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Arnold CT. Ng, MBBS, PhD, Shi Yi Goo, MBBS, Nicole Roche, MBBS, Rob J. van der Geest, PhD, William YS. Wang, MBBS, MM, PhD

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# Epicardial adipose tissue volume and left ventricular myocardial function by three-dimensional speckle tracking echocardiography

Arnold CT Ng, MBBS, PhD*;[1] Shi Yi Goo, MBBS*;[1] Nicole Roche, MBBS;[1] Rob J van der Geest, PhD;[2] William YS Wang, MBBS, MM, PhD[1]

**From:**

[1] Department of Cardiology, Princess Alexandra Hospital, The University of Queensland, Australia

[2] Department of Radiology, Leiden University Medical Center, Leiden, The Netherlands

* joint first author

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**Address for correspondence:**

Arnold CT Ng, MBBS, PhD
Department of Cardiology, Princess Alexandra Hospital, The University of Queensland
199 Ipswich Road, Woolloongabba, Brisbane, Australia 4102
Phone: +61 7 3176 2111; Fax: +61 7 3176 5399
Email address: arnoldct@hotmail.com

## SUMMARY

Coronary artery disease (CAD) and obesity are both independently associated with impaired myocardial systolic function. Epicardial adipose tissue (EAT) volume is another marker of visceral adiposity, and is associated with CAD. The association between EAT and myocardial systolic dysfunction versus other measures of obesity is unknown. This study showed that EAT volume is independently associated with myocardial systolic dysfunction, and may play a significant role in pathophysiology of diabetic, obesity and metabolic heart diseases.

## STRUCTURED ABSTRACT

**Background:** Although epicardial adipose tissue (EAT) volume is associated with increased incidence of coronary artery disease (CAD), its role in myocardial systolic dysfunction is unclear. The present study aims to identify independent determinants of EAT volume in patients without obstructive CAD, and to evaluate the association between EAT volume (versus other measures of obesity) and myocardial systolic strain analysis.

**Methods:** 130 patients without obstructive CAD on contrast-enhanced cardiac CT and normal left ventricular (LV) ejection fraction (EF) on 3D echocardiography were prospectively recruited. EAT volume was quantified from cardiac CT, and 3D multidirectional (longitudinal, circumferential, radial and area) strain were measured.

**Results:** The mean EAT volume was 97.5±43.7 $cm^3$. On multivariable analysis, measures of obesity (body mass index [BMI, p=0.007] and waist/hip ratio [p=0.001]) were independently associated with larger EAT volume. EAT volume was correlated with 3D global longitudinal (r=0.601, p<0.001), circumferential (r=0.375, p<0.001), radial (r=-0.546, p<0.001) and area (r=0.558, p<0.001) strain. On multivariable analyses, epicardial fat volume was the strongest predictor of 3D global longitudinal (standardized β=0.512, p<0.001), circumferential (standardized β=0.242, p=0.006), radial (standardized β=-0.422, p<0.001), and area (standardized β=0.428, p<0.001) strain. In contrast, other measures of obesity including BMI and waist/hip ratio were not independent determinants of 3D multidirectional global strain (all p>0.05).

**Conclusions:** EAT volume is independently associated with impaired myocardial systolic function despite preserved 3D LVEF and absence of obstructive CAD, and may play a significant role in the pathophysiology of diabetic, obesity and metabolic heart disease.


**Keywords:** Mechanics, Epicardial adipose tissue, Systolic strain, Echocardiography, Computed tomography

## INTRODUCTION

Epicardial adipose tissue (EAT) is located within the pericardial space, bounded by the serous epicardium and the fibrous pericardium. Embryologically and biochemically different from paracardial mediastinal fat (defined as adipose tissue external to the pericardium), EAT is associated with coronary artery disease (CAD), lipotoxic cardiomyopathy and atrial fibrillation.[1-7] As a metabolically active organ that releases cytokines and adipokines into the coronary arteries and myocardium [1-5], EAT may directly alter myocardial contractile function independent of CAD. A recent in-vitro study demonstrated that EAT explanted from guinea pigs secrete factors that inhibit cardiomyocyte contractile function and induce insulin resistance.[8] Recent study by Crendal and co-workers demonstrated EAT is associated with altered left ventricular (LV) myocardial strain using 2-dimensional echocardiographic speckle tracking.[9]

Two-dimensional speckle tracking longitudinal strain is a highly sensitive marker for subclinical myocardial dysfunction, and can predict all-cause mortality in patients with normal LV ejection fraction (EF).[10-12] In the present study, the authors aimed to identify independent determinants of EAT on cardiac CT in patients without obstructive CAD, and evaluate the association between EAT and myocardial systolic function using 3-dimensional (3D) speckle tracking echocardiographic multidirectional global strain analysis.

