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Multimodality Intravascular Imaging to Evaluate Sex Differences in Plaque Morphology in Stable CAD

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ABSTRACT

OBJECTIVES The aim of this study was to evaluate sex differences in plaque morphology in stable coronary artery disease (CAD) patients using a multimodality intravascular imaging approach.

BACKGROUND Differences in atherosclerotic burden and plaque morphology between men and women is a focus of treatment and preventative measures.

METHODS We retrospectively analyzed data from 383 patients with stable CAD who were referred for angiography and underwent optical coherence tomography. Among them, 128 also underwent intravascular ultrasound (IVUS)/near infrared spectroscopy.

RESULTS Of the 383 patients included in the study, 268 were men and 115 were women. Women tended to be older (66 ± 10 years of age vs. 62 ± 11 years of age; p = 0.002) and have more comorbidities including hypertension (97% vs. 90%; p = 0.031), diabetes with insulin use (18% vs. 10%; p = 0.043), obesity (body mass index 30 kg/m^2 vs. 28 kg/m^2; p = 0.022), and lower estimated glomerular filtration rate (88 ml/min/1.73m^2 vs. 98 ml/min/1.73m^2; p = 0.001). Optical coherence tomography data demonstrated that there was no sex difference in plaque morphology as characterized by maximum lipid arc, lipid length, lipid volume index, minimum cap thickness, incidence of thin cap fibroatheroma, microvessels, macrophages, and calcification. There was also no difference in maximal lipid core burden index at the 4-mm maximal segment as seen on near infrared spectroscopy. Plaque characteristics by IVUS were similar between men and women except for an increase in plaque burden in men compared to women in the reference segment (44.4 vs. 39.3; p = 0.031). After adjusting for age, body mass index, percutaneous coronary intervention history, and clinical risk factors, sex was not found to be an independent predictor of severe plaque burden by IVUS.

CONCLUSION Among men and women with stable CAD referred for coronary angiography, there was no difference in plaque characteristics as assessed by multimodality imaging. These findings, which are hypothesis generating, suggest that equally aggressive primary and secondary preventive efforts irrespective of sex must be undertaken. (J Am Coll Cardiol Img 2016;9:400–7) © 2016 by the American College of Cardiology Foundation.

Coronary artery disease (CAD) is the leading cause of death in both men and women. Data from the INTERHEART global case-control study, which included more than 27,000 men and women from 52 countries, showed that women experience their first acute myocardial infraction (MI) on average 9 years later than men (1). However, a growing body of evidence suggests that during the last 2 decades the prevalence of CAD has increased among middle-aged women, whereas the

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prevalence among similarly aged men decreased (2). Although the risk of future cardiovascular events remains higher in middle-aged men compared with middle-aged women, the gap has narrowed in recent years (2–4).

The role of traditional risk factors such as hypertension, diabetes mellitus, smoking, dietary patterns, and family history in the progression of CAD in both sexes is well established (1,3,4). The INTERHEART study attributed the difference in age of first MI largely to the higher risk factor levels at younger ages in men compared to women (1). Some researchers have suggested that women who are "relatively protected" against CAD require a greater risk factor burden before developing overt disease as a result of which women with significant CAD represent a high-risk group (5,6).

SEE PAGE 408

At a histopathological level, there are limited data from post-mortem studies to evaluate the differences in plaque morphology between men and women (7,8). Recently there has been growing interest in using in vivo intravascular imaging for characterization of plaque morphology (9–16). We sought to evaluate the differences in plaque morphology between men and women with stable CAD using a multimodality approach with intravascular ultrasound (IVUS), near infrared spectroscopy (NIRS), and optical coherence tomography (OCT) techniques.

