Sex Differences in Mortality Associated With Computed Tomographic Angiographic Measurements of Obstructive and Nonobstructive Coronary Artery Disease

An Exploratory Analysis

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Background—Sex differences exist in the prevalence and severity of obstructive coronary artery disease (CAD). Limited data are available to explore sex differences in prognosis with coronary computed tomographic angiographic (CCTA) measurements of CAD including novel nonobstructive plaque extent.

Methods and Results—A total of 1127 consecutive patients were clinically referred to 16-slice CCTA and followed for the occurrence of all-cause death. Time to death was calculated by univariable and multivariable Cox proportional hazard models. Four-year survival (92.1%) was similar by sex ($P=0.52$). Women more often had no coronary stenosis (54%) as compared with men (28%) ($P<0.0001$). Mortality worsened for both women ($P<0.0001$) and men ($P=0.002$) by the number of vessels with ≥50% stenosis. For women, overall mortality ranged from 3.5% for no CAD to 25.0% for women with 3-vessel plus left main obstructive CAD ($P<0.0001$). For men, overall mortality ranged from 2.7% for no CAD to 17.4% for males with 3-vessel plus left main obstructive CAD ($P=0.002$). Nonobstructive disease was prevalent in women (range, 24% to 66%) and men (range, 45% to 74%) ages 45 to ≥80 years. Nonobstructive CAD extent was a significant estimator of all-cause mortality when added to a model containing pretest CAD likelihood and obstructive CAD extent ($P=0.039$). For men, in a risk-adjusted model including pretest CAD likelihood and obstructive CAD, the number of nonobstructive lesions was not a significant estimator of mortality ($P=0.9$). For women, the relative hazard for mortality, in a multivariable model, was 1.3 per nonobstructive lesion ($P=0.003$), including pretest CAD likelihood and obstructive CAD as covariates. For women, risk-adjusted median mortality ranged from 2.9% to 10.9% for none to ≥4 nonobstructive lesions ($P<0.0001$).

Conclusions—Based on our preliminary analyses, CCTA obstructive and nonobstructive CAD adds incremental value to clinical assessment for risk stratification. Moreover, the extent of nonobstructive CAD by CCTA predicts mortality in women but not in men and may be helpful to optimize therapeutic strategies for women. **(*Circ Cardiovasc Imaging*. 2010;3:473-481.)**

Key Words: sex ■ prognosis ■ atherosclerosis

Considerable research has focused on sex differences in clinical presentation and outcomes for coronary artery disease (CAD).[1–6] Women frequently present for evaluation of chest pain symptoms, with an estimated 5 million women referred for a diagnostic evaluation of suspected CAD.[2] Notable differences exist in the prevalence of obstructive CAD in women as compared with men undergoing invasive coronary angiography. In a recent report from the American College of Cardiology's National Cardiovascular Data Registry (ACC-NCDR), women with stable chest pain had a 56% lower risk-adjusted odds of significant CAD than that of men ($P<0.0001$).[5]

Clinical Perspective on p 481

Recently, coronary computed tomographic coronary angiography (CCTA) was introduced as a noninvasive approach for the evaluation of CAD. Recent reports note that this modality has a high diagnostic accuracy,[7–9] including similar accuracy within a small series of women.[10] Early reports note the potential of CCTA to prognosticate CAD outcomes,[11–18] yet no study has compared risk stratification using CCTA measures of obstructive and nonobstructive CAD by sex. Given the higher prevalence of angina,[19] more atypical presentation, and notable limitations of stress testing in

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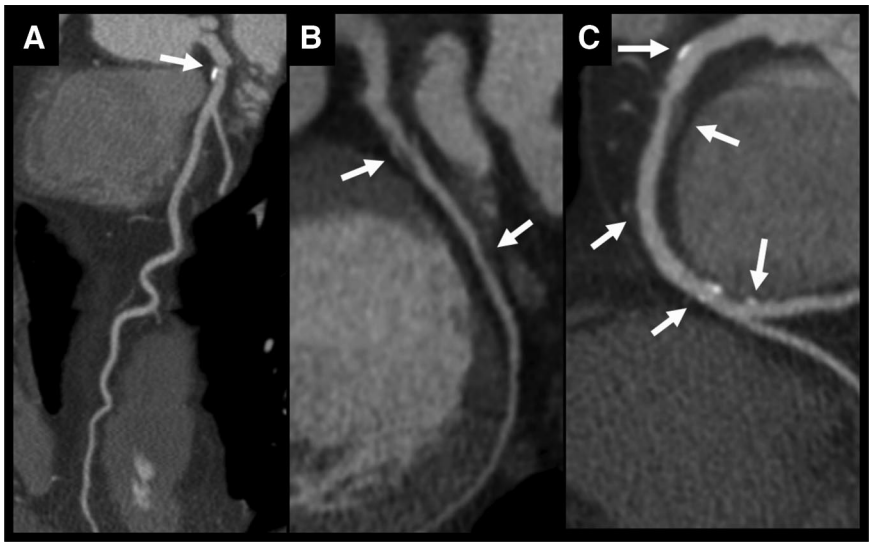


