Epicardial adipose tissue volume and coronary calcification among people living with diabetes: a cross-sectional study

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Abstract

Background Epicardial adipose tissue (EAT) has anatomic and functional proximity to the heart and is considered a novel diagnostic marker and therapeutic target in cardiometabolic diseases. The aim of this study was to evaluate whether EAT volume was associated with coronary artery calcification (CAC) in people living with diabetes, independently of confounding factors.

Methods We included all consecutive patients with diabetes whose EAT volume and CAC score were measured using computed tomography between January 1, 2019 and September 30, 2020 in the Department of Diabetology-Endocrinology-Nutrition at Avicenne Hospital, France. Determinants of EAT volume and a CAC score ≥ 100 Agatston units (AU) were evaluated.

Results The study population comprised 409 patients (218 men). Mean (± standard deviation) age was 57 ± 12 years, and 318, 56 and 35, had type 2 (T2D), type 1 (T1D), or another type of diabetes, respectively. Mean body mass index (BMI) was 29 ± 6 kg/m², mean AET volume 93 ± 38 cm^3. EAT volume was positively correlated with age, BMI, pack-year smoking history and triglyceridaemia, but negatively correlated with HDL-cholesterol level. Furthermore, it was lower in people with retinopathy, but higher in men, in Caucasian people, in patients on antihypertensive and lipid-lowering medication, in people with nephropathy, and finally in individuals with a CAC ≥ 100 AU (CAC < 100 *vs* CAC ≥ 100: 89 ± 35 vs 109 ± 41 cm^3, respectively, $p < 0.05$). In addition to EAT volume, other determinants of CAC ≥ 100 AU (n = 89, 22%) were age, T2D, ethnicity, antihypertensive and lipid-lowering medication, cumulative tobacco consumption, retinopathy, macular edema and macrovascular disease. Multivariable analysis considering all these determinants as well as gender and BMI, showed that EAT volume was independently associated with CAC ≥ 100 AU (per 10 cm^3 increase: OR 1.11 [1.02–1.20]).

Conclusions EAT volume was independently associated with CAC. As it may play a role in coronary atherosclerosis in patients with diabetes, reducing EAT volume through physical exercise, improved diet and pharmaceutical interventions may improve future cardiovascular risk outcomes in this population.

Background

Type 1 (T1D) and type 2 diabetes (T2D) are associated with an increased risk of cardiovascular disease, irrespective of improved multifactorial care [1, 2]. Epicardial adipose tissue (EAT) has recently been proposed as one determinant contributing to the pathophysiology of cardiovascular complications [3–6]. A recent meta-analysis showed that individuals with diabetes had higher EAT volumes than healthy controls, irrespective of T1D or T2D status and the method used to quantify EAT volume [3].

EAT is located between the myocardium and the visceral pericardium and is considered the heart's visceral adipose tissue [3–6]. It secretes inflammatory factors and lipid metabolites, and has been suggested as a possible determinant of accelerated atherosclerosis [3–6]. However, at the clinical level, evidence that EAT is a marker of subclinical atherosclerosis in diabetic populations is still limited [5].

Coronary artery calcium (CAC) is considered a good marker of coronary risk [7]. The CAC score assesses the volume of coronary calcifications located in atherosclerotic plaques. The CAC score increases with cardiovascular risk in both the general population and in people with diabetes [8–10]. To date, only four studies which have evaluated the association either between EAT volume [11–13] or EAT thickness [14] and CAC score in patients with diabetes have had mixed results: one study showed a positive association between EAT and CAC score in all 333 patients studied [11]; another only showed an association in the 38 individuals out of 95 studied who had early-onset T2D [13], while the remaining two studies reported no association whatsoever [12, 14].

In this context, the present study aimed to evaluate, in a large cohort of people living with diabetes, whether EAT volume was associated with CAC score, independently of confounding factors.

Methods

Study population

The present retrospective study involved each consecutive patient with diabetes admitted to the Department of Diabetology-Endocrinology-Nutrition, in Avicenne hospital, Bobigny, France, between January 1, 2019 and September 30, 2020. All had a computed tomography (CT) scan during hospitalization to evaluate their CAC score (Agatston unit).

