Diabetes Care
American Diabetes Association

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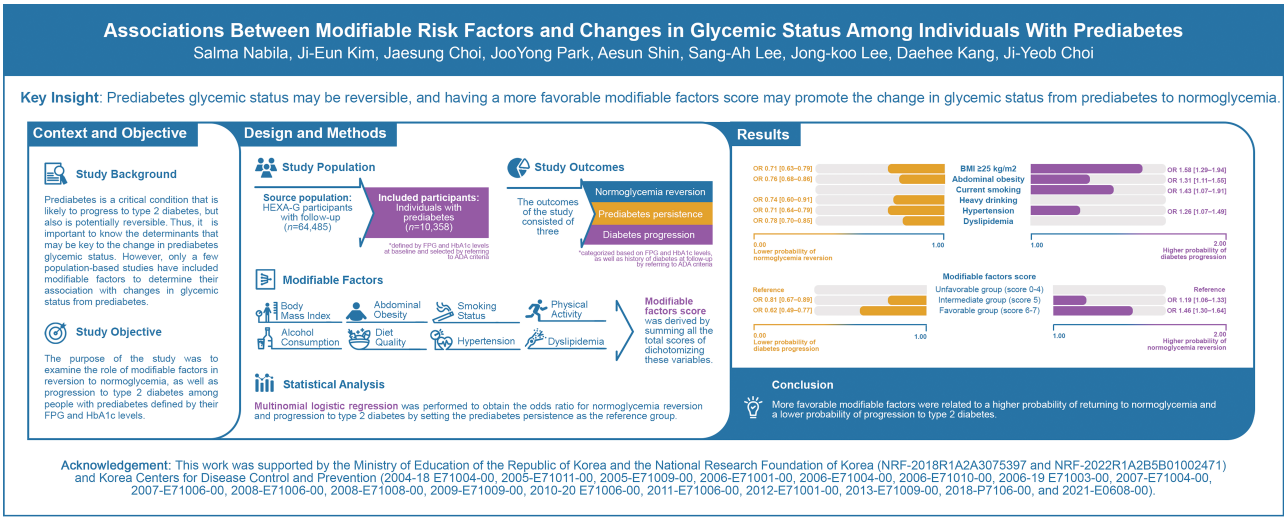
Diabetes Care 2023;46(3):535–543 | https://doi.org/10.2337/dc22-1042



Acknowledgement: This work was supported by the Ministry of Education of the Republic of Korea and the National Research Foundation of Korea (NRF-2018R1A2A3075397 and NRF-2022R1A2B5B01002471) and Korea Centers for Disease Control and Prevention (2004-18 E71004-00, 2005-E71011-00, 2005-E71009-00, 2006-E71001-00, 2006-E71004-00, 2006-E71010-00, 2006-19 E71003-00, 2007-E71004-00, 2007-E71006-00, 2008-E71006-00, 2008-E71008-00, 2009-E71009-00, 2010-20 E71006-00, 2011-E71006-00, 2012-E71001-00, 2013-E71009-00, 2018-P7106-00, and 2021-E0608-00).

ARTICLE HIGHLIGHTS

- Only a few population-based studies have included modifiable factors as the determinants of the change in prediabetes glycemic status.
- This study was conducted to examine the role of modifiable factors in prediabetes reversion to normoglycemia and progression to type 2 diabetes.
- A higher modifiable factors score was found to have a higher probability of normoglycemia reversion, as well as a lower probability of type 2 diabetes progression.
- Engaging in a healthier lifestyle and managing body composition, blood pressure, and lipid profiles may promote the prediabetes reversion to normoglycemia and prevent type 2 diabetes progression.

Associations Between Modifiable Risk Factors and Changes in Glycemic Status Among Individuals With Prediabetes

Salma Nabila,[1,2] Ji-Eun Kim,[1,2] Jaesung Choi,[2,3] JooYong Park,[1,2,4] Aesun Shin,[5,6] Sang-Ah Lee,[7] Jong-koo Lee,[8] Daehee Kang,[1,5,6,9] and Ji-Yeob Choi[1,2,3,6]

Diabetes Care 2023;46:535–543 | https://doi.org/10.2337/dc22-1042

OBJECTIVE

To examine the associations between modifiable risk factors and glycemic status changes in individuals with prediabetes.

RESEARCH DESIGN AND METHODS

A total of 10,358 individuals with prediabetes defined by their fasting blood glucose and HbA_{1c} levels from the Health Examinees-Gem study were included in the present study. Modifiable factors, including BMI, abdominal obesity, smoking status, physical activity, alcohol consumption, diet quality, hypertension, and dyslipidemia, were examined to determine their associations with changes in glycemic status during follow-up. In addition, modifiable-factor scores were calculated, and their association with changes in glycemic status was also analyzed.

RESULTS

The median follow-up time for this study was 4 years (range, 1–7 years). BMI ≥25 kg/m^2 (adjusted odds ratio [OR] 0.71 [95% CI 0.63–0.79]), abdominal obesity (OR 0.76 [95% CI 0.68–0.86]), heavy drinking (OR 0.74 [95% CI 0.60–0.91]), hypertension (OR 0.71 [95% CI 0.64–0.79]), and dyslipidemia (OR 0.78 [95% CI 0.70–0.85]) were associated with a lower possibility of normoglycemia reversion. BMI ≥25 kg/m^2 (OR 1.58 [95% CI 1.29–1.94]), abdominal obesity (OR 1.31 [95% CI 1.11–1.55]), current smoking (OR 1.43 [95% CI 1.07–1.91]), and hypertension (OR 1.26 [95% CI 1.07–1.49]) were associated with a higher probability of type 2 diabetes progression. Having more favorable modifiable factors was also associated with normoglycemia reversion (OR 1.46 [95% CI 1.30–1.64]) and type 2 diabetes progression (OR 0.62 [95% CI 0.49–0.77]).

CONCLUSIONS

More favorable modifiable factors were related to a higher probability of returning to normoglycemia and a lower probability of progression to type 2 diabetes.

Prediabetes is a condition in which blood glucose exceeds normal levels but is still below the threshold for type 2 diabetes (1). This condition has gained more attention because the prevalence is increasing globally (2,3), including in Korea (4,5), and being in this phase puts people at high risk of developing subsequent complications (1,6–9).