Figure 1. Examples of nonobstructive CAD. A, Calcified lesion in the proximal left anterior descending artery. B, Two lesions: "mixed" and noncalcified plaque in the proximal and midportion of the left circumflex artery. C, Three lesions: Calcified and noncalcified plaque in the proximal right coronary artery (RCA); noncalcified plaque in the midportion of the RCA; and calcified plaque in the distal RCA and proximal posterior descending artery.

women, development of a prognostically accurate, noninvasive test capable of detailing obstructive and nonobstructive CAD may prove useful for evaluation of cardiac risk in females. It remains uncertain whether vascular dysfunction in the setting of nonobstructive CAD may be driving symptom burden and accelerating risk in women. The current report detailed an exploratory analysis of sex differences in 4-year all-cause mortality by CCTA measurements of obstructive and nonobstructive CAD. The purpose of this exploratory analysis was to devise a preliminary model on which to guide further research on risk detection for women.

Methods

Patient Entry Criteria

The methods used in the present study were previously reported.[11] A total of 1127 stable patients with signs and symptoms suggestive of CAD were consecutively and prospectively enrolled and underwent CCTA at 1 outpatient CCTA facility. Mortality follow-up occurred retrospectively on a periodic basis. Based on age, sex, and chest pain symptoms, a pretest likelihood of CAD was determined.[20] All patients were in normal sinus rhythm and capable of breath-holding during the procedure. Each patient provided informed consent for the procedure and clinical follow-up. Follow-up procedures were approved by our center's institutional review board.

CCTA Protocol and Image Reconstruction

Patients with heart rates of ≥70 beats per minute were given 5 mg of intravenous metoprolol at 5-minute intervals (cumulative dose, 25 mg). Scans were performed using a 16-slice multidetector CT scanner (GE Lightspead Pro-16, Milwaukee, Wis). One-hundred milliliters of iodinated contrast (Bracco, Princeton, NJ) was injected followed by a 50-mL saline flush. Initial imaging of contrast was performed at 2-mm superior to take-off of the left main artery. Technical parameters of the CCTA procedure included 16×0.625 mm collimation, tube voltage of 120 mV, and effective 400 to 650 mA. Helical CT data were obtained using retrospective ECG gating. Images were reconstructed immediately after CCTA to identify motion-free coronary artery images. ECG-gated data were reconstructed at 70% to 80% of the cardiac cycle after the QRS complex to identify central diastole. Data sets were reconstructed at 40% to 50% of the cardiac cycle to identify central early diastole. Optimal phase reconstruction was assessed by comparing different phases; the phase with least arterial motion was identified for analysis. CCTA was evaluated on 2-dimensional maximum intensity projection in oblique views focusing on coronary segments. Two orthogonal thin maximal intensity projection cardiocentric views were used for the left anterior descending, left circumflex, and right coronary arteries. Three-dimensional rotation was performed to image diagonal and marginal branch vessels. Three-dimensional views using curved multiplanar reformation and short-axis cross-sectional viewing techniques were additionally used to define coronary plaque presence.

Estimated effective radiation dose was 10.7 mSv for women and 7.6 mSv for men.

CCTA Analyses

Scans were analyzed blinded to clinical data by an experienced cardiologist. Sixteen coronary segments were scored, using the American Heart Association (AHA) segmentation.[11] The arterial tree was divided into proximal, mid, and distal segments for the left anterior descending, right, left circumflex, diagonal, and obtuse marginal arteries. The left main coronary artery was also scored. Each segment was scored for the presence of coronary plaque (mixed, calcified, or noncalcified) or stenosis. The presence of atherosclerotic plaque in a segment was defined as tissue structures >1 mm^2 within or adjacent to the lumen. The number of nonobstructive lesions was summed (Figure 1). Coronary stenosis was defined as <30%, 30% to 49%, and ≥50% obstruction of luminal diameter.

Follow-Up

The primary end point was time to all-cause death. Death status was ascertained by querying the Social Security Death Index and complete in 100% of patients. Median (25th to 75th percentiles) follow-up time was 4.1 (3.8 to 4.4) years.

Statistical Analyses

Categorical variables were compared using a χ^2 statistic. For unadjusted analyses, Kaplan-Meier survival curves were plotted and compared using the log-rank statistic. Univariable and multivariable Cox models were calculated, with multivariable models including covariate adjustment with CAD pretest likelihood and risk factors (including age, hypertension, diabetes, and smoking) as covariates. When not specified as a multivariable or risk-adjusted model, CCTA variables were evaluated univariably in the overall cohort or within sex subgroups. Hazard ratios and 95% confidence intervals were calculated. From the multivariable model, predicted mortality rates were calculated. A first-order interaction of sex by CAD extent was calculated. Additionally, a first-order interaction of sex by the number of nonobstructive lesions was calculated. Model overfitting procedures were considered by limiting models to 1 variable for every 10 deaths. The proportional hazards assumption was tested by

