

Supplemental Material

Prediabetes diagnosis is associated with the progression of coronary artery calcification: the Kangbuk Samsung Health Study

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Supplemental Table S1. Odds ratios* (95% CI) of coronary artery calcification by ADA fasting glucose and HbA1c clinical categories at baseline (n = 146,436)

Coronary artery calcium score ratios	Normoglycemia FG < 100 HbA1c < 5.7	Prediabetes		
		Discordance FG 100–125 mg/dl HbA1c < 5.7%	Discordance FG < 100 mg/dl HbA1c 5.7–6.4%	Concordance FG 100–125 mg/dl, HbA1c 5.7–6.4%
Total number	81,102	21,239	24,050	20,045
CAC > 0 (%)	8.9	13.9	14.8	21.4
Age and sex adjusted model	1.00 (reference)	1.16 (1.10–1.22)	1.25 (1.19–1.31)	1.47 (1.41–1.54)
Multivariable adjusted model	1.00 (reference)	0.99 (0.94–1.04)	1.08 (1.03–1.13)	1.10 (1.05–1.16)

*Estimated from binomial logistic regression models

The multivariable model was adjusted for age and sex. Model 2: Model 1 plus adjustments for center; year of screening examination; smoking status; alcohol intake; physical activity level; education level; total energy intake; family history of CVD; dyslipidemia medication; BMI; LDL-C, HDL-C, and triglyceride levels; and SBP at baseline.

ADA, American Diabetes Association, CAC, coronary artery calcification; FG, fasting glucose; HbA1c, glycated hemoglobin; CVD, cardiovascular disease; SBP, systolic blood pressure

Supplemental Table S2. Coronary artery calcium score ratios^a (95% CI) by ADA fasting glucose and HbA1c clinical categories at baseline (n = 146,436)

Coronary artery calcium score ratios	Normoglycemia FG < 100 HbA1c < 5.7	Prediabetes		
		Discordance FG 100–125 mg/dl HbA1c < 5.7%	Discordance FG < 100 mg/dl HbA1c 5.7–6.4%	Concordance FG 100–125 mg/dl, HbA1c 5.7–6.4%
Total number	81,102	21,239	24,050	20,045
CAC > 0 (%)	8.9	13.9	14.8	21.4
Age and sex adjusted model	1.00 (reference)	1.41 (1.26–1.58)	1.65 (1.48–1.83)	2.51 (2.26–2.79)
Multivariable adjusted model	1.00 (reference)	0.99 (0.88–1.11)	1.18 (1.06–1.32)	1.28 (1.15–1.42)

* Estimated from robust Tobit regression models used with natural log(CAC + 1) as the outcome

The multivariable model was adjusted for age and sex. Model 2: Model 1 plus adjustments for center; year of screening examination; smoking status; alcohol intake; physical activity level; education level; total energy intake; family history of CVD; dyslipidemia medication; BMI; LDL-C, HDL-C, and triglyceride levels; and SBP at baseline.

ADA, American Diabetes Association, CAC, coronary artery calcification; CVD, cardiovascular disease; FG, fasting glucose; HbA1c, glycated hemoglobin; SBP, systolic blood pressure

Supplemental Table S3. Geometric mean CAC score at baseline and next visit of coronary artery calcification scores by ADA fasting glucose and HbA1c clinical categories at baseline by CAC score categories

Geometric mean CAC score (95% CI)	Normoglycemia FG < 100 mg/dl HbA1c < 5.7%	Prediabetes		
		Discordance FG 100–125 mg/dl HbA1c < 5.7%	Discordance FG < 100 mg/dl HbA1c 5.7–6.4%	Concordance FG 100–125 mg/dl, HbA1c 5.7–6.4%
CAC score 0, number	17,523	4,446	6,854	5,309
At baseline (visit 1)	0	0	0	0
At next visit (visit 2)	0.15 (0.14, 0.16)	0.21 (0.18, 0.23)	0.20 (0.18, 0.22)	0.28 (0.25, 0.30)
CAC score 1-100, number	2,482	896	1,240	1,317
At baseline (visit 1)	12.35 (11.77, 12.96)	12.58 (11.62, 13.62)	12.35 (11.50, 13.25)	13.34 (12.47, 14.25)
At next visit (visit 2)	21.52 (20.41, 22.68)	22.49 (20.61, 24.54)	21.90 (20.23, 23.69)	24.02 (22.27, 25.91)
CAC score 101-300, number	286	136	179	208
At baseline (visit 1)	157.00 (151.71, 162.47)	157.30 (149.05, 166.00)	162.61 (155.20, 170.36)	158.31 (151.73, 165.17)
At next visit (visit 2)	202.51 (190.37, 215.41)	196.79 (176.76, 219.08)	206.81 (185.69, 230.31)	215.94 (203.12, 229.56)
CAC score >300, number	64	39	47	74
At baseline (visit 1)	492.93 (439.16, 553.27)	490.56 (423.2, 568.61)	513.31 (447.21, 589.16)	572.58 (514.07, 637.75)
At next visit (visit 2)	452.67 (316.75, 646.72)	642.10 (552.76, 745.86)	558.00 (445.83, 698.33)	715.70 (637.53, 803.44)

