistical significance was defined as a two-tailed *P*-value <0.05.

Results

Baseline characteristics of the study population. A total of 412 liver biopsy tissue samples from NAFLD patients were analyzed. Among these, 75 patients who underwent wedge biopsy in relation to bariatric surgery and nine patients with incomplete results were excluded. The final analysis included a total of 328 patient samples. Mean number of portal tracts of cohort sample was 17.9 ± 8.1, and mean length was 22.5 ± 4.9 mm. Most patients showed grade 1 fibrosis (156/328, 47.5%), and among the others, 34.8% showed significant fibrosis (≥F2), and 60 subjects (18.3%) had advanced fibrosis (≥F3) (Table 1). The average age was 36.4 years, the average BMI was 28.6 kg/m2, male sex accounted for 70.7%, and patients with diabetes or abnormal fasting blood glucose reached up to 33.0%.

Risk factors for hepatic fibrosis in the Korean population. This study used univariate and multivariate analysis to suggest models for predicting advanced liver fibrosis. Subjects were divided into two groups on the basis of the degree of fibrosis (advanced fibrosis or significant fibrosis). Sixty patients had advanced fibrosis ≥F3 (18.3%). Univariate analysis showed that ALT was low while the AST/ALT ratio and the prevalence of diabetes were high in the advanced fibrosis group (Table 2). However, there was no difference in age, platelet, hypertension

Table 1 Baseline characteristics of the study population

	Mean ± *SD*
n	328
Age (years)	36.4 ± 14.0
Gender (male)	70.7%
BMI (kg/m^2)	28.6 ± 4.8
Obesity	
Normal (<23 kg/m^2)	8.7%
Overweight (23–25 kg/m^2)	11.5%
Obese (≥25 kg/m^2)	79.8%
Waist circumference (cm)	96.4 ± 11.8
Central obesity (yes)	86.6%
Hypertension (yes)	14.6%
Diabetes mellitus or IGT(yes)	33.0%
ALT (U/l)	98.5 ± 82.2
AST (U/l)	91.3 ± 67.5
AST/ALT ratio	1.26 ± 0.83
Albumin (g/dl)	4.46 ± 0.42
Total bilirubin (mg/dl)	0.86 ± 0.58
Prothrombin time (%)	102.6 ± 15.4
PT INR	0.99 ± 0.10
Glucose (mg/dl)	109.0 ± 31.8
Fasting insulin	16.3 ± 17.3
Platelet count (×10^9/l)	246 ± 68.0
AST/platelet ratio	0.40 ± 0.36
Triglycerides (mg/dl)	188 ± 99.0
HDL (mg/dl)	43.2 ± 13.4
Low HDL-cholesterol (yes)	53.8%
Fibrosis, F0 (%)	58 (17.7)
Fibrosis, F1 (%)	156 (47.5)
Fibrosis, F2 (%)	54 (16.5)
Fibrosis, F3 (%)	44 (13.4)
Fibrosis, F4 (%)	16 (4.9)

Central obesity: waist circumference ≥80 cm for men and ≥90 cm for women; low HDL-cholesterol: < 40 mg/dl in men or <50 mg/dl in women. ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; GGT, gamma-glutamyl transpeptidase; HDL-cholesterol, high density lipoprotein cholesterol; IGT, impaired glucose tolerance; PT INR, prothrombin time international normalized ratio..

co-morbidity, and BMI between the two groups. Multivariate analysis showed that only the presence of diabetes (odds ratio [OR]: 6.50, 95% confidence interval [CI]: 3.10–13.64, $P < 0.001$) and triglyceride (OR: 0.96, 95% CI: 0.92–1.00, $P = 0.0476$) was independent risk factors for advanced fibrosis (≥F3) (Table 3).