Prediabetes is a critical metabolic condition because it is likely to progress to type 2 diabetes; however, it is potentially reversible (10), and its reversion may be advantageous (11–14). Thus, previous studies were conducted to observe the

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Received 28 May 2022 and accepted 3 December 2022

This article contains supplementary material online at https://doi.org/10.2337/figshare.21743018.

determinants that may be key to the change in prediabetes glycemic status. However, only a few population-based studies have included modifiable factors in their main analysis to determine their association with changes in glycemic status (14–16). Moreover, to our knowledge, no studies have examined how modifiable factor scores are associated with glycemic-status changes from prediabetes, even though it has been widely associated with other outcomes.

The Korean Clinical Practice Guidelines for Diabetes suggest that individuals with prediabetes manage their weight by modifying their physical activity and diet. Some recommendations to control blood glucose are also mentioned, including avoiding alcohol consumption, as well as hypertension and dyslipidemia management (17). The World Health Organization stated that tobacco use, physical activity, diet, alcohol consumption, overweight or obesity, and hyperlipidemia may increase the risk of noncommunicable diseases, including diabetes (18). The American Diabetes Association (ADA) also mentioned some lifestyle factors that play a role in the prevention of type 2 diabetes, such as nutrition and physical activity. Furthermore, weight control is also considered an important key in the prevention of type 2 diabetes (10). Therefore, we conducted a study to examine the role of obesity, smoking status, physical activity, alcohol consumption, diet quality, hypertension, and dyslipidemia under the term of "modifiable factors" in prediabetes reversion to normoglycemia, as well as progression to type 2 diabetes, in a Korean population, using both fasting plasma glucose (FPG) and hemoglobin A_{1c} (HbA_{1c}) as the markers.

RESEARCH DESIGN AND METHODS

Health Examinees–Gem Study

Health Examinees-Gem (HEXA-G) is a study derived from Health Examinees of the Korean Genome and Epidemiology (KoGES_HEXA). Briefly, KoGES_HEXA is a population-based cohort study that collected epidemiological characteristics, genomic features, and gene–environment interactions of chronic diseases in the Korean population aged 40–69 years. Baseline recruitment was conducted in two phases: phase I was from 2004 to 2008, and phase II was conducted from 2009 to 2013 at 38 health examination centers and training hospitals in eight regions by performing an interview-based questionnaire survey and biological sample collection, both at the same date for each participant. A total of 167,169 participants were recruited at baseline, and 65,642 of them had completed the follow-up survey conducted from 2012 to 2016. After excluding centers that only participated in the pilot study, had different processes for data collection, and participated for less than 2 years, 139,344 people from baseline recruitment were included as HEXA-G participants, and among them, 64,485 were those who had participated in the follow-up survey. Details on participant selection for HEXA-G can be found in Supplementary Figure 1, and other details of the surveys are described elsewhere (19–21).

Study Population

This study only included participants from phase II who had completed the follow-up survey to maintain data consistency. Among the participants in the HEXA-G study who had completed their follow-up examination, 26,195 people from phase I were excluded. Individuals with no information on FPG and HbA_{1c} levels at baseline (n = 6 and 10,253, respectively) and no information on FPG and HbA_{1c} levels at follow-up (n = 2 and 9, respectively) were also excluded, leaving 27,041 participants. On the basis of their FPG and HbA_{1c} values, participants were assigned into normoglycemia, prediabetes, and type 2 diabetes groups. Individuals with normoglycemia and type 2 diabetes were excluded (n = 13,762 and 2,439, respectively), as were participants who reported a history of diabetes (n = 482). Finally, 10,358 individuals with prediabetes remained eligible for inclusion in the statistical analysis. A flowchart of participant selection is shown in Fig. 1, and more detailed information on FPG and HbA_{1c} data availability in the HEXA-G can be found in Supplementary Table 1. Although a large number of participants from phase I were excluded, the basic characteristics between the two phases did not show an imbalance in the evaluation of the standardized differences, except for age (Supplementary Table 2). Furthermore, we also confirmed that there was no imbalance found in the characteristics of participants who were included and excluded for the reason of incomplete data on the markers (Supplementary Table 2). This study was approved by the Institutional Review Board (IRB) of Seoul National University (IRB no. E-2111-024-1269).

Ascertainment of Prediabetes

Prediabetes was defined by FPG and HbA_{1c} data according to the ADA criteria (1) and history of diabetes diagnosis. The participants were considered to have prediabetes if their FPG level was between 100 and 125 mg/dL, HbA_{1c} was between 5.7% and 6.4% (39–47 mmol/mol), or both (1). Participants who reported a history of diabetes diagnosis by a physician at baseline were not included in the study population, regardless of their FPG and HbA_{1c} levels. The distribution of the glycemic status based on each marker is shown in Supplementary Table 3.

Ascertainment of Outcome

The outcomes of this study included normoglycemia reversion, prediabetes persistence, and type 2 diabetes progression based on participants' FPG and HbA_{1c} levels according to the ADA criteria at the follow-up survey. Normoglycemia reversion was defined as a normal range of both FPG $<$100 mg/dL and HbA_{1c} $<$5.7% ($<$39 mmol/mol). The presence of either or both impaired fasting glucose (100–125 mg/dL) and elevated HbA_{1c} (5.7–6.4% [39–47 mmol/mol]) was defined as prediabetes persistence. An increased level of FPG $\geq$126 mg/dL, HbA_{1c} $\geq$6.5% ($\geq$48 mmol/mol), or both was defined as progression to type 2 diabetes. In addition, participants who reported a history of being diagnosed with diabetes by a physician at follow-up were also considered to have progressed to diabetes, regardless of their FPG and HbA_{1c} levels at follow-up.