METHODS

STUDY POPULATION. This was a retrospective analysis of prospectively collected data from the institutional review board-approved clinical and multimodality imaging database. All procedures were performed in the Mount Sinai Cardiac Catheterization Lab. Our cath lab database was used to obtain the baseline demographic, clinical, procedural, and in-hospital outcomes data and imaging characteristics. As shown in **Figure 1**, our study group consisted of 420 consecutive patients with stable CAD who were referred for cardiac catheterization on whom OCT was performed. The lesion to image was based on the operator's discretion and lesions represented de novo atherosclerosis. Of these 420 patients, 37 were excluded because OCT image quality was not deemed to be optimum. The remaining 383 patients were analyzed. Of the total number, a sub-group of patients (n = 133) also underwent IVUS/NIRS imaging and 5 were excluded because of suboptimal image quality. One hundred twenty-eight patients included in the study also formed a part of the COLOR (Chemometric Observation of Lipid Core Plaques of Interest in Native Coronary Arteries) registry enrolled only from our center. Patients with renal failure (creatinine >1.5 mg/dl), contrast allergy, hemodynamic compromise, and aorto-ostial coronary artery lesions were excluded from the study.

OCT IMAGE ACQUISITION AND ANALYSIS. OCT image acquisition was performed with a commercially available C7-XR OCT Intravascular Imaging System (OCT C7 Dragonfly, St. Jude Medical, St. Paul, Minnesota). The OCT catheter was advanced at least 10 mm distal to the imaging target lesion. OCT image acquisition was then performed with automatic pullback (20 mm per second) and continuous intracoronary contrast injection (iodixanol) (total volume 12 to 16 ml injected at 3 to 4 ml/s). Each OCT catheter pullback imaged a total of 54 mm of the vessel.

OCT images were analyzed using the St. Jude Medical Offline Review Workstation at 1-mm intervals according to previously validated criteria (17,18) and as we described previously (19–22). The smallest cross-sectional area (CSA), reference CSA, and percent lumen area stenosis ([reference lumen CSA − minimum lesion lumen CSA]/reference lumen CSA × 100) were calculated for each lesion. The thinnest part of the fibrous cap was measured 3 times, and its average was reported as minimum cap thickness. In addition, OCT-dependent lipid arc was also measured at 1-mm intervals through the entire length of the lesion, and expressed in degrees. Lipid length was measured on longitudinal view (using frame analysis). Lipid volume index was calculated as the averaged lipid arc multiplied by lipid length (23). Thin cap fibroatheroma (TCFA) was defined as a plaque with lipid arc >90° and fibrous cap thickness <65 μm. Calcified plaques were defined as areas with well-delineated borders and the degree of circumferential extent of calcification was quantified at 1-mm intervals (24). A microvessel was defined as a black hole or tubular structure within a plaque, which was not connected to the vessel lumen and was clearly visible in at least 3 consecutive cross-sectional OCT images (25). Macrophages accumulation was defined as confluent or punctate highly backscattering focal regions in the artery wall. Thrombi were identified as masses protruding into the vessel lumen discontinuous from the surface of the vessel wall. Plaque rupture was detected by OCT as a ruptured fibrous cap that connects the lumen with the lipid pool, which may occur with or without a superimposed thrombus. To evaluate the interobserver variability, 2

ABBREVIATIONS AND ACRONYMS

BMI = body mass index

CAD = coronary artery disease

CSA = cross sectional area

IVUS = intravascular ultrasound

maxLCBI$_{4mm}$ = maximal lipid core burden index at the 4-mm segment

MI = myocardial infarction

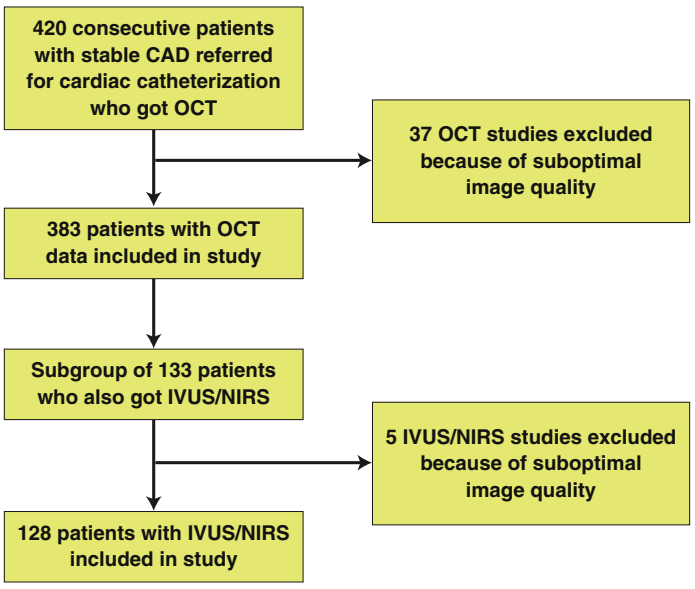
MLA = minimum luminal area

NIRS = near infrared spectroscopy

OCT = optical coherence tomography

TCFA = thin cap fibroatheroma

FIGURE 1 Flowchart Depicting Selection of Patients for the Study



The above flowchart depicts the inclusion and exclusion of patients into the study. Additionally, patients with renal failure (creatinine >1.5 mg/dl), contrast allergy, hemodynamic compromise, and aorto-ostial coronary artery lesions were excluded from the study.