CT imaging

CAC scores and EAT volume were calculated using ECG-gated cardiac CT without contrast injection. All CT scans were performed with GE (Healthcare Digital, France) or Siemens (Healthineers, France) scanners. CAC scores were calculated according to guidelines [15] using the dedicated tool available on Picture Archiving and Communication Systems (PACS) platforms (either from Carestream Health, Rochester, NY or Philips Healthcare, Best, the Netherlands). EAT volume was quantified with the software package AW VolumeShare 7 (GE Healthcare Digital). It was measured using a semi-automatic segmentation technique on every axial slice from the thoracic inlet to the beginning of the abdomen. The software automatically measured EAT volume (in cm^3) by summing appropriate pixels using a CT Hounsfield unit, range − 150 to -50 HU.

Data collection

Data were extracted from patients' medical records and collected in a secure health database. For the present study, we focused on:

- general data: current tobacco consumption and pack-year smoking history, diagnosed premature (before 55 years for men; before 65 years for women) coronary artery disease in first degree relatives; ethnicity (recorded as Caucasian, Arabic (Middle East, North Africa), Afro-Caribbean (African, African American, Caribbean), Asian (Asian continent), or other).
- medical history: routine treatments before admission, history of stroke, heart failure, or coronary artery disease. Hypertension and dyslipidaemia were self-reported and/or inferred from blood

pressure- and lipid-lowering agents, respectively. Additionally, we collected data to measure possible overweightness (body mass index (BMI) ≥ 25 kg/m²) and obesity (BMI ≥ 30 kg/m²). BMI was calculated using the formula: weight (kg) / height² (m²). Weight and height were measured within 24 hours of hospital admission.

- biomarkers: HbA1c (high performance liquid chromatography variant); total and HDL cholesterol (colorimetric assay on homogenous phase and cholesterol dosage by cholesterol oxidase), triglycerides (colorimetric assay), and LDL-cholesterol (calculated using the Friedewald formula). All these measurements were performed on plasma from fasting individuals using a Cobas 6000 analyzer (Roche diagnostics). Serum creatinine was measured (colorimetry, Kone Optima, Thermolab System, Paris La Défense, France) and creatinine clearance estimated (using the Chronic Kidney Disease-Epidemiology Collaboration equation). The urinary albumin / creatinine ratio (UACR) was measured (laser immunonephelometry, BN100, Dade-Behring, Paris, France).
- diabetes-related complications: retinopathy (defined as any medical argument for a retinopathy); nephropathy (defined as renal failure (estimated creatinine clearance < 60 ml/min) and/or albuminuria (UACR > 3 mg/mmol)); neuropathy (defined as any sign or symptoms of polyneuropathy); peripheral arterial occlusive disease (stenosis measured 50% by ultrasound examination); macroangiopathy (defined as peripheral arterial occlusive disease or history of stroke or coronary artery disease).

Statistical analyses

Continuous variables were expressed as means ± standard deviation and compared using one-way ANOVA or the Mann-Whitney's U test as appropriate. No data replacement procedure was used for missing data. Pearson's and/or Spearman's correlations were performed to identify the parameters associated with EAT. The 2 test was used to measure significant differences between the proportion of patients with a CAC score < 100 and those with a score ≥ 100 AU. Logistic regression was performed for the multivariable analysis, which included only those parameters associated with a CAC score ≥ 100 AU, as well as BMI and gender. Odds ratios with 95% confidence intervals (95 CI) for the risk of a CAC score ≥ 100 AU were calculated. Statistical analyses were performed using SPSS software (SPSS, Chicago, IL). The level of significance for all tests was $p < 0.05$.

Results

Patient characteristics

Of the 410 patients who met study inclusion criteria, 1 was not included as the EAT volume could not be measured. The characteristics of the 409 included patients are shown in Table 1.

Table 1
Patient characteristics.

	Available data	Total
Clinical characteristics:		
Age (years)	n = 409	57.1 ± 12.4
Gender (Male/Female)	n = 409	218/191
Body mass index (kg/m²)	n = 403	29.1 ± 5.9
Overweight or obese	n = 403	325 (79.5)
Obese	n = 403	158 (38.6)
Ethnicity:	n = 408	
Caucasian		88 (21.5)
Sub-Saharan Africa - Antilles		103 (25.2)
Middle East, North Africa		146 (35.7)
Asia		57 (14.0)
Other		14 (3.4)
Diabetes:		
Type	n = 409	
Type 1		56 (13.7)
Type 2		318 (77.8)
Other		35 (8.6)
Treatment		
Oral antidiabetic agents	n = 408	295 (72.1)
Glucagon-like peptid 1 agonists	n = 408	75 (18.3)
Insulin	n = 408	252 (61.6)
Time since diagnosis (years)	n = 409	14.0 ± 10.2
HbA1c, %	n = 403	9.0 ± 2.3
Retinopathy	n = 392	160 (39.1)

