Comparison of the Usefulness of the Updated Homeostasis Model Assessment (HOMA2) with the Original HOMA1 in the Prediction of Type 2 Diabetes Mellitus in Koreans

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Background

- The pathophysiology of type 2 diabetes mellitus (T2DM) involves insulin resistance (IR) and β-cell dysfunction.
- Accordingly, estimating IR and β-cell function is essential for screening high-risk subjects for T2DM and making a treatment plan.
- There are several methods for estimating IR and β-cell function, including the euglycemic or hyperinsulinemic euglycemic clamp, frequently sampled intravenous glucose tolerance, C-peptide to glucose ratio, and homeostasis model assessment (HOMA) model

The Aim of study

- The primary purpose of this study was to compare the predictive ability of HOMA1 and HOMA2 for diabetes in Korean population.

Subjects & Method (1)

- A retrospective observational study of participants in a medical health checkup program at the Health Promotion Center at Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine, Seoul, from January 2001 to December 2012.
- Participants were divided into a normal glucose tolerance (NGT) group and a pre-diabetes group according to fasting glucose and glycosylated hemoglobin levels.
- Anthropometric and laboratory data were measured at the baseline checkup, and HOMA values were calculated at the baseline and follow-up checkups.
- The hazard ratios (HRs) of the HOMA1 and HOMA2 values and the prevalence of diabetes at follow-up were evaluated using Kaplan-Meier analysis and multivariable Cox proportional hazards model

Subjects

N=136,158

N= 31,464

- history of diabetes
- taking oral hypoglycemic agents
- fasting blood glucose ≥126 mg/dL or HbA1c ≥6.5% at the baseline
- missing data
- pregnant subjects
- ect

N=104,694

Method (2)

: Calculation of HOMA

- HOMA1-IR was defined as [fasting insulin (μU/mL)× fasting glucose (mmol/L)]/22.5. HOMA1-β was calculated using (20×fasting insulin)/(fasting glucose–3.5).
- HOMA2-IR and HOMA2-β data were calculated with a HOMA2 calculator released by the Diabetes Trials Unit, University of Oxford: HOMA Calculator.
  - This calculator is available at: http://www.dtu.ox.ac.uk/homacalculator/index.php (updated January 8, 2013).
- HOMA1-β and HOMA2-β have a negative correlation with diabetes risk, so we took the inverse value to compare them with HOMA-IR or HOMA2-IR.

RESULTS

Baseline characteristics of the study participants

Characteristic	NGT group[a] (*n*=72,915)	Pre-diabetes group[b] (*n*=31,779)	Non-diabetic group[c] (*n*=104,694)	*P* value[d]
Age at first visit, yr	37.9±6.8	41.2±8.3	38.9±7.4	<0.001
BMI, kg/m^2	23±2.9	24.2±3.1	23.4±3.0	<0.001
Waist circumference, cm	78.6±9.4	82.4±9.3	79.8±9.5	<0.001
Female sex, %	29,676 (40.7)	10,996 (34.6)	40,672 (38.8)	<0.001
Family history of DM, %	9,625 (13.2)	5,402 (17.0)	15,027 (14.4)	<0.001
Current smoker, %	18,885 (25.9)	8,517 (26.8)	27,402 (26.2)	0.002
Progression to DM, %	313 (0.4)	1,626 (5.1)	1,939 (1.9)	<0.001
AST, IU/L	23.7±7.0	24.9±8.0	23.8±7.3	<0.001
ALT, IU/L	23.8±13.2	27.6±15.7	25.0±14.1	<0.001
Serum creatinine, mg/dL	1.01±0.15	1.04±0.15	1.02±0.15	<0.001
eGFR, mL/min	79.4±9.1	77.3±9.1	78.8±9.2	<0.001
SBP, mm Hg	111.5±13.0	116.2±14.7	112.9±13.7	<0.001
HbA1c, %	5.26±0.23	5.61±0.32	5.37±0.30	<0.001
Total cholesterol, mg/dL	186.6±31.7	196.3±33.4	189.6±32.5	<0.001
Triglyceride, mg/dL	115.3±73.3	140.7±92.3	123.0±80.4	<0.001
LDL-C, mg/dL	106.6±27.1	114.1±28.5	108.9±27.7	<0.001
HDL-C, mg/dL	54.5±12.3	52.4±11.7	53.9±12.2	<0.001
Non-HDL-C, mg/dL	132.1±32.1	143.9±33.4	135.7±32.9	<0.001
HOMA1-IR	1.91±0.72	2.39±0.97	2.06±0.84	<0.001
HOMA1-β	120.42±70.08	93.80±39.82	112.34±63.65	<0.001
HOMA2-IR	1.27±0.45	1.46±0.55	1.33±0.49	<0.001
HOMA2-β	100.09±35.51	93.14±31.67	97.98±34.54	<0.001