Modifiable Risk Factors

The modifiable risk factors in this study were BMI, abdominal obesity, smoking status, physical activity, alcohol consumption, diet quality, hypertension, and dyslipidemia at baseline. Diet quality was assessed using the Diet Quality Index for Koreans (DQI-K), an adapted instrument to examine the overall diet quality of the Korean population that was developed in a previous study (22). It evaluates eight components of diet habit in the analysis: daily protein intake, percentage of energy from fat, percentage of energy from saturated fat, daily cholesterol intake, daily

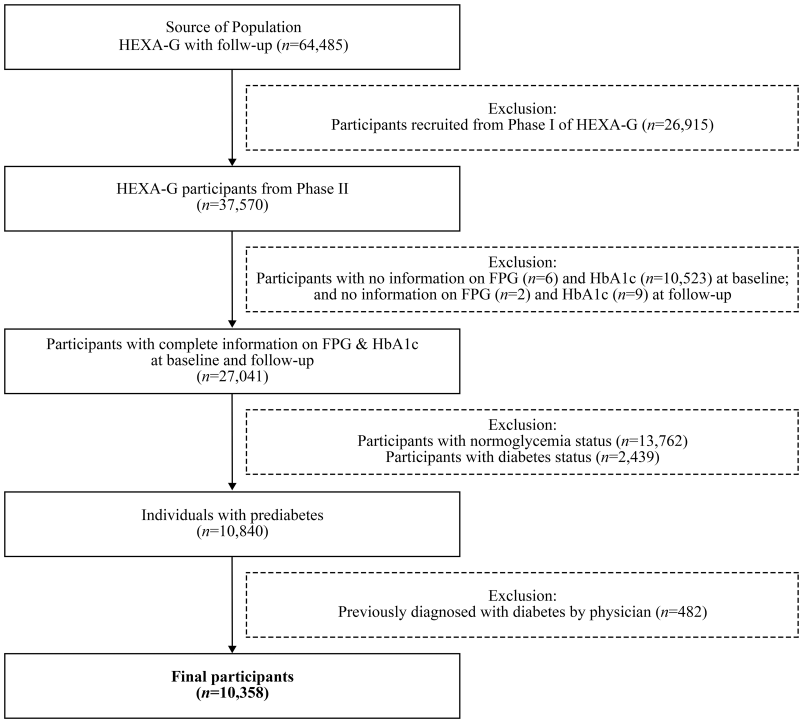

Figure 1—Flowchart of participant selection.

whole-grain intake, daily vegetable intake, daily fruit intake, and daily sodium intake. On the basis of the median value of the total DQI-K score, participants were grouped into good diet quality and poor diet quality groups (22). The definition and categories of each modifiable risk factor are detailed in the Supplementary Table 4.

Modifiable-Factors Score

The modifiable-factors score for this study was derived by summing all the total scores of the following seven parameters: dichotomizing obesity, smoking status, physical activity, alcohol consumption, diet quality, hypertension, and dyslipidemia. Smoking status was categorized as currently smoking and currently not smoking, comprising former smokers and never smokers, because only current smokers showed a significant association with glycemic status change based on the basic characteristics of the population. Alcohol consumption was grouped into nondrinkers to light drinkers and moderate drinkers to heavy drinkers. Instead of BMI, abdominal obesity was used as an indicator of obesity because central obesity is more associated with comorbidity and metabolic syndrome than is BMI (23,24). In addition, a sensitivity analysis was performed by replacing abdominal obesity with BMI as a scoring component and grouping BMI values into <23 kg/m^2 and ≥ 23 kg/m^2.

The more favorable category from each component was given a score of 1, and the other category was given a score of 0; thus, the total score ranged from 0 to 7. This approach of dichotomizing the components made it easier for the scoring and interpretation and so for us to understand modifiable risk factors and their association with glycemic status change.

On the basis of tertiles, participants' total scores were grouped into three categories: participants with scores of 0–4 were categorized into the unfavorable group, those with a score of 5 were in the intermediate group, and those with a score of 6–7 were in the favorable group. The details of the scoring are described in Supplementary Tables 5–7.

Covariates

Potential covariates of sociodemographic factors were included in this study and consisted of sex, age (grouped into 40–49, 50–59, and 60–69 years), education level (middle school or below, high school, and college or above), and income (<200, 200–399, ≥ 400 per 10,000 Korean Won). Other covariates included baseline FPG, baseline HbA_{1c} (every 0.1 increase), and family history of diabetes.

Statistical Analysis

Multinomial logistic regression analysis with a 95% CI was performed to obtain the odds ratio (OR) for reversion to normoglycemia and progression to type 2 diabetes by setting the prediabetes persistence group as the reference group. Sex (binary), age (continuous), education (categorical), income (categorical), baseline FPG (continuous), baseline HbA_{1c} (continuous), and family history of diabetes (binary) were included as the adjusting variables in the analysis. The analyses of modifiable-factors score included the analysis of continuous score, categorical (unfavorable, intermediate, and favorable), as well as the ordinal category of the score of the number of modifiable factors.

Two additional analyses were then performed. The first was to calculate the standardized differences between participants from phase I and phase II, as well as participants with and without follow-up data; a value >0.2 indicated an imbalance between the two groups (25). The other was a sex-stratified analysis to determine the difference between the ORs of glycemic status changes in men and women along with a heterogeneity test using the Cochran Q and Higgins I^2 tests; $P < 0.1$ or $I^2 < 50\%$ indicated a significant difference (26). Furthermore, three other sensitivity analyses were performed. The first was done by excluding participants with a follow-up survey of <3 years. Next was the analysis of glycemic status change from prediabetes defined only by FPG. The last was a sensitivity analysis of modifiable-factor scores by substituting abdominal obesity with BMI as one of the scoring components.

All analyses were performed using SPSS, version 26.0 (IBM Company, New York, NY); SAS statistical software, version 9.4 (SAS Institute, Cary, NC); and R Statistical Software, version 4.1.2 (R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

The median follow-up period was 4 years (range, 1–7 years). Among the 10,358 participants, 3,293 (31.8%) had their glycemic status back to normoglycemia and 843 (8.1%) progressed to diabetes. The remaining 6,222 participants (60.1%) maintained their glycemic status at the prediabetes level. The complete results of the baseline characteristics are presented in Table 1.