CAC: coronary artery calcium score; CAD: coronary artery disease

Data are n (%) or mean ± standard deviation

	Available data	Total
Macular edema	n = 382	44 (10.8)
Nephropathy	n = 390	148 (36.2)
Albuminuria	n = 389	135 (33.0)
Renal failure	n = 409	39 (9.5)
Neuropathy	n = 401	163 (39.9)
Peripheral arterial occlusive disease	n = 409	37 (9.0)
History of stroke	n = 409	13 (3.2)
History of heart failure	n = 356	5 (1.2)
Coronary artery disease (CAD)	n = 409	4 (1.0)
Additional cardiovascular risk factors:		
Family history of premature CAD	n = 149	33 (8.1)
Hypertension	n = 408	224 (54.8)
Systolic blood pressure (mmHg)	n = 408	135 ± 18
Diastolic blood pressure (mmHg)	n = 408	77 ± 13
Dyslipidemia	n = 408	238 (58.2)
Lipid parameters		
Total cholesterol (mmol/l)	n = 409	4.4 ± 1.2
HDL cholesterol (mmol/l)	n = 409	1.2 ± 0.4
Triglycerides (mmol/l)	n = 409	1.7 ± 1.2
LDL cholesterol (mmol/l)	n = 406	2.4 ± 0.9
Non HDL cholesterol (mmol/l)	n = 409	3.2 ± 1.1
Current smoking	n = 409	71 (17.4)
Smoking history (pack-year)	n = 386	8.2 ± 16.6
Computed tomography results		
Epicardial adipose tissue volume (cm^3)	n = 409	92 ± 37

CAC: coronary artery calcium score; CAD: coronary artery disease

Data are n (%) or mean ± standard deviation

	Available data	Total
CAC score (Agatston unit)	n = 409	116 ± 332
CAC: coronary artery calcium score; CAD: coronary artery disease		
Data are n (%) or mean ± standard deviation		

Parameters associated with EAT

EAT volume was positively associated with age, BMI, triglyceride levels, cumulative tobacco consumption and CAC score. It was negatively correlated with creatinine clearance and HDL-cholesterol level (Table 2). EAT volume was higher in males, overweight and obese persons, those categorized as Caucasian, patients with T2D, those with hypertension, individuals with dyslipidaemia and people with a CAC score ≥ 100 AU (Table 3). It was also higher in participants with retinopathy, nephropathy and albuminuria (Table 4).

Table 2
Correlation of epicardial adipose tissue volume with quantitative data

	R	P-value
Age, years	0.324	< 0.0001
Body mass index, kg/m²	0.288	< 0.0001
HbA1c	-0.093	0.142
Urinary albumin/creatinin ratio, mg/mmol	0.059	0.260
Creatinine clearance, ml/min	-0.237	< 0.0001
Systolic blood pressure, mmHg	-0.022	0.656
Diastolic blood pressure, mmHg	-0.035	0.483
Total cholesterol, mmol/L	-0.057	0.250
HDL cholesterol, mmol/L	-0.190	< 0.0001
Triglycerides, mmol/L	0.150	0.002
LDL cholesterol, mmol/L	-0.070	0.158
Non HDL cholesterol, mmol/L	0.005	0.925
Smoking history (pack-year)	0.233	< 0.0001
Coronary artery calcium score, Agatston unit	0.287	< 0.0001

Table 3
Epicardial adipose tissue volume according to cardio-vascular risk factors

