Assessment With Multi-Slice Computed Tomography and Gray-Scale and Virtual Histology Intravascular Ultrasound of Gender-Specific Differences in Extent and Composition of Coronary Atherosclerotic Plaques in Relation to Age

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Data evaluating gender- and age-specific differences in plaque observations on multislice computed tomography (MSCT) are scarce. Accordingly, the aim of this study was to evaluate coronary plaque patterns in men and women in relation to age using MSCT. The findings were compared to observations on grayscale intravascular ultrasound (IVUS) and virtual histology (VH) IVUS. In total, 93 patients (59 men, 34 women) underwent 64-slice MSCT followed by conventional coronary angiography with IVUS. Plaque extent and composition were assessed on MSCT, grayscale IVUS, and VH IVUS. Coronary plaque patterns were compared between men and women in 2 age groups (<65 and ≥65 years old). In patients aged <65 years, more plaques were observed on MSCT in men (6 ± 4 vs 2 ± 2 in women, p <0.001). Also, a larger plaque burden was observed on grayscale IVUS in men (45.7 ± 11.4% vs 36.3 ± 11.6% in women, p <0.001). Similarly, more mixed plaques were observed in men (3 ± 3 vs 1 ± 1 in women, p = 0.003), whereas a larger arc of calcium was detected on grayscale IVUS in men (91.7 ± 93.5° vs 25.7 ± 51.0° in women, p <0.001). On VH IVUS, the prevalence of thin-cap fibroatheroma was higher in men (31% vs 0%) compared to women. In patients aged ≥65 years old, no important differences in plaque patterns were observed between men and women. In conclusion, more extensive atherosclerosis and more calcified lesions were observed in men than in women. These differences were predominantly present in patients aged <65 years and were lost in those aged ≥65 years. **(Am J Cardiol 2010;105: 480–486)**

The direct visualization of coronary atherosclerosis rather than testing for obstructive coronary artery disease (CAD) may be more appropriate for the initial assessment of CAD in women. Although plaque burden is traditionally evaluated invasively using intravascular ultrasound (IVUS),[1,2] noninvasive imaging methods have also become available for this purpose. In previous studies, coronary calcium scoring has been used to evaluate age and gender differences in the extent of coronary calcium.[3,4] More detailed information, including stenosis severity and plaque composition, can be derived using multislice computed tomography (MSCT).[5–7] However, data evaluating gender-specific differences in plaque observations on MSCT are scarce. It is important to establish whether these observations hold true for younger and older patients. The purpose of the study was to evaluate gender-specific differences in coronary plaque extent and composition in relation to age using noninvasive MSCT. The findings were compared to invasive coronary plaque observations on grayscale IVUS and virtual histology (VH) IVUS.

Methods

A total of 93 patients were included in the study. All patients presented with chest pain suggestive of CAD. Pa-

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tients underwent 64-slice multislice computed tomographic coronary angiography, followed within 1 month by conventional coronary angiography in combination with grayscale and VH IVUS of 1 to 3 vessels. The clinical histories of the patients were evaluated before conventional coronary angiography to ensure that neither acute coronary events nor worsening of angina occurred between the examinations. Patients were excluded from the study if contraindications to MSCT were present.[8] IVUS examination was not performed if severe vessel tortuousness, severe luminal narrowing precluding the insertion of the IVUS catheter, or vessel occlusion was present. Informed consent was obtained from all patients, and the study protocol was approved by the local ethics committee.

For comparisons, the patient population was first divided on the basis of gender (men vs women) and second on the basis of age (younger [aged <65 years] vs older [aged ≥65 years] patients).

