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Original Research

Epicardial and intra-thoracic adipose tissue and cardiovascular calcifications in type 1 diabetes (T1D) in epidemiology of diabetes Interventions and Complications (EDIC): A pilot study

Panteha Rezaeian [a], Jye-Yu C. Backlund [b], Mohammed Zaveri [c], Rine Nakanishi [d], Suguru Matsumoto [e], Anas Alani [f], Aryabod Razipour [g], John M. Lachin [b], Matthew Budoff [h,*], the DCCT/EDIC Research Group

[a] Torrance Memorial Physician Network-Cedars-Sinai Health System affiliate, Torrance, CA, USA
[b] The Biostatistics Center, George Washington University, Rockville, MD, USA
[c] Department of Medicine Emanate Health Medical Group, West Covina, CA, USA
[d] Department of Cardiovascular Medicine, Toho University Graduate School of Medicine, Tokyo, Japan
[e] Department of Cardiology, Kouiki Monbetsu Hospital, Hokkaido, Japan
[f] Department of Cardiology, University of Loma Linda, Loma Linda, CA, USA
[g] Biomedical Imaging Research Institute, Cedars-Sinai Medical Center, Los Angeles, CA, USA
[h] Lindquist Research Institute, Harbor-UCLA Medical Center, 1124W Carson St, Torrance, CA 90502, USA

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ABSTRACT

Objective: Coronary artery, aortic valve, and descending aorta calcification (CAC, AVC, DAC) are manifestations of atherosclerosis, and cardiac epicardial adipose tissue (EAT) indicates heart adiposity. This study explored the association between cardiac adipose tissue and cardiovascular calcification in participants with long-standing T1D.

Methods: EAT and intra-thoracic adipose tissue (IAT) were measured in 100 T1D subjects with cardiac computed tomography (CT) scans in the EDIC study. Volume analysis software was used to measure fat volumes. Spearman correlations were calculated between CAC, AVC, DAC with EAT, and IAT. Associations were evaluated using multiple linear and logistic regression models.

Results: Participants ranged in age from 32 to 57. Mean EAT, and IAT were 38.5 and 50.8 mm^3, respectively, and the prevalence of CAC, AVC, and DAC was 43.6 %, 4.7 %, and 26.8 %, respectively. CAC was positively correlated with age (p-value = 0.0001) and EAT (p-value = 0.0149) but not with AVC and DAC; IAT was not associated with calcified lesions. In models adjusted for age and sex, higher levels of EAT and IAT were associated with higher CAC (p-value < 0.0001 for both) and higher AVC (p-values of 0.0111 and 0.0053, respectively), but not with DAC. The associations with CAC remained significant (p-value < 0.0001) after further adjustment for smoking, systolic blood pressure, BMI, and LDL, while the associations with AVC did not remain significant.

Conclusion: In participants with T1D, higher EAT and IAT levels are correlated with higher CAC scores. EAT and IAT were not independently correlated with DAC or AVC.

1. Introduction

Cardiovascular disease (CVD) is the leading cause of death in individuals with type 1 diabetes (T1D) [1–4]. Cross-sectional studies indicate that more significant pericardial fat is associated with increased coronary artery calcium (CAC) [5]. A prior DCCT/EDIC study demonstrated that the CAC score is directly associated with subsequent cardiovascular disease in T1D [6]. The data from the Multi-Ethnic Study of Atherosclerosis (MESA) and other cohorts have demonstrated extra-coronary calcification (specifically aortic and mitral valve

* Corresponding author.
E-mail address: mbudoff@lundquist.org (M. Budoff).