	Available data	Epicardial adipose tissue (cm^3)	P-value
Gender (Male/Female)			< 0.0001
Male	n = 218	100 ± 40	
Female	n = 191	85 ± 33	
Overweight or obesity			< 0.0001
No	n = 78	74 ± 30	
Yes	n = 325	98 ± 38	
Ethnicity			< 0.0001
Caucasian	n = 88	113 ± 44	
Afro-Caribbean	n = 103	75 ± 28	
Arabic	n = 146	99 ± 36	
Asia	n = 57	84 ± 29	
Other	n = 14	84 ± 35	
Type of diabetes			< 0.0001
Type 1 diabetes	n = 56	72 ± 28	
Type 2 diabetes	n = 318	99 ± 38	
Other types of diabetes	n = 35	70 ± 25	
Family history of premature CAD			0.480
No	n = 116	91 ± 36	
Yes	n = 33	96 ± 43	
Hypertension			0.028
No	n = 184	89 ± 36	
Yes	n = 224	97 ± 38	
Dyslipidaemia			< 0.0001
No	n = 170	84 ± 36	

AU: Agatston unit; CAC: coronary artery calcification score; CAD: coronary artery disease

Data: mean ± standard deviation

	Available data	Epicardial adipose tissue (cm^3)	P-value
Yes	n = 238	100 ± 37	
Current smoking			0.125
No	n = 338	92 ± 37	
Yes	n = 71	99 ± 41	
CAC ≥ 100 AU			< 0.0001
No	n = 320	89 ± 35	
Yes	n = 89	109 ± 41	
AU: Agatston unit; CAC: coronary artery calcification score; CAD: coronary artery disease			
Data: mean ± standard deviation			

Table 4
Epicardial adipose tissue volume according to diabetes-related complications

	Available data	Epicardial adipose tissue (cm^3)	P-value
Retinopathy			0.047
No	n = 232	96 ± 38	
Yes	n = 160	89 ± 37	
Macular edema			0.669
No	n = 338	94 ± 38	
Yes	n = 44	91 ± 36	
Nephropathy			0.027
No	n = 242	90 ± 36	
Yes	n = 148	98 ± 38	
Albuminuria			0.019
No	n = 254	90 ± 35	
Yes	n = 135	99 ± 39	
Renal failure			0.246
No	n = 370	92 ± 37	
Yes	n = 39	100 ± 40	
Neuropathy			0.892
No	n = 238	93 ± 38	
Yes	n = 163	94 ± 37	
Peripheral arterial occlusive disease			0.606
No	n = 372	93 ± 38	
Yes	n = 37	96 ± 34	
History of stroke			0.691
No	n = 396	93 ± 37	
Yes	n = 13	97 ± 41	
History of heart failure			0.397

Data: mean ± standard deviation

	Available data	Epicardial adipose tissue (cm^3)	P-value
No	n = 48	94 ± 30	
Yes	n = 5	107 ± 51	
Coronary artery disease			0.331
No	n = 405	93 ± 38	
Yes	n = 4	75 ± 21	
Macrovascular disease			0.733
No	n = 347	93 ± 38	
Yes	n = 62	95 ± 38	
Data: mean ± standard deviation			

Table 1 also shows that the use of the following treatments was associated with a higher EAT volume: metformin, sulfonylurea, glucagon-like peptide 1 receptor agonists, beta-blockers, statins and aspirin.

Parameters associated with CAC

Individuals with a CAC score ≥ 100 AU (*versus* < 100 AU) were older, more likely to be Caucasian (*versus* Afro-Caribbean, Arabic and Asian), more likely to have T2D (*versus* T1D), and more likely to have retinopathy, macular edema, nephropathy, macrovascular disease, hypertension and dyslipidaemia. Furthermore, they had had diabetes for a longer time and had higher pack-year smoking history (Table 5). In the multivariable analysis, after adjustment for all these parameters and both gender and BMI, EAT was independently associated with a CAC score ≥ 100 AU (Table 6).

Table 5
Patient characteristics according to Coronary artery calcium scores < or ≥ 100 Agaston units