## METHODS

### Patient population and study protocol

One hundred and thirty patients with low risk chest pain were prospectively recruited to undergo contrast-enhanced cardiac CT and 3D echocardiography. Contrast-enhanced cardiac CT was essential for assessing the presence of obstructive CAD, non-obstructive CAD and absence of CAD that could potentially confound the echocardiographic

multidirectional strain analyses. Cardiac CT examination also included quantification of EAT volume. 3D echocardiographic examination included quantifications of 3D LV mass index, end-diastolic volume index (EDVI), end-systolic volume index (ESVI), LVEF and 3D multidirectional global strain (longitudinal, circumferential, radial and area strain).

Exclusion criteria included LVEF <50%, previous cardiomyopathies, heart failure, moderate or severe valvular heart disease, congenital heart disease, previous history of myocardial infarction, percutaneous coronary intervention or coronary artery bypass grafting, obstructive CAD on cardiac CT defined as >50% stenosis, atrial fibrillation, and contraindications for cardiac CT examination. Contraindications for cardiac CT examination included supraventricular or ventricular arrhythmias, renal insufficiency (glomerular filtration rate <30 mL/min/1.73m$^2$), iodine contrast allergy, severe claustrophobia, and pregnancy. In 6 patients with intermediate 50% stenosis, ischemia was excluded by stress echocardiography (n=5) or stress technetium-99m sestamibi myocardial perfusion scan (n=1).

The mean and median dose-length product for the cardiac CT examination (including calcium scoring and CT coronary angiography) were 368.2±302.6 mGy.cm and 313.0 mGy.cm (25$^{th}$ and 75$^{th}$ percentile, 164.0 and 490 mGy.cm) respectively. Using a conversion factor of 0.014 for chest CT in adults[13], the mean and median estimated effective radiation dose were 5.2±4.2 mSv and 4.4 mSv (25$^{th}$ and 75$^{th}$ percentile, 2.3 and 6.9 mSv) respectively.

The median time difference between cardiac CT and echocardiography was 1.0 month (25$^{th}$ and 75$^{th}$ percentile, 0.4 and 1.7 months).

The study was approved by the institutional ethics committee.

**Cardiac CT data acquisition**

All patients underwent cardiac CT using a dual-source CT system (Somatom Definition Flash, Siemens Healthcare, Forchheim, Germany). Cardiac CT was acquired using prospective ECG gating triggered at 60% of the R-R interval, with a collimation of 2 x 128 x

0.6mm and a gantry rotation time of 280ms. The tube current was 80mA.s and tube voltage was 100 kV or 120 kV as determined by patient's body mass index (BMI). From the raw data, cross-sectional images were reconstructed with 0.75mm slice thickness and a soft reconstruction kernel (Siemens B26f).

Patient's heart rate and blood pressure were monitored prior to each scan and beta-blockers (25 to 100mg Metoprolol orally) were administered in the absence of contraindications. All scans were performed during mid-inspiratory breath-hold and 75mL of Ioversol (Optiray 350, Mallinckrodt Medical, St. Louis, MO) was injected. Images were subsequently exported to dedicated workstations (SyngoVia, Siemens Healthcare, Forchheim, Germany; MASS V2010-EXP, Leiden University Medical Center, Leiden, The Netherlands) for off-line post-processing. Agatston calcium score was quantified as per previous standard.[14]

**Epicardial adipose tissue quantification**

For EAT volume quantification, the pericardium was manually traced on every single cross-sectional image, starting from the level of pulmonary artery bifurcation to the diaphragm (Figure 1). Within these contour limits, a CT attenuation threshold of -50 to -200 Hounsfield Unit was used to isolate EAT as previous published.[15, 16] Mediastinal fat and pericardial fat (outside the visceral pericardium and on the external surface of the parietal pericardium) were excluded.