Table 1. Clinical Characteristics of the 646 Women and 481 Men Undergoing CCTA

	Women (n=646)	Men (n=481)	*P* Value
Age, y	60±10	59±10	0.15
Cardiac risk factors			
Hypertension	59%	54%	0.076
Hyperlipidemia	54%	50%	0.22
Diabetes mellitus	16%	18%	0.45
Family history of CHD	69%	61%	0.002
Smoking	23%	32%	0.001
Symptoms			<0.0001
Atypical chest pain	57%	45%	
Typical angina	3%	2%	
Heart failure	8%	5%	
Nonanginal symptoms	7%	6%	
Anginal equivalents*	13%	10%	0.089
Prior arrhythmia	5%	3%	0.074
Pretest CAD risk			<0.0001
Low	31%	28%	
Intermediate	54%	39%	
High	15%	33%	
No. of ≥50% stenosis			<0.0001
None	55%	28%	
1 vessel	16%	17%	
2- to 3 vessels	29%	55%	
Proximal LAD stenosis	9%	7%	0.24
Nonobstructive CAD			
None	60%	51%	0.002
1 to 3 lesions	34%	44%	
≥4 lesions	6%	5%	

CHD indicates coronary heart disease; and LAD, left anterior descending.
*Angina equivalent symptoms: nausea or excessive fatigue.
Age is presented as mean±standard deviation and compared using a *t* test. All other data are presented as frequencies and compared using a χ^2 likelihood ratio statistic or using a linear-by-linear association χ^2 statistic for CAD variable.

Schoenfeld residuals and inspection of hazard ratio plots. From the Cox model, the *C*-statistic was calculated using the method of Harrell (Stata 9.0). Risk-adjusted median mortality (25th to 75th percentiles) was plotted by the nonobstructive lesion extent and compared using an interaction term from a general linear model. As noted above, risk-adjusted mortality included nonobstructive lesion extent in a combined with pretest CAD likelihood and risk factors. For the plotting of risk-adjusted mortality, the median and interquartile ranges were calculated for risk-adjusted mortality in women and men by the number of nonobstructive lesions.

Results

Sex Differences in Clinical and CCTA Characteristics

Women generally had a greater risk factor burden and more frequent atypical symptoms (Table 1). Angina equivalents occurred in 12% of patients including exertional fatigue or nausea. Non–chest pain indications for CCTA included arrhythmias (4.3%), a positive stress test (2.9%), and an abnormal echocardiogram, ECG, or chest radiograph (6.4%).

Although the frequency of pretest likelihood varied by sex ($P<0.0001$), when categories were combined, nearly two thirds of women and men were at intermediate-high CAD likelihood ($P=0.24$). More than half of women had no coronary stenosis ≥50% as compared with 28% men ($P<0.0001$), whereas men were more likely to have multivessel CAD (55% versus 29%, $P<0.0001$).

Obstructive CAD and Nonobstructive Atherosclerosis Prevalence by Age Deciles and Sex

The prevalence of obstructive CAD increased with age for both women and men (Figure 2). As expected, there was a lower prevalence of obstructive CAD in women <80 years of age. A similar prevalence of obstructive CAD was noted for women and men ages ≥80 years ($P>0.45$).

In women and men with no coronary stenosis <50%, the prevalence and extent of nonobstructive CAD varied by sex (Figure 3). For women, there was a directly proportional relationship between age and the presence and extent of nonobstructive CAD ($P<0.0001$). However, differences in the prevalence of nonobstructive CAD across age subsets were not observed for men ($P=0.76$). Few men were included in this category of <50% stenosis, with limited frequencies in older age subsets.

All-Cause Mortality

Overall 4-year survival (92.1%) was similar by sex ($P=0.52$), with 48 and 41 deaths observed in women and men. In a Cox model controlling for obstructive CAD, sex was not a significant estimator of mortality ($P=0.37$). Chest pain was not a significant estimator of mortality ($P=0.52$). In intermediate likelihood or symptomatic patients, survival did not differ by sex ($P=0.42$).

Prognosis by CAD Extent and Severity by Sex

The absence of obstructive and nonobstructive CAD was associated with low mortality (2.2% at 4 years in 341 women and men). Obstructive CAD extent added to the estimation of all-cause mortality in a model containing pretest CAD likelihood (Table 2, $P<0.0001$). That is, for women and men, mortality worsened with the number of vessels with ≥50% stenosis (Table 3, multivariable $P<0.0001$ for the female subgroup and multivariable $P=0.004$ for the male subgroup). In subgroup analysis of women, overall mortality was 3.5%, 5.6%, 12.3%, 14.9%, and 25.0% for none, 1-vessel, 2-vessel, 3-vessel, and 3-vessel plus left main CAD, respectively ($P<0.0001$) (Figure 4). Similarly for men, overall mortality was 2.7%, 4.4%, 7.9%, 14.3%, and 17.4% for none, 1-vessel, 2-vessel, 3-vessel, and 3-vessel plus left main CAD, respectively ($P=0.002$). A first-order interaction of female sex by the number of vessels with ≥50% stenosis revealed a hazard of 1.22 (0.47 to 1.89, $P=0.68$), 2.79 (1.23 to 6.30, $P=0.014$), 2.97 (1.33 to 6.65, $P=0.008$), and 5.81 (2.31 to 14.60, $P<0.0001$), respectively for 1-, 2-, 3-, and 3-vessel plus left main CAD.