Table 1—Baseline characteristics and ORs of glycemic status change

		Events at follow-up				
		Prediabetes persistence	Normoglycemia reversion		Diabetes progression	
Variable	*N* (%)	*n* (%)	*n* (%)	OR* (95% CI)	*n* (%)	OR* (95% CI)
Sociodemographic factors						
Sex						
Men	3,545 (34.2)	2,216 (35.6)	943 (28.6)	Reference	386 (45.8)	Reference
Women	6,813 (65.8)	4,006 (64.4)	2,350 (71.4)	**1.32 (1.18–1.46)**	457 (54.2)	**0.63 (0.53–0.74)**
Age (mean ± SD)	55.4 ± 7.4	55.7 ± 7.2	54.6 ± 7.7	1.00 (0.99–1.00)	55.7 ± 7.6	**0.98 (0.97–0.99)**
Age category						
40–49	2,181 (21.1)	1,184 (19.0)	810 (24.6)	Reference	187 (22.2)	Reference
50–59	4,862 (46.9)	2,986 (48.0)	1,504 (45.7)	0.91 (0.81–1.03)	372 (44.1)	**0.59 (0.48–0.74)**
60–69	3,315 (32.0)	2,052 (33.0)	979 (29.7)	0.97 (0.84–1.11)	284 (33.7)	**0.56 (0.44–0.71)**
Education						
Middle school or less	3,413 (33.1)	2,128 (34.4)	989 (30.2)	Reference	296 (35.3)	Reference
High school	4,126 (40.0)	2,424 (39.2)	1,374 (41.9)	**1.22 (1.09–1.38)**	328 (39.1)	0.84 (0.69–1.03)
College or above	2,768 (26.9)	1,639 (26.5)	915 (27.9)	**1.22 (1.06–1.40)**	214 (25.5)	**0.69 (0.55–0.87)**
Income category (Korean 10.000 won)						
<200	3,214 (31.8)	1,935 (31.9)	1,005 (31.1)	Reference	274 (33.3)	Reference
200–399	4,554 (45.0)	2,754 (45.4)	1,435 (44.5)	0.90 (0.80–1.01)	365 (44.3)	0.90 (0.74–1.09)
≥400	2,354 (23.3)	1,382 (22.8)	788 (24.4)	0.98 (0.85–1.13)	184 (22.4)	0.95 (0.74–1.20)
Modifiable factors						
BMI, kg/m^2						
<23	3,439 (33.2)	1,894 (30.5)	1,373 (41.7)	Reference	172 (20.5)	Reference
≥23	6,910 (66.8)	4,323 (69.5)	1,919 (58.3)	**0.74 (0.67–0.81)**	668 (79.5)	**1.38 (1.14–1.67)**
<18.5	134 (1.3)	68 (1.1)	64 (1.9)	1.10 (0.75–1.61)	2 (0.2)	0.45 (0.11–1.90)
18.5–22.9	3,305 (31.9)	1,826 (29.4)	1,309 (39.8)	Reference	170 (20.2)	Reference
23–24.9	2,911 (28.1)	1,801 (29.0)	907 (27.6)	**0.78 (0.69–0.88)**	203 (24.2)	1.04 (0.82–1.31)
≥25	3,999 (38.6)	2,522 (40.6)	1,012 (30.7)	**0.71 (0.63–0.79)**	465 (55.4)	**1.58 (1.29–1.94)**
Abdominal obesity†						
No	7,590 (73.3)	4,438 (71.4)	2,636 (80.1)	Reference	516 (61.4)	Reference
Yes	2,758 (26.7)	1,779 (28.6)	655 (19.9)	**0.76 (0.68–0.86)**	324 (38.6)	**1.31 (1.11–1.55)**
Smoking status						
Never smokers	7,429 (71.9)	4,393 (70.8)	2,518 (76.6)	Reference	518 (61.7)	Reference
Former smokers	1,743 (16.9)	1,126 (18.1)	454 (13.8)	0.93 (0.77–1.12)	163 (19.4)	0.94 (0.71–1.26)
Current smokers	1,164 (11.3)	689 (11.1)	316 (9.6)	0.97 (0.79–1.18)	159 (18.9)	**1.43 (1.07–1.91)**
Smoking pack-year‡						
Never smokers	7,429 (72.1)	4,393 (71.0)	2,518 (76.7)	Reference	518 (61.8)	Reference
Light smokers	1,578 (15.3)	982 (15.9)	442 (13.5)	0.96 (0.80–1.15)	154 (18.4)	1.05 (0.79–1.40)
Moderate smokers	1,002 (9.7)	625 (10.1)	255 (7.8)	0.94 (0.76–1.17)	122 (14.6)	1.29 (0.94–1.78)
Heavy smokers	301 (2.9)	188 (3.0)	69 (2.1)	0.99 (0.71–1.38)	44 (5.3)	1.39 (0.90–2.16)
Physical activity, min/week						
No regular exercise	4,575 (44.3)	2,714 (43.8)	1,492 (45.4)	Reference	369 (44.0)	Reference
<150	1,177 (11.4)	696 (11.2)	383 (11.7)	0.96 (0.83–1.13)	98 (11.7)	1.07 (0.83–1.39)
≥150	4,570 (44.3)	2,790 (45.0)	1,408 (42.9)	0.95 (0.86–1.05)	372 (44.3)	0.98 (0.83–1.16)
Alcohol consumption§						
Nondrinkers	5,941 (57.6)	3,527 (56.9)	1,980 (60.3)	Reference	434 (51.7)	Reference
Light drinkers	2,844 (27.6)	1,689 (27.2)	923 (28.1)	1.03 (0.92–1.15)	232 (27.6)	0.94 (0.77–1.14)
Moderate drinkers	739 (7.2)	467 (7.5)	199 (6.1)	0.83 (0.68–1.02)	73 (8.7)	1.02 (0.75–1.40)
Heavy drinkers	798 (7.7)	517 (8.3)	180 (5.5)	**0.74 (0.60–0.91)**	101 (12.0)	1.20 (0.90–1.61)
Diet quality‖						
Good diet quality	5,342 (51.8)	3,222 (52.0)	1,678 (51.2)	Reference	442 (52.7)	Reference
Poor diet quality	4,971 (48.2)	2,973 (48.0)	1,602 (48.8)	0.93 (0.85–1.02)	396 (47.3)	1.02 (0.87–1.20)
Hypertension						
No	6,880 (66.5)	3,967 (63.8)	2,447 (74.4)	Reference	466 (55.5)	Reference
Yes	3,467 (33.5)	2,249 (36.2)	844 (25.6)	**0.71 (0.64–0.79)**	374 (44.5)	**1.26 (1.07–1.49)**
Dyslipidemia						
No	5,768 (55.7)	3,316 (53.3)	2,066 (62.7)	Reference	386 (45.8)	Reference
Yes	4,590 (44.3)	2,906 (46.7)	1,227 (37.3)	**0.78 (0.70–0.85)**	457 (54.2)	1.17 (0.99–1.37)
Hypercholesterolemia						
No	8,662 (83.6)	5,161 (82.9)	2,804 (85.2)	Reference	697 (82.7)	Reference
Yes	1,696 (16.4)	1,061 (17.1)	489 (14.8)	0.90 (0.79–1.02)	146 (17.3)	1.03 (0.83–1.27)
High LDL-C level						
No	8,929 (86.2)	5,323 (85.6)	2,877 (87.4)	Reference	729 (86.5)	Reference
Yes	1,429 (13.8)	899 (14.4)	416 (12.6)	**0.87 (0.76–1.00)**	114 (13.5)	0.98 (0.78–1.24)

