

Sex differences in coronary atherosclerotic plaque activity using ^{18}F -sodium fluoride positron emission tomography

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Abstract

There are sex differences in the extent, severity, and outcomes of coronary artery disease.

We aimed to assess the influence of sex on coronary atherosclerotic plaque activity measured using coronary ^{18}F -sodium fluoride (^{18}F -NaF) positron emission tomography (PET), and to determine whether ^{18}F -NaF PET has prognostic value in both women and men.

Methods

In a post-hoc analysis of observational cohort studies of patients with coronary atherosclerosis who had undergone ^{18}F -NaF PET CT angiography, we compared the coronary microcalcification activity (CMA) in women and men.

Results

Baseline ^{18}F -NaF PET CT angiography was available in 999 participants (151 (15%) women) with 4282 patient-years of follow-up. Compared to men, women had lower coronary calcium scores (116 [interquartile range, 27-434] versus 205 [51-571] Agatston units; $p=0.002$) and CMA values (0.0 [0.0-1.12] versus 0.53 [0.0-2.54], $p=0.01$). Following matching for plaque burden by coronary calcium scores and clinical comorbidities, there was no sex-related difference in CMA values (0.0 [0.0-1.12] versus 0.0 [0.0-1.23], $p=0.21$) and similar proportions of women and men had no ^{18}F -NaF uptake (53.0% ($n=80$) and 48.3% ($n=73$); $p=0.42$), or CMA values >1.56 (21.8% ($n=33$) and 21.8% ($n=33$); $p=1.00$). Over a median follow-up of 4.5 [4.0-6.0] years, myocardial infarction occurred in 6.6% of women ($n=10$) and 7.8% of men ($n=66$). Coronary microcalcification activity greater than 0 was associated with a similarly increased risk of myocardial infarction in both women (HR: 3.83; 95% CI:1.10-18.49; $p=0.04$) and men (HR: 5.29; 95% CI:2.28-12.28; $p<0.001$).

Conclusions

Although men present with more coronary atherosclerotic plaque than women, increased plaque activity is a strong predictor of future myocardial infarction regardless of sex.

By depicting calcification activity within atherosclerotic plaques, ^{18}F -sodium fluoride (^{18}F -NaF) positron emission tomography (PET) provides a non-invasive method of assessing coronary atherosclerotic disease activity (1-3). This assessment has consistently been shown to provide prognostic information, with increased activity on ^{18}F -NaF PET acting as a powerful independent predictor of disease progression and adverse outcomes (4-8). The latter application has shown hope in refining risk stratification in the particularly challenging population of patients with established multivessel coronary artery disease (9). While the complex interplay between risk factors, plaque morphology and plaque activity across the wide spectrum of coronary artery disease has been extensively studied, sex differences in coronary plaque activity and the prognostic utility of ^{18}F -NaF PET has not been investigated (8, 10-12).

There are well characterized differences in men and women in cardiovascular risk factor profiles, symptoms, prevalence of coronary artery disease and prognosis. In the current study, we aimed to assess the impact of sex on coronary ^{18}F -NaF uptake and to determine whether such plaque activity assessments provide similar prognostic information in men and women.

Methods

The current post-hoc analysis was conducted using data collected for prospective observational studies in the United Kingdom, United States of America, and Australia (NCT01749254; NCT02110303; NCT02607748; NCT02278211)(7,9,13). The study cohort comprises patients with established coronary artery disease who had either stable multivessel coronary artery disease by invasive or non-invasive coronary angiography, or recent myocardial infarction. All patients underwent baseline ^{18}F -NaF PET and were prospectively followed-up for adverse events. Inclusion and exclusion criteria have been previously described (7,9,13). The studies were conducted with the approval of the Scottish Research Ethics Committee (14/SS/0089, 15/SS/0203 and 15-SS-0059), in accordance with the Declaration of Helsinki, and with the written informed consent of each participant.

Imaging

Acquisition

^{18}F -NaF PET was performed on hybrid PET/CT scanners (64-/128-slice Biograph mCT [Siemens Medical Systems] or Discovery 690/710 [GE Healthcare]) using harmonized imaging protocols 60 min following the injection of 250 MBq ^{18}F -NaF (14). Participants underwent an attenuation correction CT scan followed by a single bed position electrocardiogram-gated emission scan of the thorax in list-mode for 30 min. The gated list-mode datasets were reconstructed using a standard ordered expectation maximization algorithm with time of flight and point-spread-function correction. Using 4 cardiac gates, the data were reconstructed on a 256×256 matrix with 75 or 47 slices using 2 iterations, 21 subsets, and 5-mm Gaussian smoothing for Siemens mCT data and 4 iterations, 24 subsets, and 5-mm

Gaussian smoothing for GE Discovery data. To compensate for coronary motion associated with heart contraction, we performed cardiac motion correction of the PET/CT images as described previously (15). After the PET scan, a low-dose non-contrast ECG-gated CT for calculation of the coronary calcium score was performed. Subsequently, a contrast-enhanced ECG-gated coronary CT angiogram was obtained in mid-diastole.

