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LETTERS TO THE EDITOR

# Gender Difference in the Prognostic Value of CTA?

The prognostic value of coronary computed tomographic angiography (CTA) is emerging, and especially detected obstructive coronary artery disease (CAD) is a strong independent predictor for events (1). Meanwhile, the pathophysiology of acute coronary syndromes in men and women differs. In contrast to events in men, coronary events in women occur more often in the absence of obstructive CAD (2) and are frequently based on plaque erosion (3,4). The goal of this study was to investigate the ability of coronary CTA to predict coronary events, in both men and women with stable chest pain.

We prospectively investigated 1,210 stable chest pain patients who underwent coronary CTA between January 1, 2007 and June 1, 2010. The institution's ethics committee approved the study. Using the American Heart Association's 16-segment model, CAD was reported for every segment as no CAD (no lesion), nonobstructive CAD (lesion with diameter stenosis <50%), or obstructive CAD (lesion with diameter stenosis ≥50%). Patients were subsequently categorized as having no CAD, any CAD (≥1 nonobstructive and/or obstructive lesions), or obstructive CAD (≥1 obstructive lesions).

The study group consisted of 640 men (53%) and 570 women (47%). Women, as compared with men, were significantly older (58 ± 11 years vs. 56 ± 11 years, $p < 0.001$), more often had a positive family history (43% vs. 33%, $p < 0.001$) and typical chest pain (15% vs. 9%, $p = 0.002$). On the other hand, men, as compared with women, more often had any CAD (70% vs. 56%, $p < 0.001$) as well as obstructive CAD (34% vs. 21%, $p < 0.001$).

Patients were followed up for a mean 1,166 ± 269 days. A total of 3 cardiac deaths, 12 myocardial infarctions, 7 unstable angina, and 38 late revascularizations (>60 days after CTA) were reported ($n = 60$ coronary events; 38 occurred in men and 22 in women, $p = 0.11$). The presence of obstructive CAD predicted significantly the occurrence of the combined endpoint, both in men and women. The annualized event rate for men with and without obstructive CAD was 5.12% and 0.15% ($p < 0.001$). For women with and without obstructive CAD, the annualized event rate was 4.83% and 0.28% ($p < 0.001$). Moreover, for men and women without any CAD, the annualized event rate was 0% and 0.39% ($p = 0.26$). There were no significant interactions between sex and obstructive or any CAD ($p = 0.54$ and $p = 0.15$). In Figure 1, Kaplan-Meier curves were calculated to assess sex differences in patients: 1) with and without obstructive CAD; and 2) with and without any CAD. The presence of obstructive CAD as well as any CAD clearly resulted in a worse outcome for both men and women. In a Cox regression model, the hazard ratio for obstructive CAD was 37.2 (95% confidence interval [CI]: 8.9 to 154.3; $p < 0.001$) in men and 18.4 (95% CI: 6.2 to 54.4; $p < 0.001$) in women. In an exploratory adjusted model, controlling for traditional risk factors, the hazard ratio for obstructive CAD remained predictive ($p < 0.001$) in women. Also in men, the presence of obstructive CAD was an independent predictor; hazard ratio = 36.9 (95% CI: 8.9 to 153.3; $p < 0.001$). Sex was not predictive of outcome ($p = 0.71$).

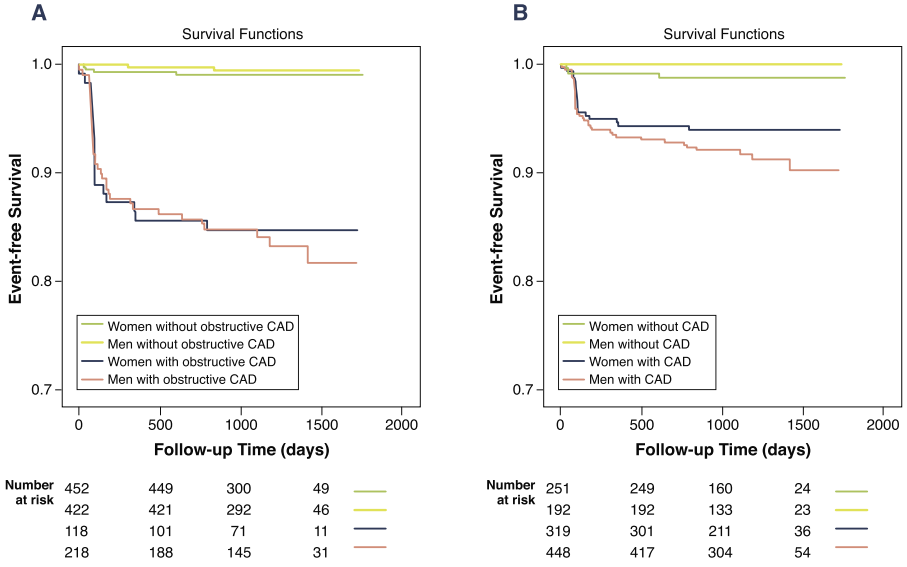


**Figure 1. Event-Free Survival for Men and Women With Different Grades of CAD**

**(A)** Kaplan-Meier curves are shown for men and women with and without obstructive coronary artery disease (CAD) (≥50% stenosis) and **(B)** for men and women with and without any CAD.