On the other hand, in the significant fibrosis (≥F2) group, the prevalence of diabetes co-morbidity and AST/ALT ratio were significant. Multivariate analysis showed the presence of diabetes (OR: 4.03, 95% CI: 2.20–7.39, $P < 0.001$) and AST/ALT ratio (OR: 0.96, 95% CI: 0.92–1.00, $P = 0.010$) were independent risk factors.

Comparison of previous non-alcoholic fatty liver disease fibrosis models in the Korean population. The predictive value of NFS, BARD, and FIB-4 were assessed in our cohort (Table 4). In the original study, the area under the curve (AUC) used to predict advanced fibrosis in NFS was 0.84 (95% CI: 0.81–0.88).[6] However, in our study, the discriminatory power (AUROC) used to predict advanced fibrosis was 0.64 of NFS, 0.58 of FIB-4, and 0.59 of BARD (Fig. 1). NPV for predicting advanced fibrosis (≥F3) using the low cutoff (−1.455) was high (86.6%). Yet PPV for predicting advanced fibrosis (≥F3) using the high cutoff (>0.676) was low (50.0%). Specificity was 98.1%, and NPV was 82.9%. Even when using FIB-4, NPV was high (83.5%), but sensitivity (22.0%) and PPV (27.1%) were low.

Discrepancy in pathological interpretation among centers. Of 328 specimens, only 142 specimens had an exactly defined fibrosis score at the time of liver biopsy by each pathologist from individual hospitals. All slides were later again reviewed by an expert pathologist with more than 20 years of experience in order to compare the results of liver fibrosis scores from individual hospitals (Table 5). The consistency rate to interpret the degree of fibrosis between individual hospitals and the experienced pathologist was 28%. Nearly 20% of interpretations were different by ±2 points in both criteria for determining fibrosis.

Discussion

In this NFS validation study using the Korean cohort, AUROC that predicts advanced fibrosis was 0.64, which was lower than AUROC in Western population cohorts (0.8–0.9). NPV using the low cutoff value was high, but PPV using the high cutoff value was low.

Nonalcoholic fatty liver disease fibrosis score uses the low cutoff value as well as the high cutoff value. When the low cutoff value (−1.455) was applied, NPV for advanced fibrosis was 93%. While using the high cutoff value (0.676), the PPV predicting advanced fibrosis was 90%.[6] Since then, an external validation of NFS was performed in Western countries which showed relatively good prediction ability compared with other fibrosis prediction models.[11–13] However, in our study, PPV was low (50%) with the high cutoff value because the Western population cohort had a higher percentage of advanced fibrosis (≥F3) and a higher BMI. External validation studies in Asian populations using NFS also showed low PPV (0–34%) with high cutoff values. For instance, in a study comprising 162 NAFLD patients from Hong Kong,[8] NPV was very high (91%) with the low cutoff value. However, PPV with the high cutoff value was low (0%). Similarly, in a multicenter research study comprised of 588 patients from eight medical centers in Japan, NPV was 98% with the low cutoff value while PPV was 43% with the high cutoff value,[7] and 27.8% patients showed advanced fibrosis. In a Cantonese cohort, patients were obese with BMI of 28.5, and 18 patients had advanced fibrosis (11%). In another external validation of NFS using the Korean cohort, the predictive ability of advanced fibrosis was very high with AUROC of 0.964.[9] However, NPV for NFS was high (100%) using the low cutoff value while PPV was low (33.3%) using the high cutoff value. In a Latin American study comprised of 228 patients from Mexico and Chile, 27 patients had advanced fibrosis (11.8%).[15] The study used the high cutoff value only, and AUROC was 0.77; and PPV was 26.0%. Moreover, 18.3% of patients had advanced fibrosis at F3, and PPV of advanced fibrosis (≥F3) using the high cutoff value (0.676) was 50.0%. Using NFS