	CAC < 100 AU	CAC ≥ 100 AU	OR [95%CI]	p
	n = 320	n = 89		
Clinical characteristics:				
Age (years)	54.7 ± 12.2	65.7 ± 8.7		< 0.0001
Gender (Male/Female)	164/156	54/35	0.7 [0.4–1.1]	0.120
Body mass index (kg/m²)	29.3 ± 6.0	28.2 ± 5.5		0.119
Ethnicity:				
Caucasian	57(17.9)	31(34.8)	REF	
Afro-Caribbean	88(27.6)	15(16.9)	0.3 [0.2–0.6]	0.001
Arabic	116(36.4)	30(33.7)	0.5 [0.3–0.9]	0.014
Asia	47(14.7)	10(11.2)	0.4 [0.2–0.9]	0.023
Other	11(3.4)	3(3.4)	0.5 [0.1–1.9]	0.316
Diabetes:				
Type				
Type 1	52(16.2)	4(4.5)	REF	
Type 2	239(74.7)	79(88.8)	4.3 [1.5–12.3]	0.006
Other	29(9.1)	6(6.7)	2.7 [0.7–10.3]	0.149
Time since diagnosis (years)	12.9 ± 9.8	17.7 ± 10.8		< 0.0001
HbA1c (%)	9.0 ± 2.3	8.7 ± 2.1		0.280
Diabetes-related complication				
Retinopathy	116(37.8)	44(51.8)	1.8[1.1–2.9]	0.025
Macular edema	28(9.3)	16(19.5)	2.4 [1.2–4.6]	0.018
Nephropathy	100(33.0)	48(55.2)	2.5 [1.5–4.1]	< 0.0001

AU: Agarston unit; CAD: coronary artery disease; OR: odds ratio; 95% CI: 95% confidence interval;

Data: mean ± standard deviation.

	CAC < 100 AU	CAC ≥ 100 AU	OR [95%CI]	p
Neuropathy	120(38.5)	43(48.3)	1.5 [0.9–2.4]	0.112
Macrovascular disease	30(9.4)	32(36.0)	5.4 [3.1–9.6]	< 0.0001
Additional cardiovascular risk factors:				
Family history of premature CAD	27(21.8)	6(24.0)	1.1 [0.4–3.1]	0.795
Hypertension	163(50.9)	61(69.3)	2.2 [1.3–3.6]	0.002
Dyslipidaemia	171(53.4)	67(76.1)	2.8 [1.6–4.8]	< 0.0001
Current smoking	52(16.2)	19(21.3)	1.4 [0.8–2.5]	0.270
Cumulative tobacco consumption (pack-year)	6.4 ± 14.1	14.7 ± 22.8		< 0.0001
AU: Agarston unit; CAD: coronary artery disease; OR: odds ratio; 95% CI: 95% confidence interval;				
Data: mean ± standard deviation.				

Table 6
Parameters explaining a coronary artery calcium score ≥ 100 Agaston units in multivariable analysis

	Odds ratio	95% confidence interval	P-value
Epicardial adipose tissue (per 10 cm^3)	1.13	1.04–1.23	0.004
Age (per year)	1.08	1.05–1.12	< 0.001
Body mass index (per kg/m^2)	0.94	0.89-1.00	0.051
Male *vs* Female			NS
Type 2 *vs* Type 1 diabetes			NS
Other diabetes types *vs* Type 1 diabetes			NS
Afro-Caribbean *vs* Caucasian			NS
Arabic *vs* Caucasian			NS
Asia *vs* Caucasian			NS
Other *vs* Caucasian			NS
Hypertension			NS
Dyslipidaemia			NS
Diabetes duration			NS
Cumulative Tobacco consumption (per pack-year)	1.03	1.01–1.04	0.002
Retinopathy	1.89	0.99–3.58	0.05
Macular edema			NS
Nephropathy			NS
Macrovascular disease	3.94	1.92–8.07	< 0.001

Discussion

Our cohort study results show that EAT volume was independently associated with CAC in people with diabetes. This reflects results from another study with a mix of individuals with and without diabetes [16]. Similarly, Yerramasu et al. found that EAT volume was an independent marker of both the presence and severity of CAC burden in 333 asymptomatic patients with T2D [11]. However, the latter finding goes against results from three others studies where no such association was found [12–14]. There are several possible reasons for this. First, these three studies had less statistical power than Yerramasu's and ours, as they only included between 95 and 200 patients [12–14]. Second, one of the three (Christensen et al.)

measured EAT thickness not volume [14]. Third, inclusion criteria differed between the three studies: only patients with T2D and elevated urinary albumin excretion rate were recruited in Christensen et al.'s study [14], while only young Native Americans with T2D were included in Reinhardt et al.'s study [13]. Our results in diabetic persons are clinically relevant as we were able to show that the association remained significant even after adjustment for numerous confounding factors.