Analysis

We measured the coronary artery calcium score in Agatston units (AU) using semiautomatic commercial software (NetraMD, ScImage, Los Altos, CA, USA). The presence of coronary atherosclerosis and the extent and severity of obstructive coronary artery disease were qualitatively evaluated on contrast-enhanced coronary computed tomography angiograms according to the Society of Cardiovascular Computed Tomography guidelines (16).

Multivessel coronary artery disease was defined as at least 2 major epicardial vessels with any combination of either >50% stenosis or previous revascularization.

Coronary ^{18}F -NaF PET image analysis was performed using a dedicated software (FusionQuant, Cedars Sinai Medical Center, Los Angeles) as described previously (5,9,13). We extracted whole-vessel tubular and three-dimensional volumes of interest (4-mm radius) from the computed tomography angiogram. Within such volumes of interest, we measured the coronary microcalcification activity, representing the overall disease activity in the vessel and based on both the volume and intensity of ^{18}F -NaF PET activity within it (similar in principle to the Agatston score used for CT calcium scoring) (17,18). Coronary microcalcification activity was defined as the integrated activity in standardized uptake value (SUV) units exceeding the corrected background blood pool mean SUV plus 2 standard

deviations (measured in the right atrium). The per-patient coronary microcalcification activity was defined as the sum of the per-vessel coronary microcalcification activity values, a coronary microcalcification activity >1.56 was considered as high ^{18}F -NaF uptake as described previously (9,13).

Clinical follow-up

The primary endpoint of the study was fatal or non-fatal myocardial infarction. Outcome status was obtained from the local and national health care record systems that integrate primary and secondary health care records or was reported by site investigators.

Categorization of these outcomes was performed blinded to the coronary PET or other study data.

Statistical Analysis

We assessed the distribution of data using the Shapiro-Wilk test. Continuous normally distributed variables are expressed as mean $\pm$ standard deviation and were compared using Student's *t*-test. Non-normally distributed data are presented as median [quartile 1 – quartile 3] and were compared using the Mann-Whitney U test. The chi-square test was used for analysis of categorical variables. Men and women were matched by coronary artery disease burden (coronary calcium score) and clinical comorbidities including diabetes, hypertension and the mode of revascularization (percutaneous or surgical). A Cox proportional hazard regression with adjustment for potential confounders was performed to determine the predictors of myocardial infarction. Statistical analysis was performed with SPSS Statistics for Windows version 27 (IBM). A two-sided P value < 0.05 was considered significant.

Results

Overall, there were 999 patients with complete baseline ^{18}F -NaF PET available for analysis, and 151 (15%) were female. Whilst women were slightly older than men (65 ± 8 versus 64 ± 8 years, $p=0.03$), there were no differences in comorbidities (including smoking habit, diabetes, hyperlipidemia and hypertension, all $p>0.10$; Table 1). Despite all patients having established coronary atherosclerosis, women had a lower extent and severity of coronary artery disease (Table 2). They presented with fewer vessels with visually assessed obstructive stenosis (2 [1-3] versus 2 [2-3], $p=0.01$), lower coronary calcium scores (116 [27-434] versus 205 [51-571] AU; $p=0.002$) and less frequently with a coronary calcium score >1000 (5.3% versus 14.1%; $p=0.002$). In line with disease burden assessments, men had more active coronary atherosclerosis on ^{18}F -NaF PET (Figure 1). A higher proportion of men than women showed coronary ^{18}F -NaF uptake (65.2% versus 47.0%, $p=0.01$) and the overall coronary microcalcification activity values were higher in men (0.5 [0.0-2.5] versus 0.0 [0.0-1.1], $p=0.01$).

To account for baseline differences in disease burden, we propensity matched a control group of 151 men who had similar CT calcium scores, segment involvement scores, and cardiovascular comorbidities to the 151 women (Table 3). Matching was successful, with no differences between men and women in any of the baseline clinical characteristics (Table 3). Similarly there were no significant differences in coronary microcalcification activity values between women and men (Table 3 and Figure 2).