experienced OCT analysts reviewed OCT pullbacks independently, and the analyses were repeated at intervals of at least 2 weeks by the first observer.

COMBINED GRAYSCALE IVUS AND NIRS IMAGING AND IMAGE ANALYSIS. Commercially available TVC Imaging System with the TVC Insight catheter (Infraredx, Burlington, Massachusetts) was used to perform grayscale IVUS and NIRS image acquisition for the same lesion. Quantitative grayscale IVUS analysis was performed using QIvus 3.0 (MEDIS, Leiden, the Netherlands) according to the American College of Cardiology consensus statement (26) and as previously described (19,20) to estimate lumen and reference CSA, external elastic membrane (EEM) CSA, plaque plus media CSA, plaque burden, and remodeling index (lesion EEM CSA/reference EEM CSA). NIRS imaging estimates the probability of the presence of an atherosclerotic lipid core. The measurements are displayed as a chemogram, which represents a spectroscopic image of the scanned lesion and allows us to calculate the lipid core burden index (27,28). The maximal lipid core burden index (LCBI) at the 4-mm segment was estimated in 4-mm pullback compartments by identifying the maximum LCBI sub-segment for every analyzed lesion ($maxLCBI_{4mm}$) as described previously (29).

IMAGE COREGISTRATION. OCT and NIRS/IVUS pullbacks were coregistered using anatomical landmarks, or fiduciary points. Vascular and perivascular markings were used to confirm simultaneous assessment of IVUS measurements and OCT analysis in the same lesion.

STATISTICAL ANALYSIS. The Shapiro-Wilk test was used to assess the normality of continuous data. All continuous measurements were expressed as mean ± SD for normally distributed variables or median and interquartile range (25th percentile, 75th percentile) for nonparametric data. Normally distributed data were compared using an unpaired Student *t* test, the Mann-Whitney test was used to compare non-normally distributed variables. Categorical variables are presented as frequencies (percentages) and were compared using the chi-square test or Fisher exact test. Multivariate linear regression analysis was also performed to examine whether sex has an independent effect on plaque morphology. Sex represented the exposure of interest in each model with dependent outcomes including different measures of plaque severity assessed by OCT (fibrous cap thickness, lipid arc), IVUS (plaque burden [PB] at reference and minimal luminal area, percent atheroma volume, and total atheroma volume), and NIRS ($maxLCBI_{4mm}$). Variables demonstrating significant differences between men and women were included as additional covariates of sex in each model. Results were reported as beta coefficients with 95% confidence intervals (CIs) and p values. All statistical analyses were performed using SPSS statistical software version 22.0 (SPSS Inc., Chicago, Illinois) with a 2-tailed probability value <0.05 considered statistically significant. Interobserver agreement and intraobserver reproducibility of imaging parameter measurements were assessed by intraclass correlation coefficients based on the random effects analysis of variance models (30).

RESULTS

BASELINE CLINICAL DEMOGRAPHICS. As shown in Table 1, of 383 patients included in the study, 268 were men and 115 were women. Women in the study tended to be older (66 ± 10 years of age vs. 62 ± 11 years of age; p = 0.002) and have more comorbidities including hypertension, diabetes with insulin use, obesity, and lower estimated glomerular filtration rates (eGFRs). More women presented with Canadian Cardiovascular Society (CCS) grades III or IV angina (78% vs. 63%; p = 0.019). Women also had higher levels of C-reactive protein (CRP), total cholesterol, high-density lipoprotein (HDL)

cholesterol and low-density lipoprotein (LDL) cholesterol. Of note, 48% of men had prior percutaneous coronary intervention (PCI) as compared to 29% of women (p = 0.001). There was no statistically significant difference in history of smoking, previous MI, or statin use. The average SYNTAX (Synergy between PCI with Taxus and Cardiac Surgery) score for both groups were low.