Multislice computed tomographic coronary angiography was performed using a 64-slice Toshiba Aquilion (Toshiba Medical Systems, Tokyo, Japan) scanner. A helical scan protocol with electrocardiographic gating was applied as described previously.[9] Images were evaluated on a remote workstation with dedicated software (Vitrea 2, Vital Images, Minnetonka, Minnesota; and Advantage, GE Healthcare, Milwaukee, Wisconsin). First, the Agatston coronary calcium score was obtained from the image data set without contrast enhancement. Subsequently, 2 experienced observers evaluated the noninvasive coronary angiograms side by side in consensus. For the assessment of intraobserver variability of plaque assessment in consensus, coronary plaques were repeatedly assessed by 2 observers >6 months later after initial assessment in a subgroup of 20 patients. The presence of coronary plaques was visually assessed as previously described.[10] First, plaques were classified as obstructive or not (≥50% luminal narrowing). Second, the plaques were classified into 3 types: noncalcified (plaques having lower density compared to the contrast-enhanced vessel lumen), calcified (plaques having only high-density structures [≥130 Hounsfield units], without any low-density tissue discernible), and mixed (plaques containing any amount of low-density element with a high-density element embedded in the noncalcified tissue). The images were evaluated on a patient level. The mean numbers of any, nonobstructive, and obstructive plaques were determined per patient. Likewise, the mean numbers of noncalcified, calcified, and mixed plaques were determined.

IVUS examinations were performed with a 20-MHz, 2.9Fr phased-array IVUS catheter (Eagle Eye; Volcano Corporation, Rancho Cordova, California). After the intracoronary administration of nitrates, the catheter was introduced to the distal coronary artery and withdrawn at a continuous speed of 0.5 mm/s to the coronary ostium using an automated pullback device. To define the starting position of the IVUS catheter, cine runs were performed.

To evaluate geometric plaque characteristics, grayscale IVUS data sets were evaluated by an experienced observer, using dedicated software (QCU CMS 4.0; Medis Medical Imaging Systems, Leiden, The Netherlands). Cross-sectional images spaced 0.5 mm apart in the pullback were analyzed within the full length of the examined vessel. The contours of the external elastic membrane (EEM) were identified, and the mean EEM area was calculated per vessel. Subsequently, the lumen-intima interface was identified and mean luminal area was calculated. Plaque area was enclosed by the contours of the EEM and the lumen. Plaque

Table 1
Patient characteristics

Patient Characteristic	Men (n = 59)	Women (n = 34)	p Value
Age (years)	61 ± 9	64 ± 8	0.2
Body mass index (kg/m^2)	27 ± 4	26 ± 4	0.3
Clinical presentation			
Atypical angina pectoris	17 (29%)	13 (38%)	0.3
Typical angina pectoris	42 (71%)	21 (62%)	0.3
Coronary artery disease risk factors			
Body mass index ≥ 30 kg/m^2	18 (31%)	8 (24%)	0.6
Hypercholesterolemia*	46 (78%)	26 (77%)	0.9
Hypertension†	30 (51%)	24 (71%)	0.06
Diabetes mellitus	11 (19%)	4 (12%)	0.4
Smoking	27 (46%)	17 (50%)	0.7
Pretest likelihood‡			
Intermediate	17 (29%)	17 (50%)	0.05
High	42 (71%)	17 (50%)	0.05
Previous myocardial infarction	10 (17%)	5 (15%)	0.8
Previous percutaneous coronary intervention	12 (20%)	8 (24%)	0.7
Medications			
Aspirin	34 (58%)	21 (62%)	0.7
Statins	38 (64%)	24 (71%)	0.5

Data are expressed as mean ± SD or number (percentage).
* Total cholesterol level ≥5 mmol/L or treatment with lipid-lowering drugs.
† Blood pressure ≥140/90 mm Hg or use of antihypertensive medications.
‡ Determined according to the method of Diamond and Forrester.

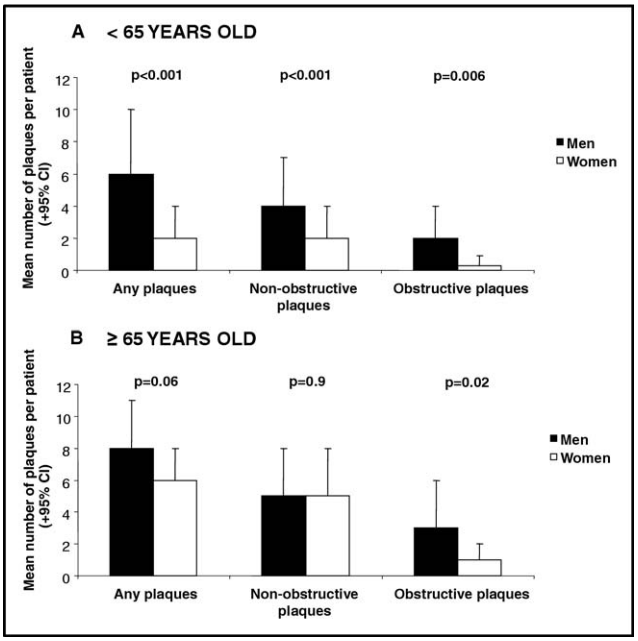

Figure 1. Coronary plaque extent on MSCT versus age and gender. *(A)* In younger (aged <65 years) patients, a higher prevalence of nonobstructive and obstructive plaques was observed in men compared with women. *(B)* In older (aged ≥65 years) patients, the number of nonobstructive plaques was identical in both genders, whereas more obstructive plaques were observed in men.

