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Sex differences in coronary plaque composition evaluated by coronary computed tomography angiography in newly diagnosed Type 2 diabetes: association with low-grade inflammation

M. Mrgan[1], J. Gram[2,3], M. Hecht Olsen[4,5], D. Dey[6], B. Linde Nørgaard[7], J. Gram[8] and N. P. Rønnow Sand[1,9]

[1]Department of Cardiology, Hospital of Southwest Denmark, Esbjerg, [2]Unit for Thrombosis Research, University of Southern Denmark, Odense, [3]Department of Clinical Biochemistry, Hospital of Southwest Denmark, Esbjerg, [4]Cardiology Section, Department of Internal Medicine, Holbæk Hospital, Holbæk, [5]Centre for Individualized Medicine in Arterial Diseases (CIMA), Odense University Hospital, University of Southern Denmark, Odense, Denmark, [6]Department of Biomedical Sciences (Biomedical Imaging Research Institute), Cedars-Sinai Medical Center, Los Angeles, CA, USA, [7]Department of Cardiology, Aarhus University Hospital, Skejby, Aarhus, [8]Department of Endocrinology, Hospital of Southwest Denmark, Esbjerg and [9]Institute of Regional Health Research, University of Southern, Odense, Denmark

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Abstract

Aim To determine differences in coronary plaque composition and inflammatory biomarkers between men and women with newly diagnosed Type 2 diabetes without known cardiovascular disease.

Methods A total of 88 people with newly diagnosed (<1 year) Type 2 diabetes underwent contrast-enhanced coronary computed tomography angiography. Advanced coronary plaque analysis was performed using semi-automated software. Plasma concentrations of inflammatory biomarkers were determined.

Results There were no significant differences between men (n=60) and women (n=28) regarding age or cardiovascular risk factors (all P>0.05). The median (quartiles) serum levels of fibrinogen [10.9 (9.8–12.6) μmol/l vs 9.7 (8.8–10.9) μmol/l], fibrin d-dimer [0.3 (0.2–0.4) mg/l vs 0.27 (0.2–0.4) mg/l] and C-reactive protein [3.1 (1.1–5.2) mg/l vs (0.8–2.6) 1.6 mg/l] were significantly higher in women (all P<0.05). Overall, men more often had multi-vessel involvement [28 men (47%) vs 4 women (14%)], and higher total plaque burden [median (quartiles) 11.6 (2.3–36.0)% vs 2.0 (0.4–5.4)%; both P<0.05]. The median (quartiles) total plaque volume [269.9 (62.6–641.9) mm^3 vs 61.1 (7.6–239.9) mm^3] and absolute calcified plaque volume [33.5 (8.3–148.3) mm^3 vs 4.7 (0.9–17.3) mm^3] were higher in men (both P<0.05). Women had a lower relative proportion of the calcified plaque component [median (quartiles) 7.8 (4.7–15.4)% vs 23.7 (8.4–31.1)%] and a higher relative proportion (median [quartiles]) of the non-low-density non-calfied plaque component [77.6 (66.0–86.0)% vs 63.6 (54.0–72.9)%; both P<0.05].

Conclusions In people with newly diagnosed Type 2 diabetes, women had lower absolute coronary plaque volumes but a more unfavourable plaque composition and enhanced systemic inflammation compared with men.

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Introduction

While male sex is an independent risk factor for cardiovascular disease in the general population, the protection conferred by female sex is reduced in those with Type 2 diabetes [1,2]; thus, the relative risk of cardiovascular disease and myocardial infarction increases by 40–50% in women with Type 2 diabetes [3]. The mechanism for the higher relative risk in women with Type 2 diabetes remains undetermined [2].

Modification of traditional cardiovascular risk factors has been the cornerstone in primary prevention of cardiovascular disease [3]; however, up to 20% of people with coronary artery disease do not present any of these conventional risk factors, which has led to an intensive search for biomarkers

Correspondence to: Monija Mrgan. E-mail: momrg@hotmail.com
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What's new?

