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LETTERS TO THE EDITOR

Differences in Underlying Culprit Lesion Morphology Between Men and Women: An IVUS Analysis From the ADAPT-DES Study



A substudy from the ADAPT-DES (Assessment of Dual Anti Platelet Therapy With Drug Eluting Stents) study (NCT00638794) assessed differences in unstable morphology between male and female patients and the interaction of patient age and sex.

The ADAPT-DES study has been described in detail (1). It was approved by the institutional review board at each participating center; eligible patients signed informed written consent. Angiograms were evaluated visually by operators during the procedure. Pre- and post-intervention grayscale and intravascular ultrasound (IVUS) virtual histology were performed using a 20 MHz catheter (Eagle Eye, Volcano Corporation, Rancho Cordova, California). Measurements included external elastic membrane (EEM), lumen,

and plaque and media (P&M) (P&M = EEM – lumen) cross-sectional area, and plaque burden (P&M/EEM). Volumes were calculated using the Simpson rule. Plaque components were color-coded as dense calcium, necrotic core, fibrofatty, or fibrotic.

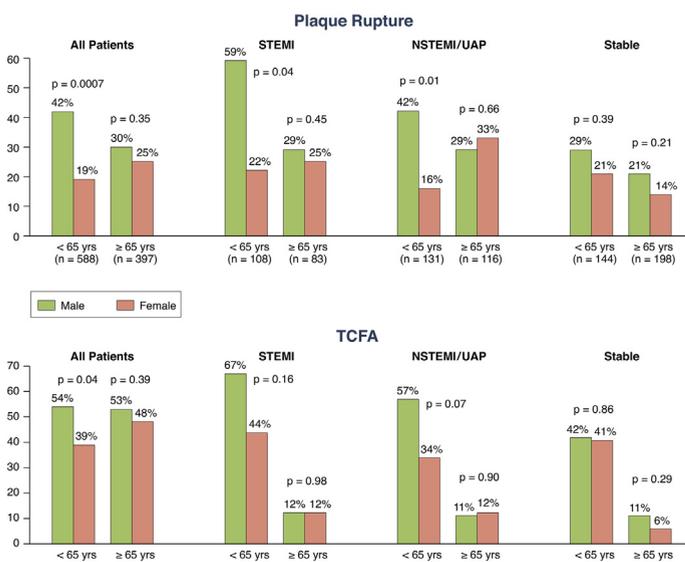
A culprit lesion was a segment that was stented and identified by comparison of pre- versus post-intervention IVUS images. Pre-intervention qualitative morphology included plaque rupture (intraplaque cavity communicating with the lumen with an overlying residual fibrous cap fragment), attenuated plaque, and calcified nodule. A thin cap fibroatheroma (TCFA) was >10% confluent necrotic core with >30° abutting to the lumen in ≥3 consecutive slices.

Categorical variables were compared by chi-square statistics. Continuous variables are presented as mean ± SD and were compared by Student *t* test. To compensate for multiple lesions in the same patients, a generalized estimating equation model was used and shown as least-squares means with 95% confidence interval. Statistical analyses were performed using SAS version 9.1.3 (SAS Institute, Cary, North Carolina).

Among 8,663 patients in the ADAPT-DES study, 2,179 were enrolled into the pre-specified IVUS substudy. Pre-intervention imaging was performed in 916 de novo culprit lesions from 780 of 2,179 patients. Men (n = 588) and women (n = 192) were compared according to 2 age groups (age <65 years vs. ≥65 years, median age of this cohort). Baseline clinical characteristics were similar between them except that renal insufficiency was more prevalent in women in both age groups: <65 years of age 3.8% men versus 11.8% women (p = 0.01) and ≥65 years of age 19.4% men versus 40.3% women (p < 0.0001). Bifurcation lesions were more prevalent in men versus women of ≥65 years of age, whereas calcification was more prevalent in women versus men <65 years of age. Angiographic diameter stenosis was more severe in men versus women <65 years of age (90.3 ± 11.0% vs. 86.9 ± 10.3%; p = 0.02) but not in patients >65 years of age.

Plaque ruptures were more common in men versus women overall (36.3% vs. 23.0%; p < 0.01) and in patients <65 years of age (42.0% vs. 19.0%; p = 0.0007) but not in patients ≥65 years of age. A similar pattern was seen in TCFA that were more common in men versus women overall (53.3% vs. 44.7%; p = 0.026) and in younger patients (53.8% vs. 39.2%; p = 0.04) but not in older patients. EEM and lumen dimensions and plaque burden were larger in men versus women in both age groups. There was no

FIGURE 1 Prevalence of Plaque Rupture and TCFA According to Patient Age and Sex



In patients <65 years of age, men presenting with ST-segment elevation myocardial infarction (STEMI) or non-ST-segment elevation myocardial infarction (NSTEMI)/unstable angina pectoris (UAP) had a greater prevalence of plaque rupture or thin cap fibroatheroma (TCFA) compared with women; this was not seen in patients presenting with stable coronary artery disease regardless of age or in patients >65 years of age regardless of presentation.

difference in prevalence of attenuated plaques or calcific nodules among any of the groups.