Table 2
Geometric and compositional characteristics of coronary atherosclerosis on grayscale and virtual histology intravascular ultrasound in younger (aged <65 years) patients

Characteristic	Men (n = 90 Vessels)	Women (n = 37 Vessels)	Correlation Coefficient (or OR) (95% CI)	p Value*
Plaque extent and composition on grayscale intravascular ultrasound				
Vessel length (cm)	7.0 ± 5.5	7.4 ± 3.8	−0.2 (−2.3 to 1.8)	0.8
External elastic membrane area (mm^2)	16.2 ± 8.5	12.2 ± 3.8	3.6 (0.8 to 6.5)	0.01
Luminal area (mm^2)	8.8 ± 4.5	8.9 ± 3.2	−0.2 (−1.8 to 1.4)	0.8
Plaque burden (%)	44.8 ± 12.3	27.9 ± 7.9	17.2 (12.9 to 21.5)	<0.001
% abnormal frames	85.9 ± 21.4	53.0 ± 26.8	32.9 (23.8 to 41.9)	<0.001
Plaque volume in most diseased 10 mm	100.0 ± 41.9	54.9 ± 24.3	45.2 (30.4 to 59.9)	<0.001
Plaque volume in least diseased 10 mm	42.1 ± 29.1	18.9 ± 13.2	23.5 (13.3 to 33.6)	<0.001
Remodeling index	1.03 ± 0.1	0.99 ± 0.1	0.03 (−0.01 to 0.06)	0.1
Positive remodeling	27 (31%)	6 (16%)	2.1 (0.8 to 5.8)	0.1
Largest arc of calcium (°)	91.7 ± 93.5	25.7 ± 51.0	67.5 (31.9 to 103.0)	<0.001
Plaque composition on virtual histology intravascular ultrasound				
Lesion length (mm)	24.6 ± 16.8	30.9 ± 17.5	0.9 (−12.3 to 11.2)	0.9
Fibrotic tissue (%)	51.1 ± 5.1	59.1 ± 8.7	−8.2 (−13.0 to −3.3)	0.001
Fibrofatty tissue (%)	27.0 ± 11.5	26.7 ± 10.2	−0.5 (−8.8 to 7.8)	0.9
Necrotic core (%)	12.8 ± 6.8	8.5 ± 4.1	4.2 (−0.3 to 8.8)	0.06
Dense calcium (%)	9.1 ± 7.8	5.7 ± 3.7	4.5 (−0.5 to 9.5)	0.08
Pathologic intimal thickening	2 (7%)	3 (23%)	0.1 (0.01 to 1.6)	0.1
Fibroatheroma	8 (28%)	5 (39%)	0.6 (0.1 to 2.7)	0.5
Thin-cap fibroatheroma	9 (31%)	0 (0%)	0.9 (0.8 to 1.0)	0.04
Fibrocalcific	10 (34%)	5 (38%)	1.8 (0.4 to 8.8)	0.4

Data are expressed as mean ± SD or number (percentage).
* Regression analysis.

burden was calculated as follows: plaque burden (%) = $[\Sigma(EEM_{area} - lumen_{area})/\Sigma EEM_{area}] \times 100$. In addition, plaque volume was determined in the 10 mm of the vessel containing the most and least plaque. The percentage of abnormal images (having plaque thickness >0.5 mm) was calculated in each examined vessel.[11] The remodeling index was calculated by dividing the EEM area at the site with most plaque by the EEM area at the proximal reference site. The latter was defined as the frame with largest luminal area located <10 mm from the most diseased frame with no major intervening side branches.[12] Positive remodeling was considered for a remodeling index ≥1.05. Finally, the largest arc of calcium in each examined vessel was obtained.

