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The Importance of Gender on Coronary Artery Size: In-Vivo Assessment by Intravascular Ultrasound

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Summary

Background: It remains controversial whether women have smaller coronary arteries than men because of a gender-specific trait, or whether the observed differences are primarily due to a difference in body size. Intravascular ultrasound (IVUS), with its ability to provide unique coronary images that allow precise measurement of arterial size in vivo, is ideally suited to address this issue.

Hypothesis: Female gender, independent of body size, is associated with smaller coronary artery size as measured by intracoronary ultrasound.

Methods: Intravascular ultrasound images of normal left main arteries were identified retrospectively from a single center database. Associations between demographic and clinical characteristics (including body size) and left main coronary dimensions were assessed with univariant and multivariate regression analyses.

Results: We identified 257 completely normal left main arteries. Mean left main arterial areas were smaller in women than in men (17.2 vs. 20.6 mm^2, $p < 0.001$), as were mean luminal areas (14.0 vs. 16.7 mm^2, $p < 0.001$). By multiple regression analysis, the independent predictors of left main lumen were body surface area ($p < 0.001$) and gender ($p = 0.003$).

Conclusions: Body surface area and gender are both independent predictors of coronary artery size, although body size has a greater influence than gender.

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Introduction

Gender is an independent predictor of outcomes after coronary revascularization.[1–10] Many have attributed this finding to the differences in clinical characteristics between men and women; women undergoing revascularization are generally older and smaller than men and have more comorbidity such as diabetes and hypertension.[1–3, 7, 8, 10]

Some investigators have postulated that poorer outcomes are related to the smaller coronary arteries in women,[1, 2, 7, 8, 10] since vessel size is related to outcomes after percutaneous coronary intervention.[11–14] However, prior investigations examining the effect of gender on coronary artery size have produced variable results. Generally, women have been found to have smaller coronary arteries,[15, 16] but others have reported that this apparent difference in artery size is due to the mass of the heart, not any specific gender trait.[17] Evaluating the potential relationship between gender and coronary artery size from earlier investigations is difficult because of the various methods (autopsied hearts[17, 18] or arteriograms[1, 5, 19–21]). Intravascular ultrasound (IVUS) provides images of coronary arteries in vivo, allowing more accurate assessment of both lumen and vessel dimensions.[22–24] This investigation was undertaken to examine further the potential influence of gender versus body size on coronary artery size as measured by intracoronary ultrasound.

Methods

Patient Selection

Patients with preinterventional IVUS imaging that included the left main artery were retrospectively identified from the database in the Ultrasound Core Laboratory at the Washington

Hospital Center. Baseline demographic and clinical data were obtained from hospital records. Patients with cardiomyopathy were excluded from the study to avoid the potential cofounding effects of an enlarged heart.

Intravascular Ultrasound Imaging and Analysis

All IVUS images were obtained after the administration of intracoronary nitroglycerin. Under fluoroscopic guidance, a 30 or 40 MHz ultrasound catheter (Boston Scientific, Maple Grove, Minn., USA) was advanced to the distal left coronary system. Continuous imaging was performed with a motorized pullback at 0.5 mm/s to the aorto-ostial junction. Images were recorded on 0.5" s-VHS tape for subsequent analysis.

Only left main arteries free of significant atherosclerotic disease (< 20% cross-sectional narrowing) were included in the final analysis in order to avoid remodeling effects.[23–25] In addition, the left main could not contain any calcification, dissections, or hematomas.