ADA, American Diabetes Association, CAC, coronary artery calcification; FG, fasting glucose; HbA1C, glycated hemoglobin

Supplementary Table S4. Conversion to normoglycemia among different prediabetes groups

Conversion to normoglycemia during the follow-up	Prediabetes		
	Discordance FG 100–125 mg/dl HbA1c <5.7% (n=5517)	Discordance FG <100 mg/dl HbA1c 5.7–6.4% (n=8320)	Concordance FG 100–125 mg/dl, HbA1c 5.7–6.4% (n=6908)
no	2062	3178	864
%	37.4	38.2	12.5

Supplementary Table S5. The change in glycemic status at the 1st follow-up visit among different prediabetes groups

Changing status at 1 st follow-up visit	Normoglycemia FBG < 100 mg/dl HbA1c < 5.7% (n=20355)	Prediabetes		
		Discordance FG 100–125 mg/dl HbA1c < 5.7% (n=5517)	Discordance FG < 100 mg/dl HbA1c 5.7–6.4% (n=8320)	Concordance FG 100–125 mg/dl, HbA1c 5.7–6.4% (n=6908)
Normoglycemia	71.2	33.2	34.2	10.2
Isolated-glucose prediabetes	16.4	44.1	10.7	14.1
Isolated-HbA1c prediabetes	7.5	6.2	30.9	47.6
Concordant prediabetes	3.9	14.0	21.4	47.6
Diabetes	0.9	2.6	2.8	13.0

Two patients had missing glycemic status at 1st follow-up (one each in the normoglycemia and concordant prediabetes categories).

Based on glycemic status at the 1st follow-up visit, glycemic status was classified as normoglycemia (FBG level <100 mg/dl and HbA1c level <5.7%), isolated-glucose prediabetes (FBG level 100–125 mg/dl, and HbA1c level <5.7%), isolated-HbA1c prediabetes (FBG level <100 mg/dl and HbA1c level 5.7–6.4%), prediabetes meeting both the FBG and HbA1c criteria (FBG level 100–125 mg/dl and HbA1c level 5.7–6.4%), and diabetes. Diabetes mellitus was defined as glucose-lowering medication use or fasting hyperglycemia based on either serum glucose of ≥ 126 mg/dL or glycated hemoglobin of $\geq 6.5\%$.

Supplemental Table S6. Ratios* (95% CI) of annual progress rates of coronary artery calcium scores by ADA fasting glucose and HbA1c clinical categories at baseline after excluding incident diabetes during follow-up (N=41,100)

ADA HbA1c concentration	Normoglycemia FBG <100 mg/dl HbA1c <5.7 %	Prediabetes		
		Discordance FBG 100–125 mg/dl HbA1c <5.7 %	Discordance FBG <100 mg/dl HbA1c 5.7–6.4 %	Concordance FBG 100–125 mg/dl HbA1c 5.7–6.4 %
Overall				
Number	20,355	5,517	8,320	6,908
Annual rates of CAC progression	1.061 (1.058–1.064)	1.090 (1.083–1.097)	1.082 (1.077–1.088)	1.110 (1.103–1.117)
Ratio of annual progression rate				
Model 1	1.000 (reference)	1.027 (1.020–1.034)	1.020 (1.014–1.026)	1.046 (1.039–1.053)
Model 2	1.000 (reference)	1.032 (1.024–1.040)	1.025 (1.018–1.031)	1.054 (1.046–1.061)
CAC = 0 at baseline				
Number	17,523	4,446	6,854	5,309
Annual rates of CAC progression	1.042 (1.040–1.045)	1.064 (1.057–1.071)	1.057 (1.052–1.062)	1.079 (1.072–1.086)
Ratio of annual progression rate				
Model 1	1.000 (reference)	1.021 (1.014–1.028)	1.014 (1.008–1.020)	1.035 (1.028–1.043)
Model 2	1.000 (reference)	1.024 (1.016–1.032)	1.016 (1.010–1.023)	1.041 (1.033–1.049)
CAC > 0 at baseline				
Number	2,832	1,071	1,466	1,599
Annual rates of CAC progression	1.210 (1.199–1.222)	1.230 (1.211–1.250)	1.223 (1.208–1.239)	1.233 (1.217–1.249)
Ratio of annual progression rate				
Model 1	1.000 (reference)	1.017 (0.998–1.036)	1.011 (0.995–1.027)	1.019 (1.003–1.036)
Model 2	1.000 (reference)	1.021 (1.001–1.041)	1.014 (0.997–1.032)	1.023 (1.005–1.041)