An experienced observer performed quantitative VH IVUS image analysis on a plaque level using dedicated software (pcVH 2.1; Volcano Corporation). Qualitative VH IVUS analysis was performed side by side in consensus by 2 experienced observers. First, 4 tissues were differentiated and labeled with different colors (fibrotic, fibrofatty tissues, necrotic core, and dense calcium).[13,14] The mean percentage of each plaque component was obtained in the full length of plaques observed on MSCT. In addition, plaques were visually assessed in 3 consecutive frames <10 mm from the minimal luminal area site and classified into 4 types: (1) pathologic intimal thickening, (2) fibroatheroma, (3) thin-cap fibroatheroma, and (4) fibrocalcific plaque.[15–17] Plaques were matched between MSCT and VH IVUS as previously described.[18]

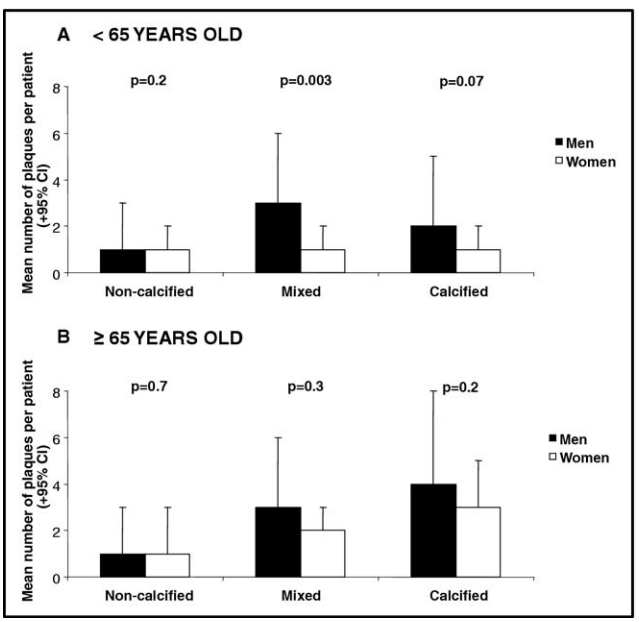

Figure 2. Coronary plaque composition on MSCT versus age and gender. *(A)* In younger (aged <65 years) patients, more mixed plaques and a trend toward more calcified plaques were observed in men compared with women. *(B)* In older (aged ≥65 years) patients, no differences in coronary plaque composition were observed between men and women.

First, gender-specific characteristics of coronary atherosclerosis were evaluated in the entire patient population by comparing observations between all men and women. Second, age-related differences between men and women were evaluated. For this purpose, the 2 patient populations (men vs women) were further divided into younger (aged <65

Table 3
Geometric and compositional characteristics of coronary atherosclerosis on grayscale and virtual histology intravascular ultrasound in older (aged ≥65 years) patients

Characteristics	Men (n = 39 Vessels)	Women (n = 42 Vessels)	Correlation Coefficient (or OR) (95% CI)	p Value*
Plaque extent and composition on grayscale intravascular ultrasound				
Vessel length (cm)	7.8 ± 3.5	9.8 ± 10.6	−2.1 (−5.9 to 1.7)	0.3
External elastic membrane area (mm^2)	15.3 ± 4.8	12.6 ± 4.6	3.5 (1.4 to 5.5)	0.001
Luminal area (mm^2)	7.9 ± 2.6	6.9 ± 2.2	1.3 (0.3 to 2.4)	0.02
Plaque burden (%)	47.6 ± 9.1	43.8 ± 8.9	4.2 (0.04 to 8.3)	0.06
% abnormal frames	92.1 ± 15.4	85.3 ± 19.8	8.3 (0.2 to 16.4)	0.06
Plaque volume in most diseased 10 mm	103.4 ± 41.8	85.4 ± 34.3	21.8 (4.1 to 39.4)	0.02
Plaque volume in least diseased 10 mm	39.7 ± 23.1	35.6 ± 27.9	5.8 (−6.3 to 18.03)	0.3
Remodeling index	1.05 ± 0.2	0.99 ± 0.1	0.04 (−0.03 to 0.1)	0.3
Positive remodeling	12 (31%)	4 (14%)	2.0 (0.6 to 6.3)	0.3
Largest arc of calcium (°)	100.1 ± 77.7	104.1 ± 60.8	−2.8 (−40.9 to 35.3)	0.9
Plaque composition on virtual histology intravascular ultrasound				
Lesion length (mm)	26.6 ± 18.3	27.4 ± 14.1	0.6 (−8.5 to 9.7)	0.9
Fibrotic tissue (%)	55.7 ± 8.3	57.0 ± 7.8	−2.8 (−6.5 to 0.8)	0.1
Fibrofatty tissue (%)	29.7 ± 12.9	25.0 ± 10.6	6.8 (1.4 to 12.2)	0.01
Necrotic core (%)	9.6 ± 5.3	11.4 ± 6.2	−2.4 (−5.2 to 0.4)	0.09
Dense calcium (%)	5.0 ± 4.0	6.6 ± 5.2	−1.6 (−3.8 to 0.7)	0.2
Pathologic intimal thickening	8 (23%)	6 (16%)	2.3 (0.6 to 8.2)	0.2
Fibroatheroma	19 (54%)	15 (41%)	1.5 (0.6 to 4.0)	0.4
Thin-cap fibroatheroma	4 (11%)	6 (16%)	0.4 (0.1 to 1.8)	0.2
Fibrocalcific	4 (11%)	10 (27%)	0.5 (0.1 to 2.0)	0.3

