

Relationship Between Carotid Intima-Media Thickness and the Presence and Extent of Coronary Stenosis in Type 2 Diabetic Patients With Carotid Atherosclerosis but Without History of Coronary Artery Disease

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OBJECTIVE—We examined the relationship between the presence and extent of coronary stenosis and carotid intima-media thickness (CIMT) in type 2 diabetic patients without history of coronary artery disease (CAD) but with carotid atherosclerosis.

RESEARCH DESIGN AND METHODS—A total of 91 type 2 diabetic patients underwent multi-slice computed tomography coronary angiography.

RESULTS—Max-IMT in the $\geq 50\%$ stenosis group by multi-slice computed tomography coronary angiography estimation was significantly greater than the 0–25 and 25–50% stenosis group (2.68 ± 0.77 vs. 1.61 ± 0.49 mm, $P < 0.0005$, and 2.14 ± 0.81 mm, $P < 0.05$, respectively), and max-IMT in the 25–50% stenosis group was significantly greater than the 0–25% stenosis group ($P < 0.05$) after adjustment for age, sex, duration of type 2 diabetes, hypertension, and dyslipidemia. In the analysis for trend through the categories of max-IMT, as max-IMT increased, the percentage of $\geq 50\%$ stenosis increased and the percentage of 0–25% stenosis decreased.

CONCLUSIONS—Our data suggest that max-IMT might be closely associated with the extent of coronary stenosis in type 2 diabetic patients without history of CAD but with carotid atherosclerosis.

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Coronary stenosis was evaluated with selective coronary angiography, but the subjects were limited to patients with a history and/or suspicion of coronary artery disease (CAD) because of its invasiveness. Therefore, little information is available regarding the relationship

between coronary stenosis and carotid intima-media thickness (CIMT) in asymptomatic type 2 diabetic patients. Recently, multi-slice computed tomography (MSCT) coronary angiography (MSCTA) enabled us to evaluate coronary stenosis accurately and noninvasively (1–3).

In this study, we performed MSCTA in patients without a history of CAD but with carotid atherosclerosis and explored the usefulness of CIMT measurement in screening for CAD in asymptomatic type 2 diabetic patients for which a useful strategy remains uncertain and controversial (4–8).

RESEARCH DESIGN AND METHODS

Study population

Among 169 type 2 diabetic inpatients in Osaka University Medical Hospital whose max-IMT was ≥ 1.1 mm and who did not have a history of CAD, which was defined as documentation of medication and history of myocardial infarction, angina pectoris, and/or previous coronary intervention, 91 patients consented to undergo MSCTA. The clinical characteristics of the subjects were as follows: men 67%; age 62 ± 10 years; duration of type 2 diabetes 13 ± 9 years; smoking 56% (definition of smoking was based on a questionnaire); hypertension 56%; dyslipidemia 76%; A1C $8.3 \pm 1.7\%$; max-IMT 2.17 ± 0.83 mm; ankle-brachial pressure index (ABPI) 1.07 ± 0.14 ; and brachial-ankle pulse wave velocity (baPWV) $1,770 \pm 394$ (cm/s).

CIMT measurement

CIMT was measured using an echotomographic system (Aplio AAS-700A; Toshiba Medical Systems, Tochigi, Japan) with a 7.5-MHz linear transducer. With the longitudinal projection of the common carotid artery, the carotid bulb, and the internal carotid artery, the site of the greatest thickness including a plaque lesion was sought along both near and far walls bilaterally (max-IMT). Carotid

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atherosclerosis was defined as max-IMT ≥ 1.1 mm according to the criteria of the Japan Academy of Neurosonology (9). In addition, all measurements of CIMT were performed by experienced physicians.

MSCT coronary angiography

Imaging was performed with a 64-slice (indicated as (64) hereafter) or 320-slice (likewise indicated as (320)) MSCT scanner (Aquilion (64) or Aquilion ONE (320); Toshiba Medical Systems). MSCTA was performed with a helical (64) or volumetric (320) scan with β -blockers and sublingual nitrates if necessary. Reconstruction with phases of fewest motion artifacts was performed and images were transferred to a remote workstation for post-processing.

MSCTA images were interpreted by two experienced observers blind to the patient's characteristics using specialized software (Ziostation; Ziosoft, Tokyo, Japan).

Using a 15-segment model according to the American Heart Association classification, presence of coronary atherosclerosis and luminal narrowing in each segment was visually graded into four classes: 0–25% stenosis, 25–50% stenosis, 50–75% stenosis, and $\geq 75\%$ stenosis.

