Significance of the Intima-Media Thickness of the Thoracic Aorta in Patients with Coronary Atherosclerosis

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Summary

Background: The prevalence and clinical significance of atherosclerotic aortic disease have now been documented in a variety of patient populations by use of transesophageal echocardiography (TEE). There are many reports that atherosclerotic aortic plaques detected by TEE are a marker for coronary artery disease (CAD).

Hypothesis: The study was undertaken to evaluate the significance of the intima-media thickness (IMT) and formation of atherosclerotic plaques of the thoracic aorta (TA) in patients with CAD, especially in terms of a correlation between the IMT of the TA and the extent of coronary atherosclerosis.

Methods: The IMT of the TA was measured using TEE. The study population comprised 100 patients (68 men, mean age 59 years). The extent of coronary atherosclerosis was divided into four groups (0, 1, 2, 3) according to the number of coronary arteries narrowed $\geq 50\%$.

Results: There was no significant difference in the IMT of the ascending TA according to the presence of significant ($> 50\%$ narrowed) coronary stenosis, but there was a significant difference in the IMT of the descending TA (1.39 vs. 1.88 mm, $p = 0.005$). There was a significant correlation between the extent of coronary atherosclerosis and the IMT of the ascending and descending TA ($r = 0.24$, $p < 0.05$; $r = 0.352$, $p < 0.001$, respectively). The plaques in the TA were seen in 7, 41, 52, and 65% of patients in Groups 0, 1, 2, and 3, respec-

tively. Among atherosclerosis risk factors, hyperlipidemia was the only factor analyzed that affected the IMT of the descending TA (2.11 vs. 1.78 mm, $p < 0.05$).

Conclusion: The IMT of the TA correlates significantly with coronary atherosclerosis, and correlation of the descending TA IMT with coronary atherosclerosis is better than that of ascending TA IMT. Age is associated with coronary atherosclerosis, and TA IMT and hyperlipidemia are associated with descending TA IMT. Therefore, although TEE is not recommended for measuring TA IMT or for evaluating aortic plaques in patients with CAD, measurement of TA IMT as well as carotid artery IMT is very helpful for understanding the extent of coronary atherosclerosis.

Key words: intima-media thickness, thoracic aorta, coronary atherosclerosis

Introduction

The prevalence and clinical significance of atherosclerotic aortic disease have now been documented in a variety of patient populations by use of transesophageal echocardiography (TEE). There are many reports that atherosclerotic aortic plaques detected by TEE are a marker for coronary artery disease (CAD).^{1, 2} However, we also frequently observe an increased intima-media thickness (IMT) of the thoracic aorta (TA) during TEE. Although there are numerous reports on increased IMT of the carotid artery associated with CAD,^{3, 4} there are no available data to our knowledge about the relation between coronary atherosclerosis and the IMT of the great vessels such as the TA as measured by TEE.

In this study we measured the IMT of the TA and examined by TEE whether atherosclerotic aortic plaque was present in 100 consecutive patients who underwent coronary angiography. The first objective of this study was to determine whether increased IMT of the TA is associated with CAD and whether IMT of the TA correlates with the extent of coronary atherosclerosis. Another objective of this study was to analyze the relation between IMT of the TA and risk factors for atherosclerosis in patients with CAD.

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Materials and Methods

Study Population

The study population consisted of 100 consecutive patients who underwent coronary angiography for (suspicious) CAD between March 2000 and July 2001. Written informed consent was obtained from all patients and the study was approved by the hospital ethics committee. Exclusion criteria were left main coronary artery involvement (because of potential risk from TEE), prior myocardial infarction or revascularization (because of eliminating the potential benefits of medicine for preexisting CAD on IMT), no consent, and New York Heart Association heart failure class >2 (because of eliminating the potential benefits of medicine for preexisting heart failure on IMT).