Data are expressed as mean ± SD or number (percentage).
* Regression analysis.

years) and older (aged ≥65 years) patients. Categorical variables were compared between groups using chi-square or Fisher's exact tests and are expressed as number (percentage). When normally distributed, continuous variables were compared using Student's *t* test for independent samples and are expressed as mean ± SD. When not normally distributed, continuous variables were compared using the nonparametric Mann-Whitney test and are expressed as median (interquartile range). All analyses were 2 tailed. To correct for (within) clustering of the variables across the patients, regression analysis was performed for data presented per vessel. For this purpose, a dummy variable was introduced, linking the vessels to different patients. Subsequently, linear regression analysis (if the dependent variable was continuous) or logistic regression analysis (if the dependent variable was categorical) was performed, including gender and the dummy variable as independent variables. The data are presented as correlation coefficients (odds ratios [ORs]) with 95% confidence intervals (CIs). To evaluate the reproducibility of coronary plaque evaluation on MSCT, Cohen's κ coefficient was calculated. A p value <0.05 was considered statistically significant. Statistical analyses were performed using SPSS version 14.0 (SPSS, Inc., Chicago, Illinois).

Results

Baseline clinical characteristics of the entire patient population are listed in Table 1. IVUS examinations were available in 208 of 279 vessels (71%) in 93 patients (129 vessels [62%] in men and 79 vessels [38%] in women). VH IVUS examinations were available in a subpopulation of 43 patients (46%) (23 men [54%] and 20 women [46%]). The characteristics of patients with VH IVUS were identical to the general patient population, whereas no differences in CAD risk factors and the use of cardiovascular medication were observed between men and women. In total, 70 vessels were available for VH IVUS analysis (37 vessels [53%] in men and 33 vessels [47%] in women).

Multislice computed tomographic coronary angiograms were of diagnostic quality in all patients. Excellent intraobserver agreement was observed for the detection of any plaque ($\kappa = 1.0$), and good intraobserver agreement was observed for the detection of obstructive plaques ($\kappa = 0.80$). Coronary plaques were more prevalent in men (6.7 ± 3.8 vs 4.0 ± 3.0 in women, $p = 0.001$). This observation was related to a higher prevalence of obstructive plaques (2.0 ± 2.2 in men vs 0.7 ± 1.1 in women, $p = 0.002$), as well as nonobstructive plaques (4.7 ± 3.1 in men vs 3.4 ± 2.8 in women, $p = 0.04$).

On grayscale IVUS, a larger plaque burden was observed in men (45.7 ± 11.4% vs 36.3 ± 11.6% in women, correlation coefficient 9.8, 95% CI 6.5 to 13.1, $p < 0.001$). The percentage of IVUS frames with plaque was also higher in men (87.8 ± 19.9% vs 70.2 ± 28.3% in women, correlation coefficient 18.3, 95% CI 11.5 to 25.0, $p < 0.001$). In addition, a trend toward a higher mean remodeling index was observed in men (1.04 ± 0.1 vs 0.99 ± 0.1 in women, correlation coefficient 0.03, 95% CI −0.004 to 0.06, $p = 0.08$).