**Echocardiography**

Transthoracic echocardiography was performed using a commercially available ultrasound system (Vivid E9, 4V probe, GE-Vingmed, Horten, Norway). A complete 2D, 3D, color, pulsed and continuous-wave Doppler echocardiogram was performed. Image contrast, depth and sector size were optimized for 3D image acquisition to include the entire myocardial wall, and an optimal frame rate of >30 frames per second. Images were obtained

during breath-hold to achieve a multi-beat 3D volume of a minimum of 4 heartbeats without artifacts.[17] The mean 3D frame rate was 34.6 frames/sec. All images were digitally stored on hard disks for offline analysis.

3D LV mass index, LVEDVI, and LVESVI were calculated using the 3D dataset and corrected for body surface area.[18] LVEF was calculated and expressed as a percentage.

**Three-dimensional speckle tracking**

3D multidirectional global strains were calculated from the 3D dataset using commercially available software (4D Auto LVQ, EchoPAC version 113, GE-Vingmed, Horten, Norway). Briefly, 3D volume datasets were initially displayed as conventional apical and short axis views. Automatic LV border contours were created after placing 2 points, one at the center of the LV base and the other at the apex, in the end-diastolic and end-systolic apical views. The LV epicardial and endocardial border contours were adjusted if required. The motion of the 3D myocardium was subsequently tracked automatically throughout the entire cardiac cycle and myocardial deformation was calculated for each segmental volume. A multidirectional 17 segments Bull's eye map with 3D global longitudinal (Figure 2), circumferential, radial and area strain results were finally generated and displayed. The software will only display 3D multidirectional global strain when ≤3 segments were excluded due to inadequate tracking.

**Statistical Analysis**

All continuous variables were tested for Gaussian distribution. Continuous variables were presented as mean ± 1 standard deviation unless otherwise stated. Categorical variables were presented as frequencies and percentages, and were compared using Chi-square test when all expected cell counts were ≥5, or Fisher's exact test if expected cell count was <5. Unpaired Student's t-test was used to compare 2 groups of continuous variables of Gaussian distribution. Pearson correlation was used to determine the association between 2 continuous

variables. Multiple linear regression analyses were performed to identify independent determinants of both EAT volume and 3D multidirectional global longitudinal, circumferential, radial and area strain, with significant univariable determinants entered simultaneously as covariates. To avoid multicollinearity, a tolerance of >0.4 was set. As the presence of diabetes, hypertension and non-obstructive coronary atherosclerosis may potentially confound the multidirectional global strain analyses, these variables were forced into all the multivariable models. In addition, to further confirm the study results, all multivariable analyses were repeated in patients without diabetes, hypertension and coronary atherosclerosis. Similarly, all analyses were repeated in patients with BMI ≤25.0 kg/m$^2$ to exclude suboptimal image quality due to obesity as a confounding factor in artificially reducing the 3D multidirectional global strain measurements. In 10 randomly selected subjects, intra- and inter-observer measurement variabilities for EAT volume and 3D multidirectional global strain were presented as mean absolute differences. A 2-tailed p value of<0.05 was considered significant. All statistical analyses were performed using IBM SPSS Statistics for Windows, version 21.0 (Armonk, NY).

**RESULTS**

The baseline clinical, cardiac CT and echocardiographic characteristics for all the patients are shown in Online supplementary Table S1. The mean age was 53±9 years, 53.1% male. Men were younger (50±9 vs. 56±8 years, p<0.001) and had significantly higher waist/hip ratio (0.97±0.06 vs. 0.89±0.06, p<0.001).

The mean EAT volume was 97.5±43.7 cm$^3$ (range 20.0 – 235.2 cm$^3$). Although there was a trend towards larger EAT volume in men (103.7±39.5 vs. 90.4±47.4 cm$^3$, p=0.08), there were no gender differences in the presence/absence of coronary atherosclerosis (p=0.19) or Agatston score (56.2±130.2 vs. 34.6±109.7, p=0.31).

Patients with coronary atherosclerosis had significantly larger EAT volume (107.4±44.9 vs. 84.4±38.8 $cm^3$, p=0.003). However, there was no correlation between EAT volume and Agatston score (r=0.089, p=0.32).

On 3D echocardiography, men had significantly larger LV volumes and lower 3D multidirectional global strain. Although there was a gender difference in LVEF, all patients had normal LVEF.