Transesophageal Echocardiography

Transesophageal echocardiography was performed on Day 1 or one day after coronary angiography by a blinded examiner using Hewlett-Packard Sonos-5500 (Philips Medical Systems/Agilent Technologies, Bothell, Wash., USA) and a multiplane probe. No patient experienced complications. All studies were videotaped for evaluation in real time. The TEE recordings of all patients were interpreted by an examiner blinded to clinical and angiographic results.

Two echogenic lines separated by a relatively anechoic space on the thoracic aortic wall were seen on TEE. These lines were generated by the blood-intima and media-adventitia interfaces, respectively.⁵ We also defined the distance between these two lines as the IMT of the TA. The atherosclerotic aortic plaque was defined as focal increased echodensity with luminal irregularity and thickening or calcification of the aortic intima disrupting the normal smooth surface of the aortic wall.

A blinded examiner first evaluated the TA in both the horizontal and longitudinal planes and examined it for plaques. If plaques were found, the maximal plaque thickness was measured in real time. The IMT was then measured in the ascending and descending TA, but not in the aortic arch, which was sometimes difficult to visualize clearly during TEE. The IMT was measured in the most thickened wall in the field visualized in end-diastole, except in the area of plaques. The far wall of the ascending TA was not always seen clearly, therefore the ascending aorta was focused upon in the near wall and a 1 cm long aortic wall segment was measured at 2 mm intervals. The descending aorta was focused upon in the far wall and again a 1 cm long segment was measured at 2 mm intervals. The average value of each of the six IMT measurements of the ascending or descending TA was taken as the evaluable IMT of the aorta.

Another examiner, also blinded to the results of coronary angiography, reviewed the recorded videotape of 20 randomly selected patients; he measured the IMT of the aorta and analyzed the presence or maximal thickness of the plaque. The correlation coefficient between the two examiners in measuring the IMT of the descending TA was 0.994 ($p < 0.001$) and

the two examiners were in 100% agreement on the identification of plaques. The first examiner reviewed the recorded videotape of 20 randomly selected patients 1 month after finishing patient enrollment, and he also measured the IMT and analyzed the presence or maximal thickness of the plaques. The correlation coefficient between the first and the second measurements of the IMT of the descending TA was 0.992 ($p < 0.001$). The presence of plaques was exactly the same in both measurements.

Coronary Angiography

Coronary angiography was performed by standard technique via the femoral artery using a Judkins catheter. No patient experienced complications during this procedure. The extent of CAD was graded as 0, 1, 2, or 3 according to the number of major coronary vessels with luminal stenosis $\geq 50\%$. Patients with left main coronary artery narrowing $\geq 50\%$ were excluded from the study. A $\geq 50\%$ obstruction in vessels other than the three major coronary arteries was graded as obstruction of the major vessel from which it arose. Coronary angiograms were always analyzed visually in more than two views. The angiographic grading was performed by a cardiologist and an experienced radiologist, both blinded to the TEE results. In the case of disagreement in angiographic grading, another cardiologist analyzed the angiographic results. Agreement between two of the three analyses was accepted as the true extent of CAD. Cases in which there was no agreement among the three observers were excluded from further analysis.

Statistical Analysis

All descriptive data were expressed in mean $\pm$ standard deviation. A p value < 0.05 was considered significant. The Spearman correlation coefficient was used to evaluate intra- and interobserver variability. The Pearson chi-square test was used to compare the discrete variables among each group, and the two-tailed t -test and one-way analysis of variance (ANOVA) were used to compare the mean difference among the groups. Pearson correlation coefficients were used to evaluate the correlation between TA IMT and the extent of CAD. All variables with potential influence on the extent of CAD were examined by multiple regression analysis.

Results

Clinical and Angiographic Findings

The mean age of the study population (68 men) was 59 ± 9 years. The number of patients with hypertension, diabetes mellitus, history of smoking, and hyperlipidemia (> 200 mg/dl total cholesterol or triglycerides) were 37, 17, 54, and 32, respectively. Of all study patients, 46 presented with angina and 39 with acute myocardial infarction.