With regard to plaque composition on multislice com-

puted tomographic coronary angiography, good intraobserver agreement was observed for the classification of plaque type ($\kappa = 0.92$). The median coronary calcium score in men was 256.0 (interquartile range 43.5 to 706.5) compared to 72.0 (interquartile range 2.3 to 155.8) in women ($p = 0.003$). Similarly, the number of calcified plaques on multislice computed tomographic coronary angiography tended to be higher (2.7 ± 3.5 in men vs 1.7 ± 1.9 in women, $p = 0.1$). Nevertheless, men had significantly more mixed plaques (2.8 ± 3.1) than women (1.3 ± 1.5) ($p = 0.01$). Interestingly, the number of noncalcified plaques was identical in men and women (1.3 ± 1.8 vs 1.0 ± 1.3, respectively, $p = 0.5$).

The arc of coronary calcium on grayscale IVUS was larger in men ($94.4 \pm 88.5°$ vs $63.6 \pm 68.1°$ in women, correlation coefficient 33.6, 95% CI 6.8 to 60.4, $p = 0.01$).

On VH IVUS, the amount of fibrotic tissue was less in the plaques of men ($53.6 \pm 7.4\%$ vs $57.5 \pm 8.0\%$ in women, correlation coefficient −5.2, 95% CI −8.2 to 2.3, $p = 0.001$). The amount of fibrofatty tissue was larger in the plaques of men ($28.5 \pm 12.2\%$ vs $25.5 \pm 10.4\%$ in women, correlation coefficient 4.9, 95% CI 0.5 to 9.3, $p = 0.03$). No differences were observed in the amount of necrotic core ($11.1 \pm 6.2\%$ in men vs $10.7 \pm 5.9\%$ in women, correlation coefficient −0.2, 95% CI −2.6 to 2.1, $p = 0.8$) and dense calcium ($6.9 \pm 6.3\%$ in men vs $6.3 \pm 4.8\%$ in women, correlation coefficient 0.6, 95% CI −1.7 to 2.8, $p = 0.6$). Likewise, no differences were observed in the prevalence of plaque types: pathologic intimal thickening was observed in 10 plaques (16%) in men and in 9 plaques (18%) in women (OR 1.1, 95% CI 0.4 to 3.3, $p = 0.8$), fibroatheroma in 27 plaques (42%) in men and 20 plaques (40%) in women (OR 1.0, 95% CI 0.4 to 2.2, $p = 0.9$), thin-cap fibroatheroma in 13 plaques (20%) in men and 6 plaques (12%) in women (OR 1.0, 95% CI 0.3 to 3.3, $p = 0.9$), and fibrocalcific plaque in 14 plaques (22%) in men and 15 plaques (30%) in women (OR 1.0, 95% CI 0.4 to 2.6, $p = 0.9$).

In total, 55 patients (59% of the total population) were aged <65 years (39 men [71%] and 16 women [29%]). The mean age was 56 ± 5 years in men and 57 ± 5 years in women ($p = 0.4$). No differences in the distribution of CAD risk factors, history of CAD, and use of cardiovascular medication were observed between men and women.

The findings of coronary plaque extent are presented in Figure 1 and listed in Table 2. On MSCT, the number of coronary plaques was higher in men than in women. The numbers of nonobstructive and obstructive plaques were higher in men (Figure 1). In total, 127 vessels were available for grayscale IVUS analysis (90 vessels in men and 37 vessels in women). Coronary artery diameters were larger in men than in women. In addition, coronary plaque burden was larger in men in the entire vessel as well as in the most and the least diseased coronary artery segments (Table 2).

The findings of coronary plaque composition are presented in Figure 2 and listed in Table 2. The median coronary calcium score on MSCT in men was 216.0 (interquartile range 4.0 to 714.0) compared to 3.5 (interquartile range 0 to 109.0) in women ($p = 0.003$). A larger number of mixed plaques was observed in men than in women (Figure 2).

