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

Xuedong Shen¹, Wilbert S. Aronow², Chandra K. Nair¹, Hema Korlakunta¹, Mark J. Holmberg¹, Fenwei Wang¹, Stephanie Maciejewski³, Dennis J. Esterbrooks¹

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 ≥ 50% stenosis of the left main coronary artery or significant 3-vessel coronary artery disease (CAD) (≥ 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 ≤ 2 died (p = 0.004). Survival by Kaplan-Meier plot in patients with AA > grade II was significantly decreased compared to patients with AA ≤ 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 ≥ 50% stenosis of the left main coronary artery or ≥ 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.
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/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 χ² 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 included in a multivariate regression model.
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 I). 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

| 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      |

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

**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 |

AA – thoracic aortic atheroma, NS – not significant

Atrial fibrillation was the reason for transesophageal echocardiography in 152 of 187 patients (81%).
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 ≤ 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

| 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
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 = 0.0002). 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.

References

1. Rubinstein R, Halon DA, Jaffe R, et al. Relation between obesity and severity of coronary artery disease in patients undergoing coronary angiography. Am J Cardiol 2006; 97: 1277-80.
2. Holmes DR, Davis KB, Mock MB, et al. The effect of medical and surgical treatment on subsequent sudden cardiac death in patients with coronary artery disease: a report from the Coronary Artery Surgery Study. Circulation 1986; 73: 1254-63.
3. Anderson TJ. Close relation of endothelial function in the human coronary and peripheral circulation. J Am Coll Cardiol 1995; 26: 1235-41.
4. Acarturk E, Demir M, Kanadasi M. Aortic atherosclerosis is a marker for significant coronary artery disease. Japanese Heart J 1999; 40: 775-81.
5. Douglas PS, Khandheria B, Stainback RF, et al. ACCF/AHA/ASE/ACCP/ASNC/SAGT/SCCT/SCMR 2007 appropriateness criteria for transthoracic and transesophageal echocardiography: a report of the American College of Cardiology Foundation Quality Strategic Directions Committee Appropriateness Criteria Working Group. 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, and the Society for Cardiovascular Magnetic Resonance. Endorsed by the American College of Chest Physicians and the Society of Critical Care Medicine. J Am Soc Echocardiogr 2007; 20: 787-805.
6. Montgomery DH, Verrieres J, McGorisk G, et al. Natural history of severe atheromatous disease of the thoracic aorta: a transesophageal echocardiographic study. J Am Coll Cardiol 1996; 27: 95-101.
7. Nihoyannopoulos P, Joshi J, Athanassopoulos G, et al. Detection of atherosclerotic lesions in the aorta by transesophageal echocardiography. Am J Cardiol 1993; 71: 1208-12.
8. Gupta V, Nanda NC, Yezhibursa D, et al. Racial differences in thoracic aorta atherosclerosis among ischemic stroke patients. Stroke 2003; 34: 408-12.
9. Persson J, Formgren J, Isacsson B, et al. Ultrasound determined intima-media thickness and atherosclerosis: direct and indirect validation. Arterioscler Thromb 1994; 14: 261-4.
10. Peter RJ, Kok WE, Havenith MG, et al. Histopathologic validation of intracoronary ultrasound imaging. J Am Soc Echocardiogr 1994; 7: 230-41.
11. Fujita A, Rubba P, Spencer MP. Prevalence of plaques and stenoses detectable by echo-Doppler examination in the femoral arteries of an elderly population. Atherosclerosis 1994; 105: 201-8.
12. Amarenco P, Cohen A, Tzourio C, et al. Atherosclerotic disease of the aortic arch and the risk of ischemic stroke. N Engl J Med 1994; 331: 1474-9.
13. Tunick PA, Rosenzweig BP, Katz ES, et al. High risk for vascular events in patients with protruding aortic atheromas: a prospective study. J Am Coll Cardiol 1994; 23: 1085-90.
14. Toyoda K, Yasaka M, Nagata S, et al. Aortogenic embolic stroke: a transesophageal echocardiographic approach. Stroke 1992; 23: 1056-61.
15. Kajanti D, Chandrasekaran K, Victor MF, et al. Recognition and embolic potential of intraaortic atherosclerotic debris. J Am Coll Cardiol 1991; 17: 73-8.
16. Fazio GP, Redberg RK Winslow T, et al. Transesophageal echocardiographically detected atherosclerotic aortic plaque is a marker for coronary artery disease. J Am Coll Cardiol 1993; 21: 144-50.
17. Tribouilloy C, Colas PL, Rida Z, et al. Multiplane transesophageal echocardiographic absence of thoracic aortic plaque is a powerful predictor for absence of significant coronary artery disease in valvular patients, even in the elderly. Eur Heart J 1997; 18: 1478-83.
18. Lai HM, Aronow WS, Rachdev A, et al. Incidence of mortality in 1,040 patients with coronary heart disease or hypertensive heart disease with normal and abnormal
left ventricular ejection fraction and with normal and abnormal QRS duration. Arch Med Sci 2008; 4: 140-2.

19. Chilappa K, Aronow WS, Rajdev A, et al. Mortality at 60-month mean follow-up in 2,057 patients with coronary angiographic evidence of no coronary artery disease, nonobstructive coronary artery disease, and revascularized obstructive coronary artery disease of 1, 2, and 3 major vessels. Med Sci Monit 2010; 16: 120-3.

20. Mintz GS, Maehara A. Insights from intravascular ultrasound on pathophysiology of acute coronary syndromes. Arch Med Sci 2010; 6, 1A: S15-24.

21. Bach RA. Acute coronary syndromes in high risk groups: patients with diabetes, the elderly, and women. Arch Med Sci 2010; 6, 1A: S89-103.

22. Barylski M, Mikhailidis DP, Rysz J, Banach M. Non-pharmacological management after acute coronary syndromes. Arch Med Sci 2010; 6, 1A: S64-75.