- It is known that Type 2 diabetes increases the risk of developing coronary artery disease more markedly in women than in men, but differences in coronary plaque composition between the sexes are poorly elucidated.
- This study found that women have smaller absolute volumes of coronary plaque components but a more unfavourable coronary plaque structure and enhanced systemic inflammation.
- The reported difference in plaque composition between men and women with a new diagnosis of Type 2 diabetes might be the basis for larger studies evaluating the impact of sex-differentiated therapeutic strategies at an early stage of Type 2 diabetes to prevent the development and progression of cardiovascular disease.

that reflect the early stages of the atherosclerotic disease [4]. As inflammation is fundamental in the development of atherosclerosis [5], there has been great interest in humoral biomarkers reflecting this component [6].

Multi-detector coronary computed tomography (CT) angiography has emerged as a valuable non-invasive method for studying coronary plaque characteristics [6]. Recently, we reported on the differences in coronary plaque composition between people with a new diagnosis of Type 2 diabetes and individuals without diabetes [7]. Others found that coronary plaque composition, rather than plaque size, calcium content or the degree of coronary artery stenosis is an independent determinant of the evolution and rupture of plaques and clinical outcomes [8]. An association between biochemical markers of inflammation and coronary plaque composition may be of importance regarding the identification of people with Type 2 diabetes who are at high risk; therefore, recognition of specific coronary plaque components and their association with inflammatory biomarkers may be important in risk stratification of Type 2 diabetes already at an early stage.

In the present study, we evaluated gender-related differences among people with a new diagnosis of Type 2 diabetes in relation to biomarkers of chronic low-grade inflammation and coronary plaque composition.

Materials and methods

Study population

Between March 2014 and August 2016, a total of 212 adults diagnosed with Type 2 diabetes [HbA_{1c} >47 mmol/mol (6.5%)] within the preceding year were identified via general practices or outpatient clinics in the region of Southern Denmark, and invited by letter to participate in the study. A total of 115 men and women (54%) agreed to participate. All participants were systematically evaluated by questionnaires and underwent examination for symptoms of or known cardiovascular disease (defined as previous myocardial infarction, angina pectoris, stroke/transient ischaemic attack and/or peripheral atherosclerosis), in which case they were excluded from the study. Pregnant women and people unable to provide informed consent were also excluded. Furthermore, for safety and technical reasons, people with renal failure (estimated GFR <45 mL/min or serum creatinine >140 μ/l), BMI >35 kg/m^2, absence of sinus rhythm, contraindications to iodinated contrast agents, and inability to perform a 10-s breath hold were excluded. A total of 88 men and women with newly diagnosed Type 2 diabetes met the inclusion criteria.

The protocol was approved by the Regional Scientific Ethical Committee for Southern Denmark (S-20140137) and by the Danish Data Protection Agency (2008-58-0035), and was conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from all individual participants included in the study.

Demographic data

Medical history, current medications and smoking habits were obtained from questionnaires. Height, weight and waist–hip ratio were measured. Brachial blood pressure was measured by oscillometry during 24 h using a TM-2430 monitor (A&D Co. Ltd, Saitama, Japan). Blood pressure was determined according to the mean values obtained from the 24-h recording.

Hypertension was defined as blood pressure ≥140/90 mmHg or treatment with at least one anti-hypertensive agent. Hypercholesterolaemia was defined as total cholesterol concentration ≥5 mmol/l, LDL cholesterol concentration ≥3 mmol/l or treatment with at least one lipid-lowering agent.

Blood collection and handling

Venous blood samples were taken under fasting conditions. Blood samples were drawn from an antecubital vein into sterile vacuum plastic tubes containing either 0.109 mmol/l citrate or no anticoagulant, and the plasma isolated after 20 min centrifugation at 2000 *g*. Samples from each participant were stored in aliquots at –80 °C until analysis. Cholesterol, direct LDL, ultra-HDL, triglyceride, creatinine, albumin and glucose levels were analysed using the Architect C16000 analyser (Abbott Diagnostics, Wiesbaden, Germany). HbA_{1c} was determined by a high-performance liquid chromatography method with a G8 analyser (Tosoh Europe, Tessenderlo, Belgium). C-reactive protein (CRP) concentrations were determined on a BN-II nephelometer using antibodies and reagents from Siemens (Siemens Healthcare GmbH, Erlangen, Germany). Concentrations of fibrinogen and fibrin-d-dimer were determined using a Star Analyser (Diagnostica Stago, Asnières, France). GFR was estimated using the Chronic Kidney Disease Epidemiology Collaboration

formula. Morning midstream urine samples were examined for urine albumin–creatinine ratio.

