

White matter hyperintensity volume in prediabetes, diabetes and normoglycemia

Supplemental material

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Supplementary Tables:

Supplementary Table 1

		Participants with prediabetes vs. normoglycemic control participants		Participants with diabetes vs. normoglycemic control participants		Participants with prediabetes vs. participants with diabetes	
		IRR (95% CI)	p-value	IRR (95% CI)	p-value	IRR (95% CI)	p-value
WMH volume	A	2.16 (1.49; 3.13)	<0.001	2.67 (1.71; 4.18)	<0.001	0.81 (0.49; 1.33)	0.396
	B	1.84 (1.26; 2.67)	0.001	1.96 (1.23; 3.12)	0.005	0.94 (0.59; 1.5)	0.789
	C	1.76 (1.20; 2.57)	0.004	1.55 (0.95; 2.53)	0.077	1.13 (0.71; 1.81)	0.605

Supplementary Table 1: Difference in WMH volume between participants with diabetes, participants with prediabetes and normoglycemic controls **in individuals with WMH (N=249)**. IRRs are from negative binomial regression models. **A:** unadjusted. **B:** adjusted for age, gender. **C:** adjusted for age, gender, hypertension, LDL-C, BMI, smoking, alcohol consumption.

Supplementary Table 2

		Participants with prediabetes vs. normoglycemic control participants		Participants with diabetes vs. normoglycemic control participants		Participants with prediabetes vs. participants with diabetes	
		IRR (95% CI)	p-value	IRR (95% CI)	p-value	IRR (95% CI)	p-value
WMH volume	A	1.45 (1.00; 2.09)	0.047	2.39 (1.47; 3.90)	<0.001	0.60 (0.37; 0.98)	0.041
	B	1.20 (0.82; 1.75)	0.351	1.59 (0.95; 2.66)	0.075	0.75 (0.48; 1.18)	0.215
	C	1.19 (0.81; 1.76)	0.379	1.38 (0.81; 2.36)	0.242	0.86 (0.55; 1.36)	0.529

Supplementary Table 2: Association of diabetes status with WMH volume **applying the definition of prediabetes and diabetes of the American Diabetes Association instead of the definition of the World Health Organization / International Diabetes Federation.** IRRs are from zero-inflated negative binomial regression models. **A:** unadjusted. **B:** adjusted for age, gender. **C:** adjusted for age, gender, hypertension, LDL-C, BMI, smoking, alcohol consumption.

Supplementary Table 3

		2-hour glucose (N=223)		Fasting glucose (N=249)		HbA1c (N=249)	
		IRR (95% CI)	p-value	IRR (95% CI)	p-value	IRR (95% CI)	p-value
WMH volume	A	1.01 (1.01; 1.02)	<0.001	1.00 (0.99; 1.01)	0.699	2.00 (1.38; 2.88)	<0.001
	B	1.01 (1.00; 1.01)	<0.001	1.00 (1; 1.01)	0.453	1.38 (1.05; 1.80)	0.019
	C	1.01 (1.00; 1.01)	<0.001	1.00 (1; 1.01)	0.590	1.20 (0.98; 1.46)	0.074

Supplementary Table 3: Association of 2-hour glucose, fasting glucose and HbA1c with WMH volume in individuals with WMH (N=249). Oral glucose tolerance test (OGTT). IRRs are from negative binomial regression models. **A:** unadjusted. **B:** adjusted for age, gender. **C:** adjusted for age, gender, hypertension, LDL-C, BMI, smoking, alcohol consumption.

Supplementary Table 4

		2-hour glucose (N=354)		Fasting glucose (N=354)		HbA1c (N=354)	
		IRR (95% CI)	p-value	IRR (95% CI)	p-value	IRR (95% CI)	p-value
WMH volume	A	1.01 (1.01; 1.02)	<0.001	1.00 (0.99; 1.02)	0.641	3.99 (2.64; 6.01)	<0.001
	B	1.01 (1.00; 1.01)	<0.001	1.00 (0.99; 1.01)	0.935	2.60 (1.73; 3.91)	<0.001
	C	1.01 (1; 1.01)	<0.001	1.00 (0.99; 1.02)	0.886	1.94 (1.22; 3.07)	0.005

Supplementary Table 4: Association of 2-hour glucose, fasting glucose and HbA1c with WMH volume **in individuals who have received an OGTT (N=354)**. Oral glucose tolerance test (OGTT). IRRs are from zero-inflated negative binomial regression models. **A:** unadjusted. **B:** adjusted for age, gender. **C:** adjusted for age, gender, hypertension, LDL-C, BMI, smoking, alcohol consumption.

