

## 1. Background

Impaired glucose regulation (IGR) is associated with detrimental cardiovascular outcomes such as cardiovascular disease risk factors (CVD risk factors) or intima-media thickness (IMT). Our aim was to examine whether these associations are mediated by body mass index (BMI), waist circumference (waist) or fasting serum insulin (insulin) in a population in the African region.

## 2. Methods

Major CVD risk factors (systolic blood pressure, smoking, LDL-cholesterol, HDL-cholesterol,) were measured in a random sample of adults aged 25-64 in the Seychelles (n=1255, participation rate: 80.2%). According to the criteria of the American Diabetes Association, IGR was divided in four ordered categories: 1) normal fasting glucose (NFG), 2) impaired fasting glucose (IFG) and normal glucose tolerance (IFG/NGT), 3) IFG and impaired glucose tolerance (IFG/IGT), and 4) diabetes mellitus (DM). Carotid and femoral IMT was assessed by ultrasound (n=496).



Age-adjusted levels of the major CVD risk factors worsened gradually across IGR categories (NFG < IFG/NGT < IFG/IGT < DM), particularly HDL-cholesterol and blood pressure (p for trend <0.001). These relationships were marginally attenuated upon further adjustment for waist, BMI or insulin (whether considered alone or combined) and most of these relationships remained significant. With regards to IMT, the association was null with IFG/NGT, weak with IFG/IGT and stronger with DM (all more markedly at femoral than carotid levels). The associations between IMT and IFG/IGT or DM (adjusted by age and major CVD risk factors) decreased only marginally upon further adjustment for BMI, waist or insulin. Further adjustment for family history of diabetes did not alter the results.

