Thoracic aortic atheroma severity predicts high-risk coronary anatomy in patients undergoing transesophageal echocardiography

Xuedong Shen[1], Wilbert S. Aronow[2], Chandra K. Nair[1], Hema Korlakunta[1], Mark J. Holmberg[1], Fenwei Wang[1], Stephanie Maciejewski[1], Dennis J. Esterbrooks[1]

[1]Cardiac Center of Creighton, University School of Medicine, Omaha, Nebraska, USA
[2]Cardiology Division, Department of Medicine, New York Medical College, Valhalla, New York, USA

Corresponding author:
Wilbert S. Aronow, MD
Cardiology Division
Department of Medicine
New York Medical College
Macy Pavilion, room 138
Valhalla, NY 10595, USA
Phone: +914 493 53 11
Fax: +914 235 62 74
E-mail: wsaronow@aol.com

Abstract

Introduction: We hypothesized a relationship between severity of thoracic aortic atheroma (AA) and prevalence of high-risk coronary anatomy (HRCA).
Material and methods: We investigated AA diagnosed by transesophageal echocardiography and HRCA diagnosed by coronary angiography in 187 patients. HRCA was defined as $\geq$ 50% stenosis of the left main coronary artery or significant 3-vessel coronary artery disease ($\geq$ 70% narrowing).
Results: HRCA was present in 45 of 187 patients (24%). AA severity was grade I in 55 patients (29%), grade II in 71 patients (38%), grade III in 52 patients (28%), grade IV in 5 patients (3%), and grade V in 4 patients (2%). The area under receiver operating characteristic curve for AA grade predicting HRCA was 0.83 (p = 0.0001). The cut-off points of AA to predict HRCA was > II grade. The sensitivity and specificity of AA > grade II to predict HRCA were 76% and 81%, respectively. After adjustment for 10 variables with significant differences by univariate regression, AA > grade II was related to HRCA by multivariate regression (odds ratio = 7.5, p < 0.0001). During 41-month follow-up, 15 of 61 patients (25%) with AA >grade II and 10 of 126 patients (8%) with AA grade $\leq$ 2 died (p = 0.004). Survival by Kaplan-Meier plot in patients with AA > grade II was significantly decreased compared to patients with AA $\leq$ grade II (p = 0.002).
Conclusions: AA > grade II is associated with a 7.5 times increase in HRCA and with a significant reduction in all-cause mortality.

Key words: high-risk coronary anatomy, transesophageal echocardiography, thoracic aortic atheroma, coronary angiography.

Introduction

High-risk coronary anatomy (HRCA) defined as $\geq$ 50% stenosis of the left main coronary artery or $\geq$ 70% obstructive 3-vessel coronary artery disease (CAD) is associated with increased mortality compared to 1-vessel and 2-vessel obstructive CAD [1, 2]. Thoracic aortic atheroma (AA) is often associated with CAD because atherosclerosis is a systemic disease that occurs in the coronary and peripheral circulation [3, 4]. The association of thoracic AA with HRCA is unknown. We hypothesized that there might be a relationship between the severity of thoracic AA and the prevalence of HRCA.

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X. Shen, W.S. Aronow, C.K. Nair, H. Korlakunta, M.J. Holmberg, F. Wang, S. Maciejewski, D.J. Esterbrooks

Material and methods

We retrospectively studied 187 consecutive patients with both transesophageal echocardiography (TEE) and coronary angiography performed at Creighton University Medical Center during January, 1994 to December, 2002. The 187 patients included 112 men and 75 women, mean age 68 ±11.2 years. The patients underwent TEE for clinical indications as recommended by American College of Cardiology/American Society of Echocardiography/American College of Emergency Physicians/American Society of Nuclear Cardiology/Society for Cardiovascular Angiography and Interventions/Society of Cardiovascular Computed Tomography/

Table I. Baseline characteristics of 187 patients

Variables	Number (%)
Men	112 (60)
Women	75 (40)
Age [years]	68 ±11
Body mass index [kg/m^2]	28 ±6
Follow-up duration [months]	41 ±32
Coronary artery disease	94 (50)
1-vessel	32 (17)
2-vessel	19 (10)
3-vessel	41 (22)
Left main	12 (6)
Hypertensive heart disease	32 (17)
Valvular heart disease	38 (20)
Dilated cardiomyopathy	9 (5)
Hypertrophic cardiomyopathy	2 (1)
Other underlying disorders	12 (6)
High-risk coronary anatomy	45 (24)
Previous myocardial infarction	28 (15)
Recent myocardial infarction	19 (10)
Coronary artery bypass surgery	61 (33)
Percutaneous coronary intervention	32 (17)
Smoking	24 (13)
Hypertension	114 (61)
Hypercholesterolemia	99 (53)
Atrial fibrillation	152 (81)
Left ventricular hypertrophy	57 (31)
Ischemic stroke or transient ischemic attack	32 (17)
Aortic stenosis	22 (12)
Aortic valve calcification	75 (40)
Mitral annulus calcification	11 (6)

Valvular heart disease includes aortic stenosis and mitral regurgitation

and the Society for Cardiovascular Magnetic Resonance guidelines [5]. Coronary angiography was performed for clinical indications in these 187 patients within 4 weeks of TEE. The 28 baseline characteristics of the 187 patients are listed in Table I.