A limitation of this study is that coronary CTA was performed within clinical workup, which could implicate referral bias. Possibly, clinical information known to the reader might have influenced coronary CTA assessment as well. The nonsignificant difference in event rate between men and women with normal coronary CTA might be due to differences in risk factors or referral patterns, which this study did not have the power to detect.

In conclusion, obstructive CAD significantly predicted events in both men and women. Despite the small numbers and hypothesis-generating nature of our study, these findings further validate the role of coronary CTA to effectively risk stratify women and men.

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# Left Atrial Volumes

## Should We Reset the Reference Standard?

Left atrial (LA) volume has been shown to be a prognostic indicator of cardiovascular (CV) events and a marker of diastolic dysfunction (1,2). Normative values for indexed LA volume (LAVi) have been established to be 22 ± 6 ml/m$^2$ (3). Yet, these values are on the basis of small sample size studies, from a period with different imaging technology and using inconsistent measurement techniques.

We aimed to re-examine the normal reference standards for LAVi in a contemporary healthy population. We searched our institutional database for a 1-year period to identify healthy subjects with normal echocardiograms. Medical records were comprehensively reviewed to select healthy patients (no CV risk factors, pulmonary or renal disease). LA volume was calculated by the biplane area–length method (3). Diastolic parameters were assessed. Furthermore, a healthy validation subset of 20 subjects was examined prospectively.

From June 2009 to June 2010, 285 healthy subjects were identified and LA volumes measured. The mean LAVi was 30.3 ± 6 ml/m$^2$ (mean age 38.3 ± 14.8 years, 61.4% women) with no difference observed between men and women (30.3 ± 7.0 ml/m$^2$ vs. 30.5 ± 6.0 ml/m$^2$, p = 0.81) and no age differences in absolute or indexed LA volumes in the entire healthy cohort or by sex.

Mean diastolic parameters were normal. Thirty percent of subjects had a LAVi ≥34 ml/m$^2$—a cutoff used to identify those with abnormal diastolic function (1). E/A, average E′, and E/E′ were not significantly different between this group and those with a LAVi <34 ml/m$^2$. The prospective cohort of 20 healthy subjects, matched to age (38.3 ± 7.0 years), sex (60% women), and body surface area (1.8 ± 0.2 m$^2$) had similar mean LAVi to the retrospective cohort (31.7 ± 6.0 ml/m$^2$ vs. 30.3 ± 7.0 ml/m$^2$; prospective vs. retrospective p = 0.35).

Reassessment of LAVi in a contemporary healthy cohort suggests that normative reference ranges of LAVi should be higher than previously reported. In the present study, the mean LAVi in healthy subjects was 30.3 ± 6.5 ml/m$^2$, 38% higher compared with current reference values for mean normal LAVi (22 ± 6 ml/m$^2$) (3) (Fig. 1).

Various factors may account for the discrepancy between previously reported values and our results. Current reference values are on the basis of relatively small sample size studies and obtained from a period with different imaging technology. With improved spatial resolution in current imaging systems, measurement of LA boundaries may be more accurate. The confluence of the pulmonary veins may also be better

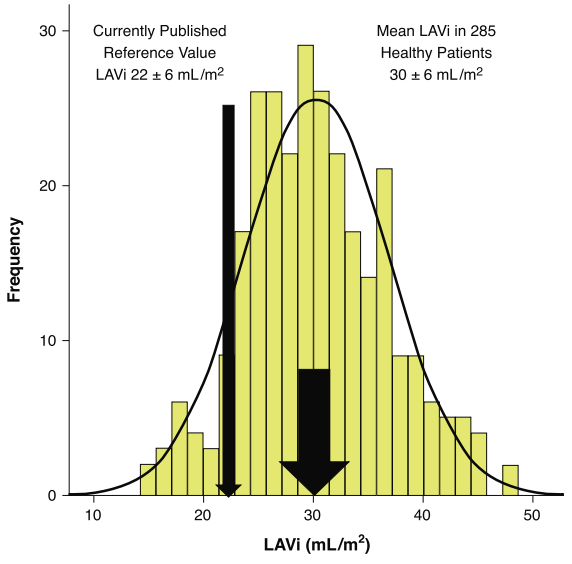


**Figure 1. Distribution of LAVi in Healthy Subjects (N = 285)**

The **short black arrow** points to the mean indexed left atrial volume (LAVi) of 30.3 ml/m$^2$, which is greater than the current published reference value of 22 ml/m$^2$ for normal **(long black arrow)**.