Continued on p. 539

Table 1—Continued

Variable	*N* (%)	Events at follow-up: Prediabetes persistence *n* (%)	Normoglycemia reversion *n* (%)	Normoglycemia reversion OR* (95% CI)	Diabetes progression *n* (%)	Diabetes progression OR* (95% CI)
Hypertriglyceridemia						
No	8,726 (84.2)	5,190 (83.4)	2,906 (88.2)	Reference	630 (74.7)	Reference
Yes	1,632 (15.8)	1,032 (16.6)	387 (11.8)	**0.79 (0.69–0.91)**	213 (25.3)	**1.30 (1.07–1.57)**
Low HDL-C level						
No	9,285 (89.6)	5,554 (89.3)	3,011 (91.4)	Reference	720 (85.4)	Reference
Yes	1,073 (10.4)	668 (10.7)	282 (8.6)	0.86 (0.73–1.01)	123 (14.6)	**1.31 (1.04–1.66)**
Other factors						
Family history of diabetes						
No	8,056 (77.9)	4,810 (77.5)	2,676 (81.4)	Reference	570 (67.9)	Reference
Yes	2,279 (22.1)	1,397 (22.5)	612 (18.6)	**0.82 (0.73–0.92)**	270 (32.1)	**1.53 (1.28–1.82)**
Baseline FPG (mean ± SD)	96.0 ± 10.2	97.1 ± 9.4	91.7 ± 9.5	**0.92 (0.92–0.93)**	104.5 ± 10.8	**1.07 (1.06–1.08)**
Baseline HbA_{1c} (mean ± SD)	5.8 ± 0.3	5.8 ± 0.3	5.7 ± 0.2	**0.73 (0.71–0.75)**	6.0 ± 0.3	**1.37 (1.33–1.42)**
DQI components						
Daily protein intake, % RNI						
<100	4,958 (48.1)	2,983 (48.2)	1,547 (47.2)	Reference	428 (51.1)	Reference
100–150	3,932 (38.1)	2,369 (38.2)	1,259 (38.4)	0.95 (0.86–1.05)	304 (36.3)	0.90 (0.75–1.07)
>150	1,423 (13.8)	843 (13.6)	474 (14.5)	0.94 (0.82–1.09)	106 (12.6)	1.02 (0.80–1.32)
Percentage of energy from fat						
<22.5	9,651 (93.6)	5,814 (93.8)	3,057 (93.2)	Reference	780 (93.1)	Reference
≥22.5	662 (6.4)	381 (6.2)	223 (6.8)	1.08 (0.89–1.30)	58 (6.9)	1.07 (0.78–1.47)
Percentage of energy from saturated fat						
<%	10,278 (99.7)	6,178 (99.7)	3,267 (99.6)	Reference	833 (99.4)	Reference
≥%	35 (0.3)	17 (0.3)	13 (0.4)	1.96 (0.84–4.57)	5 (0.6)	1.66 (0.55–5.02)
Daily cholesterol intake, mg						
<300	9,066 (87.9)	5,436 (87.7)	2,895 (88.3)	Reference	735 (87.7)	Reference
≥300	1,247 (12.1)	759 (12.3)	385 (11.7)	0.94 (0.81–1.09)	103 (12.3)	1.03 (0.81–1.31)
Daily whole-grain intake						
Nondaily	8,615 (83.2)	5,194 (83.5)	2,728 (82.8)	Reference	693 (82.2)	Reference
Daily	1,743 (16.8)	1,028 (16.5)	565 (17.2)	1.03 (0.91–1.17)	150 (17.8)	1.07 (0.87–1.32)
Daily vegetable intake, g						
<200	8,205 (79.6)	4,922 (79.5)	2,612 (79.6)	Reference	671 (80.1)	Reference
≥200	2,108 (20.4)	1,273 (20.5)	668 (20.4)	0.96 (0.86–1.08)	167 (19.9)	1.03 (0.84–1.25)
Daily fruit intake, g						
<200	6,640 (64.4)	3,997 (64.5)	2,059 (62.8)	Reference	584 (69.7)	Reference
≥200	3,673 (35.6)	2,198 (35.5)	1,221 (37.2)	0.99 (0.90–1.09)	254 (30.3)	0.90 (0.75–1.07)
Daily sodium intake, mg						
<2,000	4,263 (41.3)	2,553 (41.2)	1,367 (41.7)	Reference	343 (40.9)	Reference
≥2,000	6,050 (58.7)	3,642 (58.8)	1,913 (58.3)	0.95 (0.87–1.05)	495 (59.1)	1.02 (0.87–1.20)
Total DQI-K score (mean ± SD)	3.7 ± 1.3	3.7 ± 1.3	3.7 ± 1.2	0.98 (0.95–1.02)	3.7 ± 1.2	1.01 (0.95–1.08)

OR in bold denote statistical significance at the $P < 0.05$ level. RNI, reference nutrient intake. *OR adjusted for age (continuous), education, income, baseline FPG (continuous), baseline HbA_{1c} (continuous), and family history of diabetes. †Abdominal obesity was defined as a waist circumference ≥90 cm for men and ≥85 cm for women. ‡Smoking pack-year was grouped into light (0, 1–20 pack-years), moderate (20.1–40 pack-years), and heavy smokers (>40 pack-years). §Alcohol consumption was categorized into light (<0.1–19.9 g/day for men and 0.1–9.9 g/day for women), moderate (20–39.9 g/day for men and 10–19.9 g/day for women), or heavy drinkers (≥40 g/day for men and ≥20 g/day for women). ‖Diet quality was considered good if the DQI-K score was 0–3 and poor if the score was 4–9.