OCT IMAGING DATA. Differences in plaque morphology between men and women as characterized by OCT are summarized in Table 2. There was no significant difference in reference lumen CSA, minimum lumen CSA, or area stenosis. Furthermore, there was no difference in plaque morphology between men and women, as characterized by maximum lipid arc, lipid length, or lipid volume index. There was also no difference in minimum cap thickness, incidence of TCFA, microvessels, macrophages, and calcification. Intraclass correlation coefficient for interobserver and intraobserver variability for the maximum lipid arc was 0.98 (95% CI: 0.932 to 0.997) and 0.99 (95% CI: 0.965 to 0.998), respectively; for fibrous cap thickness it was 0.96 (95% CI: 0.875 to 0.991) and 0.98 (95% CI: 0.933 to 0.997), respectively.

IVUS/NIRS IMAGING DATA. As shown in Table 3, there was no significant difference between external elastic membrane CSA and lumen CSA in both reference and stenotic segment. There was a trend toward significance (p = 0.056) in plaque plus media CSA being higher in men as compared to women (5.8 mm^2 vs. 5.3 mm^2). There was a statistically significant increase in plaque burden among men as compared to women in the reference segment (44.4 ± 12.5 vs. 39.3 ± 10.9; p = 0.031). There was no difference in the remodeling index between the 2 groups. NIRS showed that there was no difference in $maxLCBI_{4mm}$ between men and women. To examine whether sex has an independent effect on plaque morphology, multivariate regression analysis was performed by generating several models with different plaque characteristics as dependent outcomes (Table 4). In addition to sex, we adjusted for age, body mass index (BMI), PCI history, hypertension, insulin, Canadian Cardiovascular Society angina grade III or IV, SYNTAX score, eGFR, CRP, and total cholesterol. Sex was not found to be an independent predictor of OCT fibrous cap thickness and lipid arc, IVUS PB, and NIRS $maxLCBI_{4mm}$ (Table 4). Furthermore, the trend for larger PB at the reference site did not remain significant.

DISCUSSION

Although it is well known that women presenting with symptomatic CAD are older and exhibit more

TABLE 1 Baseline Clinical Demographics

	Men (n = 268)	Women (n = 115)	p Value
Age, yrs	62 ± 11	66 ± 10	**0.002**
Hypertension	249 (90)	112 (97)	**0.031**
Dyslipidemia	217 (81)	100 (87)	0.152
Diabetes mellitus	123 (46)	61 (53)	0.214
Insulin	27 (10)	21 (18)	**0.043**
Smoking	70 (26)	24 (21)	0.267
BMI, kg/m^2	28 (25–31)	30 (27–34)	**0.022**
Previous MI	32 (12)	14 (12)	0.960
Prior PCI	129 (48)	33 (29)	**0.001**
CCS angina grade III or IV	169 (63)	90 (78)	**0.019**
SYNTAX score	6 (3–8)	8 (6–9)	**0.049**
Target lesion LAD/RCA/LCX	131/70/67 (49/26/25)	64/33/18 (56/29/15)	0.160
Statin use	193 (72)	84 (73)	0.748
Non-statin lipid lowering	24 (9)	8 (7)	0.300
eGFR (MDRD) ml/min/1.73 m^2	98 (81–119)	88 (74–103)	**0.001**
CRP	1.6 (0.6–2.9)	3.5 (1.1–8.0)	**0.001**
HBA1C	8.4 (6.8–9.9)	8.5 (7.0–10.0)	0.579
Total cholesterol, mg/dl	170 (138–200)	183 (164–231)	**<0.001**
HDL cholesterol, mg/dl	47 (37–53)	58 (47–68)	**<0.001**
LDL cholesterol, mg/dl	101 (75–126)	112 (91–137)	**0.002**
Triglyceride, mg/dl	146 (105–216)	156 (101–209)	0.867

Values are mean ± SD, n (%), or median (interquartile range). **Bold** values indicate p < 0.05.