**Determinants of epicardial adipose tissue volume**

To identify independent determinants of EAT volume, all significant univariable determinants (BMI, waist/hip ratio and systolic blood pressure) were simultaneously entered into a multiple linear regression model. Table 1 shows that only measures of obesity (BMI [p=0.007] and waist/hip ratio [p=0.001]) were independently associated with larger EAT volume.

**Determinants of 3D multidirectional global strain**

Table 2 summarizes all the univariable and multivariable determinants of 3D global longitudinal strain. On univariable analysis, patients with coronary atherosclerosis had significantly lower 3D global longitudinal strain (-14.9±3.1 vs. -16.1±3.2%, p=0.041). However, there was a non-significant association between 3D global longitudinal strain and Agatston score (r=0.125, p=0.16). Figure 3 shows the correlation between EAT volume and 3D global longitudinal strain.

As the presence of diabetes, hypertension and non-obstructive coronary atherosclerosis may potentially confound 3D global longitudinal strain, these variables were forced into the multivariable analysis. When all other significant univariable determinants of 3D global longitudinal strain were entered into the multiple linear regression model (Table 2), only EAT volume (standardized β=0.512, p<0.001) and LVESVI (standardized β=0.213, p=0.008) were independent determinants of 3D global longitudinal strain. Based on the

standardized β, EAT volume was the strongest predictor of 3D global longitudinal strain. Similar results were obtained showing that EAT volume was an independent determinant of 3D global circumferential (Table 3), radial (Table 4) and area (Table 5) strain.

**Investigation of possible confounders**

To further confirm that the study findings were not confounded by other potential disease mechanisms, all analyses were repeated in patients without diabetes, hypertension and coronary atherosclerosis (n=39). EAT volume was still significantly correlated with 3D global longitudinal (r=0.538, p<0.001), circumferential (r=0.421, p=0.008), radial (r=-0.579, p<0.001), and area (r=0.582, p<0.001) strain. On multivariable analyses, EAT volume was an independent determinant of 3D global longitudinal strain (standardized β=0.398, p=0.008). Although not significant, larger EAT volume trended towards lower 3D global circumferential (standardized β=0.126, p=0.51), radial (standardized β=-0.341, p=0.076), and area (standardized β=0.345, p=0.070) strain.

Obesity will also detrimentally affect image quality and may artificially reduce 3D multidirectional global strain measurements. Therefore, patients with BMI ≤25.0 kg/m$^2$ were selected (n=40) and all analyses were repeated. EAT volume was still significantly correlated with 3D global longitudinal (r=0.668, p<0.001), circumferential (r=0.499, p=0.001), radial (r=-0.618, p<0.001), and area (r=0.629, p<0.001) strain. On multivariable analyses, EAT volume was an independent determinant of 3D global longitudinal (standardized β=0.414, p=0.006), radial (standardized β=-0.547, p=0.006), and area (standardized β=0.575, p=0.003) strain. There was also a trend for larger EAT volume and more impaired 3D global circumferential strain (standardized β=0.215, p=0.21).

Finally, increased EAT volume may also have a direct mechanistic effect on 3D multidirectional global strain by "constricting" LV systolic and diastolic volumes. However, there were no correlations between EAT volume and LVEDVI (r=-0.09, p=0.29) or LVESVI

(r=0.08, p=0.35). Furthermore, unlike pericardial constriction where early diastolic velocities (E') by tissue Doppler imaging are usually preserved or even supranormal, there were inverse correlations between EAT volume and septal E' (r=-0.263, p=0.002) and lateral E' velocities (r=-0.285, p=0.001). Therefore, increased EAT volume was unlikely to impair 3D multidirectional global strain by physically "constricting" LV systole and diastole.

**Measurement variabilities**

Online Table S2 outlines the intra- and interobserver measurement variabilities for EAT volume and 3D multidirectional global strain analyses.