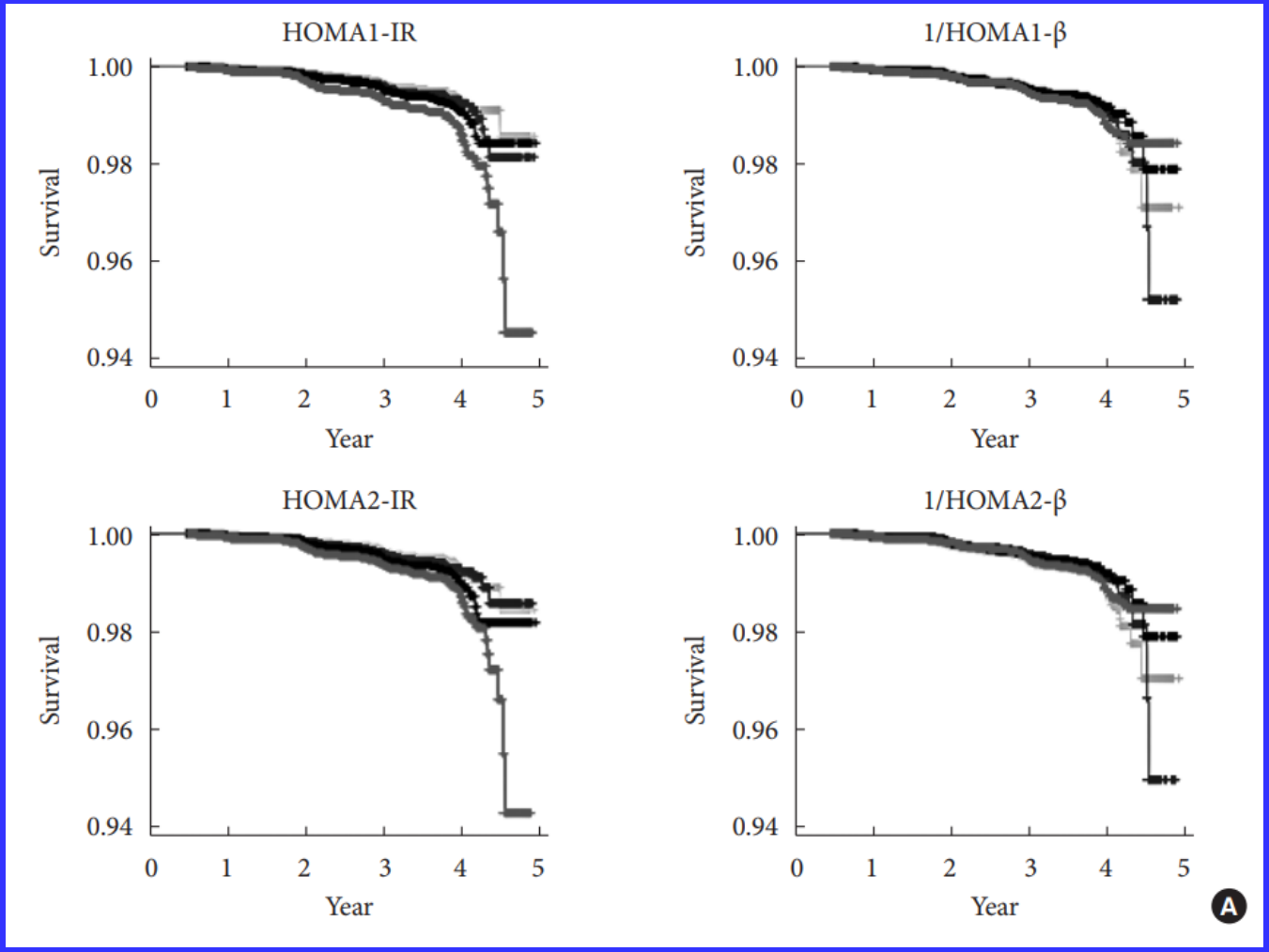
Univariate Cox proportional hazards analysis model of HOMA values for developing type 2 diabetes mellitus