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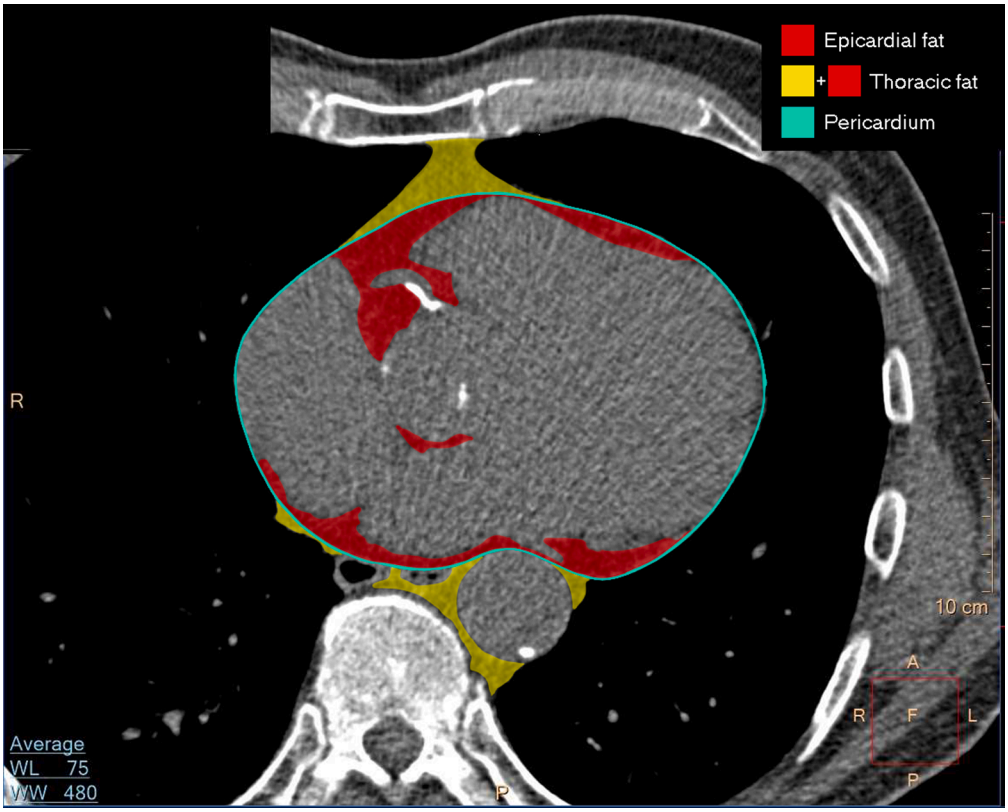


Fig. 1. Epicardial adipose tissue (red color), Intra thoracic adipose tissue (red color + Yellow color), Pericardial adipose tissue (yellow color), and Pericardium (green line).

calcification and thoracic aortic calcification) as independent indicators of atherosclerotic burden [7–10]. However, the relationship between cardiac calcification and fat volumes surrounding the heart in individuals with type 1 diabetes has not been established.

This study evaluated these relationships in a subset of participants with a long duration of T1D in the Diabetes Control and Complications Trial (DCCT) and the follow-up Epidemiology of Diabetes Interventions and Complications (EDIC) study. Cardiac computed tomography (CT) scans obtained in the EDIC study were used to measure cardiac calcification and fat volumes.

1.1. Study design and method

The methods of the DCCT and EDIC study have been described in detail [11]. Briefly, a total of 1441 participants with type 1 diabetes were randomly assigned to receive either intensive therapy ($n = 711$) aimed to lower blood glucose levels as close to the non-diabetic range as safely as possible or conventional therapy ($n = 730$) aimed at avoiding symptoms related to hyper- or hypoglycemia without specific glucose targets. The DCCT ended in 1993, after an average of 6.5 years of follow-up, and all participants were taught intensive therapy and referred to their healthcare providers for subsequent diabetes care. In 1994, 98 % of the surviving DCCT cohort enrolled in the EDIC follow-up observational study, and after an additional 20 years of follow-up, 94 % of the cohort survivors were still actively participating. The institutional review boards approved all participating centers' DCCT and EDIC protocols, and all participants provided written informed consent.