The arc of coronary calcium on grayscale IVUS was larger in men than in women (Table 2). VH IVUS was

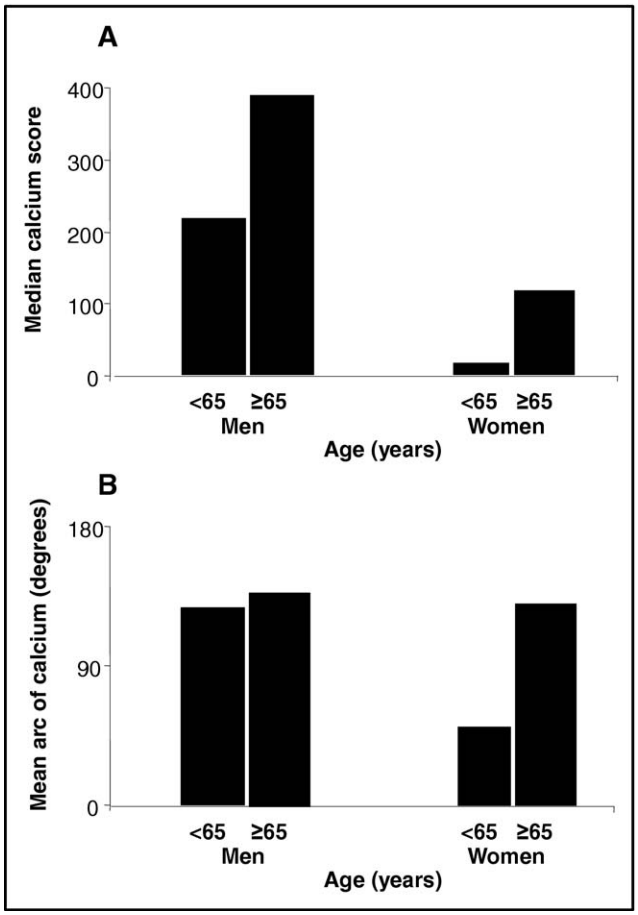

Figure 3. The progression of coronary calcium in relation to age and gender. *(A)* Higher coronary calcium scores on MSCT were observed in men. The progression of coronary calcium was more prominent after the age of 65 years old in women than in men. *(B)* For the arc of calcium on grayscale IVUS, a similar pattern of progression of coronary calcium was observed on grayscale IVUS.

available in 32 vessels of 21 patients (21 vessels in men and 11 vessels in women). The plaques in women contained more fibrotic tissue, whereas a trend toward more necrotic core was observed in the plaques of men. Thin-cap fibroatheromas were observed exclusively in the plaques of men (Table 2).

In total, 38 patients (41% of the total population) were aged ≥65 years (20 men [53%] and 18 women [47%]). The mean age was 72 ± 4 years in men and 70 ± 4 years in women ($p = 0.2$). No differences in the distribution of CAD risk factors, history of CAD, and use of cardiovascular medication were observed between men and women.

The findings of coronary plaque extent are presented in Figure 1 and listed in Table 3. No differences were observed in the prevalence of any and nonobstructive plaques. Nevertheless, obstructive plaques were still more frequently present in men (Figure 1).

In total, 81 arteries were available for grayscale IVUS analysis (39 vessels in men and 42 vessels in women). Coronary artery diameters remained larger in men than in women. Nevertheless, diffuse coronary atherosclerosis was observed in men and women, resulting in the absence of

differences of plaque burden and percentage of IVUS frames with plaque (Table 3).

The findings of coronary plaque composition are presented in Figure 2 and listed in Table 3. The average coronary calcium score on MSCT in older men was 387.0 (interquartile range 129.0 to 704.0) compared to 114.5 (interquartile range 36.0 to 363.25) in older women ($p = 0.03$). No differences in plaque composition were observed between men and women (Figure 2).

The arc of calcium on grayscale IVUS was identical in the plaques of both genders (Table 3). VH IVUS was available in 38 vessels (16 vessels in men and 22 vessels in women). No differences in the amount of necrotic core and thin-cap fibroatheroma were observed between the genders (Table 3).

Finally, the development of coronary calcium with increasing age is depicted in Figure 3. More extensive calcium was observed in men. However, progression of coronary calcium was substantially more pronounced after the age of 65 years in women compared with men.

