The Relationship Between Type 2 Diabetes Mellitus and Non-Alcoholic Fatty Liver Disease by Controlled Attenuation Parameter Using Fibroscan®

[1]Department of Endocrinology, Myongji Hospital, Goyang, Korea

[2]Department of Endocrinology, Yonsei University College of Medicine, Seoul, Korea

Jae Hyuk Lee[1]*, kwang Joon Kim[2]

BACKGROUND & AIMS

The severity of non-alcoholic fatty liver disease (NAFLD) in type 2 diabetes mellitus (T2DM) population compared with that in normal glucose tolerance (NGT) individuals has not yet been assessed by a quantitative method.

We investigated the prevalence and the severity of NAFLD in a T2DM population using controlled attenuation parameter (CAP).

METERIALS & METHODS

Subjects who underwent testing for biomarkers related to T2DM and CAP using Fibroscan® during a regular health check-up were enrolled.

CAP values of 250 dB/m and 300 dB/m were selected as the cutoffs for the presence of NAFLD and for moderate to severe NAFLD respectively.

Biomarkers related to T2DM included fasting glucose/insulin, C-peptide, HbA1c, glycoalbumin, and HOMA-IR.

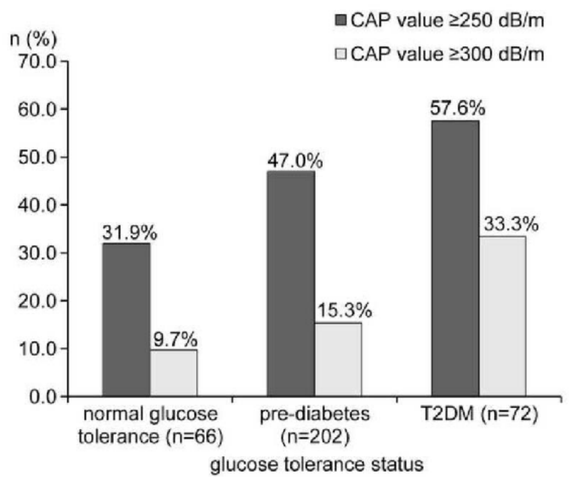
RESULTS

Table 1. Baseline characteristics of the patients

Variables	All patients (n=340)	Patients with T2DM (n=66, 19.4%)	Patients without T2DM (n=274, 80.6%)	*P*-value
Demographic variables				
Age (years)	56 ± 11	62 ± 11	55 ± 10	<0.001
Male gender	191 (56.2)	46 (69.7)	145 (52.9)	0.018
Hypertension	85 (25.0)	33 (22.4)	13 (36.1)	NS
Metabolic syndrome	85 (25.0)	22 (33.3)	63 (23.0)	NS
Family Hx of diabetes mellitus	61 (17.9)	15 (22.7)	46 (16.8)	NS
Alcohol (g/day)	5.2 ± 6.4	4.2 ± 6.4	5.4 ± 6.2	NS
Current smoker	72 (21.2)	12 (18.2)	60 (21.9)	NS
Anthropometric index				
Systolic blood pressure (mmHg)	128 ± 10	133 ± 9	127 ± 10	NS
Diastolic blood pressure (mmHg)	79 ± 9	83 ± 6	78 ± 10	NS
Body mass index (kg/m^2)	24.1 ± 3.1	25.4 ± 3.2	23.7 ± 3.0	<0.001
Laboratory variables				
Total cholesterol (mg/mL)	168.9 ± 41.2	188.9 ± 36.4	161.0 ± 42.3	NS
Triglycerides (mg/mL)	114.3 ± 63.3	135.9 ± 72.1	109.1 ± 60.0	0.006
HDL-cholesterol (mg/mL)	48.9 ± 13.9	45.0 ± 13.7	49.8 ± 13.8	0.012
LDL-cholesterol (mg/mL)	100.0 ± 29.3	114.1 ± 32.3	96.6 ± 28.6	NS
Aspartate aminotransferase (IU/L)	23.0 ± 8.6	24.2 ± 9.4	22.8 ± 8.4	NS
Alanine aminotransferase (IU/L)	23.2 ± 13.3	26.2 ± 15.1	22.5 ± 12.7	NS
Total bilirubin (mg/dL)	1.1 ± 4.6	1.9 ± 1.0	0.8 ± 1.1	NS
Gamma glutamyltransferase (IU/L)	38.3 ± 73.5	41.4 ± 39.4	37.5 ± 79.5	NS
Biomarkers related to insulin resistance				
Fasting glucose (mg/mL)	101.1 ± 55.0	137.2 ± 95.0	93.3 ± 10.3	<0.001
Fasting insulin (pm/mL)	7.1 ± 4.6	8.6 ± 6.4	6.7 ± 4.0	0.003
C-peptide (mmol/L)	2.2 ± 1.2	2.5 ± 1.3	2.1 ± 1.1	0.034
HbA1c (%)	6.0 ± 0.8	7.0 ± 1.3	5.7 ± 0.3	<0.001
Glycoalbumin (%)	12.4 ± 3.6	16.3 ± 5.9	11.4± 1.6	<0.001
HOMA-IR	1.89 ±2.20	3.11 ± 4.28	1.57 ± 1.00	<0.001
HOMA-β	77.17 ± 54.60	67.11 ± 75.22	79.71 ± 47.91	NS
High sensitive C-reactive protein (mg/L)	1.8 ± 3.1	2.0 ± 2.8	1.7 ± 3.1	NS
Liver stiffness measurement				
Liver stiffness value (kPa)	4.7 ± 2.1	5.5 ± 3.5	4.5 ± 1.6	0.001
Interquartile range (kPa)	0.7 ± 0.4	0.4 ± 0.1	0.7 ± 0.4	NS
Interquartile range/ median (%)	14.9 ± 9.5	7.5 ± 2.1	16.8 ± 9.8	NS
Controlled attenuation parameter				
CAP value (dB/m)	246.2 ± 50.4	264.5 ± 56.1	241.7 ± 48.0	<0.001
Interquartile range (dB/m)	28.4 ± 16.3	24.0 ± 13.5	29.4 ± 17.4	NS
Interquartile range/ median (%)	14.0 ± 8.4	11.8 ± 6.4	14.8 ± 9.1	NS