Variable	NGT group		Pre-diabetes group		All participants (non-diabetic group)	
	HR (95% CI)[a]	*P* value	HR (95% CI)[a]	*P* value	HR (95% CI)[a]	*P* value
HOMA1-IR	1.13 (1.1–1.17)	<0.001	1.42 (1.38–1.46)	<0.001	1.21 (1.20–1.22)	<0.001
1/HOMA1-β	0.99 (0.87–1.14)	0.922	1.13 (1.11–1.15)	<0.001	1.12 (1.11–1.13)	<0.001
HOMA2-IR	1.18 (1.13–1.23)	<0.001	1.33 (1.29–1.38)	<0.001	1.25 (1.23–1.26)	<0.001
1/HOMA2-β	0.95 (0.83–1.08)	0.418	1.26 (1.23–1.29)	<0.001	1.26 (1.25–1.28)	<0.001

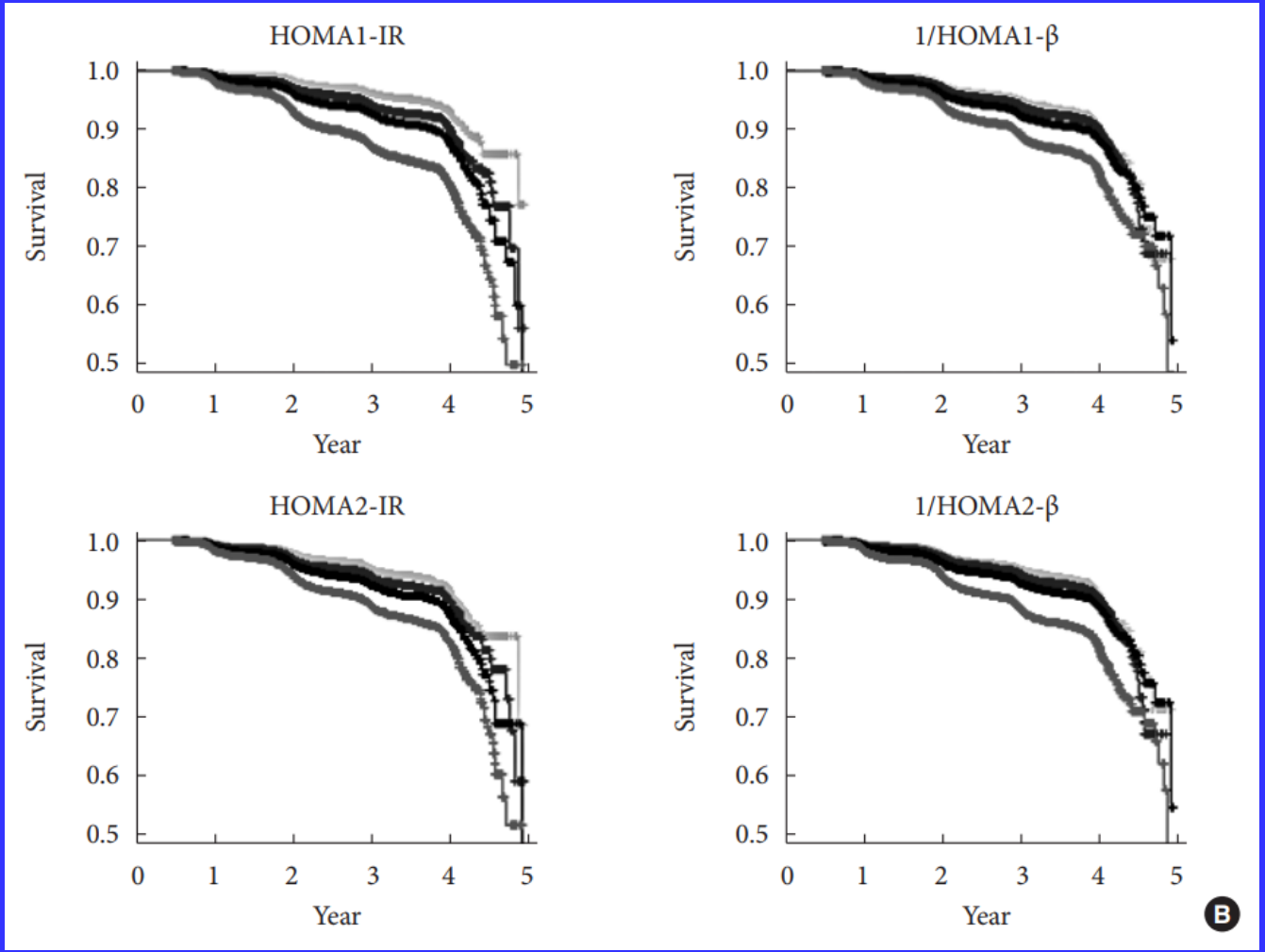
HOMA, homeostasis model assessment; NGT, normal glucose tolerance; HR, hazard ratio; CI, confidence interval; HOMA1, original HOMA; IR, insulin resistance; HOMA2, updated HOMA model.