To compare left main coronary artery size in men and women, vascular cross-sectional areas 1.0 cm proximal to the bifurcation were measured. Digitized images were measured by direct planimetry using a computer-analysis system (TapeMeasure 2.1.0; INDEC Inc., Mountain View, Calif., USA) according to the Standards for the Acquisition, Measurement, and Reporting of Intravascular Ultrasound Studies.[25]

Left Ventricular Mass

To explore the relationship between coronary artery dimension and heart size further, left ventricular (LV) mass was assessed in patients who had an echocardiogram performed within 1 year of the catheterization and IVUS. Left ventricular mass was calculated using the modified D3 formula.[26]

Statistical Analysis

Demographic and baseline clinical variables were analyzed using descriptive statistics. Continuous variables are presented as the mean ± standard deviation. Comparisons between men and women were made by an unpaired, two-sided Student's *t*-test, and $p < 0.05$ was considered significant. To identify the determinates of coronary artery size, a stepwise multiple linear regression was used, entering all parameters that were significant ($p < 0.10$) by univariant analysis. All analyses were performed using StatView 5.0.1 (SAS Institute, Inc., Cary, N.C., USA).

Results

Patients

Over a 20-month interval, 4,766 patients had IVUS imaging in association with a diagnostic or therapeutic procedure at the Washington Hospital Center. Of these, only 257 patients (141 men, 116 women) had both (1) complete imaging of the left main artery prior to an intervention with a motorized pullback, and (2) a completely normal, nondiseased left main artery.

TABLE I Demographic and clinical characteristics

Characteristic	Men (n = 141)	Women (n = 116)	Significance (p value)
Mean age (years)	59.7 ± 10.6	64.9 ± 12.1	< 0.001
Hypertension (%)	83 (58.9)	79 (68.1)	0.13
Diabetes (%)	28 (19.9)	36 (31.0)	0.04
Body surface area (m^2)	2.05 ± 0.20	1.83 ± 0.21	< 0.001

TABLE II Univariate comparison of left main coronary artery dimensions in men and women

Dimension	Men (n = 141)	Women (n = 116)	Significance (p value)
Lumen CSA (mm^2)	16.65 ± 4.04	14.0 ± 3.24	< 0.001
EEM CSA (mm^2)	20.58 ± 4.91	17.21 ± 3.97	< 0.001
MLD (mm^2)	4.26 ± 0.55	3.92 ± 0.45	< 0.001

Abbreviations: CSA = cross-sectional area, EEM = external elastic membrane, MLD = minimum lumen diameter.

Demographic and clinical characteristics are presented in Table I. Women were older (64.9 vs. 59.7 years, $p < 0.001$) and had diabetes more frequently than men. They also had a smaller mean body surface area (1.83 vs. 2.05 m^2, $p < 0.001$). There was no significant difference in the prevalence of hypertension (68 vs. 59%, $p = 0.13$).

Univariate Analysis

Univariate comparisons of left main coronary artery dimensions are listed in Table II. In the left main, uncorrected luminal and external elastic membrane cross-sectional areas (EEM CSA) were significantly smaller in women than in men (14.0 vs. 16.7 mm^2, $p < 0.001$; and 17.2 vs. 20.6 mm^2, $p < 0.001$, respectively). Minimum lumen diameter was also significantly smaller in women ($p < 0.001$). There was no significant difference in any left main IVUS measurement between those with and without hypertension or diabetes.

Body surface area had a highly significant positive correlation with EEM CSA, lumen CSA, and minimum lumen diameter (all $p < 0.001$). Neither age, height, nor weight correlated independently with arterial dimensions. Similarly, there was no significant correlation between a diagnosis of hypertension or diabetes and arterial dimensions.

Multivariate Analysis

Only gender and body surface area reached the predetermined level of statistical significance to be included in the final regression model. Analysis (Table III) demonstrated that body surface area was the strongest predictor of EEM CSA (β =

TABLE III Multiple linear regression models predicting left main coronary artery size

Dimension	Characteristic	β	Significance (p value)
Lumen CSA			
	BSA (m^2)	5.61	< 0.001
	Male	1.42	0.003
EEM CSA			
	BSA (m^2)	6.93	< 0.001
	Male	1.85	0.005

Abbreviation: BSA = body surface area. Other abbreviations as in Table II.