## DISCUSSION

Previous published studies have clearly demonstrated the independent association between EAT and coronary artery disease.[1-7] In contrast, the methodological strengths and novelties of the present study include: 1) quantification of LV myocardial function using 3D speckle tracking echocardiography; 2) quantification of EAT as a 3D volumetric measurement from cardiac CT rather than "traditional" 2D echocardiographic thickness measurement; 3) demonstrating that increasing obesity was independently associated with larger EAT volumes; 4) compared to other measures of obesity including BMI and waist/hip ratio, only EAT volume was independently associated with progressively lower 3D multidirectional global strain; and 5) the association between larger EAT volume and LV myocardial dysfunction was independent of potential confounders including obstructive CAD, hypertension, diabetes and obesity. This association is mostly mediated via myocardial steatosis and energetic.[8]

**Physiological and pathophysiological roles of epicardial adipose tissue**

Adipose tissue surrounding the heart can be divided into epicardial and paracardial fat.[19] Separated by the fibrous pericardium, EAT is bounded between the epicardium and

pericardium, whereas paracardial fat is located external to the pericardium. Similar to mesenteric and omental visceral fat, EAT is derived from the splanchnopleuric mesoderm and is embryologically different from paracardial fat.[19]

EAT has several functions affecting the human heart, including functioning as brown adipose tissue involved in thermogenesis, as an endocrine and paracrine organ that plays a significant role in coronary atherogenesis and inflammation, and as a lipid store that is actively involved in myocardial lipid and energy homeostasis, steatosis and lipotoxicity.[2, 5]

**Epicardial adipose tissue and coronary atherosclerosis**

One of the proposed pathophysiological roles of EAT is the promotion of coronary atherogenesis and inflammation.[2, 7, 16] As a metabolically active organ, EAT releases numerous pro-inflammatory cytokines that promotes atherogenesis.[2, 5] Consistent with previous publications, this present study demonstrated that patients with coronary atherosclerosis had significantly larger EAT volume.[7, 15] However, the present study was first to demonstrate an inverse relationship between EAT volume and myocardial contractile function that is independent of CAD.

One of the major strength of the present study was the exclusion of CAD as a potential confounding factor that could have impaired myocardial contractility. Firstly, all patients with obstructive CAD on contrast-enhanced cardiac CT were excluded. Secondly, the influence of non-obstructive CAD was evaluated in all the multivariable analyses. Finally, the result that EAT was associated with reduced myocardial contractility was confirmed in patients with normal coronary arteries (i.e. without any coronary atherosclerosis on cardiac CT). Therefore, the association between EAT and reduced myocardial contractility was not due to coronary atherosclerosis, but possibly a consequence of its role in myocardial lipid and energy homeostasis, steatosis and lipotoxicity.

**Epicardial adipose tissue, myocardial steatosis and contractile dysfunction**

Diabetes and obesity can lead to intramyocardial triglyceride accumulation (i.e. steatosis) in a process synonymous to "fatty liver disease".[20] When the increased availability of intramyocardial free fatty acids exceeds its cellular oxidative capacity, there is a resultant accumulation of toxic intermediates such as ceramide. Ceramide increases inducible nitric oxide synthase activity and intracellular nitric oxide concentration, eventually leading to cellular apoptosis. This process is known as lipotoxicity.[21]

Previous human physiological study has suggested that EAT may release free fatty acids directly into the myocardium, thus playing a role in myocardial lipid and energy homeostasis.[22] However, increased EAT volume may adversely result in myocardial steatosis and lipotoxicity.[23] Malavazos and co-workers demonstrated an independent correlation between EAT thickness on echocardiography and intramyocardial triglyceride accumulation on proton magnetic resonance spectroscopy.[23] In turn, it was known that intramyocardial triglyceride accumulation was independently associated with subclinical myocardial dysfunction in diabetic patients.[10] Although previous studies have shown that increased EAT was associated with increased LV mass and diastolic dysfunction [10, 24-26], the present study demonstrated an inverse independent relationship between EAT and myocardial systolic function. Even when patients with diabetes, hypertension and coronary atherosclerosis were excluded, EAT volume was still independently correlated with longitudinal myocardial function.