One thousand two hundred five participants underwent CT scanning at EDIC years 7–9 (~2000–2002). In a pilot study including a sample of 100 EDIC participants, whose selection was previously described [12], who underwent the non-enhanced cardiac computed tomography (CT) evaluation, was selected to assess the relationship between the pericardial adipose tissue volumes (including epicardial adipose tissue [EAT] and intra-thoracic adipose tissue [IAT]) with vascular calcifications (coronary artery calcification and thoracic aorta calcification) and valve calcification (aortic valve and mitral annular calcification) levels. This sub-cohort group was obtained from a case-control sample of participants enrolled in the EDIC cardiac magnetic resonance imaging study during EDIC years. We obtained access to their non-enhanced cardiac CT images were obtained from these participants, who were subsequently enrolled in the EDIC cardiac magnetic resonance imaging study [12].

The presented analyses are based on data obtained at annual visits during both the DCCT and EDIC studies, which included a detailed medical history, social history (current smoker), physical examination (e.g., blood pressure and pulse rate), and collection of biospecimens (e.g., fasting lipids, renal measures, HbA1c). Recognized and putative CVD risk factors were evaluated by standardized methods [13,14]. Hemoglobin A1c (HbA1c) was measured using high-performance liquid chromatography quarterly during the DCCT and annually during EDIC. EDIC participants who met the criteria for metabolic syndrome (central obesity, hypertension, hyperglycemia, and dyslipidemia) were investigated for the associated metabolic syndrome and the other variable, including biochemical, imaging, and clinical outcomes in T1D population. Fasting lipids, including triglycerides, total cholesterol, low-density lipoprotein cholesterol (LDL-c), and high-density lipoprotein cholesterol (HDL-c), were measured in the central laboratory annually during DCCT and every other year during EDIC, and LDL-c was calculated using the Friedewald equation [13]. The updated weighted mean of a covariate (e.g., HbA1c) measured at different intervals in DCCT vs. EDIC was computed using all values up to a particular visit, with weights proportional to the time intervals between measurements.

CT scanning procedures have been described in detail in other

Table 1
Clinical characteristics for weighted sample and the full cohort during CT scan in EDIC Year 7–9.

Variable	Weighted Sample*		Full Cohort	
	Mean	S.D.	Mean	SD.
N	100		1205	
Female (%)	47.5		47.5	
Attained Age (years)	43	6	43	7
Intensive Treatment (%)	55.2		49.5	
Study Cohort (% primary)	39.2		50.0	
Current smoker (%)	9.9		14.9	
Insulin Dose (Units/kg/day) ‡	0.67	0.27	0.68	0.23
Attained Duration of T1D (years)†	22.2	4.9	21.0	4.9
Mean HbA1c during DCCT/EDIC (%)	8.1	0.9	8.1	1.1
Body Mass Index (kg/m^2) ‡	27.2	4.2	27.5	4.4
Waist/Hip Ratio‡	0.85	0.07	0.85	0.09
Waist Circumference (cm)	88.3	1.4	89.0	12.1
SBP (mmHg)	122.2	1.4	122.2	14.4
DBP (mmHg)	76.3	1.2	76.4	9.2
Total cholesterol (mg/dL)	180.1	3.8	185.2	34.6
HDL Cholesterol (mg/dl) ‡	54	12	56	15
LDL Cholesterol (mg/dl) ‡	110	27	111	29
Triglyceride (mg/dl) ‡	80	40	90	62
Metabolic Syndrome (%)	19.3		28.3	
AER≥300 or ESRD (%) ‡	9.2		8.5	
eGFR‡	106	14	103	16
Epicardial Adipose Tissue (EAT) (mm^3)	38.5	1.9	N/A	N/A
Intrathoracic Adipose Tissue (IAT) (mm^3)	50.8	2.8	N/A	N/A
CAC > 0 (%)	43.6		31.0	
AVC > 0 (%)	4.7		N/A	N/A
DAC > 0 (%)	26.8		N/A	N/A