Supplementary Table 5

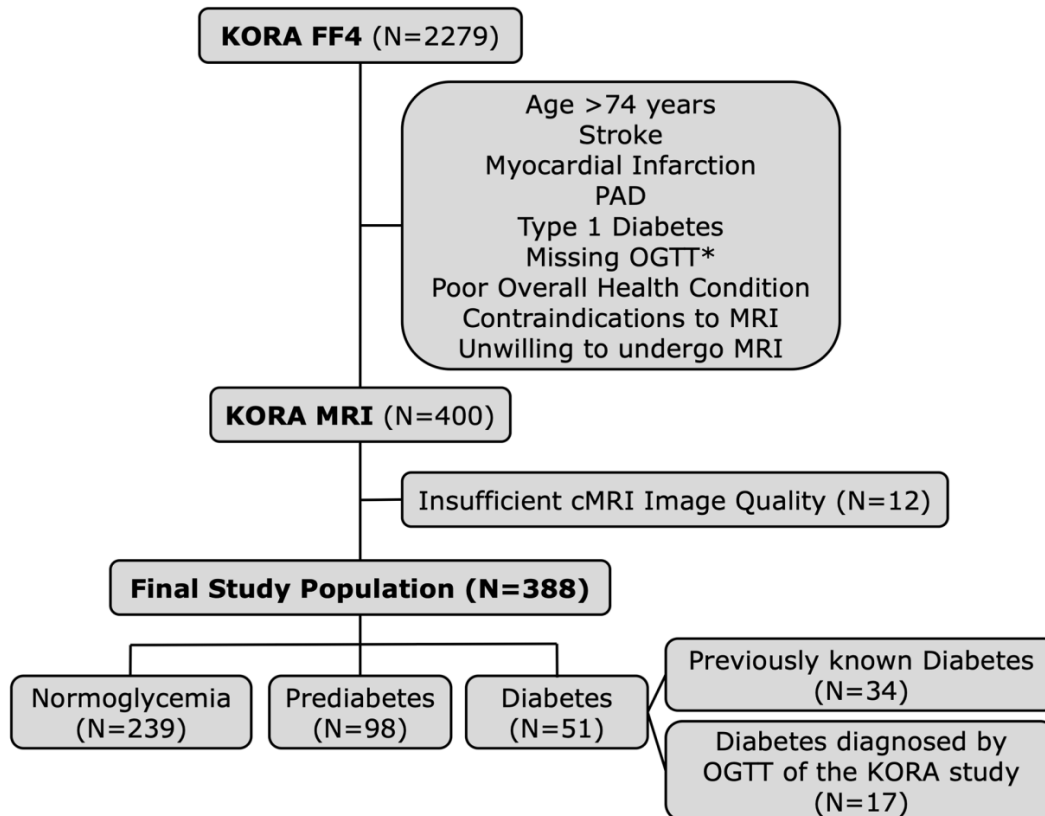
		Isolated IGT (N=44)		Isolated IFG (N=37)		Combined IGT/IFG (N=17)	
		IRR (95% CI)	p-value	IRR (95% CI)	p-value	IRR (95% CI)	p-value
WMH volume	A	2.63 (1.6; 4.34)	<0.001	1.36 (0.79; 2.36)	0.269	2.51 (1.28; 4.92)	0.007
	B	2.67 (1.62; 4.38)	<0.001	1.49 (0.88; 2.52)	0.134	1.54 (0.81; 2.91)	0.188
	C	2.59 (1.56; 4.32)	<0.001	1.69 (0.99; 2.87)	0.052	1.87 (0.96; 3.64)	0.064

Supplementary Table 5: Association of isolated IGT, isolated IFG and combined IGT/IFG with WMH volume. Impaired glucose tolerance (IGT). Impaired fasting glucose (IFG). IRRs are from zero-inflated negative binomial regression models. **A:** unadjusted. **B:** adjusted for age, gender. **C:** adjusted for age, gender, hypertension, LDL-C, BMI, smoking, alcohol consumption.

Supplementary Table 6

	Isolated IGT (N=44)	Isolated IFG (N=37)	Combined IGT/IFG (N=17)	p-value*
WMH	30 (68.2%)	24 (64.9%)	15 (88.2%)	0.198
WMH volume (mm³)	3064.6 (±6732.5)	1511.9 (±3642.6)	3780.9 (±7537.7)	0.338
Age (years)	58.3 (±9.1)	57.4 (±8.6)	61.1 (±8.6)	0.352
Male gender	29 (65.9%)	24 (64.9%)	9 (52.9%)	0.621
BMI (kg/m²)	30.9 (±4.8)	29.5 (±4.7)	31.2 (±4.4)	0.288
Hypertension^o	18 (40.9%)	16 (43.2%)	10 (58.8%)	0.437
Systolic BP (mmHg)	125.3 (±16.5)	120.1 (±13.8)	128.8 (±11.8)	0.101
Diastolic BP (mmHg)	79.1 (±9.2)	75.2 (±10.2)	79.2 (±9.2)	0.149
Total cholesterol (mg/dl)	226.1 (±32.4)	215.7 (±29.9)	229.9 (±28.3)	0.189
HDL (mg/dl)	56.3 (±12.4)	61.9 (±16.2)	57.7 (±12.2)	0.189
LDL-C (mg/dl)	148.7 (±27.5)	135.3 (±31.6)	150 (±26.3)	0.078
Triglycerides (mg/dl)	158.8 (±71.2)	132.6 (±67.2)	174.1 (±123)	0.163
HbA1c (%)	5.51 (±0.32)	5.52 (±0.28)	5.81 (±0.38)	0.003
Fasting serum glucose (mg/dl)	97.4 (±7.3)	114.4 (±3.6)	114.6 (±4.2)	<0.001
Glucose after 2-hour OGTT (mg/dl)	157.7 (±14.8)	108.8 (±18.9)	164.8 (±16)	<0.001

Supplementary Table 6: Characteristics of the study population stratified by IGT and IFG. Impaired glucose tolerance (IGT). Impaired fasting glucose (IFG). Data are means and standard deviations for continuous variables and counts and percentages for categorical variables. *p-values are from one-way ANOVA and χ^2 -test, respectively. ^oHypertension was defined as systolic blood pressure ≥ 140 mmHg, diastolic blood pressure ≥ 90 mmHg and/or use of antihypertensive medication, given that the individuals were aware of being hypertensive.

Supplementary Figures:**Supplementary Figure 1**

Supplementary Figure 1: Participant flow diagram. *Unless type 2 diabetes was diagnosed by a physician before entering the KORA FF4 study (N=34).