Coronary CT angiography

All participants underwent coronary CT angiography (SOMATOM Definition Flash; Siemens Healthcare, Forcheim, Germany). Pre-scan oral β-receptor blockers were administered, targeting a heart rate of ≤60 beats/min. Sublingual nitroglycerin was administered immediately before the scanning in each participant. A standard non-contrast cardiac CT for assessment of coronary artery calcification according to Agatston score was undertaken [9]. One experienced CT cardiologist, blinded to all clinical data, analysed the CT datasets, and one trained reader performed plaque analysis using validated semi-automated software (AutoPlaque, version 2.0, Cedars-Sinai Medical Center, Los Angeles, CA, USA). A detailed description of CT acquisition and plaque analysis has been published previously [7].

Statistical analysis

Continuous variables are presented as median (quartiles). Differences in baseline demographics were determined using Wilcoxon's rank test. Categorical variables are presented as frequencies (*n*) and corresponding percentages. Pearson's chi-squared test was used to analyse differences between groups.

Plaque data were characterized by a point mass at zero, followed by a highly skewed continuous distribution, which was why a two-part model was chosen for the univariate analysis [10]. First, a logistic regression model was used to determine the association between the presence or absence of each plaque component with all covariates (data presented as odds ratios and 95% CIs). Second, in participants with coronary plaque, the association between the extent of plaque volumes and each of the covariates was determined by a generalized linear model with the gamma distribution using link-name identity (data presented as difference and 95% CIs). The following covariates were included: age; hypertension; hypercholesterolaemia; BMI; smoking; fibrin d-dimer; fibrinogen; and CRP. Interactions between sex and each of the covariates with respect to the calcified plaque and low-density non-calcified plaque were also tested using the two-part model.

Differences in plaque composition between the sexes were tested using the Wilcoxon rank-sum test.

All statistical analyses were performed using STATA software, version 14.0 (StataCorp LLC, College Station, TX, USA).

Results

Baseline characteristics of asymptomatic population

A total of 88 people with a new diagnosis of Type 2 diabetes met the inclusion criteria. Table 1 lists the characteristics of the study population according to sex. There were no significant differences between men and women regarding age, BMI, traditional cardiovascular risk factors, and use of antidiabetic, anti-hypertensive and cholesterol-lowering medications. Serum levels of all inflammatory biomarkers were significantly higher in women (all $P<0.05$).

Prevalence and characteristics of coronary plaques

Coronary plaque characteristics are shown in Table 2. Significantly higher radiation doses were applied in men [mean (SD) 453.1 (142.1) mGycm] than in women [mean (SD) 347.9 (109.9) mGycm; P <0.001]. The Agatston score [median (quartiles)] was significantly higher in men [14 (0–173)] than in women [0 (0–21) U; $P<0.05$]. Only three participants had significant coronary stenosis and two had coronary plaques, but an Agatston score of zero.

Figure 1 shows the proportion of each plaque component in relation to the total plaque volume for men and women. Women had a lower relative proportion of the calcified plaque component [median (quartiles) 7.8 (4.7–15.4)% vs 23.7 (8.4–31.1)%] and a higher relative proportion of the non-low-density non-calcified plaque component [median (quartiles) 77.6 (66.0–86.0)% vs 63.6 (54.0–72.9)%; both $P<0.05$].

Coronary plaques and inflammation

Sex influenced the association between the extent of plaque volume and hypertension (P= 0.01), smoking (P=0.02), age ($P<0.001$) and fibrin d-dimer ($P<0.001$). Sex did not influence the association between the presence of plaque and any of the investigated risk factors/biochemical markers of inflammation.