BMI = body mass index; CCS = Canadian Cardiovascular Society; CRP = C-reactive protein; eGFR = estimated glomerular filtration rate; HBA1C = hemoglobin A1c; HDL = high-density lipoprotein cholesterol; LDL = low-density lipoprotein cholesterol; MDRD = Modification of Diet in Renal Disease; MI = myocardial infarction; PCI = percutaneous coronary intervention; SYNTAX = Synergy between PCI with taxus and cardiac surgery.

TABLE 2 OCT Imaging Data

	Men (n = 268)	Women (n = 115)	p Value
Reference lumen CSA, mm^2	6.2 (4.9–7.8)	6.3 (4.6–7.6)	0.653
Minimum lumen CSA, mm^2	1.6 (1.2–2.4)	1.8 (1.3–2.8)	0.062
Area stenosis, %	72 (61–81)	67 (61–75)	0.096
Fibrous plaque	48 (18)	29 (25)	0.165
Lipid rich plaque	204 (76)	84 (73)	0.504
Lipid arc maximum, °	166 (107–244)	171 (74–264)	0.829
Lipid arc average, °	109 (75–150)	112 (60–159)	0.965
Lipid length, mm	5 (2–9)	4 (1–10)	0.759
Lipid volume index	538 (151–1,176)	513 (95–1,312)	0.797
Minimum cap thickness, μm	90 (60–130)	90 (60–128)	0.643
TCFA	67 (25)	23 (20)	0.344
Plaque rupture	38 (14)	12 (10)	0.202
Thrombus	24 (9)	9 (8)	0.830
Microvessel	123 (46)	56 (50)	0.446
Macrophages	185 (69)	81 (70)	0.897
Calcium deposition	209 (78)	83 (72)	0.245
Calcium arc maximum, °	95 (30–141)	90 (0–145)	0.546

Values are median (interquartile range) or n (%).

CSA = cross sectional area; OCT = optical coherence tomography; TCFA = thin cap fibroatheroma.

TABLE 3 IVUS and NIRS Findings

	Men (n = 95)	Women (n = 33)	p Value
IVUS			
Reference			
EEM CSA, mm^2	13.5 (10.7–15.8)	13.1 (10.6, 15.7)	0.551
Lumen CSA, mm^2	6.8 (5.7–9.1)	7.1 (6.0–9.0)	0.526
PM CSA, mm^2	5.8 (4.4–8.3)	5.3 (3.6–6.7)	0.056
Plaque burden, %	44.4 ± 12.5	39.3 ± 10.9	**0.031**
Minimum lumen site			
EEM CSA, mm^2	13.0 (10.5–14.7)	12.5 (9.7–16.8)	0.537
Lumen CSA, mm^2	2.6 (2.1–3.2)	2.8 (2.1–3.5)	0.477
PM CSA, mm^2	13.8 (10.8–16.4)	13.2 (10.7–15.1)	0.279
Plaque burden, %	78.3 ± 7.2	75.7 ± 8.7	0.070
PAV, %	62.3 (55.1–68.8)	63.0 (53.6–65.9)	0.410
TAV, mm^3	126.4 (104.3–176.4)	117.9 (97.0–164.0)	0.334
Remodeling index	0.96 (0.82–1.1)	0.96 (0.88–1.1)	0.827
Lesion length	17.7 ± 5.7	18.2 ± 8.4	0.790
NIRS			
$maxLCBI_{4mm}$	388.0 ± 215.0	368.0 ± 247.0	0.633

Values are median (interquartile range) or mean ± SD. **Bold** value indicates $p < 0.05$.

EEM = external elastic membrane; IVUS = intravascular ultrasound; $maxLCBI_{4mm}$ = maximal lipid core burden index at the 4-mm segment; NIRS = near infrared spectroscopy; PAV = percent atheroma volume; PM = plaque plus media; TAV = normalized total atheroma volume; other abbreviation as in Table 2.

comorbidities (5), debate has been ongoing regarding their prognosis as compared to men (3,6). Whereas many studies have documented that females with symptomatic CAD fare worse than their male counterparts, carefully controlled analyses have suggested that differences in outcome may be due to age and other comorbidities, and not due to the nature of their coronary disease itself (6,31). The findings of our study also suggest that there is no significant difference in atherosclerotic plaque between men and women in a select cohort of patients with stable CAD. Additional key aspects of this study include that, to our knowledge: 1) it is the largest study to utilize OCT to evaluate differences in plaque morphology between men and women; 2) it is the first OCT study to evaluate plaque morphology between men and women with stable CAD; and 3) it provides correlation of multiple modalities such as IVUS, NIRS, and OCT.