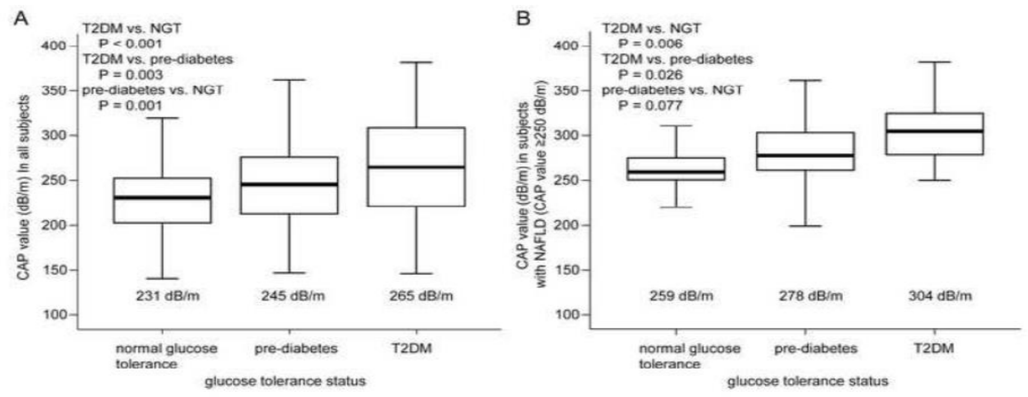
Variables are expressed as mean ± SD (range) or n (%). NS, not significant (*P*-value>0.05); T2DM, type 2 diabetes mellitus; HDL, high-density lipoprotein; LDL, low-density lipoprotein; HbA1c, hemoglobin A1c; HOMA-IR, homeostasis model assessment of insulin resistance of insulin resistance; HOMA-β, homeostasis model assessment of beta cell function; hs-CRP, high sensitivity C-reactive protein; CAP, controlled attenuation parameter

Figure 1. Prevalence of NAFLD according to the glucose tolerance



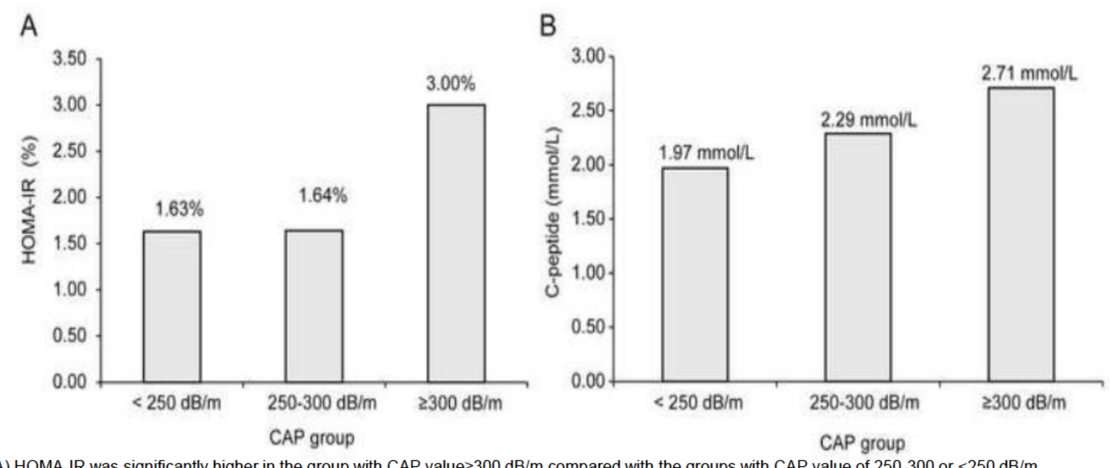
The proportion of subjects with presence of NAFLD (CAP value≥250 dB/m) increased according to the glucose tolerance status (31.9% in NGT, 47.0% in pre-diabetes, 57.6% in T2DM; NGT *vs.* pre-diabetes, *P*=0.027; NGT *vs.* T2DM, *P*=0.003; pre-diabetes *vs.* T2DM, *P*=0.157) (dark gray bar). The proportion of subjects with moderate to severe NAFLD (CAP value ≥300 dB/m) also increased according to the glucose tolerance status (9.7% in NGT, 15.3% in pre-diabetes, 33.3% in T2DM; NGT *vs.* pre-diabetes, *P*=0.321; NGT *vs.* T2DM, *P*=0.001; pre-diabetes *vs.* T2DM, *P*=0.02) (light gray bar). NAFLD, non-alcoholic fatty liver disease; CAP, controlled attenuation parameter; NGT, normal glucose tolerance; T2DM, type 2 diabetes mellitus.

