A1C Is Associated With Intima-Media Thickness in Individuals With Normal Glucose Tolerance

**OBJECTIVE** — One-hour glucose during an oral glucose tolerance test (OGTT) was recently proposed as a valuable marker to identify individuals with normal glucose tolerance (NGT) and increased intima-media thickness (IMT). However, central markers of glycemic control were not considered. The aim of this study was to identify which marker of glycemic control is most informative with respect to the variation of IMT in individuals with NGT.

**RESEARCH DESIGN AND METHODS** — Cardiovascular risk factors, glucose metabolism (OGTT), and IMT were determined in 1,219 nondiabetic individuals (851 women, 368 men; 558 with NGT).

**RESULTS** — One-hour glucose and A1C levels were significantly correlated to carotid IMT in individuals with NGT, whereas fasting and 2-h glucose levels were not informative. Only A1C was associated with IMT independent of other confounders, whereas 1-h glucose was not informative. Comparable results were found in the total cohort, including individuals with IFG and IGT.

**CONCLUSIONS** — A1C was the most informative glycemic marker with respect to IMT in individuals with NGT.

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calculated to identify independent relations between potential risk factors and variation of IMT. An α-error <5% was considered to be statistically significant.

RESULTS — The 1-h glucose correlated moderately with IMT in individuals with NGT (IMTACC: $r = 0.136, P = 0.002$; IMTbulbus: $r = 0.172, P < 0.001$; IMTtotal: $r = 0.166, P < 0.001$). A stronger correlation was found between A1C and IMT in this group with NGT (IMTACC: $r = 0.310, P < 0.001$; IMTbulbus: $r = 0.238, P < 0.001$; IMTtotal: $r = 0.286, P < 0.001$). No relation was found between IMT and fasting glucose, 2-h glucose, or fasting insulin. Multivariate analysis within individuals with NGT revealed that only A1C was independently associated with IMT after adjustment for age, sex, waist, smoking, systolic blood pressure, and HDL/total cholesterol ratio. A1C contributed 4.4% to the variation of IMT. In contrast, 1-h glucose was not further informative (Table 1).

Comparable results were found in the total cohort, which also included individuals with IFG and IGT. Correlations within the crude analysis were comparable to the results in individuals with NGT (data not shown). Again, only A1C was independently associated with IMTACC and IMTtotal ($P = 0.005$ and 0.032, respectively), although only a rather small proportion (2.3%) of the IMT variation was explained. The 1-h glucose was not independently associated with IMT. Additional risk markers, which were significantly associated with IMT, were age, systolic blood pressure, smoking, and the HDL/total cholesterol ratio, depending on the model calculated. In total, the investigated risk markers explained up to 26% of the variation of IMT. None of the correlations were indicative for a threshold in the relation between IMT and 1-h glucose or A1C.

CONCLUSIONS — Numerous studies suggested that individuals with diabetes or IGT have an increased cardiovascular risk (5,6). The relation between markers of glucose metabolism and IMT in individuals with NGT is less clear. Recently, 1-h glucose was associated with increased IMT (3). The authors proposed a cutoff value for 1-h glucose of 155 mg/dl, which was suggested to be of additive information to identify individuals with NGT and increased IMT. The results of the study presented here do not support those findings. Although the crude analysis revealed moderate correlations between 1-h glucose and IMT, this relation was not confirmed after adjustment for established cardiovascular risk factors. However, A1C was more strongly correlated to IMT than 1-h glucose and was the only marker that was independently associated with IMT in individuals with NGT. Nevertheless, the informative value of A1C was also limited by explaining only ~4% of the variation of IMT. Therefore, even A1C is not helpful in the identification of individuals with NGT and increased IMT. In previous reports, some risk factors were more strongly correlated to IMTACC, whereas others related stronger to IMTbulbus (7). Interestingly, crude correlation between A1C and IMTACC tended to be stronger than that with IMTbulbus. In some contrast, 1-h glucose was slightly more strongly related to IMTbulbus. However, whether this observation has physiological relevance is unclear, and our study was not designed to address this topic.

We conclude that A1C was the most informative glycemic marker with respect to IMT in individuals with NGT. In general, this independent relation of A1C to IMT suggests that glycemic control might have a pathophysiologic relevance in the development of atherosclerosis, even in individuals with NGT.

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