The patient was given conscious sedation for TEE with intravenous Versed and Fentanyl. A 3.7/5.0 MHz omniplane transesophageal transducer was placed in the posterior pharynx and advanced into the esophagus. The proximal ascending aorta was visualized in the horizontal and longitudinal planes. After the examination of the proximal ascending aorta, the transducer was rotated posteriorly and advanced to the distal esophagus to obtain the images of the descending aorta. Finally, the probe was slowly withdrawn to obtain the images of the distal portion of the ascending aorta and aortic arch. The distal portion of the ascending aorta was only partially visualized because of interference of the trachea. The thoracic aorta was monitored from the level of the stomach (40-45 cm from the incisors) to approximately 18-20 cm from the incisors. The TEE recording of all patients was interpreted independently by 2 experienced observers who had no knowledge of the clinical and coronary angiographic data. The AA severity was classified as grade I (normal or minimal intimal thickening); grade II (extensive intimal thickening); grade III (atheroma < 5 mm); grade IV (atheroma ≥ 5 mm); and grade V (mobile lesion) [6]. An AA > grade II was defined as significant.

Follow-up information was obtained from the hospital and outpatient clinic records. The patients' clinical characteristics and critical events were recorded during the follow-up. Ischemic cerebrovascular accident included either a stroke defined as a definite focal neurological deficit of acute onset consistent with a vascular event lasting for > 24 hours and confirmed by computerized tomography or magnetic resonance imaging scans or a transient ischemic attack defined as a focal neurological deficit of sudden onset that resolved completely in < 24 hours with a negative computerized tomographic scan or magnetic resonance imaging scan. Follow-up information was obtained on ischemic cerebrovascular accident because of its high association with CAD and AA. All-cause mortality was documented.

Continuous data were presented as a mean ± standard deviation. Continuous variables were compared using the Student's t-test. Categorical data were assessed with the χ^2 or Fisher-exact tests. The correlation between AA grade and HRCA was analyzed by linear regression. A receiver operating characteristic (ROC) curve was used for evaluation of the cut-off value of AA grade to predict HRCA. Variables that achieved a significance level of $p < 0.1$ by univariate regression were

reevaluated using multivariate logistic regression. Actuarial survival from all-cause mortality was plotted by the Kaplan-Meier method using software PASW version 17.0. A *p* value of < 0.05 was considered statistically significant.

Results

HRCA was present in 45 of 187 patients (24%). The AA severity was grade I in 55 patients (29%), grade II in 71 patients (38%), grade III in 52 patients (28%), grade IV in 5 patients (3%), and grade V in 4 patients (2%). Forty-five patients (24%) had HRCA including

12 patients with left main coronary artery disease. Table II shows the association of baseline variables with an AA > grade II versus an AA ≤ grade II. Table II also shows levels of statistical significance.

Table III shows the ability of the AA grade to predict 1-vessel, 2-vessel, 3-vessel, and left main CAD and HRCA. The area under the ROC curve (AUC) for AA grade to predict HRCA was 0.83 (*p* = 0.0001, Figure 1). The cut-off points of AA grade to predict HRCA was > II. The sensitivity, specificity, positive and negative predictive values of AA > grade II were 76%, 81%, 56% and 91%, respectively. The AA grade was also able to predict

Table II. Association of baseline variables with aortic atheroma grade > II versus grade ≤ II

Variable	AA > grade II	AA ≤ grade II	*p* value
Age [years]	71 ±10	66 ±11	0.001
Men	42/61 (69%)	70/126 (56%)	NS
Body mass index [kg/m^2]	27 ±5	29 ±7	NS
High risk coronary anatomy	34/61 (56%)	11/126 (9%)	< 0.001
Left main disease	8/61 (13%)	4/126 (8%)	0.02
1-vessel disease	8/61 (13%)	24/126 (19%)	NS
2-vessel disease	8/61 (13%)	11/126 (9%)	NS
3-vessel disease	33/61 (54%)	8/126 (6%)	< 0.001
Previous myocardial infarction	18/61 (30%)	10/126 (8%)	< 0.001
Recent myocardial infarction	9/61 (15%)	10/126 (8%)	NS
Coronary artery bypass surgery	38/61 (62%)	23/126 (18%)	< 0.001
Percutaneous coronary intervention	16/61 (26%)	16/126 (13%)	0.04
Smoking	5/61 (8%)	19/126 (15%)	NS
Hypertension	41/61 (67%)	73/126 (58%)	NS
Diabetes mellitus	14/61 (23%)	22/126 (17%)	NS
Hypercholesterolemia	36/61 (59%)	63/126 (50%)	NS
Atrial fibrillation	49/61 (80%)	103/126 (82%)	NS
Left ventricular hypertrophy	20/61 (33%)	37/126(29%)	NS
Aortic stenosis	10/61 (16%)	12/126 (10%)	NS
Aortic valve calcification	29/61 (48%)	46/126 (37%)	NS
Mitral annulus calcification	6/61 (10%)	5/126 (4%)	NS