N/A Not Applicable.
* Adjusting for the inverse probability sample weight.
† At the time of the CT scan or prior visit.
‡ Measured at the last available visit before or at cardiac CT.
AER: albumin excretion rate; AVC: aortic valve calcification; CAC: coronary artery calcium; CT: cardiac computed tomography; DAC: descending aorta calcification; DBP: diastolic blood pressure; DCCT: Diabetes Control and Complications Trial; EDIC: Epidemiology of Diabetes Interventions and Complications study; eGFR: estimated glomerular filtration rate; ESRD: end stage renal disease; HDL: high-density lipoprotein; LDL: low-density lipoprotein; SBP: systolic blood pressure; SD: Standard deviation; T1D: Type 1 Diabtes Melitus.

studies [15]. In this study, all participants underwent 64 multi-slice calcium scanning. Two experienced and trained readers blinded to all demographics and the original DCCT treatment group assignment evaluated the cardiac CT scans. All tissue measurements were performed on axial slices of non-contrast studies of the heart using GE Advantage Windows 4.6 Workstations. The GE 64 protocol included a gantry rotation time of 350 ms, kVp 120, 320 mA; Standard Filter, with a slice thickness of 2.5 mm. [16] Subsequently, 50 participants were randomly chosen for reproducibility evaluation. Another reader remeasured CT scans to interreader reproducibility and agreement.

1.2. Measurements of adipose tissue

Epicardial and intra-thoracic fat quantification was measured using the Advantage workstation (version 4.6, General Electric, Milwaukee, WI). All adipose tissue measurements were performed on the axial slices of non-contrast studies of the heart. Intra-thoracic fat comprises all the fat within the chest that surrounds the heart, encompassing both epicardial adipose tissue and paracardial adipose tissue. Epicardial adipose tissue (EAT) was measured on axial images starting from 10 mm above the superior extent of the left main coronary artery ostium to the last slice containing the pericardial sac and obtained by manually tracing out the pericardium every 2-3 slices below the start point, with software automatically tracing out the segments between the selected slices. Measurement of intra-thoracic adipose tissue (IAT) was performed using the same superior boundary described above. The diaphragm defined the inferior boundary for IAT. The anterior border of the

Table 2
Distribution of calcification and fat variables.

	N	CAC > 0 (%)	AVC > 0 (%)	DAC > 0 (%)	EAT (mean ±SD†)	**IAT (mean ±SD)**
Sex						
Females	22	46.5	5.2	22.5	34 ± 3	41 ± 4
Males	78	40.9	4.3	30.7	43 ± 2 $p^{\ddagger}$=0.0159	60 ± 3 p = 0.0003
DCCT Treatment Group						
Intensive	49	42.8	3.2	26.5	38 ± 3	49 ± 4
Conventional	51	44.6	6.6	27.1	39 ± 2	52 ± 4
Study Cohort						
Primary	47	42.6	0	27.1	43 ± 3	59 ± 5
Secondary	53	44.2	7.8	26.6	35 ± 2 p = 0.0426	45 ± 3 p = 0.0160
Current Smoker						
No	90	39.9	5.2	23.8	38 ± 2	50 ± 3
Yes	10	77.0 p = 0.0166	0	53.8	45 ± 3 p = 0.0358	59 ± 6
BMI ≥ 25 (kg/m^2)						
No	28	41.9	9.9	28.9	32 ± 3	39 ± 4
Yes	71	44.9	1.9	25.9	42 ± 2 p = 0.0132	57 ± 4 p = 0.0013
T1D Duration ≥ 20 (years)						
No	45	37.0	1.4	28.4	44 ± 3	61 ± 5
Yes	55	47.3	6.5	25.9	35 ± 2 p = 0.0376	45 ± 3 p = 0.0102
Metabolic Syndrome						
No	81	38.6	5.2	30.6	35 ± 2	46 ± 3
Yes	19	64.4	2.7	10.7 p = 0.0190	53 ± 6 p = 0.0018	71 ± 8 p = 0.0040