The numbers of patients with CAD extent graded 0, 1, 2, and 3 were 15, 42, 23, and 20, respectively. There were no significant differences among groups 0, 1, 2, and 3 in age, gender,

TABLE I Characteristics of the study subjects according to the number of narrowed (>50%) coronary vessels

CAD extent	0	1	2	3
No. of patients	15	42	23	20
Age (years)	56 ± 8	57 ± 9	59 ± 9	64 ± 11
Sex (M:F)	7:8	31:11	18:5	12:8
Hypertension (%)	5 (33)	16 (38)	7 (30)	9 (45)
Diabetes (%)	1 (7)	8 (19)	2 (9)	6 (30)
Smoking (%)	4 (27)	27 (61)	13 (57)	10 (50)
Hyperlipidemia (%)	5 (33)	12 (29)	5 (22)	10 (50)
Diagnosis				
Angina (%)	0 (0)	26 (62)	14 (61)	6 (30)
MI (%)	0 (0)	16 (38)	9 (39)	14 (70)
Ejection fraction (%)	66 ± 7 ^a	63 ± 9 ^a	61 ± 9	53 ± 13
Total cholesterol (mg/dl)	193 ± 31	190 ± 41	200 ± 49	220 ± 54
Triglyceride (mg/dl)	200 ± 124	216 ± 153	256 ± 228	244 ± 140
HDL-cholesterol (mg/dl)	39.8 ± 8.7	36.2 ± 6.7	41.5 ± 8.9	38.5 ± 12.4
Glucose (mg/dl)	119 ± 33 ^b	139 ± 56 ^b	146 ± 62	195 ± 100

Data were expressed as mean ± 1 standard deviation.

^a $p < 0.01$.

^b $p < 0.05$ compared with CAD extent 3.

Abbreviations: CAD = coronary artery disease, M = male, F = female, MI = myocardial infarction, HDL = high-density lipoprotein.

hypertension, diabetes, history of smoking, hyperlipidemia, diagnosis (of those in groups 1, 2, 3), total cholesterol, triglycerides, and high-density lipoprotein (HDL) cholesterol, except in ejection fraction and fasting glucose levels. Although there was no significant difference among groups, age was associated with a greater extent of CAD ($r = 0.266$, $p = 0.006$). Compared with patients with CAD extent 3, those with CAD extent 0 and 1 had higher ejection fractions and lower fasting glucose levels (Table I).

Transesophageal Echocardiography Findings

The IMT of the descending TA in patients with significant coronary arterial narrowing (CAD extent 1, 2, or 3, $n = 85$) was significantly increased (1.883 ± 0.6 vs. 1.389 ± 0.6 mm, $p < 0.01$) compared with that in patients without significant CAD (CAD extent 0, $n = 15$). The IMT of the ascending TA in the former group of patients was also increased (1.619 ± 0.6 vs. 1.482 ± 0.5 mm, NS) compared with the latter group.

Mean descending TA IMT in patients with CAD extent 0, 1, 2, and 3 was 1.389 ± 0.6 , 1.759 ± 0.6 , 1.864 ± 0.6 , and 2.166 ± 0.6 mm, respectively. Compared with patients with CAD extent 0, only patients with CAD extent 3 showed significant ($p < 0.005$) thickening of the descending TA, although there was an increasing tendency toward thickening according to the CAD extent. However, an excellent correlation was found between descending TA IMT and CAD extent ($r = 0.352$, $p < 0.001$, Fig. 1). Mean ascending TA IMT in patients with CAD extent 0, 1, 2, and 3 was 1.482 ± 0.5 , 1.515 ± 0.6 , 1.539 ± 0.5 , and 1.930 ± 0.8 mm, respectively, with an increasing tendency toward thickening according to the CAD extent. There were no significant differences in IMT among any of the groups, but an excellent correlation was found between ascending TA IMT and CAD extent ($r = 0.24$, $p < 0.05$, Fig. 1).