Nonobstructive Disease and Mortality by Sex

Nonobstructive CAD extent was a significant estimator of all-cause mortality when added to a model containing pretest CAD likelihood and obstructive CAD extent (Table 2,

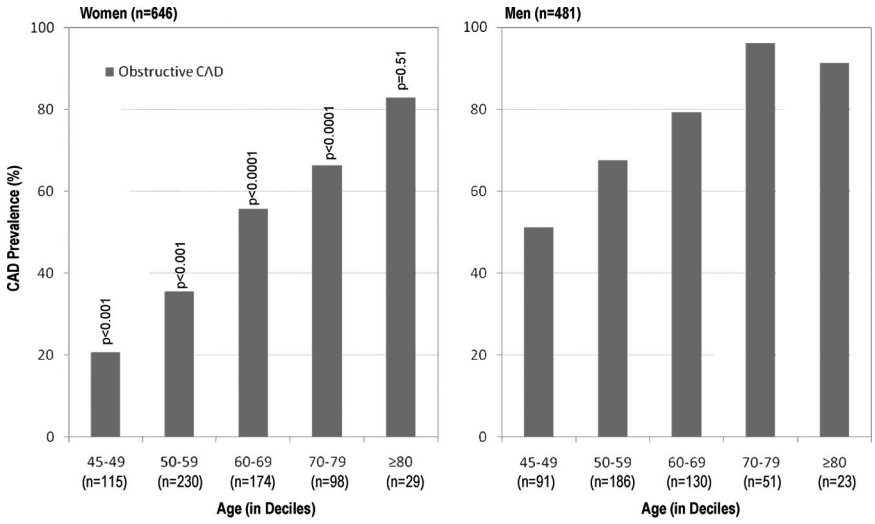


Figure 2. Prevalence of obstructive CAD in women and men by age deciles. Probability values at the top of each column represent the comparative percent of CCTA obstructive CAD in women versus similarly aged men.

$P=0.039$). For women, the relative hazard for mortality in a multivariable model was 1.3 per nonobstructive lesion ($P=0.003$), including pretest CAD likelihood and obstructive CAD as covariates. For men, the number of nonobstructive lesions was not a significant estimator of mortality (multivariable $P=0.95$, Table 3). Figure 5 plots the risk-adjusted (controlling for CAD pretest likelihood, number of vessels with CAD, hypertension, diabetes, and smoking) overall mortality for women by the number of nonobstructive lesions. For women, risk-adjusted median mortality ranged from 2.6% to 10.9% for none to ≥4 nonobstructive lesions (general linear model, $P<0.0001$). For men, risk-adjusted median mortality ranged from 2.9% to 8.8% for none to ≥4 nonobstructive lesions (general linear model, $P<0.0001$). A first-order interaction of female sex by the number of nonobstructive lesions revealed a hazard of 3.17 (1.30 to 7.70, $P=0.011$), 8.67 (3.32 to 22.63, $P<0.0001$) for 1 to 3 and ≥4 lesions.

In a subset analysis of 490 patients with no CAD stenosis ≥50%, the number of nonobstructive lesions was a significant estimator of time to death in a Kaplan-Meier survival analysis ($P=0.001$) (Figure 6). Kaplan-Meier survival by the number of nonobstructive lesions was nonsignificant for men ($P=0.75$) yet highly significant in women ($P<0.0001$, Figure 6). Women with 1 to 3 and ≥4 nonobstructive lesions had a relative hazard of 1.6 (univariable $P=0.046$) and 2.9 (univariable $P=0.021$) when compared with those with no nonobstructive CAD. Given that only 20 deaths occurred in this subset, we limited our covariates to only smoking and age. In this adjusted model, nonobstructive CAD remained a significant estimator of mortality ($P=0.008$).

Discussion

The current report provides an exploratory analysis of the mortality risk associated with CCTA obstructive combined with the novel imaging parameter nonobstructive CAD in women and men. These preliminary findings reveal that CCTA is effective at delineating mortality risk in women, an important finding given the technical limitations and challenges with conventional stress testing.[21] These results highlight a unique risk marker provided by CCTA, that is, the ability to noninvasively visualize obstructive combined with nonobstructive CAD, providing confirmatory evidence as to