* Adjusting for the inverse probability sample weight. † SD: Standard Deviation. ‡only p-values less than 0.05 are reported.
AER: albumin excretion rate; AVC: aortic valve calcification; BMI: Body mass index; CAC: coronary artery calcium; CT: cardiac computed tomography; DAC: descending aorta calcification; DCCT: Diabetes Control and Complications Trial; EAT: epicardial adipose tissue; IAT: intra-thoracic adipose tissue; SD: Standard deviation; T1D: Type 1 Diabtes Melitus.

volume was determined by the chest wall, and the posterior border by the aorta, bronchi, and esophagus. Intra-thoracic adipose tissue was manually measured by tracing the respective boundaries every 2-3 slices and interpolated by software. The observer was given interactive access to the coronal and sagittal images to help facilitate accurate measurements, and the software isolated the region of interest (ROI).

Since absolute Hounsfield units of the pixels corresponding to the properties of that tissue were selected, volume analysis software (a histogram-based statistical program) was used to discern fat from other tissues using a threshold of voxels between -190 and -30 Hounsfield Units. Pericardial Adipose Tissue (PAT) included intra-thoracic fat surrounding the pericardium (Fig. 1), and PAT was calculated by subtracting EAT volume from IAT volume. Adipose tissue measurements were performed blinded to participant characteristics, DCCT treatment assignment, and CAC score.

1.3. Measurements of coronary and extra-coronary calcifications

Coronary artery calcium (CAC), aortic valve calcification (AVC), and descending aorta calcification (DAC) score were computed using the Agatston method from non-contrast cardiac CT scans. Conferring to this method, three contiguous pixels with a density of over 130 Hounsfield

Table 3
Spearman correlation* between selected covariates and coronary artery calcification, aortic valve calcium, and descending aortic calcification (Adjusting for sex).

Covariate at the time of or before the CT scan	Coronary Artery Calcification*		Aortic Valve Calcium*		Descending Aortic Calcification*	
	Correlation coefficient	p-value	Correlation coefficient	p-value	Correlation coefficient	p-value
Epicardial Fat Volume (mm^3)	**0.24**	**0.0149**	-0.06	0.5668	0.06	0.5736
Intrathoracic Fat Volume (mm^3)	0.16	0.1168	-0.07	0.5178	0.05	0.6093
Age (years)	**0.37**	**0.0001**	0.10	0.3246	0.006	0.9560
T1D Duration (years)	0.14	0.1645	0.17	0.1000	0.009	0.9277
BMI (kg/m^2)	0.03	0.7434	**-0.22**	**0.0303**	0.06	0.5398
Waist Circumference (cm)	0.16	0.1140	-0.13	0.1923	0.0004	0.9971
SBP (mmHg)	-0.006	0.9524	0.04	0.6967	-0.12	0.2289
DBP (mmHg)	-0.07	0.4858	0.05	0.6348	0.009	0.9297
Total cholesterol (mg/dL)	0.04	0.6958	0.01	0.8967	0.11	0.2690
HDL (mg/dL)	-0.07	0.5066	0.02	0.8306	-0.01	0.9152
LDL (mg/dL)	0.07	0.4896	-0.02	0.8327	0.14	0.1741
Triglycerides (mg/dL)	0.04	0.7279	0.05	0.6461	0.05	0.6031
$HbA1_C$ Mean during DCCT/EDIC (%)	0.10	0.3365	**-0.20**	**0.0455**	0.07	0.5043
eGFR (ml/min per 1.73 m^2)	-0.16	0.1177	-0.15	0.1426	-0.05	0.6213

* log (calcification score)-log(0.92)
earson partial correlation was adjusted for sex and corrected with sample weight.
BMI: Body mass index; CT: cardiac computed tomography; DBP: diastolic blood pressure; DCCT: Diabetes Control and Complications Trial; EDIC: Epidemiology of Diabetes Interventions and Complications study; eGFR: estimated glomerular filtration rate; HbA1c: Hemoglobin A1c; HDL: high-density lipoprotein; LDL: low-density lipoprotein; SBP: systolic blood pressure; SD: Standard deviation; T1D: Type 1 Diabtes Melitus.

