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Gender differences in the prevalence of coronary artery tortuosity and its association with coronary artery disease

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ABSTRACT

Background: Little is known about the significance of severe coronary tortuosity (SCT) despite it being a relatively common finding on coronary angiography. We examined whether the presence of tortuosity was influenced by gender or cardiac risk factors.

Methods and results: We examined 870 patients (Men = 589, Women = 281) who presented to Westmead Hospital, Sydney, Australia for invasive coronary angiography for the assessment of chest pain due to suspected CAD. Female gender and age were significantly associated with SCT ($p < 0.001$ for age) with 45.2% of women having SCT as opposed to 19.7% of men ($p < 0.001$). Men with SCT had lower Extent scores only compared than those without tortuosity (22.4 vs. 32.4, $p = 0.003$). However, women with SCT had less severe coronary artery disease than those with no SCT as measured by both the Extent score (12.4 vs. 19.1, $p = 0.03$) and Gensini score (10.4 vs. 15.5, $p = 0.02$).

Conclusion: There is a significant relationship between coronary artery tortuosity and gender. Women with severe tortuosity are more likely to have normal coronary arteries or less severe disease than men despite presenting with chest pain.

1. Introduction

Tortuosity of the coronary arteries is not an uncommon finding on coronary angiography however it is seldom reported by cardiologists. Whether tortuosity plays a role in angina is not known despite some evidence that people with severe coronary tortuosity (SCT) and normal coronary arteries display myocardial perfusion defects [1]. Aging and hypertension are thought to be known risk factors for the development of tortuosity in coronary, femoral, cerebral and carotid arteries [2,3]. Tortuosity may not be a benign entity. Traditional reporting of angiograms using stenosis severity is the predominant method of evaluating suspected ischemic chest pain with functional imaging used in intermediate or uncertain cases. This may lead to a lack of representation of mechanisms other than obstructive epicardial disease in the development of ischemic chest pain syndromes.

There is a paucity of literature on the clinical significance of coronary tortuosity and the association of gender and cardiac risk factors on its development. We conducted this study to further evaluate the relationship between coronary artery tortuosity in patients presenting for coronary angiography for the investigation of chest pain.

2. Methods

2.1. Study population

1680 participants were recruited for the AHES from January 2010 and January 2012. These were people who presented to Westmead Hospital, Sydney, Australia for invasive coronary angiography for the assessment of chest pain due to suspected CAD. Patients were referred for investigation by a cardiologist for outpatient or inpatient investigation. The decision to pursue angiography was made by the referrer who was not involved in the subsequent recruitment of the patients to the study. Participants were consented to the study prior to or following invasive coronary angiography. Exclusion criteria were presentation with acute myocardial infarction, unstable angina, cardiogenic shock. Of the 1680 examined in the AHES study, 870 patients (Men = 589, Women = 281) were included in this analysis. 489 participants were excluded because they had a previous history of coronary artery bypass

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grafting (n = 191) and/or previous coronary artery stent (n = 298). A further 321 were excluded if the tortuosity could not be assessed in all three vessels.

Patients were interviewed to obtain demographic characteristics, medical history and behavioral habits. Both interview and review of medical record were used to determine the presence of risk factors and to obtain medication use and confirm medical history. The study was approved by the Westmead Hospital (Sydney West Local Health Network) ethics committee, and was performed in accordance with the Declaration of Helsinki. All patients provided written informed consent.

2.2. Evaluation of coronary artery disease

Diagnostic coronary angiography was performed via a femoral or radial approach. The technique employed was determined by vascular accessibility of the patient and operator preference. Selective coronary injections were performed after intracoronary nitroglycerin and filmed in standard projections with a Siemens Bi-Plane radiographic unit (Siemens Healthcare, Germany). All angiograms were filmed at 15 frames/s. Cine runs were stored at the time of acquisition in DICOM format.

Angiograms were analyzed offline by a cardiologist (author J.C.) blinded to the medical history and adjunctive investigations. Two orthogonal views were examined in end-diastole to maximize contrast enhancement and vessel diameter. The image with the most severe stenosis was used for each evaluated segment of the coronary arteries. To allow more accurate assessment and classification of lesion severity [4] each lesion that was visually scored as greater than 50% luminal obstruction in a vessel that was ≥1.5 mm diameter was further analyzed by quantitative coronary analysis (QCA) using validated computerized edge-detection software (QCAPLUS, Sanders data Systems, Palo Alto, California, USA). Coronary angiograms were analyzed systematically for:

1) *Vessel score*: A Vessel score was calculated based on the number of vessels with significant obstructive coronary disease. The American College of Cardiology (ACC) taskforce definition from 2011 uses 50% stenosis to define significant vessel disease [5]. This definition was used for the left main coronary artery, right coronary, left anterior descending and left circumflex arteries. Scores ranged from 0 to 4, depending on the number of vessels with greater than 50% stenosis [6]. Left main artery stenosis was scored as double vessel disease.
2) *Gensini score:* This was calculated using the results of the QCA analysis and visual estimation of stenosis severity [7]. This score divides the three coronary arteries into several sub-segments. The percent diameter stenosis is scored from zero to 32 depending on the severity of the stenosis: Zero if normal, 1 for 1–25%, 2 for 25–50%, 4 for 50–75%, 8 for 75–90%, 16 for 99% and 32 for total occlusion. Each segment is given a multiplying factor (from 0.5 for the distal segment to 5 for the left main coronary artery) depending on the significance of the myocardial area supplied by that segment. The sum of the scores gives the Gensini score, which provides an indication of the severity of coronary artery disease stenoses and has been used as a tool to assess the relationship between coronary and other vascular disease [7–10].
3) *Extent score:* this score indicates the percentage of the coronary arterial tree involved by angiographically detectable coronary atheroma independent of the stenosis severity [11]. Luminal irregularity as identified on angiography represents coronary atherosclerosis. The proportion of the vessel with irregularity is multiplied by a factor for each vessel representing the length of the artery. The scores are: left main artery, 5; left anterior descending artery, 20; main diagonal branch (or branches), 10; first septal perforator, 5; left circumflex artery, 20; obtuse marginal artery and posterolateral branch each, 10; right coronary artery, 20; and main posterior descending branch, 10. When the major lateral wall branch was a large obtuse marginal or intermediate vessel with no posterolateral branches, these were given a factor of 20, and the left circumflex artery a factor of 10. The scores for each vessel were added to give a total score out of 100, that is the percentage of the coronary intimal surface area containing coronary atheroma. When a vessel was occluded and the distal vessel was incompletely visualized by coronary collateral flow, the proportion of the vessel not visualized was given the mean score of the remaining arteries.
4) Tortuosity: was identified by the presence of ≥3 bends (defined as ≥45° change in vessel direction) along the main trunk of at least one coronary artery (LAD, LCX, RCA) present in both systole and diastole as previously described [12,13]. We defined severe coronary tortuosity (SCT) as the presence of at least one vessel with tortuosity consistent with our definition.

3. Statistical analysis

Data were analyzed using SAS 9.2 (Statistical Analysis Package, SAS Institute, 2011, North Carolina, USA). All categorical data were reported as percentages and continuous variable expressed as mean ± standard deviation (SD). Student's *t*-test was used for the comparison of demographic data that were continuous variables and chi-squared analysis for categorical variables. Relationships between SCT, gender, age, cardiovascular risk factors (hypertension, diabetes, smoking and hyperlipidemia) and the three coronary artery scores were assessed using Pearson correlations using binary variables for the analysis of risk factors. The odds ratio for tortuosity by gender was examined using logistic regression with men being the reference. A general linear model adjusting for age was used to test the difference in Extent and Gensini scores for men and women with SCT and no SCT. Statistical significance was considered present when $p < 0.05$.

4. Results

4.1. Patient characteristics

The study cohort was predominantly male (67%) with an average age of 59.3 years. Men were of significantly younger age than women (Table 1). There were no significant differences in the presence of traditional cardiac risk factors except for a higher proportion of women having hypertension (75.5 vs. 66.4%, $p = 0.02$) and more men having a history of smoking (73.1% vs. 41.9%, $p < 0.001$). As expected, women were shorter and had a lower body weight ($p < 0.001$). A larger proportion of women had SCT compared to men (45.2% vs. 19.7%, $p < 0.001$). The Gensini, Extent and Vessel scores were substantially higher for the cohort of men compared to women ($p < 0.001$ for all scores).

4.2. Gender comparison of arteries affected by severe coronary tortuosity

The arterial distribution of SCT by gender is shown in Table 2. The LAD was the single artery most affected by SCT. A large number of people had severe tortuosity in both the LAD and LCx. More women had all three vessels affected (19.7% vs. 6.0%), whereas men predominantly had a single vessel affected (63.2% vs. 48%).

Table 3 shows that women were significantly more likely to have tortuosity in any major epicardial coronary artery compared to men. The odds ratio for a woman to have any vessel affected by SCT, compared to a man, was 2.71 ($p < 0.001$).

4.3. Prevalence of risk factors in the cohort with severe coronary tortuosity

Table 4 shows the prevalence of risk factors in the study population comparing those with severe coronary tortuosity to those without it. The overall prevalence of SCT was 28% (244/870). Women contributed