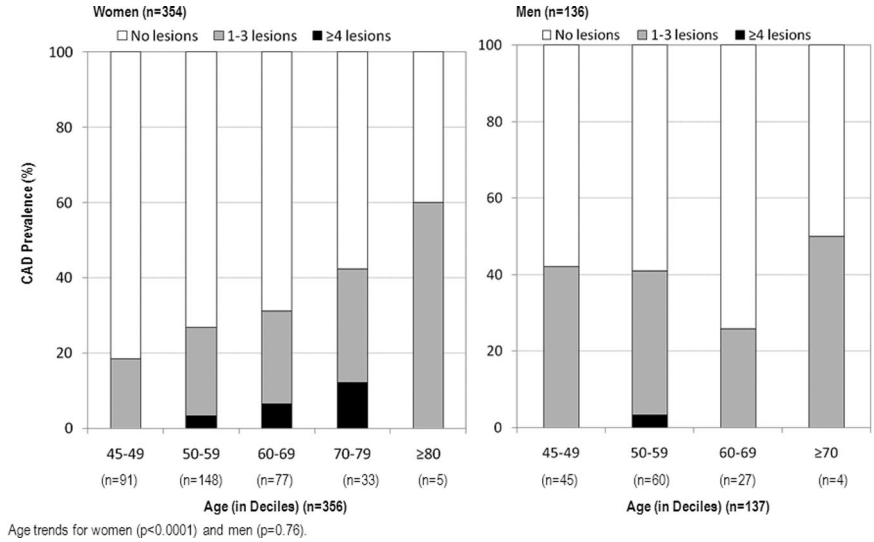


Figure 3. Prevalence of nonobstructive CAD in women and men by age deciles in 490 patients with <50% coronary stenosis. For men, ages 70 and older were combined (n=4).

Table 2. Cox Proportional Hazards Models Including the Added Value of Nonobstructive and Obstructive CAD

	Hazard Ratio	95% Confidence Interval	*P* Value
I. Clinical model (model $\chi^2=19$, $P<0.0001$)			
Pretest CAD likelihood (per risk category)	1.9	1.4–2.6	<0.0001
C statistic=0.63			
II. Adding obstructive CAD extent (model $\chi^2=37$, $P<0.0001$)			
Pretest CAD likelihood (per risk category)	1.6	1.1–2.1	0.005
Vessels with ≥50% stenosis (per vessel)	1.4	1.2–1.7	<0.0001
+Obstructive CAD			
C statistic=0.69			
III. Adding nonobstructive CAD extent (model $\chi^2=58$, $P<0.0001$)			
Pretest CAD likelihood (per risk category)	1.5	1.1–2.1	0.006
Vessels with ≥50% stenosis (per vessel)	1.3	1.1–1.5	0.005
Nonobstructive lesions (per lesion)	1.1	1.1–1.3	0.039
+Nonobstructive lesions			
C statistic=0.72			

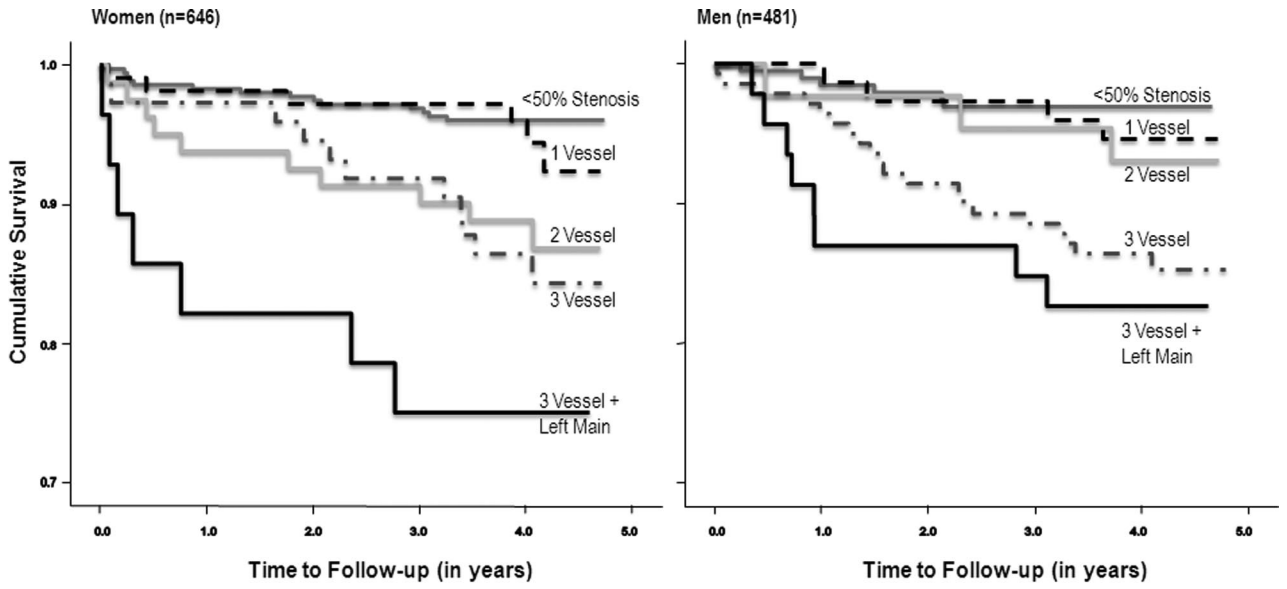
the underlying burden of atherosclerosis that may be etiologic for symptoms. This approach requires prospective validation in larger cohorts than presented herein but may have appeal to clinicians vexed with the optimal evaluation of suspected cardiac symptoms in women.