First, EAT volume was positively correlated with male gender and older age. Elsewhere, EAT volume has been associated with all the components of metabolic syndrome in people with T2D [16, 17] and those with T1D [18, 19]. Similarly, we found an association between EAT volume and higher BMI, increased triglycerides levels, lower HDL-cholesterol levels and antihypertensive treatment. This result is in line with previous studies which showed a higher EAT volume in individuals with T2D than those with T1D [12, 19]. Additionally, cumulative tobacco consumption, which is associated with insulin resistance and metabolic syndrome [20], was positively correlated with EAT volume in our study. Finally, we also found that EAT volume was higher in individuals of Caucasian ethnicity. Similarly, the difference in EAT thickness between persons with and without metabolic syndrome was more evident in Caucasians [17, 21]. Other studies have also found that EAT levels differ according to racial/ethnic group in the general population [22–25].

The association between EAT and CAC in our study suggests that EAT might play a role in subclinical atherosclerosis in diabetes. There are arguments to support this hypothesis. First, in the present study, we also found an association between EAT and other target organ damage, specifically the eyes and kidneys. Indeed, retinopathy and nephropathy are also known markers of poor cardiovascular prognosis in people with diabetes [8, 10]. Second, increased EAT volume/thickness has been associated with markers of subclinical atherosclerosis other than CAC score, such as coronary artery disease and cardiac dysfunction [5]. Third, whereas EAT is physiologically cardioprotective - as it provides mechanical protection and energy to the myocardium and has anti-inflammatory properties - abnormally increases in EAT volume is proinflammatory [3–6]. Similarly, EAT volume has been associated with plaque vulnerability, which may contribute to acute coronary syndrome [26]. Fourth, prospective studies have shown that high EAT volume/thickness is associated with more cardiovascular events in the general population [27], in patients with T2D without participant-selection study criteria [28] and T2D patients with microalbuminuria [14].

Our study has several limitations. Its design was observational, which prevented us from being able to draw conclusions about causal relationships between EAT volume and CAC. Neither were we able to make a conclusion about the role of therapy on EAT volume. Furthermore, in order to evaluate the prognostic value of EAT volume, we used a marker of subclinical atherosclerosis (i.e., CAC) instead of measuring the incidence of cardiovascular events. Moreover, we only included patients who had been admitted to our hospital department and who had their CAC score measured. Therefore, our results may not be representative of all patients with diabetes. Finally, we did not have data on waist circumference, which could have influenced the association between EAT volume and CAC. However, we did adjust for several confounders, including BMI.

The main strength of our study is that we measured EAT and not pericardial (or total cardiac) adipose tissue. EAT lies between the myocardium and the visceral layer of the pericardium and is different from pericardial fat which is located externally to the myocardium. There is no fascia separating EAT and myocardium. Therefore both tissues are in direct contact [3–6, 29]. To date, EAT is the only type of cardiac adipose tissue which has been observed to predict incident cardiovascular events in T2D patients [28]. Furthermore, we applied a robust methodology - CT acquisition and assessment following standard methods - as well as cardiac software to automatically quantify EAT. Only 1 EAT measure out of the 410 performed (study population) could not be interpreted. CT scans are considered the gold standard for EAT as, unlike echography, they measure EAT volume not thickness [4, 14].

Conclusions

We showed that in individuals with diabetes, EAT volume was higher in males, persons of Caucasian ethnicity and those who met the criteria for the components of metabolic syndrome. More importantly, we demonstrated that EAT was independently associated with subclinical coronary atherosclerosis in our study population. This suggests that measuring EAT volume might improve assessment of cardiovascular prognosis [14, 27, 28]. There are also therapeutic implications of our work. EAT volume can be modified by lifestyle such as diet and/or exercise, bariatric surgery and pharmaceutical interventions [29, 30]. For example, thiazolidinediones, dipeptidyl peptidase-4 inhibitors, glucagon-like peptide-1 receptor agonists and sodium-glucose cotransporter 2 inhibitors have all been reported to reduce EAT volume [31].

Abbreviations

BMI: body mass index

CAC: coronary artery calcium

CT: computed tomography

EAT: epicardial adipose tissue

PACS: Picture Archiving and Communication Systems

T1D: type 1 diabetes

T2D: type 2 diabetes

UACR: urinary albumin / creatinine ratio

Declarations

Authors’ contributions

EC and HB conceived and designed this study and had full access to all the study data. EC is responsible for the integrity of the data and the accuracy of the data analyses. IR and PYB collected the data. EC drafted the paper, with help from MTN, IR, ST, PYB and HB. MTN performed the analyses. All authors critically revised the manuscript for important intellectual content and gave final approval for publication.