Tables 3 and 4 show the associations between calcified plaque and low-density non-calcified plaque and different variables. Neither the presence of calcified plaque nor the presence of low-density non-calcified plaque was associated with any of the covariates in women. By contrast, age was associated with the presence of both calcified plaque and low-density non-calcified plaque in men. In women, the extent of calcified plaque was associated with age, hypercholesterolaemia and fibrinogen, while the extent of low-density non-calcified plaque was associated with fibrinogen. In men, the extent of calcified plaque was associated with age, while the extent of low-density non-calcified plaque was associated both with age and fibrinogen.

Discussion

Type 2 diabetes increases the risk of having coronary artery disease more markedly in women than in men [1,2], but sex differences in coronary plaque composition are still poorly elucidated, especially in the early stages of Type 2 diabetes. The main findings of the present study in men and women

Table 1 Clinical characteristics

	Women $n = 28$	Men $n = 60$	P
Demographics			
Age, years	56.9 (50.1–67.7)	55.5 (50.1–65.3)	0.85
Risk factors			
BMI (kg/m^2)	29.1 (26.5–33.3)	29.8 (26.7–32.4)	0.90
Waist–hip ratio	0.9 (0.9–1.0)	1.0 (1.0–1.1)	0.01
Smoking	25 (89)	35 (58)	0.36
Hypertension	17 (61)	40 (67)	0.38
Hypercholesterolaemia	25 (89)	47 (78)	0.17
Medical therapy			
Cholesterol-lowering medication	16 (57)	40 (67)	0.75
Anti-hypertensive medication	13 (46)	30 (50)	0.10
Oral antidiabetic medication	23 (82)	47 (78)	0.46
Insulin	1 (4)	5 (8)	0.38
24-h blood pressure			
Systolic blood pressure, mmHg	127 (122–133)	132 (125–140)	0.14
Diastolic blood pressure, mmHg	75 (70–79)	77 (73–82)	0.08
Pulse rate, beats/min	73 (70–79)	72 (66–79)	0.54
Laboratory findings			
Fibrin d-dimer, mg/l	0.3 (0.2–0.4)	0.2 (0.2–0.4)	0.05
Fibrinogen, µmol/l)	10.9 (9.8–12.6)	9.7 (8.8–10.9)	0.01
CRP, mg/l	3.1 (1.1–5.2)	1.6 (0.8–2.6)	0.04
Total cholesterol, mmol/l	4.7 (3.9–5.4)	4.2 (3.7–4.7)	0.15
LDL cholesterol, mmol/l	2.8 (1.8–3.4)	2.5 (1.9–2.9)	0.21
HDL cholesterol, mmol/l	1.2 (0.9–1.4)	1.1 (0.9–1.3)	0.10
Triglycerides, mmol/l	1.7 (1.2–2.3)	1.6 (1.2–2.5)	0.86
HbA_{1c}, mmol/l	44 (41–49)	46 (43–50)	0.42
HbA_{1c}, %	6.2 (5.9–6.7)	6.4 (6.1–6.7)	0.42
Estimated GFR, ml/min	80.0 (68.0–93.5)	90.0 (83.0–98.0)	0.02
Serum creatinine, µmol/l	68.5 (57.5–74.5)	77.5 (71.0–85.0)	0.01
Urine albumin–creatinine ratio, mg/g	8 (14–7)	6 (12–5)	0.18

CRP, C-reactive protein.
Data shown are median (quartiles) or n (%).

Table 2 Coronary plaque characteristics

	Women $n = 28$	Men $n = 60$	P
Affected coronary vessels, n (%)			
0	16 (57)	24 (40)	
1	8 (29)	8 (13)	
2	2 (7)	10 (17)	0.02
3	2 (7)	18 (30)	
Agatston score, U			
0	16 (57)	24 (40)	
1–99	10 (36)	14 (24)	0.02
100–400	2 (7)	11(18)	
> 400	0 (0)	11 (18)	
Coronary plaque composition	***n* =12**	***n* = 38**	
Total plaque volume, mm^3	61.1 (7.6–239.9)	269.9 (62.6–641.9)	0.04
Calcified plaque volume, mm^3	4.7 (0.9–17.3)	33.5 (8.3–148.3)	0.01
Non-calcified plaque volume, mm^3	55.5 (7.4–221.2)	206.8 (51.2–420.4)	0.07
a) Non-low-density non-calcified plaque volume	48.6 (6.9–186.3)	183.5 (45.2–301.9)	0.07
b) Low-density non-calcified plaque volume	3.1 (0.6–34.9)	26.6 (9.7–83.5)	0.09
Remodelling index	2.1 (1.5–4.9)	3.1 (2.7- 7.1)	0.04
Plaque length, mm	25.0 (10.7–54.5)	63.9 (28.1–107.4)	0.03
Total plaque burden (%)	2.0 (0.4–5.3)	11.6 (2.3–36.0)	0.01