## 3. Results

Variable	NFG	IFG / NGT	IFG / IGT	DM	z-trend*
<b>Men</b>					
Clinical and metabolic data (n)	316	98	73	81	
Age (years)	42.5 ± 0.6	45.1 ± 0.9	49.3 ± 1.1	52.7 ± 1.0	8.1
Body mass index (kg/m <sup>2</sup> )	24.6 ± 0.3	26.6 ± 0.4	26.6 ± 0.5	27.7 ± 0.6	5.9
Waist circumference (cm)	85.8 ± 0.6	92.5 ± 1.0	93.0 ± 1.4	97.5 ± 1.3	8.2
Serum fasting insulin (pmol/l)	10.8 ± 0.4	14.2 ± 0.8	19.8 ± 2.4	20.9 ± 2.1	7.8
Triglycerides (mmol/l)	0.97 ± 0.03	1.20 ± 0.07	1.56 ± 0.19	1.76 ± 0.17	6.9
LDL cholesterol (mmol/l)	3.42 ± 0.07	3.60 ± 0.13	3.83 ± 0.14	3.75 ± 0.17	2.5
HDL cholesterol (mmol/l)	1.42 ± 0.03	1.29 ± 0.05	1.27 ± 0.06	1.20 ± 0.05	-3.8
Systolic blood pressure (mmHg)	127 ± 0.9	132 ± 1.6	137 ± 1.9	145 ± 2.3	8.0
Mean intima-media thickness (n)	104	46	48	50	
Carotid (mm)	0.72 ± 0.01	0.71 ± 0.02	0.78 ± 0.03	0.75 ± 0.02	2.4
Femoral (mm)	0.93 ± 0.06	0.92 ± 0.09	1.20 ± 0.10	1.41 ± 0.13	5.2
Total (mm)	0.76 ± 0.02	0.82 ± 0.04	0.90 ± 0.03	1.04 ± 0.04	4.9
<b>Women</b>					
Clinical and metabolic data (n)	480	47	77	103	
Age (years)	41.4 ± 0.5	52.1 ± 1.4	50.1 ± 1.0	54.4 ± 0.8	11.9
Body mass index (kg/m <sup>2</sup> )	27.1 ± 0.3	31.5 ± 0.9	31.8 ± 0.7	31.8 ± 0.5	8.4
Waist circumference (cm)	86.7 ± 0.6	100.1 ± 2.1	97.4 ± 1.4	101.5 ± 1.1	10.7
Serum fasting insulin (pmol/l)	13.8 ± 0.4	21.1 ± 1.9	19.4 ± 1.4	25.4 ± 2.1	8.4
Triglycerides (mmol/l)	0.82 ± 0.02	1.07 ± 0.08	1.10 ± 0.1	1.35 ± 0.08	8.8
LDL cholesterol (mmol/l)	3.44 ± 0.05	4.11 ± 0.19	3.81 ± 0.14	4.20 ± 0.14	5.8
HDL cholesterol (mmol/l)	1.40 ± 0.02	1.32 ± 0.05	1.28 ± 0.0	1.21 ± 0.04	-5.0
Systolic blood pressure (mmHg)	120 ± 0.7	137 ± 3.8	138 ± 2.1	139 ± 1.9	10.3
Mean intima-media thickness (n)	155	30	45	76	
Carotid (mm)	0.69 ± 0.01	0.75 ± 0.02	0.74 ± 0.04	0.84 ± 0.03	5.6
Femoral (mm)	0.71 ± 0.03	0.88 ± 0.09	0.84 ± 0.06	1.16 ± 0.07	6.5
Total (mm)	0.76 ± 0.02	0.82 ± 0.04	0.90 ± 0.03	1.04 ± 0.04	7.4
<b>Overall</b>					
Clinical and metabolic data (n)	776	145	150	184	
Age (years)	41.8 ± 0.4	47.4 ± 0.8	49.7 ± 0.7	53.7 ± 0.6	14.3
Body mass index (kg/m <sup>2</sup> )	26.0 ± 0.2	27.8 ± 0.4	29.0 ± 0.5	29.7 ± 0.4	9.5
Waist circumference (cm)	86.3 ± 0.4	94.3 ± 1.0	95.1 ± 1.0	99.5 ± 0.9	13.4
Serum fasting insulin (pmol/l)	12.5 ± 0.3	15.9 ± 0.8	19.6 ± 1.4	23.3 ± 1.5	11.1
Triglycerides (mmol/l)	0.89 ± 0.02	1.17 ± 0.05	1.35 ± 0.10	1.55 ± 0.09	11.2
LDL cholesterol (mmol/l)	3.43 ± 0.04	3.73 ± 0.11	3.82 ± 0.10	3.98 ± 0.11	5.8
HDL cholesterol (mmol/l)	1.41 ± 0.02	1.30 ± 0.04	1.27 ± 0.04	1.21 ± 0.03	-6.5
Systolic blood pressure (mmHg)	123 ± 0.6	134 ± 1.6	136 ± 1.4	142 ± 1.5	13.1
Mean intima-media thickness (n)	258	76	93	126	
Carotid (mm)	0.71 ± 0.01	0.72 ± 0.01	0.76 ± 0.02	0.80 ± 0.02	5.9
Femoral (mm)	0.81 ± 0.03	0.91 ± 0.07	1.04 ± 0.06	1.27 ± 0.07	8.3
Total (mm)	0.76 ± 0.02	0.82 ± 0.04	0.90 ± 0.03	1.04 ± 0.04	8.7

**Table 1.** Distribution of selected clinical and metabolic factors across categories of impaired glucose regulation

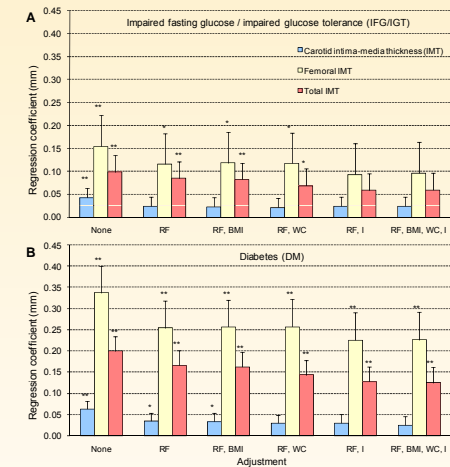
Values displayed are age-standardized means ± standard error. \*z-value for trend; all corresponding p-values <0.01.