Table 4
Association of epicardial adipose tissue and intra-thoracic adipose tissue with coronary artery calcification, descending aortic calcification, and aortic valve calcification.

		Geometric mean ratio of CAC		Geometric mean ratio of DAC		Geometric mean ratio of AVC	
Model*	Variables	Scores (95 % C.I.)	p-value	Scores (95 % C.I.)	p-value	Scores (95 % C.I.)	p-value
1	EAT	1.08 (1.06, 1.10)	<0.0001	1.01 (0.99, 1.04)	0.3756	0.88 (0.80, 0.97)	0.0111
1	IAT	1.04 (1.03, 1.05)	<0.0001	1.00 (0.98, 1.02)	0.8923	0.91 (0.85, 0.97)	0.0053
2	EAT	1.08 (1.06, 1.11)	<0.0001	1.00 (0.97, 1.02)	0.7274	0.98 (0.90, 1.07)	0.6335
2	IAT	1.04 (1.03, 1.06)	<0.0001	0.99 (0.97, 1.01)	0.1802	0.98 (0.93, 1.04)	0.5558

* Tobit regression models using log (calcification score)-log (0.92) adjusted for sex and age (Model 1), and for sex, age, smoking, BMI, SBP and LDL (Model 2).
AVC: aortic valve calcification; BMI: Body mass index; CAC: coronary artery calcification; CI: confidence interval; DAC: descending aorta calcification; EAT: epicardial adipose tissue; IAT: intra-thoracic adipose tissue; LDL: low-density lipoprotein; SBP: systolic blood pressure.

(HUs) qualified as an atherosclerotic plaque. The CAC, AVC, and CAD score for an individual lesion is defined as the product of that lesion's area, and the maximal HU observed in that lesion. Each region's total calcium score was quantified separately for three major areas (coronary artery, aortic valve, and descending aorta wall). The lesion score was calculated using the area density method by multiplying the lesion area by a density factor derived from the maximal HU within the area.

AVC is calculated as any calcified lesion within the aortic valve leaflets. Any calcified focus that extended to the aortic root was considered aortic valve calcium. Lesions were qualified as aortic-valve calcification if they were deposited within the aortic-valve leaflets, commissures, or aortic annulus, excluding proximal aorta and coronary arteries. AVC score, by the Agatston method, was measured in every participant. The absence of AVC was assigned a score of 0. DAC was defined as any calcium deposition on the descending aortic wall from the lower edge of the pulmonary artery bifurcation superiorly to the cardiac apex inferiorly.

1.4. Statistical analysis

The analyses were weighted using the inverse probability of selection probability for the 100 participants in this study out of the 1205 DCCT/EDIC participants with CT scans to obtain unbiased results. The sample probabilities were calculated for each participant in the pilot study based on gender and tertiles of age, six strata total (three age strata for women and three age strata for men). After the inverse probability sample weight adjustment, the sample cohort of 100 participants in this study had similar characteristics to the entire cohort (53 % males, mean age 43 years, and mean HbA1c 8.1 %) (Table 1).

Clinical characteristics were based on the annual visit data at the time the cardiac CT was obtained or from the last visit before the cardiac CT. Spearmen correlations were calculated between selected covariates and EAT and IAT volumes, adjusted for sex. Moreover, the distribution of EAT and IAT volumes by covariates was also evaluated. Finally, univariate and multivariate analyses, unadjusted and adjusted for age and sex, were performed. Tobit-censored regression models for a mixed outcome (such as coronary autonomic neuropathy) assessed the adipose tissue's effect on the calcification score adjusted for age and sex (basic models). Additional models further adjusted for smoking, body mass index (BMI), systolic blood pressure (SBP), and low-density lipoprotein cholesterol (LDL).

