INTENSIVE GLUCOSE-LOWERING THERAPY REDUCES CARDIOVASCULAR DISEASE EVENTS IN VETERANS AFFAIRS DIABETES TRIAL PARTICIPANTS WITH LOWER CALCIFIED CORONARY ATHEROSCLEROSIS.


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OBJECTIVE: This study investigated the hypothesis that baseline calcified coronary atherosclerosis may determine cardiovascular disease events in response to intensive glycemic control within the Veterans Affairs Diabetes Trial (VADT). RESEARCH DESIGN AND METHODS: At baseline, 301 type 2 diabetic participants in the VADT, a randomized trial comparing the effects of intensive versus standard glucose lowering on cardiovascular events, had baseline coronary atherosclerosis assessed by coronary artery calcium (CAC) measured by computed tomography. Participants were followed over the 7.5-year study for development of cardiovascular end points. RESULTS: During a median follow-up duration of 5.2 years, 89 cardiovascular events occurred. Although intensive glucose-lowering therapy did not significantly reduce cardiovascular events in the substudy cohort as a whole, there was evidence that the response was modified by baseline CAC, as indicated by significant P values for treatment by log(CAC + 1) interaction terms in unadjusted and multivariable-adjusted models (0.01 and 0.03, respectively). Multivariable-adjusted hazard ratios (HRs) for the effect of treatment indicated a progressive diminution of benefit with increasing CAC. Subgroup analyses were also conducted for clinically relevant CAC categories: those above and below an Agatston score of 100. Among those randomized to intensive treatment, for the subgroup with CAC >100, 11 of 62 individuals had events, while only 1 of 52 individuals with CAC < or = 100 had an event. The multivariable HR for intensive treatment for those with CAC >100 was 0.74 (95% CI 0.46-1.20; P = 0.21), while for the subgroup with CAC < or = 100, the corresponding HR was 0.08 (0.008-0.77; P = 0.03), with event rates of 39 and 4 per 1,000 person-years, respectively. CONCLUSIONS: These data indicate that intensive glucose lowering reduces cardiovascular events in those with less extensive calcified coronary atherosclerosis.