Serum insulin levels are associated with plaque composition in the carotid artery

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Background: Impaired insulin and glucose levels are implicated in the etiology of cardiovascular disease, however, their influence on the formation and composition of atherosclerotic plaque remain unclear.

Methods: In 1740 participants (mean age 72.9 years, 46% women, 14.4 % diabetes mellitus) from the population-based Rotterdam Study, we assessed carotid atherosclerosis using MRI and evaluated the presence of calcification, lipid core, and intraplaque hemorrhage. All participants also underwent blood sampling to obtain information on serum insulin and glucose levels. Using logistic regression models, we assessed the association of serum insulin and glucose levels (per standard deviation (SD) and tertiles) with the different plaque components in the carotid artery, while adjusting for sex, age, and cardiovascular risk factors.

Association of serum insulin and glucose levels with carotid artery plaque composition (n=1740)

Insulin (per SD)	IPH OR (95%CI)	Lipid core OR (95%CI)	Calcification OR (95%CI)
Model 1	1.27 (1.05–1.55)	0.76 (0.63–0.90)	0.93 (0.74–1.16)
Model 2	1.39 (1.09–1.76)	0.88 (0.72–1.09)	1.05 (0.80–1.38)
Model 3	1.43 (1.14–1.81)	0.88 (0.72–1.09)	1.05 (0.80–1.38)
Glucose (per SD)			
Model 1	1.04 (0.55–1.96)	0.51 (0.29–0.91)	1.19 (0.58–2.47)
Model 2	0.49 (0.20–1.21)	1.08 (0.49–2.37)	1.22 (0.44–3.34)
Model 3	0.48 (0.19–1.19)	1.10 (0.50–2.41)	1.18 (0.43–3.24)

Odds ratio (OR), given with a 95% confidence interval (CI), express the relationship between serum insulin and glucose (per SD increment) with intraplaque hemorrhage (IPH), lipid core and calcification. Model 1 = adjusted for sex, age, intima-media thickness and time difference between insulin and glucose measurements and MRI scan. Model 2 = model 1 + smoking, high-density lipoprotein, total cholesterol, systolic and diastolic blood pressure, body mass index, use of antihypertensive medication and *glucose or †insulin levels. Model 3 = model 2 + use of lipid lowering medication, vitamin K antagonists and antiplatelet agents.

Conclusions: Higher serum insulin levels are associated with the presence of intraplaque hemorrhage, and with a lower frequency of lipid core in carotid atherosclerosis. These findings suggest a complex role for serum insulin in the pathophysiology of carotid atherosclerosis and in plaque vulnerability.

Results: High serum insulin levels were associated with a higher presence of intraplaque hemorrhage [adjusted odds ratio (OR) per 1-SD increase: 1.27 (95% confidence interval (CI) 1.05–1.55)] and with a lower presence of lipid core [adjusted OR: 0.76 (95%CI: 0.63–0.90)]. We found no association with the presence of calcification. We found similar results when investigating insulin categories. Sensitivity analyses in individuals free of diabetes mellitus yield similar results. No association was found between serum glucose and any of the plaque components.

Association of serum insulin and glucose levels with carotid artery plaque composition in individuals free of DM (n=1489)

Insulin (per SD)	IPH OR (95%CI)	Lipid core OR (95%CI)	Calcification OR (95%CI)
Model 1	1.32 (1.05–1.66)	0.78 (0.64–0.96)	0.98 (0.75–1.29)
Model 2	1.46 (1.12–1.90)	0.86 (0.68–1.09)	1.13 (0.82–1.56)
Model 3	1.49 (1.14–1.95)	0.87 (0.69–1.11)	1.12 (0.81–1.54)
Glucose (per SD)			
Model 1	0.71 (0.20–2.57)	0.90 (0.30–2.67)	1.31 (0.32–5.38)
Model 2	0.40 (0.10–1.54)	1.85 (0.56–6.13)	0.92 (0.20–4.28)
Model 3	0.41 (0.11–1.59)	1.86 (0.56–6.19)	0.94 (0.20–4.41)

Odds ratio (OR), given with a 95% confidence interval (CI), express the relationship between serum insulin and glucose (per SD increment) with intraplaque hemorrhage (IPH), lipid core and calcification. Model 1 = adjusted for sex, age, intima-media thickness and time difference between insulin and glucose measurements and MRI scan. Model 2 = model 1 + smoking, high-density lipoprotein, total cholesterol, systolic and diastolic blood pressure, body mass index, use of antihypertensive medication and *glucose or †insulin levels. Model 3 = model 2 + use of lipid lowering medication, vitamin K antagonists and antiplatelet agents.