Data are shown as median (quartiles) or n (%).
Only men and women who actually had plaque are included in the data on plaque morphology in the lower panel of the table.

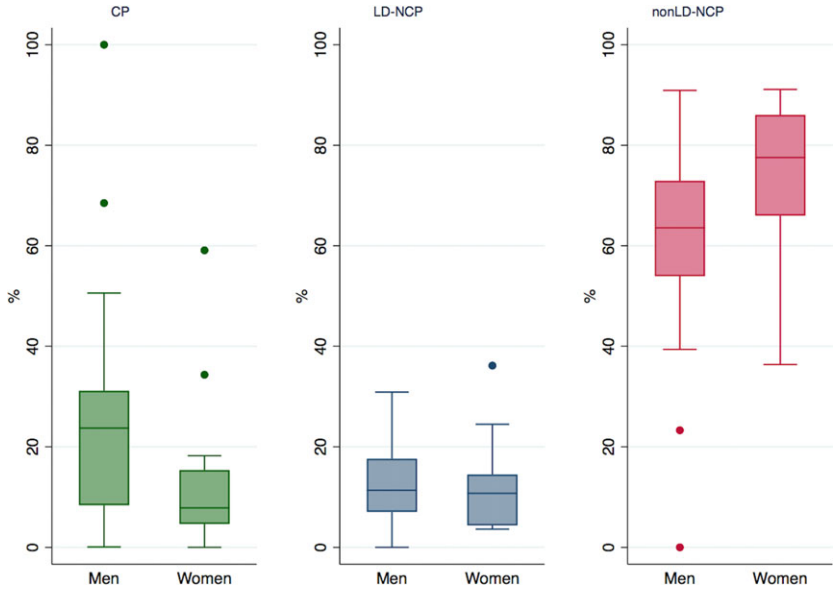

FIGURE 1 Sex-specific proportions of coronary plaque components in relation to total coronary plaque volume. calcified plaque. (CP), low-density non-calcified plaque (LD-NCP) non-low-density non-calcified plaque (nonLD-NCP)

Table 3 Sex-specific associations between the occurrence and extent of the calcified coronary plaque component and selected independent variables. Univariate analysis

	Presence of plaque Logistic regression			Extent of plaque Generalized linear model (gamma distribution with identity link)		
Calcified plaque	Odds ratio	CI	*P*	Difference	CI	*P*
Women						
Age, years	1.1	1.0–1.1	0.13	0.57	0.1–1.0	0.02
BMI, kg/m^2	1.0	0.85–1.2	0.91	1.6	–1.1–4.2	0.24
Hypercholesterolemia, *n*	1.3	0.1–16.7	0.82	14.6	1.6–27.7	0.03
Smoker, *n*	1.7	0.4–7.9	0.49	1.8	–22.5–26.0	0.89
Hypertension, *n*	2.4	0.5–12.1	0.30	12.5	–3.8–28.7	0.13
Fibrin d-dimer, mg/l	12.7	0.1–7454	0.43	61.8	–6.3–129.9	0.07
Fibrinogen, µmol/l	0.9	0.4–2.6	0.94	9.2	1.5–16.9	0.02
CRP, mg/l	1.0	0.8–1.1	0.58	0.2	–1.8–2.3	0.84
Men						
Age, years	1.2	1.1–1.3	0.01	6.9	4.0–9.8	0.01
BMI, kg/m^2	1.0	0.9–1.2	0.79	-5.68	–16.5–6.2	0.30
Smoker, *n*	2.3	0.8–6.8	0.13	-7.6	–78.0–62.7	0.83
Hypercholesterolemia, *n*	0.7	0.2–2.7	0.62	-69.5	–187.2–48.3	0.25
Hypertension, *n*	1.7	0.6–5.11	0.35	25.9	–39.3–91.2	0.44
Fibrin d-dimer, mg/l	0.9	0.3–3.0	0.88	171.8	–187.6–531.2	0.35
Fibrinogen, µmol/l	1.3	0.9–1.7	0.12	0.5	–26.4–27.4	0.97
CRP, mg/l	1.0	0.9–1.0	0.28	–1.6	–5.1–2.0	0.39