Table 2 Risk factors for hepatic fibrosis in the Korean population

	Advanced fibrosis (≥ F3)		*P* value*	Significant fibrosis (≥ F2)		*P* value*
	Fibrosis =0–2	Fibrosis =3–4		Fibrosis =0–1	Fibrosis =2–4	
n	268	60	—	214	114	—
Age (years)	36.1 ± 13.7	37.6 ± 15.3	0.4447	35.3 ± 13.2	38.2 ± 15.3	0.0732
Gender (male)	71.6%	66.7%	0.4439	72.0%	68.4%	0.5020
BMI (kg/m2)	28.6 ± 4.6	28.8 ± 5.7	0.7642	28.5 ± 4.8	29.0 ± 4.9	0.3752
Obesity	—	—	0.3348	—	—	0.9366
Normal (<23 kg/m^2)	7.6%	13.6%	—	8.6%	8.8%	—
Overweight (23–25 kg/m^2)	11.8%	10.2%	—	12.0%	10.6%	—
Obese (≥25 kg/m^2)	80.6%	76.3%	—	79.4%	80.5%	—
Waist circumference (cm)	96.2 ± 9.8	97.3	0.8083	97.5 ± 9.4	95.2	0.4490
Central obesity (yes)	84.6%	93.3%	0.6715	83.3%	90.3%	0.4885
Hypertension (yes)	14.6%	15.0%	0.9293	13.1%	17.5%	0.2765
Diabetes mellitus or IGT (yes)	27.7%	56.7%	<.0001	23.5%	50.9%	<.0001
ALT (U/l)	102.6 ± 85.3	80.1 ± 64.3	0.0235	104.7 ± 85.0	87.0 ± 75.8	0.0637
AST (U/l)	91.3 ± 67.7	91.2 ± 67.2	0.9851	90.9 ± 68.8	92.1 ± 65.4	0.8826
AST/ALT ratio	1.21 ± 0.80	1.47 ± 0.90	0.0246	1.16 ± 0.77	1.44 ± 0.90	0.0052
Albumin (g/dl)	4.48 ± 0.41	4.40 ± 0.48	0.2031	4.47 ± 0.42	4.45 ± 0.43	0.7628
Total bilirubin (mg/dl)	0.86 ± 0.59	0.87 ± 0.54	0.8741	0.87 ± 0.62	0.84 ± 0.48	0.6579
PT	102.3 ± 15.1	103.5 ± 16.9	0.5893	101.9 ± 10.6	103.7 ± 14.5	0.3268
PT INR	1.00 ± 0.11	0.98 ± 0.07	0.1839	1.00 ± 0.12	0.98 ± 0.06	0.1336
Glucose (mg/dl)	108.2 ± 30.8	109.3 ± 30.3	0.3110	107.2 ± 30.3	112.3 ± 34.2	0.1695
Fasting insulin	16.2 ± 17.9	17.1 ± 15.0	0.7706	16.8 ± 19.4	15.5 ± 12.8	0.5862
Platelet count (×10^9/l)	249 ± 67.0	235 ± 70.0	0.1428	251 ± 65.0	238 ± 72.0	0.0903
AST/platelet ratio	0.41 ± 0.38	0.39 ± 0.29	0.7270	0.39 ± 0.33	0.42 ± 0.42	0.5282
Triglycerides (mg/dl)	192 ± 99.0	171 ± 97.0	0.1497	191 ± 97.0	184 ± 102.0	0.5533
HDL (mg/dl)	43.4 ± 13.9	42.3 ± 1.12	0.6234	43.1 ± 14.5	43.3 ± 11.4	0.9286
Low HDL-cholesterol (yes)	53.1%	56.9%	0.6261	53.7%	54.0%	0.9581

**P*-values are calculated by Pearson chi-squared test, Fisher's exact, or student's *t*-test as appropriate.

Central obesity: waist circumference ≥80 cm for men and ≥90 cm for women; low HDL-cholesterol: <40 mg/dl in men or <50 mg/dl in women.ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; GGT, gamma-glutamyl transpeptidase; HDL-cholesterol, high density lipoprotein cholesterol; IGT, impaired glucose tolerance; PT INR, prothrombin time international normalized ratio.