We divided patients into: 1) ST-segment elevation myocardial infarction (STEMI); 2) non-STEMI or unstable angina; and 3) stable coronary artery disease. In patients <65 years of age (but not ≥65 years of age), a difference in plaque rupture and TCFA prevalence was seen in patients with STEMI or non-STEMI/unstable angina but not in patients with stable coronary artery disease, with a similar trend in the prevalence of TCFA (Figure 1).

Multivariate analysis showed that male sex was an independent predictor for plaque rupture (odds ratio: 1.85 [95% confidence interval: 1.26, 2.71]; $p = 0.0017$) and for TCFA (odds ratio: 1.41 [95% confidence interval: 1.01, 1.96]; $p = 0.045$) after adjustment of other variables. However, age as a continuous variable was not an independent predictor for plaque rupture or TCFA.

The present study demonstrated that ruptured plaques and TCFA were more common in men than in women <65 years of age, but these differences disappeared in older patients (≥65 years of age). Some selection bias is expected because these patients were referred for coronary intervention. IVUS use was per operator discretion; IVUS was not performed in all coronary arteries; and pre-intervention IVUS was only performed in a subset. Nevertheless, we included the entire cohort of patients in the IVUS substudy of the ADAPT-DES study with pre-intervention imaging.

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<http://dx.doi.org/10.1016/j.jcmg.2015.02.019>

Please note: The ADAPT-DES study was sponsored by the Cardiovascular Research Foundation, with funding provided by Boston Scientific, Abbott Vascular, Medtronic, Cordis, Biosensors, the Medicines Company, Daiichi-Sankyo, Eli Lilly, Volcano, and Accumetrics. Dr. Wang has received grants from Boston Scientific and InfraRedx; has received fellowship support from Boston Scientific; has received honoraria from ACIST Medical Systems; and has served on Speakers Bureaus for Boston Scientific. Dr. Mintz has received grants and consulting fees from Volcano and Boston Scientific. Dr. Witzentichler has received speaker honoraria from Boston Scientific, Abbott Vascular, Volcano, Atrium Medical, and Ilixir Medical; and has received consulting fees from Volcano. Dr. Metzger has received consulting fees from Abbott Vascular, ev3, IDEV, and Medtronic. Dr. Rinaldi has received consulting fees from Abbott Vascular. Dr. Duffy has received speaker honoraria from Volcano. Dr. Weisz has received consulting fees from InfraRedx. Dr. Stuckey has served on an advisory board for and received speaker honoraria from Boston Scientific and Lilly/Daiichi-Sankyo. Dr. Kirtane has received institutional grants from Medtronic, Boston Scientific, Abbott Vascular, Abiomed, Vascular Dynamics, St. Jude Medical, and Eli Lilly. Dr. Stone has received consulting fees from Volcano, InfraRedx, and Boston Scientific. Dr. Maehara has received grants from Boston Scientific; has received consulting fees from Boston Scientific and ACIST Medical Systems; and has received speaker honoraria from St. Jude Medical and Volcano. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose. Morton Kern, MD, served as Guest Editor for this paper.

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Sex Differences in the Progression of Aortic Stenosis and Prognostic Implication



The COFRASA-GENERAC Study

In patients with aortic stenosis (AS), degree of aortic valve calcification (AVC) measured using multislice computed tomography is closely related to hemodynamic severity as assessed using transthoracic echocardiography (1); but for similar hemodynamic severity, AVC load is lower in females than in males and AS progresses faster as hemodynamic or anatomic severity increases (2,3). The impact of sex on AS progression accounting for baseline AS (hemodynamic or anatomic) severity has never been specifically evaluated.

Patients enrolled between November 2006 and September 2013 in 2 ongoing prospective studies, COFRASA (Aortic Stenosis in Elderly: Determinant of Progression) (NCT00338676) and GENERAC (Genetic of Aortic Valve Stenosis-Clinical and Therapeutic Implications) (NCT00647088) with at least 2 years of follow-up constituted our study population. Population and methodology has been described elsewhere (3). Briefly, all participants had pure, isolated, at least mild, asymptomatic, degenerative AS and underwent, the same day, a comprehensive clinical, transthoracic echocardiography, and multislice computed tomography evaluation at inclusion and yearly thereafter. The degree of AVC was quantitatively assessed according to the Agatston method (calcium score) expressed in arbitrary units (AU). Correlations