CRP, C-reactive protein.

with a new diagnosis of Type 2 diabetes were that, although women had lower absolute coronary plaque volumes, lower plaque burden and less coronary calcification than men, the relative size of the non-calcified part of the plaque was higher in women while the relative size of the calcified plaque component was lower. Moreover, women had significantly higher concentrations of inflammatory biomarkers, including fibrinogen, which was associated with plaque phenotypes in both men and women.

Previous reports [13,14] on healthy populations without diabetes have verified that women overall have less coronary calcification than men. Our findings are in concordance with these studies, demonstrating that 57% of women had an Agatston score of zero as opposed to 40% of men. In

Table 4 Sex-specific associations between the occurrence and extent of the low-density non-calcified coronary plaque component and selected independent variables. Univariate analysis

	Presence of plaque Logistic regression			Extent of plaque Generalized linear model *(gamma distribution)*		
Low-density non-calcified plaque	Odds ratio	CI	*P*	Difference	CI	*P*
Women						
Age, years	1.1	1.0–1.1	0.14	1.8	–0.9–3.6	0.06
BMI, kg/m^2	1.0	0.8–1.1	0.97	5.9	–6.2–18.0	0.34
Smoker, *n*	1.2	0.3–5.8	0.74	43.7	–43.7–131-2	0.33
Hypercholesterolaemia, *n*	1.6	0.1–19.7	0.73	41.7	–10.7–94.1	0.12
Hypertension, *n*	3.0	0.6–15.4	0.19	49.6	–10.0–109.2	0.10
Fibrin d-dimer, mg/l	5.6	0.01–2889	0.59	222.4	–19.6–464.3	0.07
Fibrinogen, µmol/l	1.0	0.7–1.5	0.85	8.3	–0.002–16.7	0.05
CRP, mg/l	0.9	0.8–1.1	0.47	0.04	–6.1–6.2	0.99
Men						
Age, years	1.2	1.1–1.3	0.01	3.9	0.3–7.4	0.03
BMI, kg/m^2	1.0	0.9–1.2	0.68	–3.9	–17.3–9.5	0.56
Smoker, *n*	2.0	0.7–5.8	0.20	18.5	–47.9–84.9	0.58
Hypercholesterolemia, *n*	0.7	0.2–2.4	0.53	–55.6	–188.0–76.7	0.41
Hypertension, *n*	1.5	0.5–4.5	0.45	42.0	–14.2–98.2	0.14
Fibrin d-dimer, mg/l	1.0	0.3–3.3	0.99	147.4	–160.1–454.8	0.35
Fibrinogen, µmol/l	1.3	1.0–1.9	0.05	–8.0	–14.9–1.1	0.02
CRP, mg/L	1.0	0.9–1.0	0.31	–2.0	–4.5–0.5	0.12

CRP, C-reactive protein.

addition, 18% of men had an Agatston score >400, while no women had a score >400. Contrast-enhanced coronary CT angiography has the ability to discriminate among different plaque components [11], and studies have shown that a more lipid-rich coronary plaque content is present in people with acute coronary syndrome and abnormal glucose tolerance [12].