Over a median of 4.5 [4.0 to 6.0] years and 4282 patient-years of follow-up, myocardial infarction occurred in 6.6% of women (n=10) and 7.8% of men (n=66) (Table 4, supplemental data). We observed no difference in the coronary microcalcification activity between women and men who experienced an event (1.55 [0.32 to 3.5] versus 2.28 [0.58 to 4.42], p=0.53). There were no differences in the coronary calcium scores in both women and men who subsequent had a myocardial infarction compared to those without events (p=0.31 and p=0.26, respectively). Coronary microcalcification activity greater than zero was an independent predictor of myocardial infarction in multivariable analysis (hazard ratio 4.39; 95% confidence interval 2.07 to 9.29; p<0.001), independent of sex (hazard ratio 0.76; 95% confidence interval 0.37 to 1.58; p=0.46), and the coronary calcium score (hazard ratio 1.24, 95% confidence interval 0.82 to 1.73; p=0.30). Coronary microcalcification activity greater than 0 was associated with a 4-fold increased risk of myocardial infarction in women (hazard ratio 3.83; 95% confidence interval 1.10 to 18.49; p=0.04) and 5-fold increase in men (hazard ratio 5.29; 95% confidence interval 2.28 to 12.28; p<0.001; Figure 3 and 4).

Discussion

In a comprehensive post-hoc pooled analysis of prospective multicenter studies, we have demonstrated that women have lower coronary atherosclerotic plaque activity than men. Consistent with well-established differences in disease burden, this appears to be largely driven by the extent of coronary atherosclerosis, since both sexes had comparable coronary atherosclerotic plaque activity for a given burden of coronary atherosclerosis. Moreover, amongst those patients who subsequently had a myocardial infarction, women had a similar coronary atherosclerotic plaque activity as men. Finally, we have found that coronary atherosclerotic plaque activity was a robust predictor of myocardial infarction irrespective of sex.

Our findings complement recent studies which characterized the sex differences in the extent, severity, presentation, management, and outcomes in coronary artery disease. Registries have consistently shown that women with acute myocardial infarction are much less likely to receive guideline-recommended therapies and that this population has greater in-hospital mortality rates than men (19,20). Women with stable coronary artery disease have a smaller volume of calcified plaque and fewer calcified lesions yet may suffer from more diffuse disease (21). As demonstrated by the Coronary Artery Calcium Consortium, women may require more comprehensive disease phenotyping to provide optimal risk stratification (22). In line with these discrepancies on coronary CT angiography, women show less obstructive coronary disease and fewer plaques with adverse morphological features when compared to men (23,24).

Over the past decade, ^{18}F -NaF PET has been repurposed for imaging cardiovascular disease and emerged as a powerful tool for prediction of disease progression and adverse outcomes across a wide range of conditions (5,9,13,25,26). In coronary artery disease, initial studies have linked increased ^{18}F -NaF uptake with risk factors, culprit lesions in patients with acute coronary syndromes, and plaques with adverse morphology on CT angiography or intravascular imaging (27,28). More recently, post-hoc analyses of prospective studies reported that ^{18}F -NaF coronary uptake acts as an independent predictor of adverse events in patients with established disease (5,9). This finding was recently confirmed in the context of the prospective multicenter Prediction of Recurrent Events With ^{18}F -Fluoride (PRE ^{18}F FIR) study (13). Despite this wealth of observational studies to date, we lack data on sex differences in plaque activity. This was predominantly because women were largely underrepresented in past analyses. In the current study, we aimed to combine independent datasets to provide an opportunity to characterize sex differences in coronary atherosclerotic plaque activity.

Our current study provides further evidence to support fundamental sex differences and similarities in coronary artery disease. In line with previous studies focused on disease burden assessments, we observed that women have lower overall plaque activity (21). This difference appears to be driven by the discrepancies in plaque burden as on a subsequent sensitivity analysis, there were no differences in the coronary atherosclerotic plaque activity between men and women when matched according to the burden of coronary artery disease. Most importantly, coronary atherosclerotic plaque activity was equally predictive for adverse events in men and women suggesting that despite lower disease burden, imaging plaque activity with PET can be used for risk stratification regardless of the patient's sex. This

predictive value of PET resembles sex differences and similarities with respect to the low-attenuation plaque burden on coronary CT angiography. As shown by Williams et al, quantitative low-attenuation plaque is a powerful predictor of myocardial infarction in women and men, with a low-attenuation plaque burden exceeding 4% associated with a 6-fold increase in the risk of adverse outcomes (29). These observations are also in line with studies focused on patients presenting with an acute event which demonstrated that although women with stable coronary artery disease have different plaque characteristics and plaque progression, the morphology of the culprit lesions appear to be similar irrespective of sex (24). The available evidence would suggest that while there are substantial sex differences in disease extent and burden, plaque activity and adverse morphology remain predictive of outcomes in both women and men.