Table 3 Multiple regression analysis for risk factors of hepatic fibrosis

	Advance fibrosis (≥F3)			Significant fibrosis (≥F2)		
	OR	95% CI	**P*	OR	95% CI	**P*
Age (years)	0.99	0.96–1.01	0.322	1.01	0.99–1.03	0.367
BMI (kg/m^2)	0.96	0.89–1.04	0.324	1.01	0.95–1.06	0.870
Diabetes mellitus or IGT (yes)	6.50	3.10–13.64	<0.001	4.03	2.20–7.39	<0.001
AST/ALT ratio	1.47	0.98–2.19	0.062	1.49	1.10–2.02	0.010
PT INR	0.09	0.36–6.95	0.277	0.18	0.01–3.99	0.278
Glucose (mg/dl)	—	—	—	0.62	0.25–1.51	0.289
Platelet count (×10^9/l)	0.60	0.36–1.01	0.052	0.77	0.52–1.14	0.185
Triglycerides (mg/dl)	0.96	0.92–1.00	0.047	—	—	—

**P*-values are calculated by multivariable regression analysis as appropriate.

ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; CI, confidence interval; IGT, impaired glucose tolerance; OR, odds ratio; PT INR, prothrombin time international normalized ratio.

in a cohort with a small percentage of advanced fibrosis yields relatively high AUROC and NPV values and a relatively low PPV value. Therefore, the use of the high cutoff value in predicating PPV of NFS in Korean NAFLD patients with a small percentage of advanced fibrosis should be considered. Although the NFS showed the highest value of AUROC (0.64) among the other non-invasive models in our study, the prediction ability of NFS was relatively lower than in Western studies.[6,11] This is because our study cohort had lower BMI (28.6 kg/m^2), younger average age, and low diabetes comorbidity (8.6%). Moreover,

Table 4 Predictive value of previous noninvasive panels to discriminate advance fibrosis

—	NAFLD fibrosis score		BARD	FIB-4	
AUROC	0.64 (95% CI:0.56–0.72)		0.594	0.58 (95% CI:0.51–0.66)	
Cutoff	Low (−1.455)	High (0.676)	2 points	Low (1.30)	High (2.67)
Sensitivity (%)	53.4	8.6	83.3	55.9	22.0
Specificity (%)	66.7	98.1	36.7	56.0	86.9
PPV (%)	26.3	50.0	22.5	21.9	27.1
NPV (%)	86.6	82.9	90.9	85.2	83.5

AUROC: Area under receiver operating characteristic curve; FIB-4; fibrosis-4; NAFLD, non-alcoholic fatty liver disease; NPV: negative predictive value; PPV: positive predictive value.

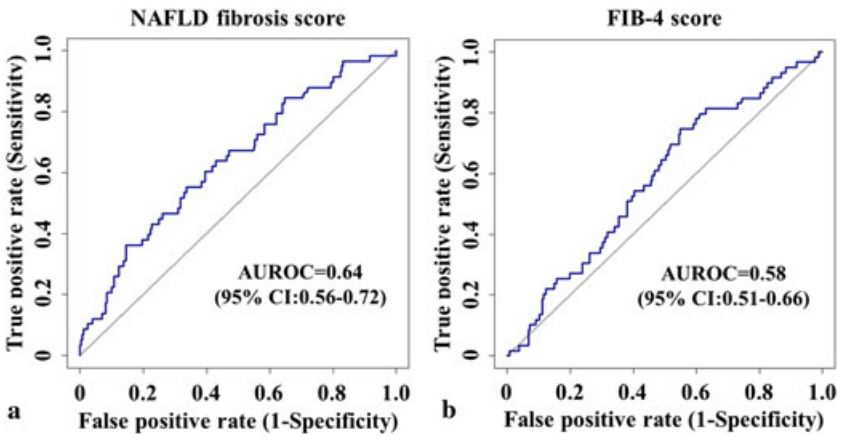

Figure 1 Receiver operating characteristic to assess advanced fibrosis according to non-alcoholic fatty liver disease (NAFLD) fibrosis score and fibrosis-4 (FIB-4) score. [Color figure can be viewed at wileyonlinelibrary.com]

