P-0619 The fatty liver index as a predictor of incident chronic kidney disease in a 10-year prospective cohort study

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BACK GROUND

Chronic Kidney Disease (CKD) has become a worldwide health problem that results in high morbidity and mortality in various chronic diseases, consuming substantial healthcare costs. Non-alcoholic fatty liver disease (NAFLD) is the most common cause of chronic liver disease, with a prevalence as high as 30% of the general population in developed countries. NAFLD and CKD may share many important common cardio-metabolic risk factors such as insulin resistance, chronic inflammation, and obesity.

Although NAFLD is considered to be associated with CKD, long-term follow up data is lacking. We investigated whether NAFLD, as determined by the fatty liver index (FLI), could predict incident CKD in 10-year prospective cohort study. We also assessed the clinical utility of FLI to predict the development of CKD.

Methods

6,238 adults aged 40 to 69 years without baseline CKD from the Ansan - Ansung cohort were examined. Patients were classified according to FLI as follows: FLI<30, no NAFLD; FLI≥60, NAFLD; and 30≤FLI<60, intermediate. Incident CKD was defined as estimated glomerular filtration rate (eGFR) <60 ml/min per 1.73 m². The clinical utility of FLI in predicting incident CKD was estimated via area under the receiver-operating characteristic curve (AUC), net reclassification improvement (NRI), and integrated discrimination improvement (IDI) analyses.

Results

Baseline characteristics of participants based on the development of CKD over the 10-year follow up period are shown in Table 1. Among the 4,761 subjects, 15.21 % (N=724) developed CKD during the follow-up period. Incident CKD group had significantly higher baseline age, waist circumference, BMI, blood pressure, total cholesterol, LDL-cholesterol, TG, and hsCRP levels than non-incident CKD group. There were not significant differences in AST, ALT, and GGT levels at baseline among the incident and non-incident CKD groups. Baseline FLI levels were higher in the incident CKD group than in the non-incident CKD group (33.66±23.92 vs. 28.03±22.39, P<0.001).

Table 1. Baseline characteristics according to incident CKD

Baseline variables	Incident CKD(+) N=724 (15.21 %)	Incident CKD(-) N=4037 (84.79 %)	p-value
Age(years)	58.74±8.00	50.72±8.03	<.0001
Sex (men)	254 (35.08%)	1554 (38.49%)	0.08
BMI (kg/m ²)	24.87±3.27	24.53±3.05	0.01
Waist circumference (cm)	84.43±9.07	81.74±8.75	<.0001
HTN	258 (37.55%)	796 (20.82%)	<.0001
Systolic BP (mmHg)	126.4±19.80	119.3±17.50	<.0001
Diastolic BP (mmHg)	81.55±11.08	79.06±11.09	<.0001
Diabetes mellitus	86 (11.96%)	171 (4.26%)	<.0001
HbA1c (%)	6.08±1.35	5.69±0.72	<.0001
FPG (mg/dL)	89.43±26.67	84.79±16.74	<.0001
Total cholesterol (mg/dL)	196.9±35.96	188.7±33.68	<.0001
HDL- cholesterol (mg/dL)	43.41±9.55	44.41±9.72	0.01
LDL-cholesterol (mg/dL)	119.0±32.13	113.8±31.76	<.0001
Triglyceride (mg/dL)	172.2±108.6	152.4±92.91	<.0001
e-GFR(mL/min per 1.73 m ²)	83.60±12.27	95.45±12.20	<.0001
HOMA-IR	1.78±1.30	1.62±1.08	0.003
AST (IU/L)	28.33±12.13	27.99±17.23	0.52
ALT (IU/L)	25.98±18.39	26.41±31.08	0.61
GGT (IU/L)	29.55±81.19	24.62±29.18	0.11
FLI	33.66±23.92	28.03±22.39	<.0001
Albumin (g/dL)	4.23±0.29	4.23±0.31	0.70
hsCRP (mg/dL)	0.26±0.35	0.21±0.59	0.007
Current smoking	125 (17.27%)	750 (18.58%)	0.54
Current alcohol intake	229 (31.98%)	1555 (38.90%)	0.0008
Regular exercise (none)	231 (32.31%)	1221 (30.81%)	0.43
Protein intake (g/day)	59.89±26.27	66.49±29.22	<.0001

Table 2 presents the characteristics of study participants according to baseline FLI levels. A total of 601 (12.62%) subjects had NAFLD as assessed by FLI (≥60), and 2889 (60.68%) subjects did not have NAFLD (FLI<30). Subjects with higher FLI had lower eGFR at baseline.

Table 3 shows the risk of incident CKD according to the baseline FLI groups. With the FLI<30 group as the reference, the odds ratios for incident CKD increased across FLI groups.

After adjustment for confounding variables, this trend remained statistically significant (Model 2). In a fully adjusted model (Model 3), the odds ratios (95% CI) for incident CKD in the 30≤FLI<59 and FLI ≥60 groups were 1.16 (0.93-1.43) and 1.43 (1.07-1.89) compared to those in the FLI<30 group (P for trend=0.0439).