Evidence consistently reports a lower rate of obstructive CAD in symptomatic women referred for invasive coronary angiography,[3–5] and this has important implications for the use of CCTA. For women, their high rate of no obstructive CAD often leads to an exclusion of a cardiac diagnosis prompting further evaluation for a noncardiac symptom etiology. The inclusion of CCTA-defined nonobstructive disease provided novel prognostic information not available from other noninvasive imaging techniques. The degree to which nonobstructive CAD may inform the cardiac diagnosis has important implications for the balance between the benefits of CCTA in women and its associated risks from radiation exposure (mean effective dose, 11.5 mSv; ≈30% higher doses for women).[22] The benefit of nonobstructive CAD in clinical decision making may offer promise by augmenting the intensity of preventive efforts when compared with the patient without any detectable plaque or stenosis.

There is a paradox for women with a reported higher prevalence of angina and lower risk of acute coronary syndromes, yet a greater number of total deaths related to coronary heart disease and more hospitalizations for angina and heart failure.[23] The current data are intriguing in that they put forth the concept that a missing link within our diagnostic paradigm may be nonobstructive CAD. Importantly, nonobstructive disease was a significant estimator of mortality in women ($P<0.0001$), whereas for men, nonobstructive disease was not additive beyond that of obstructive CAD. An important limitation that remains unexplored herein is the degree to which a coronary artery calcium scan may suffice for risk stratification purposes in women while minimizing radiation exposure. Despite this, prior reports have noted the importance of nonobstructive disease as a harbinger of future CAD events.[24–29] Data such as these underscore the need of assessing more than obstructive CAD burden in women presenting for evaluation of chest pain symptoms. We believe that documentation of nonobstructive disease by CCTA may reduce indecision and improve the rapidity of therapeutic decision-making for women.

Table 3. Sex Differences in Prognosis With Nonobstructive and Obstructive CAD

	Hazard Ratio	95% Confidence Interval	*P* Value
Obstructive CAD extent subgroup analysis			
Ia. Adjusted model (including covariate-pretest CAD likelihood) for obstructive CAD extent in women (model $\chi^2=35$, df=2, $P<0.0001$)			
No. of vessels with ≥50% stenosis (per vessel)	1.5	1.2–1.9	<0.0001
Ib. Adjusted model (including covariate-pretest CAD likelihood) for obstructive CAD extent in men (model $\chi^2=12$, df=2, $P=0.002$)			
No. of vessels with ≥50% stenosis (per vessel)	1.6	1.2–2.1	0.004
Nonobstructive lesion extent subgroup analysis			
IIa. Adjusted model (including covariates-pretest CAD likelihood) for nonobstructive CAD extent in women (model $\chi^2=27$, df=3, $P<0.0001$)			
No. of vessels with ≥50% stenosis (per vessel)	2.1	1.3–3.4	0.003
No. of nonobstructive lesions (per lesion)	1.3	1.1–1.5	0.005
IIb. Adjusted model (including covariate-pretest CAD likelihood) for obstructive CAD extent in men (model $\chi^2=18$, df=3, $P=0.0001$)			
No. of vessels with ≥50% stenosis (per vessel)	1.5	1.2–2.0	0.002
No. of nonobstructive lesions (per lesion)	1.1	0.8–1.3	0.95



	Risk-Adjusted Annual Death Rates (Controlling for Pretest CAD Likelihood, Nonobstructive CAD Including a First Order Interaction of Gender x Obstructive CAD Extent)	
	Women	Men
<50% Stenosis:	0.9% ± 0.6%	0.8% ± 0.3%
1 Vessel:	2.0% ± 0.8%	1.5% ± 0.5%
2 Vessel:	2.8% ± 1.7%	2.3% ± 0.7%
3 Vessel:	3.9% ± 2.4%	3.3% ± 1.1%
3 Vessel Plus Left Main	4.7% ± 3.6%	4.9% ± 5.0%