[a]When increased by the standard deviation from the mean value of each HOMA value. Reference is the mean value of each HOMA model.

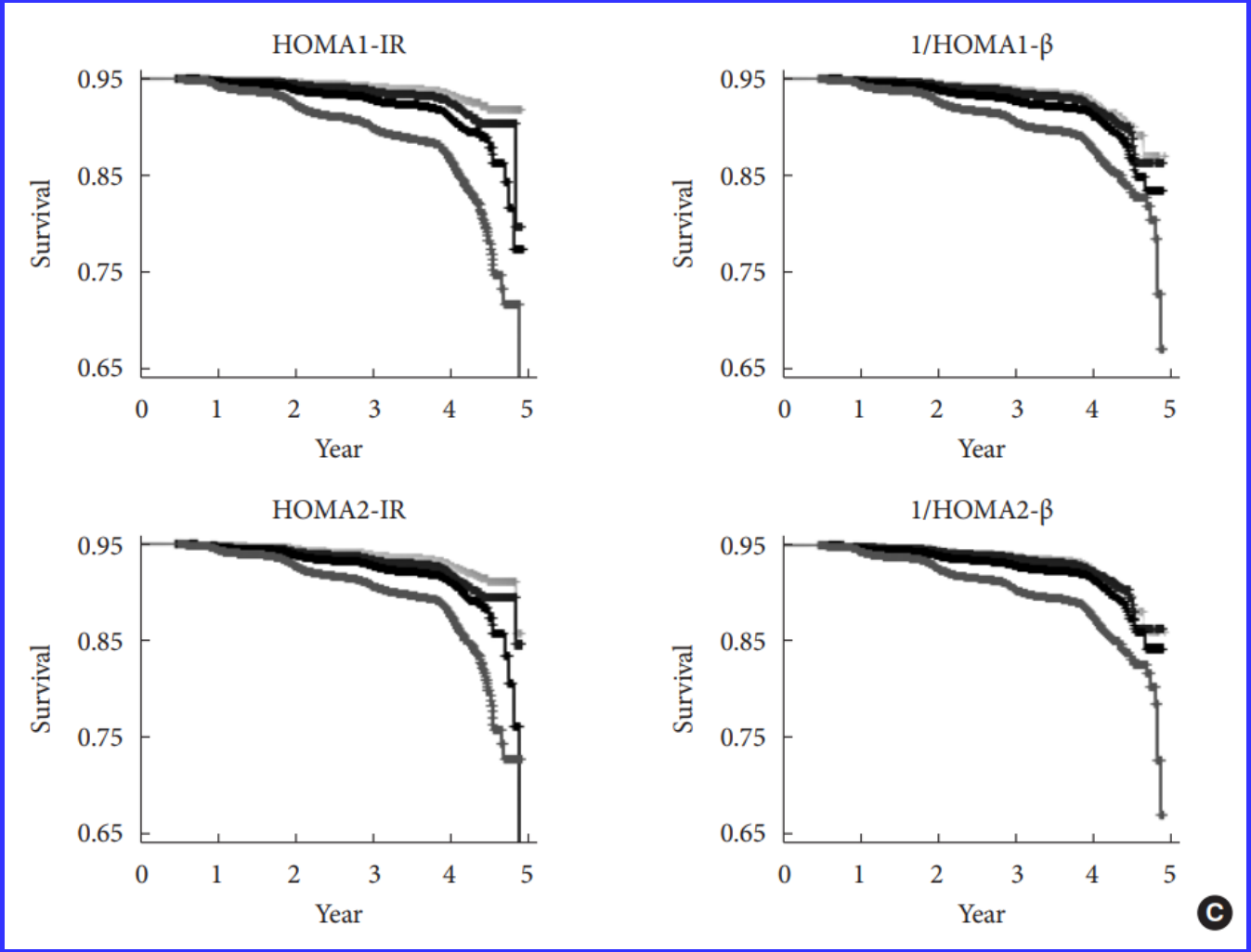
Kaplan-Meier curves for the cumulative prevalence of T2D for the quartile of HOMA values in the normal glucose tolerance group