There is a strong association between adverse plaque morphology, low-attenuation plaque, and ^{18}F -NaF uptake (10-12). Although this might serve to question the rationale for PET imaging, the key aspect of our analysis is the study population. Subjects with multivessel coronary atherosclerosis with a past medical history of revascularization or acute events have not been targeted by CT imaging and in clinical practice are challenging to risk stratify (30). By depicting plaque activity, ^{18}F -NaF PET has the potential to address this clinical need. Clinical applications of this imaging modality could include guiding therapeutical decisions such as allocation of more potent lipid lowering therapies or medication targeting residual inflammation within the coronary arteries.

Limitations

While the overall number of patients and events in our study remains modest, the current analysis represents the largest dataset of 999 patients who underwent coronary ^{18}F -NaF PET. Nevertheless, as often observed in coronary artery disease studies, women have been underrepresented in our analysis and consequently in the multivariable analysis, only a limited number of factors could be included. Our models are therefore potentially prone to overfitting. While all participants had advanced multivessel coronary artery disease, we have included patients with stable disease and subjects imaged within 3 weeks following myocardial infarction. Although this increases the heterogeneity of the analysed cohort, as shown previously ^{18}F -NaF coronary uptake acts as a predictor of myocardial infarction regardless of the patients past medical history (9). In the future, our findings require further external validation, ideally within studies which would assess the clinical application of ^{18}F -NaF coronary PET imaging.

Conclusions

Whilst men present with more pronounced coronary atherosclerotic plaque activity than women, coronary ^{18}F -NaF uptake on PET is a strong predictor of future myocardial infarction regardless of sex.

Statements & Declarations

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Competing Interests

The authors have no relevant financial or non-financial interests to disclose.

Compliance with Ethical Standards

The authors have no relevant financial or non-financial interests to disclose. The studies were conducted with the approval of the Scottish Research Ethics Committee (14/SS/0089, 15/SS/0203 and 15-SS-0059), in accordance with the Declaration of Helsinki, and with the written informed consent of each participant.

Data availability

The datasets analyzed during the current study are available from the corresponding author on reasonable request.

Author Contribution

All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by Jacek Kwiecinski, Evangelos Tzolos and Kang-Ling Wang. Alastair Moss, Marwa Daghem, Philip D Adamson, Patrycja Molek-Dziadosz, Dana Dawson, Parthiban Arumugam, Nikant Sabharwal, John P Greenwood, John N Townend, Patrick A Calvert, James HF Rudd, Daniel Berman and Johan W Verjans played a critical role in data acquisition. Damini Dey and Piotr Slomka provided software support for image analysis. Michelle Williams, Marc Dweck and David Newby provided essential data interpretation and enhanced the intellectual content of the manuscript. The first draft of the manuscript was written by Jacek Kwiecinski and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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Tables

Table 1. Baseline Characteristics of Female and Male Participants

	Overall (n=999)	Female (n=151)	Male (n=848)	P value
Age (years)	64.1±8.4	65.5±8.3	63.9±8.3	0.03
Cerebrovascular disease	43 (4.3%)	5 (3.3%)	38 (4.5%)	0.51
Peripheral vascular disease	37 (3.7%)	5 (3.3%)	32 (3.7%)	0.78
Smoking status				
- Current	258 (25.8%)	41 (27.1%)	217 (25.6%)	0.69
- Ex-smoker	366 (36.6%)	48 (31.8%)	318 (36.5%)	0.26
- Non-smoker	375 (37.5%)	60 (39.7%)	315 (37.9%)	0.66
Hypertension	527 (52.8%)	86 (57.0%)	441 (52.0%)	0.26
Diabetes Mellitus	179 (17.9%)	28 (18.5%)	151 (17.8%)	0.83
Hyperlipidemia	668 (66.8%)	111 (73.5%)	557 (65.7%)	0.15
Medication				
Aspirin	941 (94.2%)	141 (93.4%)	800 (94.3%)	0.83
P2Y12 antagonist	733 (73.4%)	110 (72.8%)	623 (73.5%)	0.79
Statin	915 (91.6%)	140 (92.7%)	775 (91.4%)	0.86
Beta blocker	769 (77.0%)	92 (60.9%)	677 (79.8%)	0.57
ACE inhibitor/ARB	820 (82.1%)	119 (78.8%)	701 (82.7%)	0.83

ACE - angiotensin converting enzyme; ARB - angiotensin receptor blocker;

n (%), mean ± standard deviation

Table 2. Coronary Artery Calcium Score and Coronary Artery Disease Activity on Computed Tomography and Positron Emission Tomography