**2D versus 3D speckle tracking**

In the present study, multidirectional myocardial function was quantified using 3D speckle tracking. 3D speckle tracking is a relatively new imaging modality and early research experience suggests it is not directly comparable to 2D speckle tracking.[27] Theoretically, 3D speckle tracking provides additional advantages over 2D such as avoidance of foreshortening of apical images and out-of-plane motion, and complete quantification of all multidirectional

strain analyses from a single volume of interest. However, this is usually at the expense of lower volume rate and 3D strain values are not directly comparable with 2D measurements.[28]

**Study limitations**

Although the present study demonstrated an independent association between EAT volume and impaired 3D multidirectional global strain, it does not necessarily indicate increased EAT volume was the cause of the myocardial dysfunction that will eventually lead to clinical heart failure. However, previous in-vitro study have demonstrated that EAT explanted from guinea pigs secrete factors that inhibited isolated cardiomyocyte contractile function and induced insulin resistance.[8] Secondly, while the present study suggested that increasing obesity was independently associated with larger EAT volumes and larger EAT volumes was independently associated with reduced myocardial contractile function, it is unclear if increased EAT volume and impaired myocardial function were all a manifestation of metabolic syndrome, or represents an independent pathophysiological process. Finally, no comparisons were made between the sensitivity of 2D versus 3D echocardiographic speckle tracking in detecting myocardial dysfunction.

**Future directions**

Obesity is known to be associated with myocardial dysfunction and heart failure.[29-31] Although the pathophysiology is unclear, it may be secondary to myocardial steatosis and lipotoxicity from fatty acid intermediates such as diacylglycerol and ceramide as seen in diabetic patients.[10, 32] In the present study, the stronger association between EAT volume and myocardial dysfunction compared to BMI and waist/hip ratio suggest EAT may exert a direct local paracrine effect on myocardial energetics and contractility.[22] Therefore, future studies on diabetic, obesity and metabolic heart disease should consider quantification of EAT volume by cardiac CT/magnetic resonance imaging, in addition to intramyocardial triglyceride content by proton magnetic resonance imaging. Finally, as EAT is known to

contain brown adipose tissue, it may potentially have implications for understanding the pathogenesis and treatment of obesity and metabolic syndrome.[5]

## CONCLUSIONS

EAT volume is a marker of visceral obesity, and is associated with subclinical myocardial systolic dysfunction. This association is independent of CAD, diabetes and hypertension, and is superior to other measures of obesity such as BMI and waist/hip ratio. Future studies on diabetic, obesity and metabolic heart diseases should include quantification of EAT volume when evaluating LV myocardial function.

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**Figure legends**

Figure 1. Quantification of epicardial adipose tissue on cardiac CT.

Epicardial adipose tissue is defined as fat between the heart and the fibrous pericardium, whereas paracardial adipose tissue is external to the pericardium (left panel). Contours were drawn along the pericardium and epicardial adipose tissue is automatically identified by the software (red color) (right panel).

Figure 2. Examples of epicardial adipose tissue volumes and 3D speckle tracking in 2 female patients. Both patients had comparable LV mass index, volumes and EF, but 3D global longitudinal strain was significantly more impaired in the patient with larger epicardial adipose tissue volume. 3D: 3-dimensional; LV: left ventricular; EAT: epicardial adipose tissue; EDVI: end-diastolic volume index; ESVI: end-systolic volume index; EF: ejection fraction; LVMI: left ventricular mass index; GLS: global longitudinal strain.

Figure 3. Correlation between epicardial adipose tissue volume and 3D global longitudinal strain. Patients with larger epicardial adipose tissue volume have significantly more impaired myocardial function despite a preserved LVEF. 3D: 3-dimensional.

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Table 1. Univariable and multivariable linear regression models for epicardial adipose tissue volume

| | Univariable | | Multivariable | |
|---|---|---|---|---|
| Variable | Standardized β | p value | Standardized β | p value |
| Body mass index | 0.382 | <0.001 | 0.230 | 0.007 |
| Waist/hip ratio | 0.359 | <0.001 | 0.266 | 0.001 |
| Systolic BP | 0.305 | <0.001 | 0.129 | 0.18 |
| Diastolic BP | 0.316 | <0.001 | 0.131 | 0.17 |