Kaplan-Meier curves for the cumulative prevalence of T2D for the quartile of HOMA values in the pre-diabetic group



Kaplan-Meier curves for the cumulative prevalence of T2D for the quartile of HOMA values in the non-diabetic group



Multivariate a Cox proportional hazards analysis model of HOMA values for developing T2D

Variable	NGT group		Pre-diabetes group		All participants (non-diabetic group)	
	HR (95% CI)[b]	*P* value	HR (95% CI)[b]	*P* value	HR (95% CI)[b]	*P* value
HOMA1-IR	1.09 (1.04–1.14)	<0.001	1.23 (1.19–1.28)	<0.001	1.14 (1.12–1.15)	<0.001
1/HOMA1-β	1.07 (0.97–1.17)	0.177	1.14 (1.12–1.16)	<0.001	1.13 (1.11–1.14)	<0.001
HOMA2-IR	1.11 (1.04–1.19)	0.001	1.13 (1.08–1.18)	<0.001	1.12 (1.09–1.15)	<0.001
1/HOMA2-β	1.05 (0.93–1.20)	0.428	1.29 (1.26–1.31)	<0.001	1.27 (1.25–1.29)	<0.001

HOMA, homeostasis model assessment; NGT, normal glucose tolerance; HR, hazard ratio; CI, confidence interval; HOMA1, original HOMA; IR, insulin resistance; HOMA2, updated HOMA model.

[a]All estimates reflect adjustment for age, sex, body mass index, family history of diabetes, history of smoking, systolic blood pressure, glycosylated hemoglobin, triglyceride, and high density lipoprotein cholesterol, [b]When increased by the standard deviation from the mean value of each HOMA value. Reference is the mean value of each HOMA model.

Summary

- All of the HOMA values except HOMA1-β and HOMA2-β in the NGT group were significant predictors of the progression to diabetes.
- In the NGT group, there was no significant difference in HOMA1-IR and HOMA2-IR
- In the pre-diabetes group, HOMA2-β was a more powerful marker than HOMA1-IR or HOMA1-β
- In the non-diabetic group (NGT+pre-diabetes), HOMA2-β was also a stronger predictor of diabetes than HOMA1-IR or HOMA1-β

Conclusion

- HOMA2 is more predictive than HOMA1 for the progression to diabetes in pre-diabetes or non-diabetic Koreans.

Homeostatic model assessment

- **The original HOMA (HOMA1)** has been broadly used due to its simplicity and cost effectiveness. Previous studies show that an increase of HOMA1-IR and a decrease of HOMA1-β are associated with an increased incidence of diabetes and future cardiovascular events in patients with T2DM.
- **An updated HOMA (HOMA2)**, the correctly solved computer model that considers such variations, was announced in 1998. HOMA2 was recalibrated to give steady-state β-cell function (% B) and insulin sensitivity (% S) of 100% in normal young adults when using currently available assays for insulin, specific insulin, or C-peptide

$$\text{HOMA-IR} = \frac{\text{Glucose} \times \text{Insulin}}{22.5}$$

$$\text{HOMA-}\beta = \frac{20 \times \text{Insulin}}{\text{Glucose} - 3.5}\%$$

Glucose in Molar Units mmol/L

available at: http://www.dtu.ox.ac.uk/homacalculator/index.php (updated January 8, 2013).