TABLE 4 Association Between Sex and Plaque Characteristics by Linear Multivariate Regression Analysis

Model Number	Plaque Characteristics/ Model Outcomes	Standardized Coefficient (95% CI)	p Value
	OCT		
1	Fibrous cap thickness	0.05 (-9.2 to 20.0)	0.459
2	Lipid arc (maximal)	0.07 (-12.1 to 42.2)	0.277
	IVUS		
3	PB reference	0.15 (-2.1 to 10.3)	0.196
4	PB at MLA	0.22 (0.1 to 7.6)	0.050
5	PAV	0.14 (-1.7 to 7.9)	0.199
6	TAV	0.14 (-10.4 to 49.8)	0.197
	NIRS		
7	$maxLCBI_{4mm}$	0.09 (-71 to 160)	0.447

Several multivariate regression models were generated with sex representing the exposure of interest in each model, whereas model outcomes included different measures of plaque severity assessed by OCT, IVUS, and NIRS. Age, BMI, PCI history, hypertension, insulin, CCS angina grade III or IV, SYNTAX score, eGFR, CRP, and total cholesterol were included as additional covariates of sex in each model.

CI = confidence interval; MLA = minimal luminal area; PB = plaque burden; other abbreviations as in Tables 1, 2, and 3.

Given the relative paucity of histopathological data in this regard, the utilization of in vivo imaging techniques assumes paramount importance. In recent times, several modalities such as multislice computed tomography (MSCT) (13,32), IVUS (11,12), NIRS (28), and OCT (14,16,20) have been used for this purpose. The OCTAVIA (Optical Coherence Tomography Assessment of Gender Diversity In Primary Angioplasty) trial (n = 140) showed that in patients presenting with ST-segment elevation myocardial infarction undergoing primary PCI, no differences in culprit plaque morphology and factors associated with coronary thrombosis were observed between age-matched men and women (14). Similarly, another OCT study performed in the acute coronary syndrome (ACS) setting demonstrated that frequency of lipid-rich plaques, TCFA, calcification, thrombus, and plaque disruption were similar between men and women (16). However, there have been no prior OCT studies performed on patients with stable CAD. Our present study on plaque morphology in stable CAD is in congruence with and extends earlier findings to a stable CAD population.

Studies utilizing IVUS for plaque characterization between men and women have reported conflicting findings which are likely due to differences in age, comorbidities, and presentation of CAD (stable CAD versus ACS). Nicholls et al. (33) analyzed 978 patients and found that despite the presence of more risk factors, the percent of atheroma volume was lesser in women. However, the median age of women and men in their study was 57 years and 56 years, respectively, which is significantly lower than our study population. Another smaller study (n = 93) that utilized both MSCT and virtual histology IVUS to compare plaque morphology found that more extensive atherosclerosis and more calcified lesions were observed in men than in women (13). These differences were predominantly present in patients aged <65 years and were attenuated in those aged ≥65 years. Similar findings have been reported even in the setting of ACS. Results from the PROSPECT (Providing Regional Observations to Study Predictors of Events in the Coronary Tree)

study also demonstrate that despite having more comorbid risk factors than men, women have less extensive CAD by both angiographic and IVUS measures. Lesions in women compared with men had less frequent plaque rupture, smaller necrotic core and calcium, and smaller lumens but similar plaque burden. They also suggested that TCFA might be a stronger marker of plaque vulnerability in women than in men (12). Another independent IVUS study of 468 patients in the ACS setting showed that coronary plaque ruptures were more often associated with thrombus and acute presentations in women than in men (9). However, 2 studies that used IVUS virtual histology reported that women tend to have more calcified plaque as compared to men (10,34). Another study by Kornowski et al. (35) reported that women and men had similar reference and lesion plaque burden, eccentricity, and calcium, and concluded that there were no quantitative or qualitative differences in coronary atherosclerotic plaques. An IVUS sub-study from the ADEPT-DES (Assessment of Dual Anti Platelet Therapy With Drug Eluting Stents) study recently reported that 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 ACS but not in patients with stable CAD, with a similar trend in the prevalence of TCFA (36).