Discussion

The findings of this study can be summarized as follows. More extensive atherosclerosis and more advanced calcified lesions were observed in men on MSCT than in women. Conversely, in women, atherosclerosis tended to be nonobstructive, with a relatively larger contribution of noncalcified plaque. Comparison of the observations with regard to age revealed that the differences of coronary plaque observations were predominantly present in younger patients and were lost or minimal in older patients. The findings were confirmed on invasive grayscale IVUS and VH IVUS.

In the present study, fewer coronary plaques were observed in younger (aged <65 years) women than in younger men on MSCT and on grayscale IVUS. This observation is in line with previous IVUS studies. Indeed, in a recent investigation by Nicholls et al[2] (including 251 women, mean age <65 years), coronary plaque burden was significantly lower in women. In contrast, Kornowski et al,[19] who performed preinterventional IVUS in slightly older women (average age 66 years) and compared the findings to those in a significantly younger male population (average age 60 years), failed to show any differences in plaque burden. Similarly, the difference in plaque extent was also lost in our study when comparing patients aged >65 years. Nevertheless, diffuse (nonobstructive) coronary atherosclerosis was observed in women across all ages on MSCT and on grayscale IVUS. Possibly, the presence of nonobstructive atherosclerosis in the absence of evident obstructive lesions may reflect a different manifestation of CAD in women and should not necessarily be considered benign. Indeed, 4 years of follow-up in the Women's Ischemia Syndrome Evaluation (WISE) study revealed that women with no or minimal stenoses on invasive coronary angiography still had a 9.4% risk for death or myocardial infarction.[20] Accordingly, the traditional diagnostic workup on the basis of luminography may result in underappreciation of CAD in women, and atherosclerosis imaging may be preferable.

In the present study, lesions in men tended to be more calcified, whereas the relative contribution of noncalcified plaques to the total plaque burden was higher in women on MSCT. Whereas the smaller amount of calcium in younger women may reflect less progressed atherosclerosis, the differences in plaque composition in younger patients may reveal particular patterns of plaque progression in the genders. Indeed, in the present study, more fibrotic tissue and a trend toward a higher proportion of pathologic intimal thickening were observed in the plaques of younger women on VH IVUS. In contrast, in patients aged <65 years, thin-cap fibroatheromas were exclusively observed in men, and the percentage of necrotic core tended to be higher. This is in line with observations in postmortem studies. Indeed, Mautner et al,[21] who investigated plaque composition in the histologic specimens of men and women with a mean age at death of <65 years, observed that plaques in women contained significantly more cellular fibrous tissue than those in men. In contrast, in men as well as in older women, ruptured lesions with large necrotic cores and disrupted fibrous caps were frequently observed.[15]

Coronary calcium score on MSCT was still lower in older women than in men, whereas the number of calcium-containing lesions was the same between the genders. The possible explanation for this phenomenon may be twofold. First, a similar calcium score may actually imply a higher percentage atheroma volume in women due to smaller vessel caliber. Second, the relative contribution of noncalcified atherosclerosis to total plaque burden may be higher in women. Accordingly, noninvasive coronary angiography with MSCT may be superior to calcium scoring because it may provide a more reliable estimate of total plaque burden. Nevertheless, it is important to realize that MSCT currently provides only general information on extent the (noncalcified) plaque burden compared with invasive IVUS. Accordingly, further studies are necessary to determine whether noninvasive characterization of plaque burden with MSCT may translate into more accurate risk stratification in women.

Compared to men, a more pronounced increase in coronary calcium was observed in women aged >65 years on MSCT, which was confirmed on grayscale IVUS. In line with these observations, pathologic and other noninvasive imaging studies have previously shown that an initial lag of about 10 years in the development of calcium exists. However, this phenomenon disappears during the sixth and seventh decades in women, as also observed in the present study.[3,20]

The following limitations need to be recognized. Observations in the present study were obtained in a relatively small patient population, and grayscale IVUS was not available in all vessels. As a result, the present results are restricted to vessels suitable for IVUS investigation. In addition, VH IVUS data were available in a limited patient population. No follow-up data were available. In general, MSCT is still associated with elevated radiation exposure, although radiation doses are rapidly decreasing with newer acquisition protocols.[22,23] Also, no dedicated algorithms that allow the quantification of plaque stenosis or volume are available for MSCT at present. Finally, an important limitation of VH IVUS is that the technique is relatively new and not widely available.

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