AA – thoracic aortic atheroma, NS – not significant
Atrial fibrillation was the reason for transesophageal echocardiography in 152 of 187 patients (81%)

Table III. Ability of thoracic aortic atheroma grade to predict 1-vessel, 2-vessel, 3-vessel, and left main coronary artery disease and high-risk coronary anatomy

	AUC	SE	95% CI	*P* value	Cutoff point	Sensitivity [%]	Specificity [%]	PPV [%]	NPV [%]
1-vessel	0.52	0.06	0.44-0.59	0.74	≤ 2	75	34	19	87
2-vessel	0.60	0.07	0.53-0.67	0.17	> 1	84	31	12	95
3-vessel	0.84	0.04	0.78-0.89	0.0001	> 2	81	81	54	94
Left main	0.73	0.08	0.66-0.79	0.007	> 2	67	70	13	97
HRCA	0.83	0.04	0.77-0.88	0.0001	> 2	76	81	56	91

HRCA – high-risk coronary anatomy, AUC – area under receiver operating characteristic curve, SE – standard error, PPV – positive predictive value, NPV – negative predictive value
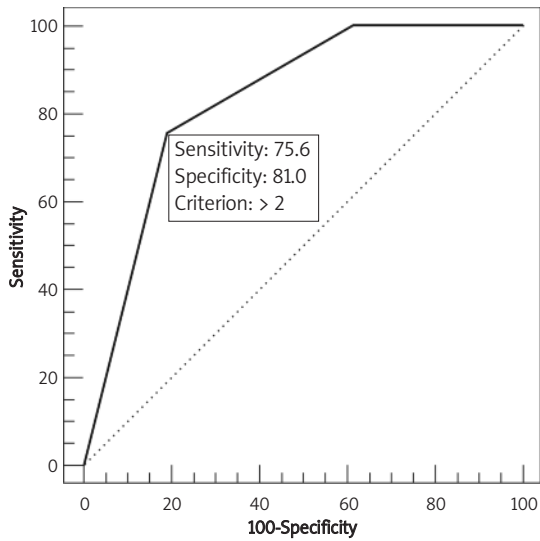
Figure 1. The area under the ROC curve (AUC) for AA grade to predict HRCA was 0.83 ($p = 0.0001$)
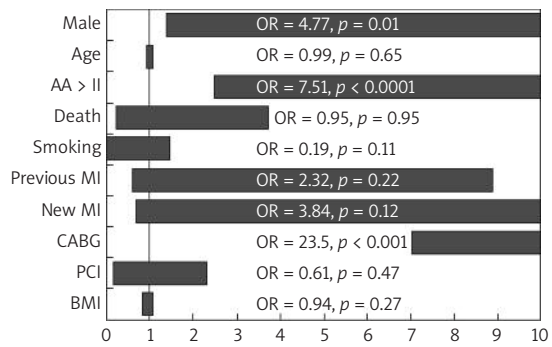

Figure 2. After adjustment for the variables with significant differences by univariate regression, an AA > II grade was continuously related to HRCA by multivariate regression ($p < 0.0001$). The odds ratios for predicting HRCA for male gender, age, an AA > grade II, death, smoking, previous myocardial infarction (MI), new MI, coronary artery bypass grafting (CABG), percutaneous coronary intervention (PCI), and body mass index (BMI) are shown

the presence of left main CAD (AUC = 0.73, $p = 0.007$) and 3-vessel CAD (AUC = 0.84, $p = 0.0001$).

Table IV and Figure 2 shows the multivariate regression analysis for HRCA after adjustment for 10 variables with significant differences by univariate regression. After adjustment for these 10 variables, an AA > grade II was related to HRCA by multivariate regression (odds ratio = 7.51, $p < 0.0001$).