	Overall (n=999)	Female (n=151)	Male (n=848)	P value
Coronary artery calcium score (AU)	190 [48-338]	116 [27-434]	205 [51-571]	0.002
Coronary artery calcium score group (AU)				
0	64 (6.4%)	8 (5.2%)	56 (6.6%)	0.34
1–99	329 (32.9%)	60 (39.7%)	269 (31.7%)	0.053
100–399	286 (28.6%)	42 (27.8%)	244 (28.8%)	0.81
400–999	192 (19.2%)	33 (21.9%)	159 (18.8%)	0.35
≥1,000	128 (12.8%)	8 (5.3%)	120 (14.1%)	0.002
Number of vessels with obstructive disease	2 [2-3]	2 [1-3]	2 [2-3]	0.01
1-vessel disease	102 (10.2%)	18 (11.9%)	84 (9.9%)	0.45
2-vessel disease	574 (57.5%)	109 (72.2%)	465 (54.8%)	<0.001
≥3-vessel disease	323 (32.3%)	24 (15.9%)	299 (35.3%)	<0.001
Coronary Microcalcification Activity	0.41 [0.0-2.4]	0.0 [0.0-1.12]	0.53 [0.0-2.54]	0.01
Coronary Microcalcification Activity Group				
0	375 (37.5%)	80 (53.0%)	295 (34.8%)	<0.001
0.01-1.56	279 (27.9%)	38 (25.2%)	241 (28.4%)	0.41
>1.56	345 (34.5%)	33 (21.8%)	312 (36.8%)	<0.001
Plaques with ¹⁸ F-sodium fluoride uptake	2 [1–3]	2 [0-3]	2 [1-3]	0.07
Plaques with uptake (number of vessels)				
0	375 (37.5%)	80 (53.0%)	295 (34.8%)	<0.001
1-2	382 (38.2%)	38 (25.2%)	344 (40.6%)	<0.001

≥3	242 (24.2%)	33 (21.9%)	209 (24.6%)	0.46
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n (%), median [interquartile range]

AU, Agatston Units

Table 3.

Men and Women Propensity Matched According to Plaque Burden and Comorbidities

	Female (n=151)	Male (n=151)	P value
Age (years)	65.5±8.3	64.8±8.3	0.74
Cerebrovascular disease	5 (3.3%)	5 (3.3%)	1.0
Peripheral vascular disease	5 (3.3%)	6 (4.0%)	0.76
Smoking status			
- Current	41 (27.1%)	42 (27.8%)	0.90
- Ex-smoker	48 (31.8%)	47 (31.1%)	0.90
- Non-smoker	60 (39.7%)	60 (39.7%)	1.0
Hypertension	86 (57.0%)	90 (59.6%)	0.64
Diabetes Mellitus	28 (18.5%)	28 (18.5%)	1.0
Hyperlipidemia	111 (73.5%)	113 (74.8%)	0.79
Coronary artery calcium score (AU)	116 [27-434]	115 [27-431]	0.99
Coronary artery calcium score group (AU)			
0	8 (5.2%)	9 (5.9%)	0.80
1–99	60 (39.7%)	59 (39.1%)	0.91
100–399	42 (27.8%)	42 (27.8%)	1.00
400–999	33 (21.9%)	33 (21.9%)	1.00
≥1,000	8 (5.3%)	8 (5.3%)	1.00
Number of vessels with obstructive disease	2 [1-3]	2 [2-3]	0.10
1-vessel disease	18 (11.9%)	17 (11.0%)	0.86

2-vessel disease	109 (72.2%)	110 (72.8%)	0.90
≥3-vessel disease	24 (15.9%)	24 (15.9%)	1.00
Coronary Microcalcification Activity	0.0 [0.0-1.12]	0.0 [0.0-1.23]	0.21
Coronary Microcalcification Activity Group			
0	80 (53.0%)	73 (48.3%)	0.42
0.01-1.56	38 (25.2%)	45 (29.8%)	0.37
>1.56	33 (21.8%)	33 (21.8%)	1.00
Plaques with ¹⁸ F-NaF uptake (n)	2 [0-3]	2 [0-3]	0.37
Plaques with uptake – group			
0	80 (53.0%)	73 (48.3%)	0.42
1-2	38 (25.2%)	41 (27.2%)	0.69
≥3	33 (21.9%)	37 (24.5%)	0.58

n (%), mean ± standard deviation, median [interquartile range]

AU, Agatston Units

Table 4. Patients clinical and imaging characteristics according to gender and outcomes during follow-up.