2. Results

Among the 100 participants, the weighted mean age was 43 years (range 32–57), and 53 % were male (Table 1). The mean and standard deviation (SD) volume of EAT and IAT in men were 43 ± 2 mm^3 and 60 ± 3 mm^3, respectively. Women's EAT and IAT were 34 ± 3 mm^3 and 41 ± 4 mm^3, respectively, with a significant difference between men and women (p-value = 0.0159 for EAT, and p-value = 0.0003 for IAT) (Table 2).

Current smokers had higher EAT (p-value = 0.0358). The group with BMI > 25 kg/m^2 had higher EAT and IAT but not CAC, DAC, or AVC, while the normal weight group (BMI less than 25) had a higher AVC. The

normal weight BMI participants had significantly less EAT and IAT (p-value = 0.0132 and p-value = 0.0013, respectively). Participants with metabolic syndrome had significantly higher EAT and IAT volumes (p-value = 0.0018 and p-value = 0.0040, respectively) (Table 2).

EAT and age correlated with CAC (p-value = 0.0149 and p-value = 0.0001, respectively). BMI was inversely correlated with AVC (p-value = 0.0303). DCCT/EDIC weighted glycosylated hemoglobin (HbA1C) before CT was inversely associated with AVC (p-value = 0.0455). However, no association was found between coronary and extra-coronary calcification and lipid panel results or blood pressure values (Table 3).

Tobit regression models (Table 4) adjusted for sex and age showed significant positive associations between EAT and CAC (geometric mean ratio of CAC 1.08; 95 % confidence interval 1.06, 1.10; p-value < 0.0001), between IAT and CAC (geometric mean ratio of CAC 1.04; 95 % confidence interval 1.03, 1.05; p-value < 0.0001), between EAT and AVC (geometric mean ratio of CAC 0.88; 95 % confidence interval 0.80, 0.97; p-value = 0.0111), and between IAT and AVC (geometric mean ratio of CAC 0.91; 95 % confidence interval 0.85, 0.97; p-value = 0.0053). However, there is no association between EAT and DAC or IAT and DAC (p-value = 0.3756 and p-value = 0.8923, respectively). Further adjusted for smoking, BMI, SBP, and LDL, the associations of CAC with EAT and IAT remained highly significant (<0.0001); however, the associations of AVC with EAT and IAT were no longer significant.

3. Discussion

This exploratory study found that men with T1D had significantly higher amounts of epicardial and intrathoracic adipose tissue than women with T1D, which aligned with our previous findings [12]. Our previous study also reported that EAT and IAT were highly associated with higher BMI, larger waist-to-hip ratio, higher triglyceride levels, and higher mean-weighted HbA1C [12]. Prior studies discovered the EAT and IAT associations with angiographic CAD severity and future ASCVD events in the general population [17–19,3,20,21]. The current data showing increased EAT levels are associated with increased CAC prevalence in this T1D cohort is particularly noteworthy [3,22–24]. While our previous study reported the association of EAT and IAT with cardio-metabolic risk factors (BMI, weight-hip ratio, HbA1c, and triglyceride level), in the current study, we demonstrated the association of concrete cardiovascular diseases characterized as coronary artery calcification, aortic valve and descending aorta calcification documented by cardiac CT imaging.

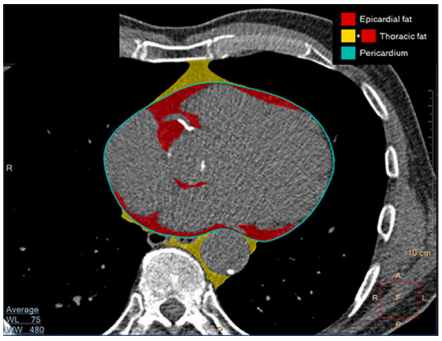
The correlation between EAT and BMI was considerably higher than the association of EAT with other components of metabolic syndrome [25]. Previously, it has been shown that EAT but not IAT has an independent predictive value for CAC and future coronary events in individuals without proven CAD in the general population [26–28]. Our study demonstrated an association between EAT and CAC scores in persons with T1D. BMI was positively associated with EAT and IAT levels. CAC may alert healthcare providers about subclinical coronary artery diseases and indicate the need for intensified medical therapy, such as initiating or intensifying statin therapy in individuals with T1D [3,29,30,31].