Twenty-five of 187 patients (13%) died during 41 ±32-month follow-up. All deaths were cardiac in origin. Of these 25 patients, 11 (44%) had coronary artery bypass surgery, and 4 (16%) had percutaneous coronary intervention. The mean left

ventricular ejection fraction was 44 ±14% in patients who died versus 51 ±13% in patients who survived ($p = 0.02$). During follow-up, 15 of 61 patients (25%) with AA > grade II and 10 of 126 patients (8%) with AA grade ≤ 2 died ($p = 0.004$). The survival by Kaplan-Meier plot in patients with AA > grade II was significantly decreased compared to patients with AA ≤ grade II ($p = 0.002$) (Figure 3). Of the 25 patients who had died, 11 had coronary artery bypass graft surgery.

Discussion

TEE is a valuable tool to image AA with high resolution and accuracy [7, 8]. The interobserver and intraobserver concordance were 92.5% and 95%, respectively [6]. Ultrasound technology is able to assess the lesion size and extent [9], composition [10], and dynamic effect on flow [11]. The AA not
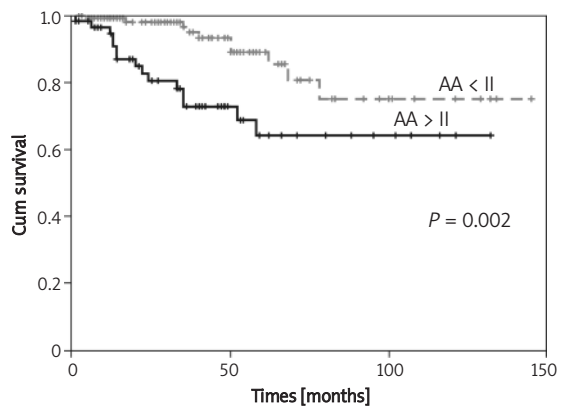
Table IV. Multivariate regression analysis for high-risk coronary anatomy after adjustment for 10 variables with significant differences by univariate regression

Variable	Odds ratio	P value	95% CI for odds ratio	
			Lower	Upper
Men	4.77	0.01	1.38	16.52
Age	0.99	0.65	0.93	1.05
AA > II grade	7.51	< 0.0001	2.50	22.56
Death	0.95	0.95	0.25	3.70
Smoking	0.19	0.11	0.02	1.45
Previous MI	2.32	0.22	0.61	8.91
Recent MI	3.84	0.12	0.70	21.16
CABS	23.45	< 0.001	7.05	78.01
PCI	0.61	0.47	0.16	2.31
Body mass index	0.94	0.27	0.84	1.05

AA – thoracic aortic atheroma, MI – myocardial infarction, CABS – coronary artery bypass surgery, PCI – percutaneous coronary intervention

Figure 3. The survival curves by Kaplan-Meier plot show that patients with an AA > grade II have a significantly decreased survival than patients with an AA ≤ grade II ($p = 0.002$)

only is a risk factor for ischemic stroke [12-15], but also is a marker for CAD [16]. The AA detected by TEE has a high sensitivity and specificity for presence of significant CAD [17]. Tribouilloy *et al.* [17] studied 278 patients with valvular heart disease and found that the presence of AA on TEE had a sensitivity of 91% and a specificity of 82%, respectively, for significant CAD. However, this study did not address the relationship between AA and HRCA.

The principal findings of our study were that the prevalence of HRCA in patients with AA > grade II was significantly higher than in patients with an AA ≤ grade II (56% vs. 9%, $p < 0.001$). The AUC for AA grade predicting HRCA was 0.83 ($p = 0.0001$). The cut-off points of AA grade to predict HRCA was > grade II. The sensitivity, specificity, positive and negative predictive values of AA > grade II to predict HRCA were 76%, 81%, 56% and 91%, respectively. After adjustment for variables, an AA > grade II was related to HRCA by multivariate regression (odds ratio = 7.5, $p < 0.0001$). The AA grade was also able to predict the presence of left main CAD (AUC= 0.73, $p = 0.007$) and 3-vessel CAD (AUC = 0.84, $p = 0.0001$).

Patients with HRCA are at increased risk for mortality [18, 19]. Our study also showed that the all-cause mortality in patients with an AA > grade II (25%) was significantly higher than in patients with an AA ≤ grade II (8%) ($p = 0.004$). The survival by Kaplan-Meier plot in patients with an AA > grade II was significantly decreased than in patients with an AA ≤ grade II ($p = 0.002$). The survival in patients with an AA > grade II was decreased probably because of the high prevalence of HRCA in these patients. This statement is based on the fact that in 12 patients with an AA > grade II who died, 8 (67%) had HRCA and 4 (33%) did not ($p < 0.01$). These data confirm previous observations that atherosclerosis is a systemic disease [20-22].

Thus, patients with an AA > grade II detected by TEE should be further evaluated for severe CAD. However, it is difficult to imagine that TEE would be performed to investigate atherosclerosis in the aorta in order to assess the probability of HRCD and to make the further clinical decision as to diagnosis by invasive or noninvasive coronary angiography and treatment.

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