The present study extends previous findings by showing that women and men differ with regard to plaque phenotype, as we found a significantly lower proportion of calcified plaque and a higher proportion of non-calcified plaque in women. These observations seem to be consistent with previous studies showing that coronary plaque in women contains larger amounts of cellular tissue and less dense fibrous tissue or calcium [15,16]. Moreover, a study in which intravascular ultrasonography was performed in patients with chest pain indicated a more vulnerable plaque structure in women [17]. These fragile plaque features have been associated with worse prognosis and adverse haemodynamic consequences [14,15]. Currently, it is not fully elucidated whether coronary plaque with a preponderance of non-calcified plaque material represents a less advanced or less stabilized atherosclerotic plaque subtype as compared with plaque dominated by calcification; however, recent studies indicate that medical treatment with statins changes plaque composition to a more stable condition [16].

Possible sex differences in coronary plaque composition in people with Type 2 diabetes are still poorly elucidated. Although well validated, it should be acknowledged that rates of macrovascular disease are lower in premenopausal women than in men. Interestingly, this sex difference, which normally vanishes after the menopause [17], is less pronounced in premenopausal women with Type 2 diabetes. Traditional cardiac risk factors cannot completely account for sex differences in cardiovascular mortality because up to 20% of all coronary events in women occur in the absence of these factors [18]. In the present study, women had significantly higher levels of fibrinogen, CRP and fibrin d-dimer than men; however, only fibrinogen was associated with the extent of plaque phenotypes. Biomarkers reflecting various pathways of atherogenesis, including inflammation, cell stress and coagulation, have been shown to be significant markers for cardiovascular events [19]. Both elevated fibrinogen [20] and fibrin d-dimer levels were predictors for development of cardiovascular disease in prior studies [19]. Recently, an elevated CRP level was correlated with an increased risk of future ischaemic events in patients with acute coronary syndrome [21], and high CRP levels predicted the presence of vulnerable plaques [22] in the acute setting. Hak *et al.* [23] found a stronger association of inflammatory biomarkers with insulin concentrations in elderly women than in men, and in addition that an elevated CRP level was a significant predictor for development of diabetes and metabolic syndrome in women only, independent of obesity and insulin resistance.

It may be speculated that low-grade inflammation may have a role in perturbing insulin action in women, or inflammatory biomarkers may interact with female sex hormones, resulting in decreased protective effects of oestrogens on body fat distribution and insulin action [24]. All

available evidence suggests a female advantage in human healing rates, whilst oestrogens have a positive effect by reducing inflammation and accelerating wound healing [25]. If Type 2 diabetes itself changes this process, resulting in a decreased protective effect of oestrogens and thereby promoting destabilization of pre-existing atherosclerotic plaques, remains to be settled.

The major finding of the present study is related to sex differences in coronary plaque composition and level of inflammatory status in newly diagnosed Type 2 diabetes. The study shows that men with newly diagnosed Type 2 diabetes have a higher degree of coronary atherosclerosis than women with newly diagnosed Type 2 diabetes, whilst women have significantly elevated inflammatory blood biomarkers and a less dense plaque structure compared with men. It might be speculated that either plaques in women are less stable or that humoral factors change in an atherogenetic manner [26], which might explain the higher increase in cardiovascular events in women after a diagnosis of Type 2 diabetes. This might call for gender-differentiated therapeutic strategies in cardiovascular disease prevention.

The present study has some limitations. The number of participants in the study was small; as only 54% of those asked agreed to participate, we cannot exclude some degree of bias, meaning that caution should be exercised in making strict conclusions based on this explanatory study. It should be noted, however, that the percentages of men and women who gave informed consent for participation in the study were equal. In men with Type 2 diabetes, a significantly higher radiation dose was applied, probably because of a different composition of fat and muscle in men and women. There was no significant difference in BMI between men and women. Both the duration of cholesterol-lowering and antihypertensive medication and the changes in cholesterol and blood pressure levels might have had an impact on plaque composition, which could not be accounted for in the study, as these data were not available.

The present study adds to the knowledge in this area by showing a different coronary plaque composition in women and men, both in absolute and relative terms. Moreover, women had significantly higher concentrations of inflammatory biomarkers, with fibrinogen being associated with plaque phenotypes both in men and women newly diagnosed with Type 2 diabetes. Future studies are required to approve these results and to help elucidate the precise role of sex in the inflammation and healing of coronary plaques.

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Competing interests

None declared.

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Supporting Information

Additional supporting information may be found online in the Supporting Information section at the end of the article.