Table 5 Discrepancy in pathological interpretation among centers

		Interpretation of hepatic fibrosis (Local hospital)				
		F0	F1	F2	F3	F4
Interpretation of hepatic fibrosis (Central Laboratory)	F0	**0**	4	13	7	0
	F1	0	**32**	29	7	2
	F2	0	11	**6**	3	1
	F3	0	8	13	**2**	0
	F4	0	2	1	1	**0**

only 60 out of 328 patients had advanced fibrosis (18.3%), which might have affected the results. This result reinforces that Korea needs a new prediction model on the basis of the relatively lower BMI and lower incidence of advanced fibrosis in the Korean population. There was a similar previous study that found that the top five non-invasive markers (AST/ALT ratio, APRI index, enhanced liver fibrosis panel, FIB-4, and liver stiffness) were excellent predictors to exclude the presence of advanced fibrosis; however, there was poor agreement to diagnose advanced fibrosis in a type 2 diabetes cohort.[16,17]

Another interesting finding from our data is that diabetes or impaired fasting glucose was the sole risk factors of significant as well as advanced fibrosis. Several recent studies also point out the importance of insulin resistance as a key player in the development of NAFLD.[18,19] Insulin resistance is an independent risk factor for all histological features of NASH and fibrosis.[18]

This study has several limitations. First, as it was a retrospective study, the indications for liver biopsy were very different among the hospitals, and fatty liver patient cohorts were quite distinct. Nine medical centers participated in this study. The comparison of NAS of liver biopsy showed wide variation with the average NAS from 1.38–5.56. Moreover, the average diabetes comorbidity was low (8.6%), although the diabetes comorbidity at certain hospitals was much higher (45.5%). The average age of patients who received a liver biopsy at the different hospitals was also different. This indicates that patient characteristics included in the cohort varied among the participating hospitals. Second, participating hospitals did not use a standardized questionnaire

for the calculation of alcohol consumption and did not use a uniform protocol to exclude toxic hepatitis. All subjects were carefully examined for medication history, and a single pathologist examined the slide specimens to exclude toxic hepatitis. However, the diagnosis of toxic hepatitis depended on the local hepatologist. Third, there were only a few cases in which additional parameters such as waistline, fasting insulin concentration, serum ferritin, and CK-18 were evaluated. Therefore, such data were unavailable for this study collectively. Fourth, because past infection of hepatitis B virus with longstanding liver injury is reported in the Korean population, the sensitivity analysis of IgG-HBcAb positive subjects was additionally required. But it was not performed because of insufficient data. Fifth, although lots of pre-existing prediction models such as NFS, AST/ALT index, APRI (AST-to-platelet ratio index), ELF (enhanced liver fibrosis panel), and FibroTest have been studied to predict advanced fibrosis ≥F3 in NAFLD patients, unfortunately, we focused on NFS, FIB-4, and BARD among them in our analysis. Finally, to avoid inter-observer variation, all histology slides were reviewed by an experienced pathologist. All biopsy results were compared with the individual results interpreted by each hospital. The consistency in interpretation of degrees of fibrosis by individual hospitals and by an experienced pathologist was 28%. We conclude that a consensus for NAFLD pathological diagnosis is needed in Korea.

In conclusion, external validation of NFS using the Korean NAFLD cohort showed that NPV using the low cutoff value was high. However, PPV using the high cutoff value was relatively low. Additional research on a unique NAFLD cohort with a small percentage of advanced hepatic fibrosis patients and non-obese NAFLD patients using the high cutoff value for NFS is needed.

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