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Availability of data and materials

Data for the present analysis can be provided from the first author on reasonable request.

Ethics approval and consent to participate

In Avicenne hospital and in general in the various Public Assistance Hospitals in Paris, all patients are informed at admission that their medical records may be used for research, unless they indicate their opposition. For the present study, no patient indicated opposition. Approval for the use of patient data was provided by the local ethics committee (approval number: CLEA-2020-148). Data were analyzed anonymously. No patient opposed.

Consent for publication

Not applicable

Competing interests

The authors declare that they have no competing interests.

References

1. Gregg EW, Li Y, Wang J, Burrows NR, Ali MK, Rolka D, et al. Changes in diabetes-related complications in the United States, 1990-2010. N Engl J Med. 2014;370:1514–23.
2. Vergès B. Cardiovascular disease in type 1 diabetes: A review of epidemiological data and underlying mechanisms. Diabetes Metab. 2020;46:442–9.
3. Li Y, Liu B, Li Y, Jing X, Deng S, Yan Y, et al. Epicardial fat tissue in patients with diabetes mellitus: a systematic review and meta-analysis. Cardiovasc Diabetol. 2019;18:3.

4. Villasante Fricke AC, Iacobellis G. Epicardial Adipose Tissue: Clinical Biomarker of Cardio-Metabolic Risk. Int J Mol Sci. 2019;20.
5. Christensen RH, von Scholten BJ, Lehrskov LL, Rossing P, Jørgensen PG. Epicardial adipose tissue: an emerging biomarker of cardiovascular complications in type 2 diabetes? Ther Adv Endocrinol Metab. 2020;11:2042018820928824.
6. Iacobellis G, Barbaro G. Epicardial adipose tissue feeding and overfeeding the heart. Nutrition. 2019;59:1–6.
7. Greenland P, Blaha MJ, Budoff MJ, Erbel R, Watson KE. Coronary Calcium Score and Cardiovascular Risk. J Am Coll Cardiol. 2018;72:434–47.
8. Cosentino F, Grant PJ, Aboyans V, Bailey CJ, Ceriello A, Delgado V, et al. 2019 ESC Guidelines on diabetes, pre-diabetes, and cardiovascular diseases developed in collaboration with the EASD. Eur Heart J. 2020;41:255–323.
9. Fox CS, Golden SH, Anderson C, Bray GA, Burke LE, de Boer IH, et al. Update on Prevention of Cardiovascular Disease in Adults With Type 2 Diabetes Mellitus in Light of Recent Evidence: A Scientific Statement From the American Heart Association and the American Diabetes Association. Diabetes Care. 2015;38:1777–803.
10. Valensi P, Belle EV, Cosson E, Emmerich J, Prevost G, Ferrières J, et al. Risk stratification and screening for coronary artery disease in asymptomatic patients with diabetes mellitus. Diabetes Metab. 2020;
11. Yerramasu A, Dey D, Venuraju S, Anand DV, Atwal S, Corder R, et al. Increased volume of epicardial fat is an independent risk factor for accelerated progression of sub-clinical coronary atherosclerosis. Atherosclerosis. 2012;220:223–30.
12. Zobel EH, Christensen RH, Winther SA, Hasbak P, Hansen CS, von Scholten BJ, et al. Relation of cardiac adipose tissue to coronary calcification and myocardial microvascular function in type 1 and type 2 diabetes. Cardiovasc Diabetol. 2020;19:16.
13. Reinhardt M, Cushman TR, Thearle MS, Krakoff J. Epicardial adipose tissue is a predictor of decreased kidney function and coronary artery calcification in youth- and early adult onset type 2 diabetes mellitus. J Endocrinol Invest. 2019;42:979–86.
14. Christensen RH, von Scholten BJ, Hansen CS, Heywood SE, Rosenmeier JB, Andersen UB, et al. Epicardial, pericardial and total cardiac fat and cardiovascular disease in type 2 diabetic patients with elevated urinary albumin excretion rate. Eur J Prev Cardiol. 2017;24:1517–24.
15. Hecht HS, Cronin P, Blaha MJ, Budoff MJ, Kazerooni EA, Narula J, et al. 2016 SCCT/STR guidelines for coronary artery calcium scoring of noncontrast noncardiac chest CT scans: A report of the Society of Cardiovascular Computed Tomography and Society of Thoracic Radiology. J Thorac Imaging. 2017;32:W54–66.
16. Wang C-P, Hsu H-L, Hung W-C, Yu T-H, Chen Y-H, Chiu C-A, et al. Increased epicardial adipose tissue (EAT) volume in type 2 diabetes mellitus and association with metabolic syndrome and severity of coronary atherosclerosis. Clin Endocrinol (Oxf). 2009;70:876–82.