Normoglycemia Reversion

Compared with men, women appeared to have a higher probability of normoglycemia reversion (OR 1.32, 95% CI 1.18–1.46). Similarly, people with higher education (OR 1.22, 95% CI 1.09–1.38 for high school level; and OR 1.22, 95% CI 1.06–1.40 for college or above level) were more likely to have normoglycemia reversion. Furthermore, among the modifiable factors, BMI ≥25 kg/m^2 (OR 0.71, 95% CI 0.63–0.79), abdominal obesity (OR 0.76, 95% CI 0.68–0.85), heavy drinking (OR 0.74, 95% CI 0.60–0.91), hypertension (OR 0.71, 95% CI 0.64–0.79), and dyslipidemia (OR 0.78, 95% CI 0.70–0.85) lowered the probability of normoglycemia reversion. Similarly, a family history of diabetes (OR 0.82, 95% CI 0.73–0.92), higher baseline FPG (OR 0.92, 95% CI 0.91–0.93), and higher baseline HbA_{1c} (OR 0.73, 95% CI 0.71–0.71) also decreased the probability.

Type 2 Diabetes Progression

In the results of the sociodemographic factors, a lower probability of type 2 diabetes progression was found in women (OR 0.63 [95% CI 0.96–0.99], compared with men) and older age categories (OR 0.59 [95% CI 0.48–0.73] for the 50–59 years age group; and OR 0.56 [95% CI 0.44–0.71] for the 60–69 years age group) and participants with an education level of college or above (OR 0.69, 95% CI 0.54–0.87). Furthermore, among the modifiable-factors analyses results, a higher risk of type 2 diabetes progression was observed with BMI ≥25 kg/m^2 (OR 1.58, 95% CI 1.29–1.94), abdominal obesity (OR 1.31, 95% CI 1.11–1.55), current

Table 2—Associations between modifiable-factors score and glycemic status change

		Events at follow-up				
		Prediabetes persistence	Normoglycemia reversion		Diabetes progression	
Variable	*N* (%)	*n* (%)	*n* (%)	OR* (95% CI)	*n* (%)	OR* (95% CI)
Modifiable-factors score† (continuous; mean ± SD)	4.6 ± 1.3	4.5 ± 1.3	4.9 ± 1.2	**1.15 (1.10–1.19)**	4.1 ± 1.3	**0.88 (0.82–0.93)**
Modifiable-factors category						
Unfavorable group	4,502 (43.8)	2,850 (46.2)	1,162 (35.6)	Reference	490 (58.5)	Reference
Intermediate group	3,049 (29.7)	1,814 (29.4)	1,013 (31.1)	**1.19 (1.06–1.33)**	222 (26.5)	**0.81 (0.67–0.98)**
Favorable group	2,717 (26.5)	1,507 (24.4)	1,085 (33.3)	**1.46 (1.30–1.64)**	125 (14.9)	**0.62 (0.49–0.77)**
Modifiable-factors score, *n*‡						
0	22 (0.2)	17 (0.3)	3 (0.1)	0.38 (0.10–1.39)	2 (0.2)	0.82 (0.18–3.78)
1	110 (1.1)	71 (1.2)	13 (0.4)	**0.47 (0.25–0.90)**	26 (3.1)	**1.90 (1.10–3.30)**
2	487 (4.7)	312 (5.1)	109 (3.3)	0.78 (0.61–1.01)	66 (7.9)	1.32 (0.94–1.86)
3	1,322 (12.9)	859 (13.9)	312 (9.6)	**0.78 (0.66–0.92)**	151 (18.0)	1.20 (0.94–1.53)
4	2,561 (24.9)	1,591 (25.8)	725 (22.2)	0.90 (0.79–1.02)	245 (29.3)	1.20 (0.97–1.49)
5	3,049 (29.7)	1,814 (29.4)	1,013 (31.1)	Reference	222 (26.5)	Reference
6	2,147 (20.9)	1,217 (19.7)	827 (25.4)	**1.19 (1.05–1.35)**	103 (12.3)	**0.77 (0.59–1.00)**
7	570 (5.6)	290 (4.7)	258 (7.9)	**1.39 (1.14–1.70)**	22 (2.6)	0.71 (0.43–1.18)

OR in bold denote statistical significance at the $P < 0.05$ level. *OR adjusted for age (continuous), education, income, baseline FPG (continuous), baseline HbA_{1c}, and family history of diabetes. †All modifiable-factors score is the sum of abdominal obesity, smoking status, physical activity, alcohol consumption, diet quality, hypertension, and dyslipidemia scores. ‡All factors score was divided into three groups on the basis of tertiles scores. Scores of 0–4 were categorized as unfavorable, 5 as intermediate, and 6–7 as favorable.

smokers (OR 1.43, 95% CI 1.07–1.91), and hypertension (OR 1.26, 95% CI 1.07–1.49). Similarly, a family history of diabetes (OR 1.53, 95% CI 1.28–1.82), increase in baseline FPG (OR 1.07, 95% CI 1.06–1.08), and every 0.1 increase in baseline HbA_{1c} (OR 1.37, 95% CI 1.33–1.42) increased the risk of type 2 diabetes progression.