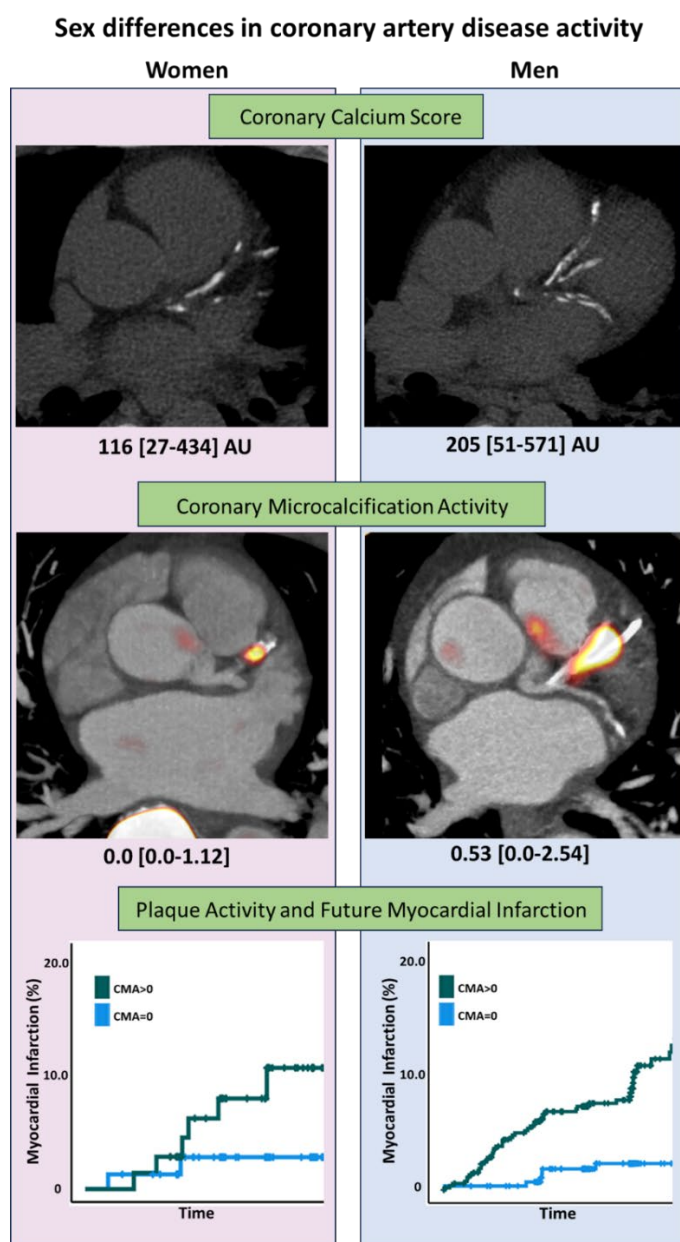
	Overall (n=999)		P value	Female (n=151)		P value	Male (n=848)		P value
Myocardial Infarction during follow-up	Yes n=76	No n=923		Yes n=10	No n=141		Yes n=66	No n=782	
Age (years)	65.2±8.9	63.9±8.6	0.59	65.3±1 3.1	65.5±9.2	0.48	64.8±9. 1	63.8±8. 6	0.53
Cerebrovascular disease	4 (5.2%)	39 (4.2%)	0.68	0	5 (3.5%)	N/A	4 (6.1%)	34 (4.3%)	0.51
Peripheral vascular disease	11 (14.5%)	26 (2.8%)	0.003	1 (10%)	4 (2.8%)	N/A	10 (15.1%)	22 (2.8%)	0.02
Smoking	51 (67.1%)	624 (62.1%)	0.12	7 (70%)	89 (58.2)	0.19	44 (66.7%)	491 (62.8%)	0.23
Hypertension	41 (53.9%)	527 (52.7%)	0.58	6 (60%)	86 (56.7%)	0.31	35 (53.0%)	406 (51.9%)	0.36
Diabetes Mellitus	20 (26.3%)	159 (17.2%)	0.09	3 (30%)	28 (17.7%)	0.10	17 (25.7%)	134 (17.1%)	0.13
Hyperlipidemia	50 (65.8%)	668 (67.0%)	0.71	8 (80%)	111 (73.1%)	0.47	42 (63.6%)	515 (65.8%)	0.55

Coronary artery calcium score (AU)	301 [50- 833]	205 [48-526]	0.14	122 [43- 301]	132 [48- 434]	0.31	327 [70- 928]	204 [49- 547]	0.26
Coronary Microcalcificatio n Activity	1.5 [0.1- 4.4]	0.4 [0.0- 2.3]	0.002	0.2 [0.0- 3.2]	0.0 [0.0- 1.1]	0.06	1.8 [0.2- 4.4]	0.4 [0.0- 2.5]	0.001

Figures

Figure 1. Sex differences in coronary artery disease activity (Graphical Abstract).