Atherosclerotic TA plaques were more frequently ($p < 0.005$) found in patients with significant CAD (49.4%, 42/85) than in patients without CAD (6.7%, 1/15). Of the patients with significant CAD, 40.5% (17/42) with CAD extent 1, 52.5% (12/23) with CAD extent 2, and 65% (13/20) with CAD extent 3 showed atherosclerotic TA plaques. The plaques were significantly more frequent with advanced CAD extent ($p < 0.01$).

FIG. 1 Correlation between intima-media thickness of thoracic aorta and the extent of coronary atherosclerosis in the study patients.

Among patients with significant CAD ($n = 85$), there were no significant differences in ascending TA IMT according to gender (men: $n = 61$, 1.607 ± 0.59 mm, women: $n = 24$, 1.651 ± 0.76 mm); this also holds true for descending TA IMT (men: 1.914 ± 0.65 mm, women: 1.804 ± 0.53 mm). The presence of hypertension, diabetes mellitus, and history of smoking obviously could not affect the IMT of the ascending and descending TA and the presence of TA plaques. Only hyperlipidemia was associated with greater descending TA IMT (2.11 ± 0.6 vs. 1.78 ± 0.6 mm, $p < 0.05$), but not with ascending TA IMT or TA plaques (Table II). Age was associated with higher ascending ($r = 0.279$, $p = 0.005$) and descending ($r = 0.371$, $p < 0.001$) TA IMT; however, IMT of the ascending or descending TA showed no significant difference in ejection fraction and fasting glucose levels.

Multiple regression analysis revealed that IMT of the descending TA was the only independent predictor of CAD extent ($p = 0.026$). Age, IMT of the ascending TA aorta, and hyperlipidemia were not valuable predictors of CAD extent during this analysis.

Discussion

Our study shows that the IMT of the TA correlates significantly with the extent of coronary atherosclerosis, while descending TA IMT is associated with age and hyperlipidemia in patients with CAD. Furthermore, the IMT of the descending TA is an independent predictor of the extent of coronary atherosclerosis. These results suggest that the increased IMT of the TA, especially the descending TA, during TEE is a marker of coronary atherosclerosis and that hyperlipidemia is the most important risk factor affecting IMT of the descending TA in patients with CAD. We believe that the measure-

ment of TA IMT during TEE provides important information about coronary atherosclerosis, although TEE for the measurement of TA IMT alone is not indicated. To our knowledge, this is the first study demonstrating a correlation between IMT of the TA and the extent of coronary atherosclerosis, as well as implicating an association between IMT of the TA and atherosclerosis risk factors in patients with CAD.

The cut-off value of TA IMT differentiating between patients with and without CAD could not be obtained from our study because the number of patients without significant CAD was too small for comparison and because of the wide confidence ranges of IMT.

Increased IMT of the carotid artery is associated with ischemic heart disease, stroke, and atherosclerosis risk factors.^{4,6} However, Adams *et al.* reported that although carotid IMT correlates significantly with the extent and severity of CAD, the relationship is weak ($r = 0.23$).⁷ Several studies reported that carotid bulb IMT and common femoral IMT correlate more closely with the extent of coronary atherosclerosis.^{3,8} This was explained by a low oscillatory shear stress in the carotid bulb and the coronary arteries, and by characteristic curves of the femoral and coronary arteries compared with the common carotid artery, which is a straight arterial segment with high shear stress.^{3,9} Although the carotid bifurcation, the coronary arteries, the infrarenal abdominal aorta, and the vessels supplying the lower extremities are at highest risk of atherosclerosis,⁹ Pearson *et al.* showed a close correlation between thickness and distensibility in the carotid artery and the descending TA.¹⁰ Our study also showed that the correlation between descending TA IMT and coronary atherosclerosis is better ($r = 0.352$, $p < 0.001$) than that between common carotid IMT and the extent of coronary atherosclerosis ($r = 0.23$, $p < 0.001$).⁷

Each risk factor may affect different segments of the carotid artery; that is, age, hypertension, and smoking affect all seg-

TABLE II Intima-media thickness of thoracic aorta and presence of plaque in patients with more than one narrowed ($> 50\%$) coronary arteries according to the presence of risk factors