Table 2. Baseline characteristics according to incident FLI category

Baseline variables	FLI			p-value
	<30 N=2889 (60.68 %)	30-59 N=1271(26.70 %)	≥60 N= 601(12.62 %)	
Age(years)	51.24±8.58	53.24±8.36	52.54±8.23	<.0001
Sex (men)	899 (31.12%)	564 (44.37%)	345 (57.40%)	<.0001
BMI (kg/m ²)	23.09±2.35	26.22±2.30	28.30±2.78	<.0001
Waist circumference(cm)	77.53±6.78	87.37±5.83	93.29±6.57	<.0001
HTN	431 (15.48%)	384 (32.85%)	239 (42.83%)	<.0001
Systolic BP (mmHg)	116.75±17.63	124.44±16.88	128.97±17.70	<.0001
Diastolic BP (mmHg)	76.93±10.73	82.40±10.56	85.23±10.45	<.0001
Diabetes mellitus	81 (2.82%)	100 (7.91%)	76 (12.75%)	<.0001
HbA1c (%)	5.59±0.68	5.89±0.95	6.17±1.17	<.0001
FPG (mg/dL)	82.94±14.82	87.42±19.70	93.98±27.92	<.0001
Total cholesterol(mg/dL)	184.22±32.42	195.67±32.82	205.29±38.12	<.0001
HDL-cholesterol(mg/dL)	46.46±9.72	41.39±8.72	39.73±8.35	<.0001
LDL-cholesterol (mg/dL)	114.15±28.90	117.41±32.12	110.50±39.22	<.0001
Triglyceride (mg/dL)	118.04±46.37	184.39±81.98	275.30±158.74	<.0001
e-GFR(mL/min per 1.73 m ²)	94.62±13.00	92.37±12.39	91.70±13.27	<.0001
HOMA-IR	1.43±0.85	1.85±1.26	2.31±1.55	<.0001
AST (IU/L)	25.89±8.17	28.76±13.39	36.85±37.06	<.0001
ALT (IU/L)	20.94±9.72	29.91±28.43	44.78±65.07	<.0001
Total bilirubin (mg/dL)	0.58±0.30	0.56±0.27	0.61±0.36	0.005
GGT (IU/L)	15.42±9.79	29.79±26.66	63.86±98.64	<.0001
Albumin (g/dL)	4.21±0.30	4.24±0.30	4.28±0.31	<.0001
hsCRP (mg/dL)	0.19±0.59	0.24±0.52	0.31±0.45	<.0001
Current smoking	441 (15.26%)	261 (20.54%)	173 (28.79%)	<.0001
Current alcohol intake	1007 (35.26%)	486 (38.51%)	291 (48.91%)	<.0001
Regular exercise (none)	909 (32.05%)	377 (30.14%)	166 (28.09%)	0.12
Protein intake (g/day)	65.19±29.12	64.94±27.61	68.15±30.29	0.06

Table 3. Odds ratio (95% Confidence Interval) for incident CKD according to the FLI groups

	FLI			P for trend
	<30	30~60	≥60	
Incident CKD	379 (13.12%)	224 (17.62%)	121 (20.13%)	<.0001
Crude odds ratio	1	1.42 (1.18~1.70)	1.67 (1.33~2.09)	<.0001
Model 1	1	1.22 (1.01~1.48)	1.64 (1.29~2.10)	0.0002
Model 2	1	1.17 (0.94~1.44)	1.45 (1.10~1.91)	0.024
Model 3	1	1.16 (0.93~1.43)	1.43 (1.07~1.89)	0.044

Model 1: Adjusted for age and sex

Model 2: Model 1 + further adjusted for baseline eGFR, smoking, regular exercise, alcohol intake, protein intake, systolic BP and DM

Model 3: Model 2 + further adjusted for total cholesterol and log hsCRP

We next evaluated the incremental predictive value of FLI when added to a base model of established clinical CKD risk factors. The addition of FLI to a clinical model predicting incident CKD resulted in a modest increase in the AUC (from 0.816 to 0.818, P = 0.0615) (Table 4). Incorporation of FLI also led to significant improvements in reclassification [category-free NRI, 17%; 95% CI, 8.9-25%]. The category-free NRI for event components was -8% (P-value= 0.0359), and that for non-events was 25% (P-value <0.001). This finding indicates that FLI correctly reclassified subjects without events as lower risk. The addition of FLI to the traditional CKD model improved the IDI significantly (IDI, 0.002; 95% CI, 0.0046-0.0143; P-value=0.0466).

Table 4. Discrimination and reclassification improvement for incident CKD by FLI

	Incident CKD	
	Values	P-value
AUC (95% CI)		
Traditional model ^a	0.816 (0.80~0.833)	
Traditional model ^a +FLI	0.818 (0.802~0.835)	0.061 ^b
NRI (95% CI)		
Category-free NRI (% [95% CI])	17% (8.9 to 25%)	< 0.001
% of events correctly reclassified	-8%	0.036
% of non-events correctly reclassified	25%	<.0001
IDI (95% CI)	0.002 (0.0046-0.0143)	0.046

^a Traditional model includes age, gender, baseline eGFR, smoking, regular exercise, alcohol intake, protein intake, systolic BP, DM, total cholesterol and log hsCRP. ^b P-value (Traditional model vs. Traditional model + FLI)

Conclusion

The presence of NAFLD determined by FLI substantially increased the risk of incident CKD over a 10-year period in an adult population. Furthermore, we presented that FLI provided modest to substantial improvement in reclassification of incident CKD beyond traditional risk factors. Our findings suggest that FLI is useful to better classify CKD risk in individuals. Given the increasing prevalences of both CKD and NAFLD and their direct effects on the acceleration of cardiovascular disease, further large-scale studies are warranted to confirm the utility of FLI as a predictor for incident CKD.