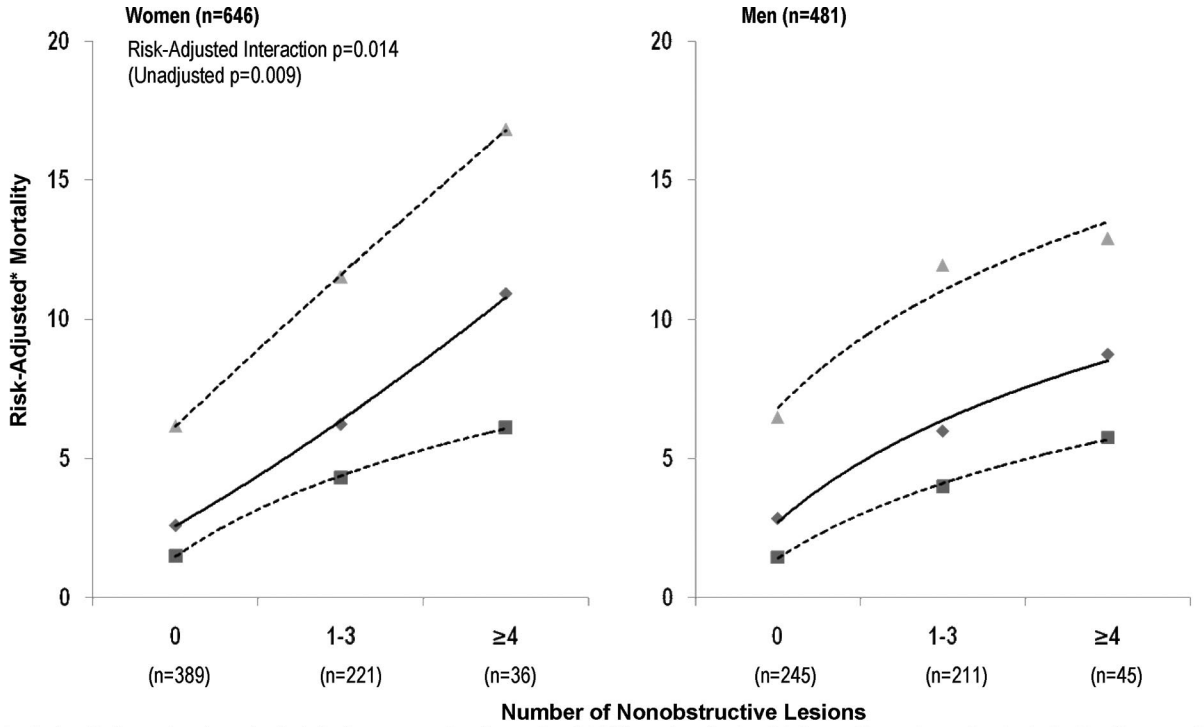
Figure 4. Unadjusted, all-cause 4-year Kaplan-Meier survival in 1127 symptomatic women and men by the number of vessels with ≥50% stenosis. Tables, below the figures, report adjusted annual mortality rates.

Several reports have documented a moderate correlation between coronary plaque by CCTA and intravascular ultrasound.[30–32] Intravascular ultrasound–documented nonobstructive atheroma frequently comprises features consistent with vulnerable plaque,[33] leading to more progressive disease and clinical instability.[33–37] Within the current series, nonobstructive disease was prevalent in both younger and older women and associated with higher mortality risk. Significant and extensive calcified plaque has similarly elevated risk in women as compared with men.[24,29] The observed higher risk of nonobstructive disease in women supports a hypothesis of a sex-specific pathophysiology for atherosclerosis. It remains plausible that a differential symptom presentation in women may relate to underlying vascular dysfunction in the setting of nonobstructive disease. In a recent report in 142 patients with evidence of mild CAD, atheroma burden and eccentricity was significantly greater in men than women.[38] However, maximal coronary flow reserve was significantly lower in women than men ($P<0.001$), suggesting that impaired flow in the setting of subcritical disease may figure prominently in symptom burden for women.[38]

Another important observation from the current report is the higher mortality risk in women as compared with men with multivessel CAD. This finding is consistent with numerous reports and AHA statistics noting that women with CAD have higher worsening cardiac outcomes.[2–5,23,39–41] Prior results have indicated that women with high-risk coronary calcification are also at higher risk than their male counterparts.[24,29] From the ACC-NCDR Registry, women with multivessel CAD had a nearly 2-fold higher in-hospital mortality when compared with men ($P=0.013$).[5] From our report, 3-vessel CAD including significant left main stenosis was associated with a higher 4-year mortality in women as compared with men, even when controlling for an array of clinical covariates.

Study Limitations

Clinical outcomes data require lengthy follow-up times, and the current data represent extended follow-up with 16-slice CCTA. Our report is exploratory and requires validation in larger patient series, consistent with established imaging modalities. The current sample size is small and underpowered for the estimation of sex-specific mortality differences. Importantly, we included a consecutive series of women and men including those without appropriate indications for imaging that may have influenced our findings. CCTA has been reported to overestimate percent stenosis when compared with invasive angiography, the degree to which this influences outcomes is unknown. Only visual estimates of nonobstructive CAD were applied herein because validated quantification algorithms are not currently available. We also did not have available the location and composition (ie,