Adjustment in addition to age and sex	IFG / NGT			IFG / IGT			DM		
	Coef.	SE	p	Coef.	SE	p	Coef.	SE	p
<b>Triglycerides (mmol/l)</b>									
None	0.19	0.07	0.01	0.39	0.07	0.00	0.59	0.07	0.00
BMI	0.14	0.07	0.05	0.33	0.07	0.00	0.52	0.07	0.00
Waist	0.10	0.07	ns	0.31	0.07	0.00	0.46	0.07	0.00
Insulin	0.15	0.07	0.03	0.29	0.07	0.00	0.48	0.08	0.00
BMI, Waist, Insulin	0.09	0.07	ns	0.25	0.07	0.00	0.41	0.08	0.00
<b>Low-density lipoprotein cholesterol (mmol/l)</b>									
None	0.26	0.11	0.02	0.29	0.12	0.02	0.39	0.12	0.00
BMI	0.19	0.11	0.09	0.21	0.12	0.07	0.30	0.12	0.01
Waist	0.15	0.11	ns	0.19	0.12	ns	0.24	0.12	0.04
Insulin	0.22	0.11	0.05	0.20	0.12	ns	0.23	0.12	0.06
BMI, Waist, Insulin	0.15	0.11	ns	0.15	0.12	ns	0.16	0.12	ns
<b>High-density lipoprotein cholesterol (mmol/l)</b>									
None	-0.14	0.04	0.00	-0.19	0.05	0.00	-0.27	0.05	0.00
BMI	-0.08	0.04	0.05	-0.12	0.04	0.01	-0.19	0.04	0.00
Waist	-0.06	0.04	ns	-0.11	0.04	0.02	-0.16	0.04	0.00
Insulin	-0.11	0.04	0.01	-0.14	0.05	0.00	-0.20	0.05	0.00
BMI, Waist, Insulin	-0.05	0.04	ns	-0.09	0.04	0.04	-0.14	0.05	0.00
<b>Systolic blood pressure (mmHg)</b>									
None	5.43	1.49	0.00	7.02	1.56	0.00	10.82	1.54	0.00
BMI	4.15	1.48	0.01	5.55	1.56	0.00	9.14	1.54	0.00
Waist	3.67	1.49	0.01	5.39	1.55	0.00	8.38	1.56	0.00
Insulin	4.57	1.50	0.00	5.72	1.59	0.00	9.48	1.64	0.00
BMI, Waist, Insulin	3.45	1.50	0.02	4.87	1.58	0.00	8.42	1.64	0.00

**Table 2.** Associations between categories of impaired glucose regulation and selected cardio-metabolic risk factors

ns: p ≥ 0.10

NFG: normal fasting glucose; IFG: impaired fasting glucose; NGT: normal glucose tolerance; IGT: impaired glucose tolerance; DM: diabetes mellitus; BMI: body mass index; waist: waist circumference; insulin: serum fasting insulin.



**Figure.** Associations between intima-media thickness (IMT) and categories of impaired glucose metabolism upon incremental adjustment for covariates (regression coefficients with their standard errors). Panel A: impaired fasting glucose / impaired glucose tolerance (IFG/IGT); Panel B: diabetes (DM).

\* p: 0.05-0.09  
\*\* p < 0.05

All associations between impaired fasting glucose / normal glucose tolerance (IFG/NGT) and IMT were statistically not significant and are thus not shown

None: no adjustment; RF: major risk factors (low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, systolic blood pressure, smoking); BMI: body mass index; WC: waist circumference; I: serum fasting insulin.

## 4. Conclusions

We found graded relationships between IGR categories and both major CVD risk factors and carotid/femoral IMT. These relationships were only partly accounted for by BMI, waist and insulin. This suggests that increased CVD-risk associated with IGR is also mediated by factors other than the considered markers of adiposity and insulin resistance. The results also imply that IGR and associated major CVD risk factors should be systematically screened and appropriately managed.