Statistical analysis

Max-IMT was compared by ANCOVA with Holm adjustments. Analysis of trend through categories of max-IMT was performed with the χ^2 test for trend. The receiver operating characteristic (ROC) curve analysis was used to determine the optimal cutoff value of max-IMT for $\geq 50\%$ coronary stenosis. CIs of ROC values were calculated through bootstrap resampling, and there were 2,000 bootstrap samples, according to the percentile method. The threshold of statistical significance was defined as $P < 0.05$.

RESULTS

MSCTA results

A total of 1,330 coronary segments were analyzed, and 17 were undiagnosable because of motion ($n = 12$) or calcification ($n = 5$). A total of 29 patients (32%) had at least one segment of $\geq 50\%$ stenosis, 37 (41%) had at least one segment of 25–50% stenosis, and 25 (27%) had only 0–25% stenosis.

Relationship between CIMT and coronary stenosis

Max-IMT was significantly greater in the $\geq 50\%$ stenosis group (2.68 ± 0.77 mm)

compared with the 0–25% stenosis group (1.61 ± 0.49 mm) ($P < 0.0005$) and the 25–50% stenosis group (2.14 ± 0.81 mm) ($P < 0.05$), and the max-IMT of the 25–50% stenosis group was significantly greater than the 0–25% stenosis group ($P < 0.05$) after adjustment for age, sex, duration of type 2 diabetes, hypertension, and dyslipidemia (Fig. 1A).

In the analysis for trend through the categories of max-IMT, as max-IMT

increased, the percentage of $\geq 50\%$ stenosis increased ($P < 0.00005$) and the percentage of 0–25% stenosis decreased ($P < 0.0001$) (Fig. 1B).

ROC curve analysis for $\geq 50\%$ stenosis

The area under the ROC curve (AUC) of max-IMT, ABPI, and baPWV were 0.78 (95% CI 0.70–0.86), 0.72 (0.63–0.83), and 0.73 (0.62–0.83), respectively. The