17. Pierdomenico SD, Pierdomenico AM, Cuccurullo F, Iacobellis G. Meta-analysis of the relation of echocardiographic epicardial adipose tissue thickness and the metabolic syndrome. Am J Cardiol. 2013;111:73–8.
18. Colom C, Viladés D, Pérez-Cuellar M, Leta R, Rivas-Urbina A, Carreras G, et al. Associations between epicardial adipose tissue, subclinical atherosclerosis and high-density lipoprotein composition in type 1 diabetes. Cardiovasc Diabetol. 2018;17:156.
19. Svanteson M, Holte KB, Haig Y, Kløw NE, Berg TJ. Coronary plaque characteristics and epicardial fat tissue in long term survivors of type 1 diabetes identified by coronary computed tomography angiography. Cardiovasc Diabetol. 2019;18:58.
20. Cena H, Fonte ML, Turconi G. Relationship between smoking and metabolic syndrome. Nutr Rev. 2011;69:745–53.
21. Salami SS, Tucciarone M, Bess R, Kolluru A, Szpunar S, Rosman H, et al. Race and epicardial fat: the impact of anthropometric measurements, percent body fat and sex. Ethn Dis. 2013;23:281–5.
22. Willens HJ, Gómez-Marín O, Chirinos JA, Goldberg R, Lowery MH, Iacobellis G. Comparison of epicardial and pericardial fat thickness assessed by echocardiography in African American and non-Hispanic White men: a pilot study. Ethn Dis. 2008;18:311–6.
23. Apfaltrer P, Schindler A, Schoepf UJ, Nance JW, Tricarico F, Ebersberger U, et al. Comparison of epicardial fat volume by computed tomography in black versus white patients with acute chest pain. Am J Cardiol. 2014;113:422–8.
24. El Khoudary SR, Shin C, Masaki K, Miura K, Budoff M, Edmundowicz D, et al. Ectopic cardiovascular fat in middle-aged men: effects of race/ethnicity, overall and central adiposity. The ERA JUMP study. Int J Obes (Lond). 2015;39:488–94.
25. Adams DB, Narayan O, Munnur RK, Cameron JD, Wong DTL, Talman AH, et al. Ethnic differences in coronary plaque and epicardial fat volume quantified using computed tomography. Int J Cardiovasc Imaging. 2017;33:241–9.
26. Nerlekar N, Brown AJ, Muthalaly RG, Talman A, Hettige T, Cameron JD, et al. Association of Epicardial Adipose Tissue and High-Risk Plaque Characteristics: A Systematic Review and Meta-Analysis. J Am Heart Assoc. 2017;6.
27. Mahabadi AA, Berg MH, Lehmann N, Kälsch H, Bauer M, Kara K, et al. Association of epicardial fat with cardiovascular risk factors and incident myocardial infarction in the general population: the Heinz Nixdorf Recall Study. J Am Coll Cardiol. 2013;61:1388–95.
28. Christensen RH, von Scholten BJ, Hansen CS, Jensen MT, Vilsbøll T, Rossing P, et al. Epicardial adipose tissue predicts incident cardiovascular disease and mortality in patients with type 2 diabetes. Cardiovasc Diabetol. 2019;18:114.
29. Rafeh R, Viveiros A, Oudit GY, El-Yazbi AF. Targeting perivascular and epicardial adipose tissue inflammation: therapeutic opportunities for cardiovascular disease. Clin Sci (Lond). 2020;134:827–51.

30. Launbo N, Zobel EH, von Scholten BJ, Faerch K, Jørgensen PG, Christensen RH. Targeting epicardial adipose tissue with exercise, diet, bariatric surgery or pharmaceutical interventions: A systematic review and meta-analysis. Obes Rev. 2020;
31. Xourgia E, Papazafiropoulou A, Melidonis A. Effects of antidiabetic drugs on epicardial fat. World J Diabetes. 2018;9:141–8.