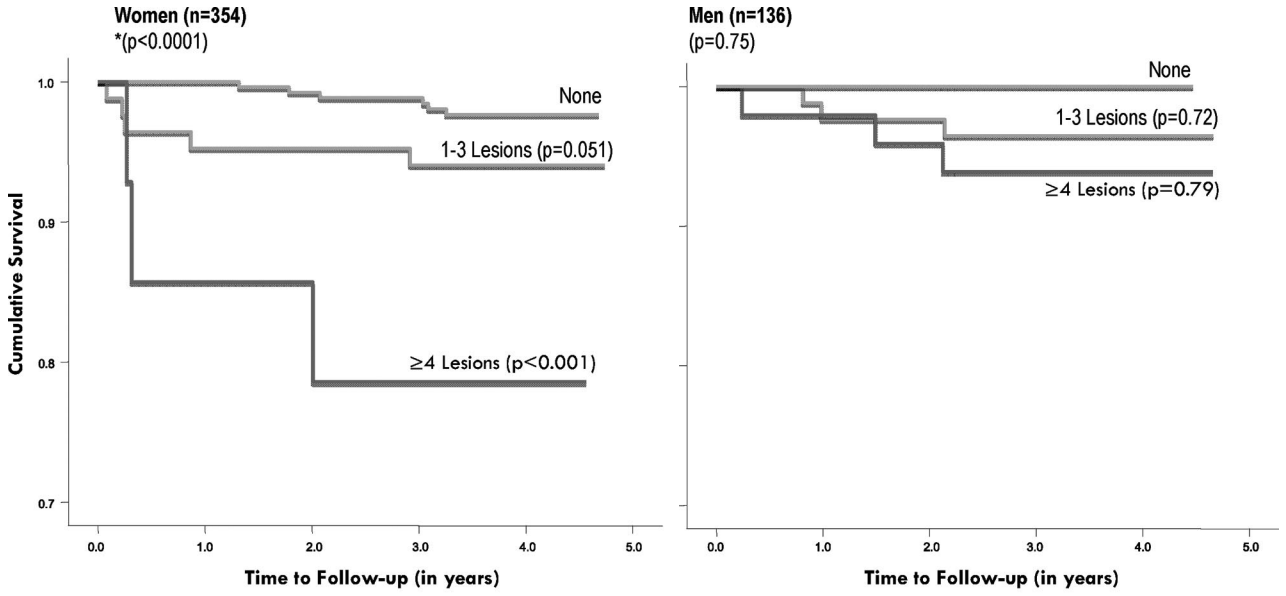


*Risk-adjustment by the number of vessels with obstructive coronary artery disease stenosis ≥50%, age, hypertension, diabetes, smoking, and presenting chest pain. Trend for men and women (p<0.0001) based on GLM interaction term of gender by the number of nonobstructive lesions. This analysis was performed initially unadjusted and then with covariate adjustment.

Figure 5. Risk-adjusted (controlling for CAD extent, symptoms, and risk factors) overall median (25th to 75th percentiles) mortality, predicted from a Cox proportional hazards model, by the number of nonobstructive lesions in women and men.

calcified versus noncalcified) of nonobstructive disease that may have further refined risk detection. Several reports have noted a prominent role of smaller arterial size in women that was not evaluated herein.[4] Data were available only on all-cause mortality and could be improved with inclusion of nonfatal events. Downstream invasive coronary angiography and medical therapy data were unavailable and could have improved our understanding of CCTA prognostication.

CCTA results in substantial radiation burden to the patient and should be used in cases in which the benefit in terms of diagnosis and risk assessment outweighs the risk associated with radiation.



*(p<0.0001) in Women is based on a subset survival analysis.
(p=0.75) in Men is based on a subset survival analysis.

Figure 6. Unadjusted Kaplan-Meier survival in 490 women and men with <50% stenosis.

Conclusions

A wealth of evidence notes more frequent nonobstructive CAD in women referred for invasive coronary angiography.[3,4] The current preliminary analyses elaborate on this evidence by evaluating the prevalence and prognostic significance of obstructive and nonobstructive CAD in women and men undergoing CCTA. As expected, women with extensive CAD, including 3-vessel CAD with left main disease, had a higher mortality when compared with men with the same extent of CAD. Despite less extensive and severe obstructive CAD in women, the novel inclusion of CCTA-defined nonobstructive CAD provided enhanced detection of risk. For men, nonobstructive disease was not significantly predictive of mortality beyond the extent of obstructive CAD. We hypothesize a sex-specific pathobiologic process for atherosclerotic disease that potentially explains this differential prognostic finding.

Our findings require validation, yet CCTA appears promising for the evaluation of suspected cardiac symptoms in women due to its ability to detect risk based on the extent and severity of obstructive CAD. We believe that an integrated interpretation focused on the combination of obstructive CAD and nonobstructive disease has the potential to reduce indecision and focus disease management to at-risk women.

Disclosures

None.

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CLINICAL PERSPECTIVE

Despite the nearly decade of published data on the diagnostic and prognostic accuracy with coronary computed tomographic angiography (CCTA), minimal data are available on its differential accuracy in women. This statement is important because women comprise a large segment of CCTA referrals, and many imaging modalities have decided limitations and technical artifact challenges in women. The possibility exists that the introduction of a novel test such as CCTA may prove useful to "rule-in" or "rule-out" coronary artery disease, given a reduced radiation profile. Although the data we present in the current report are from older technology, currently it is possible to achieve an adequate diagnostic test at <8 mSv. Given this critical statement, the benefits of CCTA include an examination of more than obstructive stenosis and include nonobstructive plaque. Within the women's health literature, we have always believed that the higher burden of cardiac symptoms coupled with a high prevalence of nonobstructive coronary artery disease indicate the potential for vasculopathy or nonobstructive plaque as an important harbinger of risk. The inclusion of a noninvasive test examining the extent and severity of nonobstructive plaque can have important implications for risk stratification of women. This intriguing finding opens the possibility of a unique combination of markers available with CCTA to provide the missing link in effective diagnostic testing for women. Prospective validation of the current findings remains a vital component to utilization of the results presented in this report.