*Annual CAC progression rates and ratios were estimated from mixed models with random intercepts and slopes with natural log(CAC + 1) as the outcome and inverse probability weighting

Multivariable model 1 was adjusted for age at baseline and sex. Model 2 was adjusted for smoking status; alcohol intake; physical activity level; total energy intake; dyslipidemia medication; BMI; LDL-C, HDL-C, and triglyceride levels; and SBP as time-dependent variables and age at baseline, sex, center, year of screening examination, education level, and family history of CVD as time-fixed variables.

ADA, American Diabetes Association, CAC, coronary artery calcification; CVD, cardiovascular disease; FG, fasting glucose; HbA1c, glycated hemoglobin; SBP, systolic blood pressure

Supplemental Table S7. Geometric mean CAC score at baseline and next visit of coronary artery calcification scores by ADA fasting glucose and HbA1c clinical categories at baseline by age and sex

Geometric mean CAC score (95% CI)	Normoglycemia FG < 100 mg/dl HbA1c < 5.7%	Prediabetes		
		Discordance FG 100–125 mg/dl HbA1c < 5.7%	Discordance FG < 100 mg/dl HbA1c 5.7–6.4%	Concordance FG 100–125 mg/dl, HbA1c 5.7–6.4%
Men aged <40 at baseline, number	8,554	2,082	2,938	2,001
At baseline (visit 1)	0.21 (0.19, 0.23)	0.22 (0.18, 0.27)	0.24 (0.2, 0.28)	0.33 (0.27, 0.38)
At next visit (visit 2)	0.41 (0.38, 0.44)	0.45 (0.38, 0.52)	0.52 (0.45, 0.58)	0.68 (0.59, 0.77)
Men aged 40-49 at baseline, number	8,361	2,747	3,728	3,682
At baseline (visit 1)	0.77 (0.72, 0.82)	0.99 (0.89, 1.10)	0.88 (0.80, 0.97)	1.10 (1.00, 1.21)
At next visit (visit 2)	1.26 (1.18, 1.33)	1.70 (1.54, 1.87)	1.49 (1.36, 1.62)	1.98 (1.82, 2.15)
Men aged ≥50 at baseline, number	939	429	542	758
At baseline (visit 1)	3.97 (3.39, 4.63)	7.27 (5.76, 9.13)	6.6 (5.34, 8.12)	6.59 (5.52, 7.84)
At next visit (visit 2)	5.9 (5.04, 6.87)	10.82 (8.57, 13.59)	9.96 (8.07, 12.23)	10.06 (8.42, 11.99)
Women aged <40 at baseline, number	1,007	76	309	100
At baseline (visit 1)	0.04 (0.02, 0.07)	0.06 (-0.02, 0.14)	0.06 (0.02, 0.11)	0.06 (-0.02, 0.16)
At next visit (visit 2)	0.06 (0.03, 0.09)	0.13 (-0.02, 0.31)	0.12 (0.05, 0.19)	0.13 (-0.01, 0.28)
Women aged 40-49 at baseline, number	1,296	147	592	256
At baseline (visit 1)	0.15 (0.11, 0.20)	0.12 (0.02, 0.23)	0.12 (0.07, 0.18)	0.22 (0.11, 0.35)
At next visit (visit 2)	0.24 (0.18, 0.30)	0.26 (0.10, 0.43)	0.24 (0.16, 0.32)	0.47 (0.29, 0.69)
Women aged ≥50 at baseline, number	198	36	211	111
At baseline (visit 1)	0.83 (0.50, 1.23)	0.95 (0.10, 2.43)	2.08 (1.41, 2.93)	2.51 (1.47, 3.99)
At next visit (visit 2)	1.15 (0.74, 1.67)	1.45 (0.31, 3.61)	2.89 (1.97, 4.10)	3.45 (2.02, 5.56)

ADA, American Diabetes Association, CAC, coronary artery calcification; FG, fasting glucose; HbA1C, glycated hemoglobin