6.93, 95% confidence interval [CI] 4.29–9.58, $p < 0.001$). This means that every 1.0 m^2 increase in body surface area, the EEM CSA would increase 6.93 mm^2 (with a 95% CI of 4.29–9.58 mm^2). However, even after correcting for body surface area, male gender remained a significant predictor of larger EEM CSA ($\beta = 1.85$, 95% CI 0.64–3.06, $p = 0.003$). This association with gender was also true for lumen CSA ($\beta = 1.42$, 95% CI 0.43–2.41, $p = 0.005$) and minimum lumen diameter ($\beta = 0.19$, 95% CI 0.05–0.33, $p = 0.007$).

Echocardiographic Analysis

Echocardiographic information on LV dimensions within 1 year of the IVUS was available in 45 patients (19 men, 26 women). The left main IVUS measurements were similar in the echocardiography subgroup compared with the entire study population. While men tended to have a larger LV mass than women, there was no significant difference in LV mass once corrected for body surface area (112.03 ± 30.22 vs. 109.72 ± 25.97 g/m^2, $p = 0.79$).

As in the entire study population, only gender and body surface area reached the predetermined level of statistical significance to be included in the final regression model. Multiple linear regression analysis demonstrated that, after correcting for LV mass, male gender remained an independent predictor of larger lumen CSA ($\beta = 3.23$, $p = 0.004$), EEM CSA ($\beta = 4.37$, $p = 0.002$), and minimum lumen diameter ($\beta = 0.36$, $p = 0.02$).

Discussion

In this population of patients undergoing IVUS with non-diseased left main coronary arteries, women had significantly smaller arteries than men. This difference was independent of body surface area or LV mass.

The association of gender with coronary artery size is consistent with prior pathologic and angiographic investigations. Roberts and Roberts[17] examined necropsy hearts and reported smaller mean CSAs of coronary arteries in women than in men (5.9 vs. 7.7mm^2, $p < 0.001$). An angiographic investigation by MacAlpin *et al.*[19] found a significantly smaller mean diameter of the left main in normal women than in normal men. Dodge *et al.*[15] reviewed over 9,000 consecutive catheterization studies to identify only those films with no evidence of atherosclerotic plaque. Normal arteriograms were obtained from only 83 patients (73 men, 10 women). They reported significantly smaller epicardial diameter in women. However, unlike studies using various methods with only a fair ability to measure small differences in coronary size, this analysis used IVUS, with its high-resolution images. Kornowski *et al.*[23] also used IVUS and found no difference in size between the genders after correcting for body surface area, but this study was limited by the selection of several different vessel locations that were not always completely free of disease. Similarly, the study by Sheifer *et al.*[16] did not select disease-free vessels, which may have confounded the results due to vascular remodeling.

It has long been known that ventricular mass correlates strongly with body size,[27, 28] and that the ventricular mass strongly predicts the size of the coronaries. Multiple investigators have reported a positive correlation between the amount of myocardium and the size of the coronary arteries, regardless of the methodology employed.[15, 17–21, 29, 30] This investigation also found a strong positive correlation between body surface area and coronary artery size. Multivariate regression revealed that after correcting for LV mass, gender remained an independent predictor of the size of the coronary lumen. Unlike some prior reports, the use of echocardiography for assessing LV mass and IVUS to determine coronary size probably accounts for the increased power in this study to detect small differences due to gender compared with the larger differences in coronary size due to body and heart size.

Conclusion

The mechanism of a gender-specific difference in coronary artery size is not known and will require further investigation. Gender-specific hormone levels may play some role. Current data suggest that, among other actions, estrogen affects vasodilation and inhibits the development of atherosclerosis.[31, 32] It is possible that estrogen may affect the development and growth of coronary vessels or alter its chronic vasomotor tone. Further investigation into the influences of gender on basic anatomy may provide insight into cardiovascular pathophysiology that ultimately benefits both men and women.

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