Risk factors	Hypertension		Diabetes	
	(+)	(-)	(+)	(-)
Number (n)	32	53	16	69
IMT (mm)				
Descending thoracic Ao	1.96 ± 0.6	1.84 ± 0.6	1.92 ± 0.6	1.86 ± 0.6
Ascending thoracic Ao	1.66 ± 0.7	1.59 ± 0.6	1.71 ± 0.9	1.60 ± 0.6
Plaque, number (%)	19 (59)	23 (43)	7 (44)	35 (51)
Risk factors	Smoking		Hyperlipidemia	
	(+)	(-)	(+)	(-)
Number (n)	50	35	27	58
IMT (mm)				
Descending thoracic Ao	1.85 ± 0.7	1.93 ± 0.6	2.11 ± 0.6	1.78 ± 0.6^a
Ascending thoracic Ao	1.59 ± 0.5	1.66 ± 0.8	1.79 ± 0.7	1.54 ± 0.6
Plaque, number (%)	25 (50)	17 (49)	13 (48)	29 (50)

Data were expressed as mean $\pm$ 1 standard deviation.

^a $p < 0.05$ compared with hyperlipidemia group.

Abbreviations: IMT = intima-media thickness, Ao = aorta.

ments of the carotid artery equally, while gender and diabetes mellitus affect the bifurcation and internal carotid artery more than they do the common carotid artery.^{11, 12} These studies also suggest that each risk factor can affect the IMT of different arterial segments inhomogeneously. Several reports found that race, in addition to variable risk factors, affects carotid artery IMT.^{13, 14} Aortic wall thickness or atherosclerosis expressed as average sclerotic length and average sclerotic area was associated with increasing age, hypercholesterolemia, smoking, and diabetes mellitus, while age and hypertension were associated with aortic wall stiffness.^{10, 15, 16} Furthermore, atherosclerosis of the descending TA could be improved with cholesterol-lowering therapy in familial hypercholesterolemia.¹⁷ These studies suggest that each risk factor may not affect aortic wall thickness homogeneously.^{10–17} Increasing age and hyperlipidemia are associated with a more significant thickening of the descending TA; however, there is no significant association between TA IMT and other risk factors (hypertension, diabetes mellitus, and smoking) in our study. Our results are somewhat different from those in previous reports regarding aortic wall thickness and the involvement of risk factors.^{10, 15–17} While the population in our study consisted of 85 patients with significant CAD, the population in previous studies^{10, 15–17} had no significant CAD. This, in addition to the racial difference, may explain the different results. From our study results, we know that age and hyperlipidemia are still important factors in determining TA IMT even in patients with significant CAD.

In our study, the sensitivity and specificity of aortic plaque in detecting significant CAD are 49.4 and 93.3%, respectively. Matsumura *et al.* reported that sensitivity and specificity of aortic plaques in predicting significant CAD were 93 and 47%, respectively.¹⁸ Others have reported sensitivity and specificity ranging from 76 to 90% and from 68 to 90%, respectively.^{1, 19} The relatively low sensitivity of aortic plaques in detecting significant CAD in our study could be explained by racial and regional differences from the studies. However, specificity was excellent compared with that in other studies. This is also explained by a relatively low incidence of aortic plaques in Korean individuals.

Conclusions

The IMT of the TA correlates significantly with coronary atherosclerosis, and correlation of the descending TA IMT with coronary atherosclerosis is better than that of ascending TA IMT. Age is associated with coronary atherosclerosis, and TA IMT and hyperlipidemia are associated with descending TA IMT. Other risk factors such as gender, hypertension, diabetes mellitus, and history of smoking are not related with TA IMT or coronary atherosclerosis in our study. The sensitivity and specificity of aortic plaques in detecting significant CAD are relatively good. Therefore, although TEE is not recommended for measuring TA IMT or for evaluating aortic plaques in patients with CAD, measurement of TA IMT as well as ca-

rotid artery IMT during TEE is very helpful for understanding the extent of coronary atherosclerosis.

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