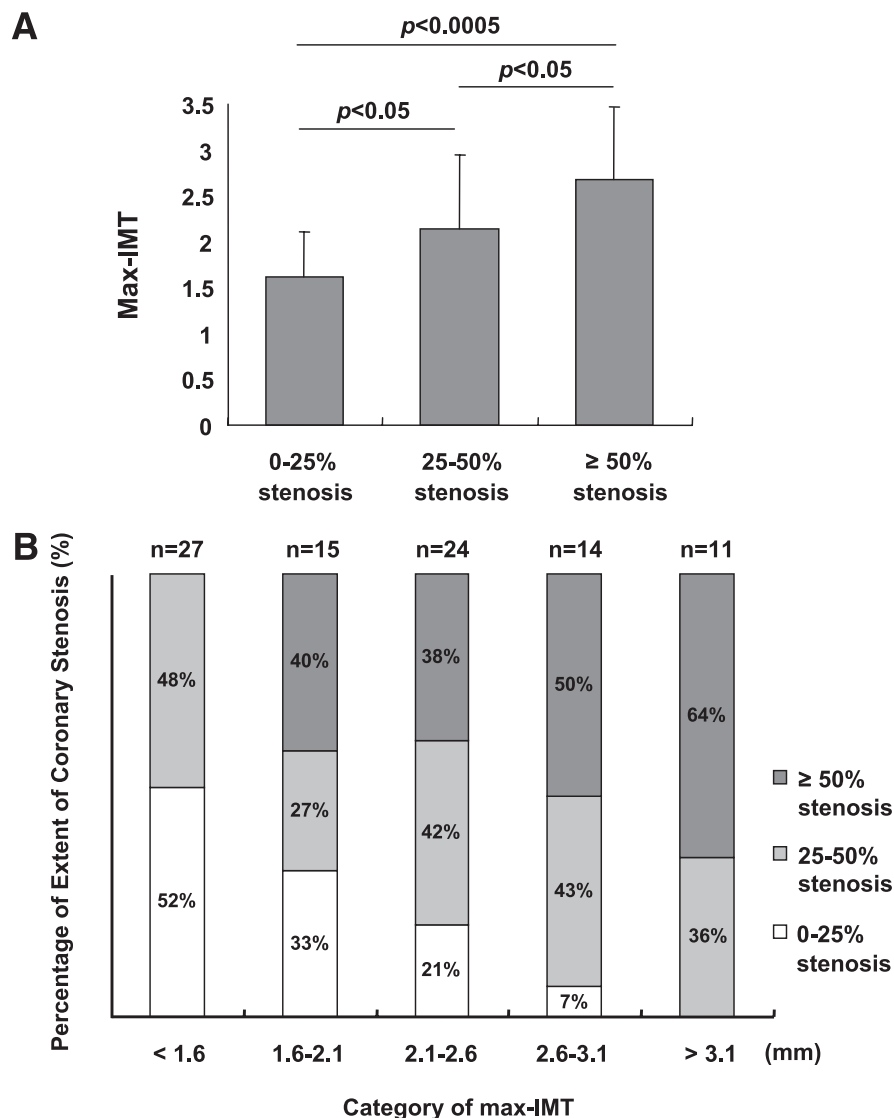


Figure 1—A: The relationship between CIMT and coronary stenosis. Max-IMT was significantly greater in the $\geq 50\%$ stenosis group (2.68 ± 0.77 mm) than the 0–25% stenosis group (1.61 ± 0.49 mm) ($P < 0.0005$) and the 25–50% stenosis group (2.14 ± 0.81 mm) ($P < 0.05$). In addition, the max-IMT of the 25–50% stenosis group was significantly greater than the 0–25% stenosis group ($P < 0.05$). B: The extent of coronary stenosis in each max-IMT category. In the max-IMT < 1.6 mm group, the percentage of $\geq 50\%$ stenosis was 0%, whereas in the patients whose max-IMT was ≥ 1.6 mm, the percentage of $\geq 50\%$ stenosis was 45%. Furthermore, in the analysis for trend through the categories of max-IMT, as max-IMT was increased, the percentage of $\geq 50\%$ stenosis was increased ($P < 0.00005$) and the percentage of 0–25% stenosis was decreased ($P < 0.0001$).

cutoff level of max-IMT providing the maximal sum of sensitivity and specificity was 1.90 mm (95% CI 1.6–2.5). At this cutoff level, sensitivity was 0.93 (95% CI 0.71–1.00) and specificity was 0.55 (0.42–0.83). The positive predictive value was 0.49 (95% CI 0.39–0.69), and the negative predictive value was 0.94 (0.84–1.00).

When max-IMT was combined with baPWV and ABPI, the AUC of max-IMT was 0.83 (95% CI 0.75–0.92) at a max-IMT cutoff level of 1.60 mm (1.6–2.1), a baPWV cutoff level of 1,430 cm/s, and an ABPI cutoff level of 1.19. At these cutoff values, sensitivity was 0.97 (95% CI 0.87–1.00) and specificity was 0.68 (0.60–0.83). Positive predictive value was 0.58 (95% CI 0.49–0.75), and negative predictive value was 0.98 (0.92–1.00).

CONCLUSIONS—Our data suggest that max-IMT might be closely associated with the presence and extent of coronary stenosis in type 2 diabetic patients without history of CAD but with carotid atherosclerosis and that max-IMT measurement might have a passable AUC, high sensitivity, high negative predictive value, low specificity, and low positive predictive value for significant coronary stenosis. We propose a hypothesis that max-IMT measurement might be useful for distinguishing patients who need not undergo workup for coronary stenosis but that max-IMT might be insufficient to determine patients who should undergo workup for coronary stenosis. We consider this study not conclusive but hypothesis generating. When this study was designed, available information was so little to calculate an appropriate sample

size. Consequently, our study population of 91 was insufficient to calculate clinically useful cutoff values with narrower 95% CIs and to compare usefulness of max-IMT, ABPI, and baPWV. Another limitation of this study was CIMT measurements, which were performed by three operators as daily clinical routine examinations and should inevitably involve operator variability. Larger replication studies need to be designed with appropriate sample size calculations, and our results may provide a rationale to conduct such studies.

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R.K. researched data and wrote the manuscript. H.K. supervised this work, contributed to the discussion, and reviewed and edited the manuscript. S.S. wrote and reviewed and edited the manuscript. K.Y., T.K., K.T., T.Y., and A.K. researched data and wrote the manuscript. N.K. researched data, planned and supervised this work, contributed to the discussion, and reviewed the manuscript. M.M. planned and supervised this work, contributed to the discussion, and reviewed the manuscript. T.-a.M. and I.S. contributed to the discussion and reviewed and edited the manuscript.

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