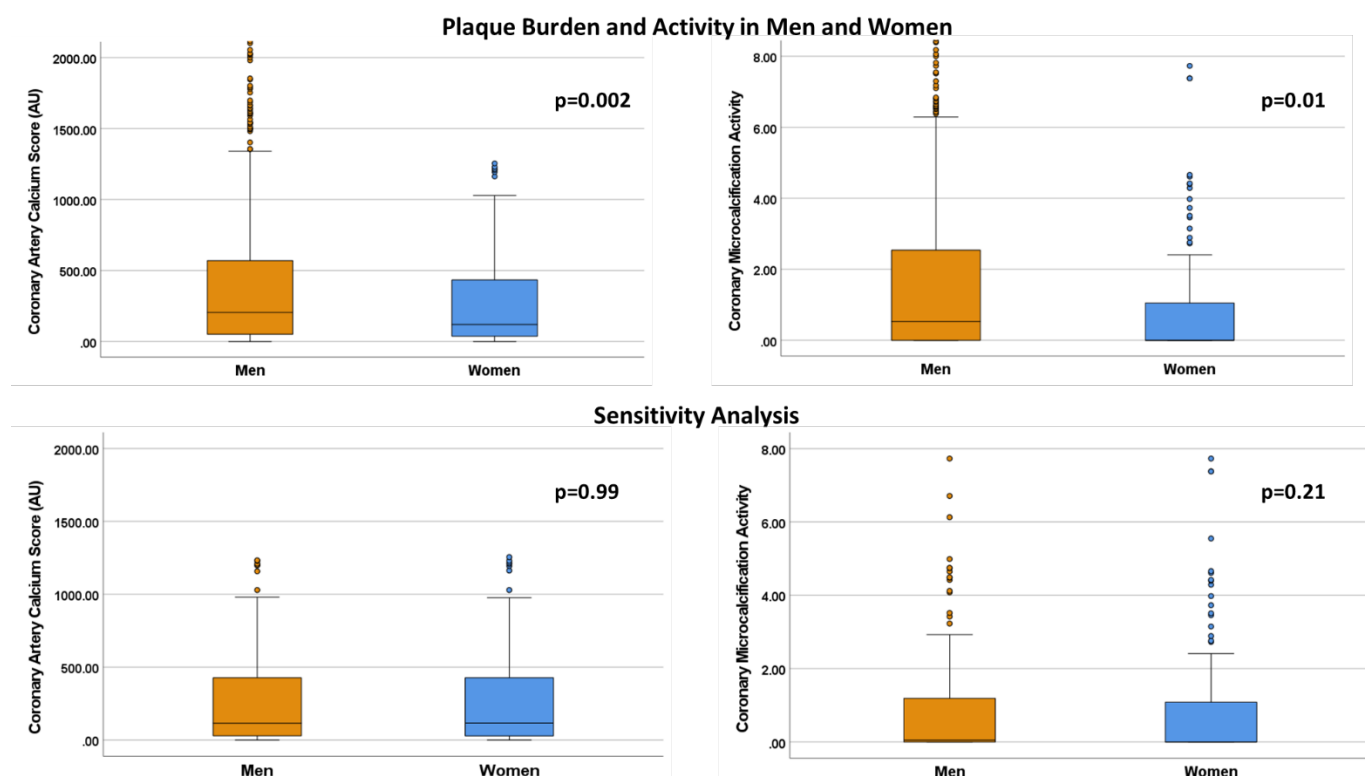
While women have lower disease burden and plaque activity on 18F-sodium fluoride positron emission tomography than men, the coronary microcalcification activity is a strong predictor of subsequent myocardial infarction regardless of sex.



median [interquartile range]; AU, Agatston Units; CMA, coronary microcalcification activity

Figure 2. Plaque burden and activity in men and women.

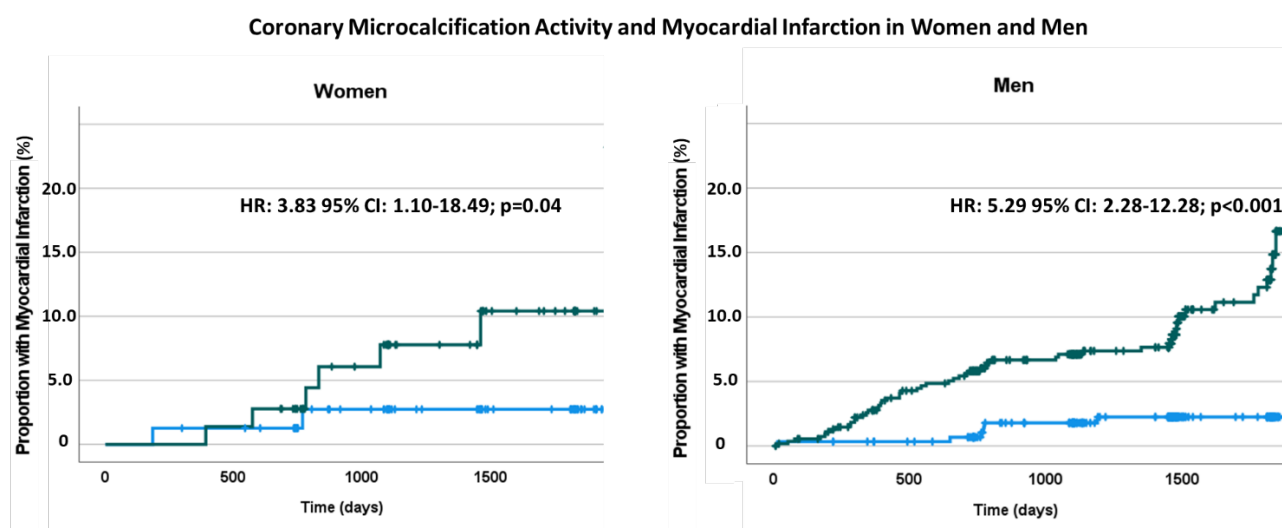
Men (n=848) have higher coronary calcium scores and coronary microcalcification activity than women (n=151). However, when patients were matched according to disease burden, there was no difference in coronary 18F-sodium fluoride uptake in men (n=151) and women (n=151).