Modifiable-Factors Score

The results from the scoring analyses are presented in Table 2, which shows that along with the increase in modifiable-factors score, the probability for normoglycemia reversion increased (OR 1.15, 95% CI 1.10–1.19) and type 2 diabetes progression decreased (OR 0.88, 95% CI 0.82–0.93). The median score was 5, comprising 30.9% of the participants, and those who scored lower were less likely to have normoglycemia reversion and likely to have type 2 diabetes progression, whereas the opposite trend was observed for those who scored higher. Similar results were found in the categorical analysis, where the favorable group was more likely to regress to normoglycemia (OR 1.46, 95% CI 1.30–1.64) and less likely to progress to type 2 diabetes (OR 0.62, 95% CI 0.49–0.77).

Figure 2*A* shows the adjusted ORs of each component of the modifiable score for glycemic status change and indicates that of all components, hypertension (OR 1.42 [95% CI 1.28–1.58] for having hypertension compared with no presence of hypertension) had the highest probability of normoglycemia reversion and smoking status (OR 0.69 [95% CI 0.54–0.87] for currently smoking compared with currently not smoking) were associated with the highest risk of type 2 diabetes progression. Although the figure indicates that some components, such as physical activity and diet quality, have similar ORs for normoglycemia reversion and type 2 diabetes progression, Fig. 2*B* shows that there are differences in the distribution of people with favorable modifiable scores for each component. The higher the modifiable-factors score, the larger is the proportion of people with higher scores for each component (Fig. 2*B*).

Additional and Sensitivity Analyses

Of all participants in the HEXA-G recruited from phase II, only 35,570 (50.6%) had follow-up data; however, the comparisons between those with and without follow-up data using standardized differences did not show a noteworthy imbalance (Supplementary Table 2). Results from stratified analysis by sex showed that most of the ORs of changes in glycemic status were not different between men and women (Supplementary Tables 8 and 9). The variable that showed a significant difference was the educational level of college in normoglycemia reversion. The sensitivity analysis, after excluding participants with a follow-up time of <3 years, showed consistent results (Supplementary Table 10). The results of sensitivity analysis using only FPG to define the glycemic status appeared to be similar to the main analysis in terms of significance, except for sex and hypertension, which showed nonsignificant associations with diabetes progression (Supplementary Table 11). Furthermore, the result of the analysis after replacing abdominal obesity with BMI in the scoring component was also comparable to the main result of the modifiable-factor score (Supplementary Table 12).

CONCLUSIONS

Among 27,041 participants from the original study with all the needed information on FPG and HbA_{1c}, 10,358 participants (37.8%) were defined as having prediabetes and were included in our study. Using only FPG, 4,443 patients (16.4%) were identified with prediabetes. Meanwhile, if only HbA_{1c} was used as the marker, 8,976 patients (33.2%) with prediabetes were identified. Therefore, using both markers increased the sensitivity of detecting individuals with prediabetes.

The results of this study suggest that most of the participants (60.1%) managed to maintain their plasma glucose

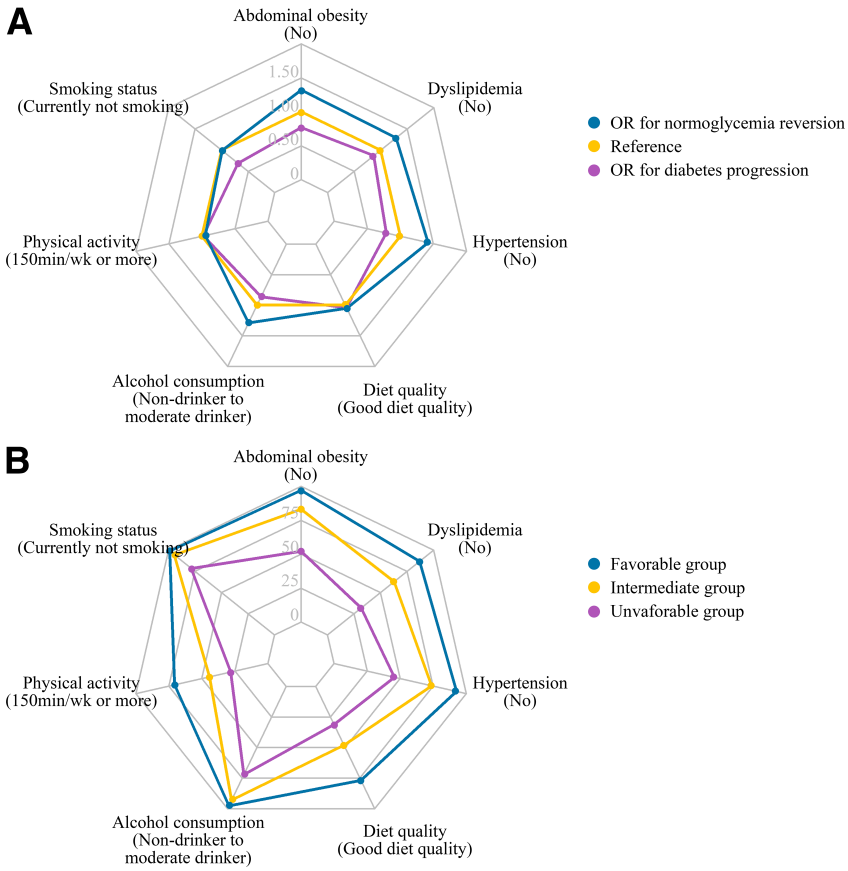

Figure 2—ORs of glycemic status change of each modifiable-factors score component and distribution of participants with a favorable score in each component. *A*) ORs of glycemic status change of each modifiable-factors score component adjusted for age (continuous), education, income, baseline FPG (continuous), baseline HbA_{1c} (continuous), and family history of diabetes. *B*) Distribution of participants with a favorable score in each component (i.e., participants who were given a score of 1 in each scoring component): no abdominal obesity: 97.1%, 83.3%, 52.2%; currently not smoking: 99.0%, 44.3%, 28.2%; 150 min/week of physical activity: 70.7%, 44.3%, 28.2%; nondrinker to moderate drinker of alcohol: 97.7%, 93.1%, 72.1%; good diet quality: 76.8%, 48.0%, 31.2%; no hypertension: 92.6%, 73.9%, 45.7%; and no dyslipidemia: 87.0%, 62.9%, 31.8% for the favorable group, intermediate group, and unfavorable groups, respectively.

levels within the prediabetes range for 4 years. Among the rest, more people showed their glycemic status regressed to normoglycemia (31.8%) than those who progressed to type 2 diabetes (8.2%). The prevalence of blood glucose transition differed depending on the indicator used. Nevertheless, previous studies analyzing prediabetes changes using cutoff points from ADA reported similar findings, suggesting that cases of regression from prediabetes to normoglycemia are more frequent (27).