NIRS has been used to assess lipid content of plaques by identifying the presence of cholesterol monohydrate and cholesterol ester. This has been validated in histopathological studies (27) and in comparison to OCT (20). Presence of larger lipid-core plaques by NIRS has been shown to be associated with a greater risk of periprocedural MI following PCI presumably due to distal embolization of plaque contents (37). Furthermore, NIRS has been used to predict cardiovascular outcomes in patients with CAD. In a study of 203 patients which included patients with stable CAD and ACS, an increased LCBI in a nonculprit coronary artery was associated with a 4-fold increase in the risk of cardiovascular events at 1-year follow-up (38). Our study did not find any significant difference in LCBI between men and women in a select cohort of patients with stable CAD.

Each of the intravascular imaging modalities has their own relative advantages and disadvantages, thereby lending greater credibility to a comprehensive study utilizing multimodality assessment. The superiority of a hybrid OCT-IVUS imaging approach acting complementary to each other to improve reliability of plaque characterization has been reported (39,40). The superiority of OCT over IVUS for characterization of plaque morphology is because of its unprecedented resolution (10 μm to 20 μm), which is approximately 10 times higher than that of IVUS (41,42). Additionally, there is autopsy data demonstrating that OCT measurements of plaque and estimates of vessel lumen are closer to those obtained from histopathology than IVUS-derived measurements (43). However, OCT has a lower axial penetration (1 mm to 2 mm) as compared to IVUS (4 mm to 8 mm), thereby rendering IVUS as the only imaging modality to estimate PB (39). In a head-to-head comparison between the 3 modalities, OCT-defined TCFA was characterized by positive vessel remodeling, high PB and greater lipid core burden as assessed by dual NIRS-IVUS imaging (20).

The clinical implications of our study findings need to be viewed in the context of increasing CAD among women (2) and the fact that women presenting with symptomatic CAD are older with more comorbidities (5) and have worse prognosis compared to men (3). Post-mortem histomorphological data from fatal MI patients have shown fibrous cap thickness, macrophage infiltration, and necrotic core to be the most important predictors of plaque vulnerability (44). Our multimodality imaging data suggests that the aforementioned plaque characteristics are no different between men and women in a select cohort of patients with stable CAD. Therefore, equally aggressive primary and secondary prevention measures must be undertaken irrespective of sex. This is especially important in the light of the findings from studies that have shown clear sex biases in the use of evidence-based medical therapy (3). Women with stable angina were less likely to receive antiplatelets, lipid-lowering drugs, and revascularization even in the presence of symptomatic, angiographically significant disease (45). In fact, the SATURN (Study of Coronary Atheroma by Intravascular Ultrasound: Effect of Rosuvastatin Versus Atorvastatin) trial demonstrated that women with coronary disease demonstrate greater coronary atheroma regression than men when empirically prescribed guideline-driven potent statin therapy (15). Our findings of similar plaque morphology between men and women also support the recent suggestion that sex-based differences in outcome following PCI are attributable to age and comorbidities (6).

STUDY LIMITATIONS. The limitations of our study are that it is a retrospective single-center study and there is a disparity in the number of cases investigated with different modalities of imaging. Despite

multivariate adjustment the possibility of residual confounding cannot be excluded and the use of propensity analysis would have necessitated a larger sample size. The findings of our study are hypothesis-generating and require larger multicenter studies for confirmation.

CONCLUSIONS

Our study suggests that in a select cohort of men and women with stable CAD referred for coronary angiography, there was no difference in PB on IVUS or plaque morphology as assessed by OCT and NIRS.

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PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE: Multimodality intravascular imaging utilizing OCT, IVUS, and NIRS suggests that there is no difference in plaque morphology and characteristics between men and women in a select cohort of stable CAD who were referred for coronary angiography.

TRANSLATIONAL OUTLOOK: Additional multicenter studies utilizing various modalities of imaging are needed to further elucidate plaque characteristics in men and women with stable CAD, which is a growing cohort. Nevertheless, the findings of our study call for equally aggressive preventative and treatment measures in those at risk for CAD, irrespective of their sex.

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