AU – Agatston units

Figure 3. Coronary microcalcification activity and myocardial infarction in women and men.

Cumulative incidence plots of myocardial infarction in women and men showing the difference in events between those with (green) and without (blue) a coronary microcalcification activity above 0.

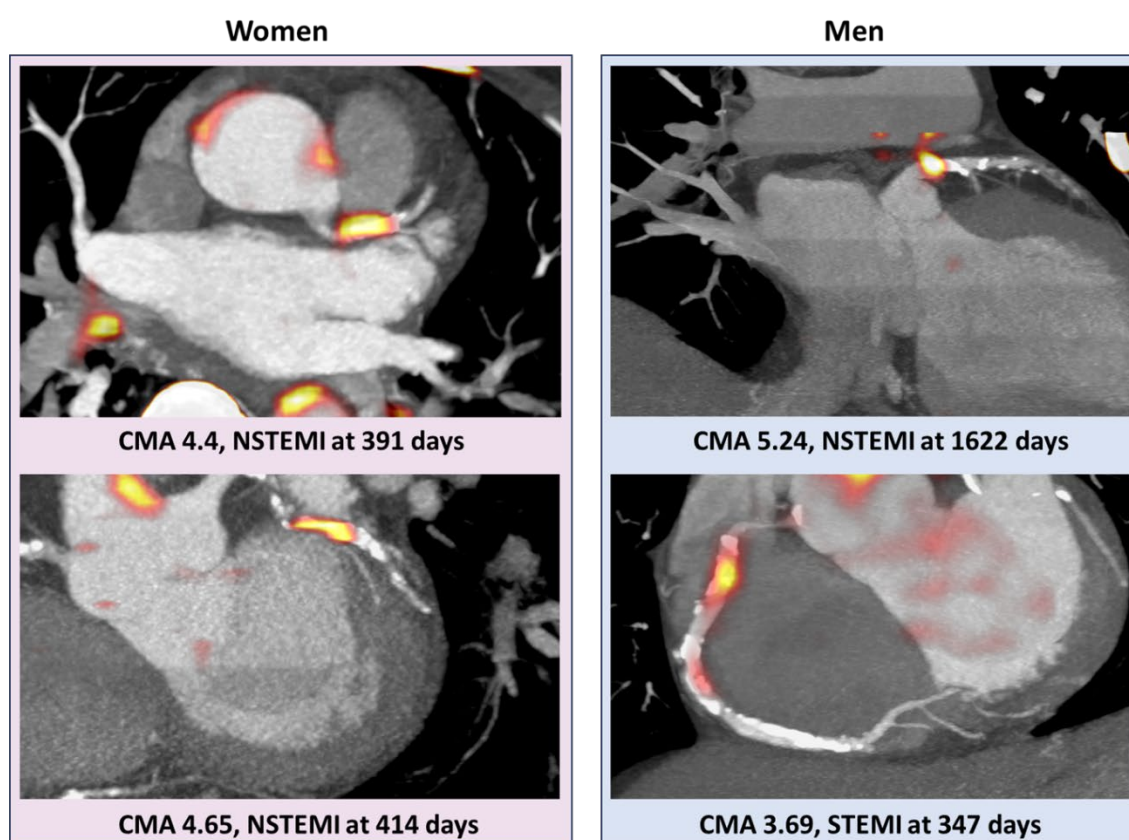


CI, confidence interval; HR, hazard ratio

Figure 4. Case examples of patients who experienced a myocardial infarction during follow-up.

Despite sex-related discrepancies in disease burden there was no difference in the coronary microcalcification activity between women and men who experienced an event during follow-up.

Case examples of patients who experienced a myocardial infarction during follow-up



CMA, coronary microcalcification activity; NSTEMI, non-ST elevation myocardial infarction; STEMI, ST elevation myocardial infarction