In our study, higher EAT and IAT levels were not significantly associated with AVC levels, which is in direct contrast to our expectations [30,32,33]. Epicardial fat is likely to induce local inflammation and is situated in the peri-coronary space, thus being correlated with an increased presence of coronary atherosclerosis. The aortic valve and aortic valve, being distanced from the fat beds, are probably unaffected by this perivascular effect. Aortic wall and aortic wall calcification are more closely linked to mechanical stress. The initiation of aortic sclerosis is believed to be triggered by mechanical stress causing endothelial damage, leading to inflammatory cell infiltration and lipid deposition similar to the early stages of atherosclerosis.

We acknowledge several limitations in our study.The relatively small sample size (n = 100) of the cohort employed in these analyses may have provided low power to detect associations and prevented us from conducting analyses adjusted for more standard risk factors; therefore, we only presented basic models adjusting for age and sex, and for age, sex, smoking, BMI, SBP, and LDL. However, our study has several important strengths, including the unique information related to adipose tissue surrounding the heart, CAC score, and extra-coronary calcification extracted from cardiovascular computed tomography in a cohort of individuals with long-standing T1D. More importantly, the association between heart adiposity and coronary, valvular, and aortic wall calcification in a T1D population has yet to be established.

4. Conclusions

In conclusion, our exploratory study in individuals with type 1 diabetes found that EAT and IAT are strongly associated with coronary artery calcification and with various cardio-metabolic risk factors such as higher BMI, waist-to-hip ratio, triglyceride levels, and mean-weighted HbA1c. Importantly, we found that higher EAT and IAT levels were not associated with aortic valve calcification (AVC), or descending aorta calcification. While EAT and IAT may contribute to local inflammation and coronary atherosclerosis, DAC and AVC appear to be more closely linked to mechanical stress. These results highlight the significance of EAT and IAT in coronary artery athrosclerosis among individuals with type 1 diabetes. This underscores the importance of using such markers to inform the commencement or escalation of medical interventions, such as statin therapy, aimed at reducing cardiovascular risk. Further research is warranted to elucidate the complex interplay between adipose tissue distribution and cardiovascular pathology in individuals with type 1 diabetes.



The selected sample of participants with type 1 diabetes (N = 100) shows higher epicardial adipose tissue (EAT) and higher intra-thoracic adipose tissue (IAT) are associated with higher coronary artery calcium (CAC) scores.

Author agreement

We confirm that the manuscript has been read and approved by all named authors and that there are no other persons who satisfied the criteria for authorship but are not listed. We further confirm that the order of authors listed in the manuscript has been approved by all of us.

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CRediT authorship contribution statement

Panteha Rezaeian: Writing – review & editing, Writing – original draft, Validation. **Jye-Yu C. Backlund:** Writing – review & editing, Writing – original draft, Validation, Formal analysis. **Mohammed Zaveri:** Writing – review & editing, Validation. **Rine Nakanishi:** Writing – review & editing, Validation. **Suguru Matsumoto:** Writing – review & editing, Validation. **Anas Alani:** Writing – review & editing, Validation. **Aryabod Razipour:** Writing – review & editing, Validation. **John M. Lachin:** Writing – review & editing, Validation, Formal analysis. **Matthew Budoff:** Writing – review & editing, Writing – original draft, Conceptualization.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Matthew Budoff reports financial support was provided by National Institutes of Health. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.ajpc.2024.100650.

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