In this study, older adults with prediabetes were less likely to have type 2 diabetes progression. These results were comparable with those of previous studies that examined the progression of type 2 diabetes among older adults with prediabetes (28,29). Findings from these two studies suggest that the conversion rate of diabetes progression is lower than that of normoglycemia reversion, mortality, and prediabetes persistence. Our study showed a significant negative association with type 2 diabetes progression and an inverse association with normoglycemia reversion (although no significance was found), suggesting that, rather than a change in glycemic status, older people were more likely to remain in prediabetes.

Higher education was associated with a higher possibility of normoglycemia reversion and a lower risk of developing type 2 diabetes. The sex-stratified analysis (Supplementary Table 8) indicated that the association with normoglycemia reversion was only significant among women. Although it is not clear, this finding could be explained by the effect of education on normoglycemia reversion that might be confounded by engagement in a healthy lifestyle. Particularly in our study, education was associated with the modifiable-factors score among women but not men (Supplementary Table 13). The difference then may cause the probability of normoglycemia reversion to appear disparate between men and women.

This study indicated that among the modifiable risk factors, obesity, heavy alcohol consumption, hypertension, and dyslipidemia were associated with a lower possibility of normoglycemia reversion. In contrast, obesity, current smoking, and hypertension increased the risk of type 2 diabetes. Consistent with findings of previous studies, high BMI and waist circumference–defined abdominal obesity were inversely associated with reversion to normoglycemia (14,27,30) and positively associated with progression to diabetes (30,31). The presence of hypertension was associated with a lower possibility of normoglycemia reversion and a higher possibility of type 2 diabetes progression. Authors of a previous study reported a similar finding that showed a lower likelihood of reversion to normoglycemia among people with hypertension, using the same definition of glycemic status that we used in the present study (27). Furthermore, other previous studies using the ADA criteria of HbA_{1c}-defined prediabetes likewise found that hypertension in people with prediabetes increased the risk of developing type 2 diabetes mellitus (31,32), especially those whose HbA_{1c} values were higher (32).

A healthy lifestyle is beneficial for preventing diseases. Previous studies have shown that adherence to a healthier lifestyle is associated with a lower risk of developing type 2 diabetes (33,34). Correspondingly, the findings of the present study also imply that individuals who adhered to more healthy or favorable modifiable factors were less likely to progress to diabetes. To our knowledge, no study has reported the association of lifestyle or modifiable-factors scores with reversion to normoglycemia among people with prediabetes. As for the findings from the present study, people with prediabetes who had more favorable modifiable factors had a higher possibility of normoglycemia reversion. The results were consistent when either abdominal obesity or BMI was considered as one of the scoring components, indicating that either of these variables can be used to evaluate adherence to lifestyle factors or modifiable risk factors

to promote normoglycemia reversion and prevent type 2 diabetes.

The strength of this study is that it was based on a large prospective study among the Korean population and included a scoring analysis of modifiable factors for normoglycemia reversion from prediabetes. However, this study had some limitations. First, the follow-up rate of participants in phase II was low (50.6%), which caused a large number of participants to be excluded from the study. However, our analysis indicated that those with follow-up data did not differ from those without follow-up data in terms of the measured characteristics critical to this study. Second, because some parts of the data were collected using a self-report questionnaire, there could be a possibility of bias in the collected information. Third, information regarding medication type was not assessed; thus, it was not possible to see the role of any type of medication in the glycemic status change among participants. However, people with a history of being diagnosed with diabetes by a physician were excluded from the study participants and this minimized the effect of diabetes medication use by participants in altering glycemic status change. Fourth, owing to the availability of biomarker information, the glycemic status in this study was only defined by two parameters. The oral glucose tolerance test results were not collected in the original cohort study; therefore, there could be other individuals with prediabetes who were not included. More studies regarding the glycemic status change among people with prediabetes are recommended to perform a wider range of analyses using all the markers of glycemic status definitions to provide more detailed evidence that could be useful in the future. A study to examine more comprehensive associations between sociodemographic factors and normoglycemia reversion is also suggested.

Conclusion

This study observed associations between modifiable risk factors and normoglycemia reversion, as well as type 2 diabetes progression, among people with prediabetes. The results showed that most participants remained in the prediabetes level at follow-up. Having more favorable modifiable factors was associated with a higher probability of returning to normoglycemia and a lower probability of progression to type 2 diabetes. These findings can be used as evidence to encourage the public, especially individuals with prediabetes, to engage in a healthier lifestyle and manage their weight and body composition, blood pressure, and lipid profiles to promote glycemic status reversion to the normal range and prevent type 2 diabetes progression.

Funding. This work was supported by the Ministry of Education of the Republic of Korea and the National Research Foundation of Korea (grants NRF-2018R1A2A3075397 and NRF-2022R1A2B5B01002471) and Korea Centers for Disease Control and Prevention (grants 2004-E71004-00, 2005-E71011-00, 2005-E71009-00, 2006-E71001-00, 2006-E71004-00, 2006-E71010-00, 2006-E71003-00, 2007-E71004-00, 2007-E71006-00, 2008-E71006-00, 2008-E71008-00, 2009-E71009-00, 2010-E71006-00, 2011-E71006-00, 2012-E71001-00, 2013-E71009-00, 2018-P7106-00, and 2021-E0608-00).

Duality of Interest. No potential conflicts of interest relevant to this article were reported.

Author Contributions. S.N. contributed to the study concept and design, data analysis and interpretation, manuscript drafting, and discussion. J.E.K., J.C., and J.P. contributed to data acquisition and discussion. A.S., S.-A.L., J.-k.L., and D.K. contributed to the article discussion. J.-Y.C. contributed to the study concept and design, manuscript drafting, and discussion, and is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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