Figure 2. Severity of NAFLD according to the glucose tolerance



(A) Subjects with T2DM had significantly higher median CAP values than those with NGT (265 *vs.* 231 dB/m, *P*<0.001) or pre-diabetes (265 *vs.* 245 dB/m, *P*=0.003). (B) In subjects with presence of NAFLD (CAP value ≥250 dB/m), the median CAP value increased according to the glucose tolerance status: 259 dB/m, 278 dB/m, and 304 dB/m in NGT, prediabetes, and T2DM groups, respectively (comparison between groups: T2DM *vs.* NGT,*P*=0.006; T2DM *vs.* pre-diabetes, *P*=0.026; pre-diabetes *vs.*NGT, *P*=0.077). CAP, controlled attenuation parameter; T2DM, type 2 diabetes mellitus; NGT, normal glucose tolerance

Figure 3. HOMA-IR and C-peptide level according to CAP



(A) HOMA-IR was significantly higher in the group with CAP value≥300 dB/m compared with the groups with CAP value of 250-300 or <250 dB/m (HOMA-IR, 3.00 ± 1.99 *vs.* 1.64 ± 1.04 *vs.* 1.63 ± 2.59 %, respectively; *P*<0.001). (B) Subjects with CAP value >300 dB/m showed significantly higher serum C-peptide than those with CAP value of250-300 dB/m or<250dB/m (C-peptide, 2.71 ± 0.95 *vs.* 2.29 ± 1.62 *vs.* 1.97 ± 0.88 mmol/L, respectively; *P*<0.001).HOMA-IR, homeostasis model assessment of insulin resistance of insulin resistance; CAP, controlled attenuation parameter.

Table 2. Multiple logistic regression analyses for T2DM

Model controlling for age, gender, BMI, triglyceride, HDL-cholesterol, and LSV		
	Odds ratio (95% CI)	*P*-value
Age	1.08 (1.05–1.11)	<0.001
Triglyceride	1.01 (1.00–1.03)	0.046
CAP value (group 0 vs. 1)	1.14 (0.61–2.15)	0.068
CAP value (group 0 vs. 2)	2.36 (1.13–4.86)	0.022

T2DM, type 2 diabetes mellitus; BMI, body mass index; HDL, high-density lipoprotein; CAP, controlled attenuation parameter.
Group 0, CAP value <250 dB/m; Group 1, 250 dB/m ≤CAP value <300 dB/m; Group 3, CAP value ≥300 dB/m

Table 3. Correlations between CAP value and biomarkers related to T2DM

Variable	Correlation	
	ρ	*P*-value
Fasting glucose (mg/mL)	0.379	<0.001
Fasting insulin (pm/mL)	0.395	<0.001
C-peptide (mmol/L)	0.402	<0.001
HbA1c (%)	0.345	<0.001
Glycoalbumin (%)	0.097	0.079
HOMA-IR	0.407	<0.001
HOMA-β	0.132	<0.001
High sensitive C-reactive protein	0.277	0.001

CAP, controlled attenuation parameter; T2DM, type 2 diabetes mellitus; HbA1c, hemoglobin A1c; HOMA-IR, homeostasis model assessment of insulin resistance; HOMA-β, homeostasis model assessment of beta cell function.

CONCLUSIONS

This study proved that subjects with T2DM had a higher prevalence of severe NAFLD than those with NGT. Moreover, increased hepatic steatosis was independently associated with the presence of T2DM, and insulin resistance induced by hepatic fat may be an important mechanistic connection.

Longitudinal prospective studies are anticipated to investigate the clinical implication of the relationship between CAP value and biomarkers related to T2DM and their association with the prognosis of T2DM

17 ECE
458--EP
Diabetes (complications & therapy)
JAEHYUK LEE
DOI: 10.3252/pso.eu.17ece.2015
Poster presented at: ECE2015 16–20 May 2015 DUBLIN, IRELAND 17th EUROPEAN CONGRESS OF ENDOCRINOLOGY