BP: blood pressure

Table 2. Univariable and multivariable linear regression models for 3-dimensional global longitudinal strain

| | Univariable | | Multivariable | |
|---|---|---|---|---|
| | Standardized β | p value | Standardized β | p value |
| Male gender | 0.294 | 0.001 | 0.114 | 0.23 |
| Hypertension | 0.180 | 0.040 | 0.115 | 0.14 |
| Diabetes | 0.164 | 0.06 | 0.080 | 0.26 |
| Body mass index | 0.215 | 0.014 | -0.108 | 0.17 |
| Waist/hip ratio | 0.361 | <0.001 | 0.080 | 0.38 |
| Systolic BP | 0.324 | <0.001 | 0.064 | 0.46 |
| Diastolic BP | 0.298 | 0.001 | 0.078 | 0.34 |
| LVESVI | 0.350 | <0.001 | 0.213 | 0.008 |
| Presence of coronary atherosclerosis | 0.179 | 0.041 | -0.016 | 0.83 |
| Epicardial adipose tissue volume | 0.601 | <0.001 | 0.512 | <0.001 |

BP: blood pressure; ESVI: end-systolic volume index; LV: left ventricular.

Table 3. Univariable and multivariable linear regression models for 3-dimensional global circumferential strain

| | Univariable | | Multivariable | |
|---|---|---|---|---|
| | Standardized β | p value | Standardized β | p value |
| Hypertension | 0.299 | 0.001 | 0.243 | 0.003 |
| Diabetes | 0.228 | 0.009 | 0.090 | 0.25 |
| Body mass index | 0.283 | 0.001 | -0.011 | 0.90 |
| Waist/hip ratio | 0.271 | 0.002 | 0.102 | 0.21 |
| Systolic BP | 0.230 | 0.009 | -0.072 | 0.43 |
| Diastolic BP | 0.233 | 0.008 | 0.107 | 0.23 |
| LV mass index | -0.194 | 0.027 | -0.179 | 0.024 |
| LVESVI | 0.429 | <0.001 | 0.350 | <0.001 |
| Presence of coronary atherosclerosis | 0.055 | 0.54 | -0.061 | 0.42 |
| Epicardial adipose tissue volume | 0.375 | <0.001 | 0.242 | 0.006 |

BP: blood pressure; ESVI: end-systolic volume index; LV: left ventricular.

Table 4. Univariable and multivariable linear regression models for 3-dimensional global radial strain

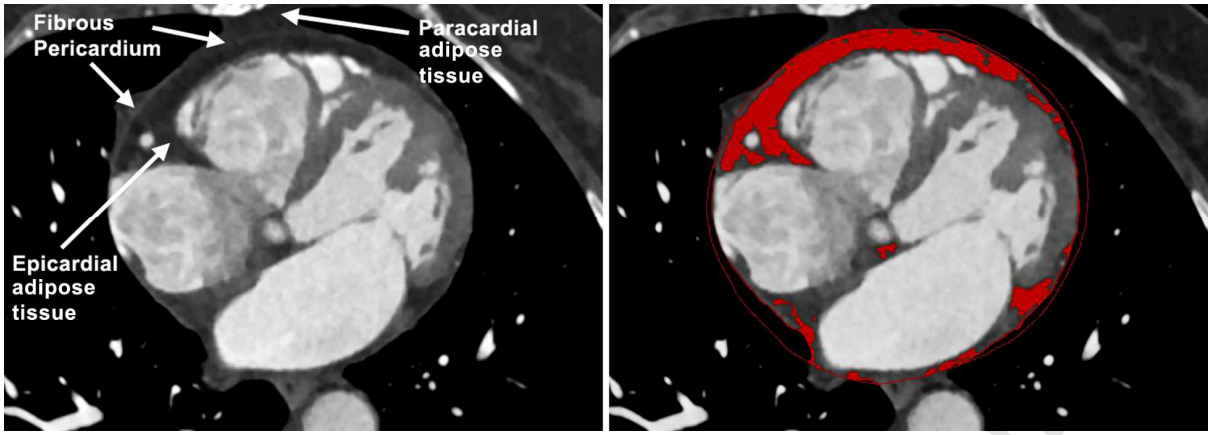
| | Univariable | | Multivariable | |
|---|---|---|---|---|
| | Standardized β | p value | Standardized β | p value |
| Male gender | -0.211 | 0.016 | 0.020 | 0.83 |
| Hypertension | -0.245 | 0.005 | -0.179 | 0.022 |
| Diabetes | -0.220 | 0.012 | -0.088 | 0.22 |
| Body mass index | -0.296 | 0.001 | 0.070 | 0.39 |
| Waist/hip ratio | -0.353 | <0.001 | -0.149 | 0.10 |
| Systolic BP | -0.283 | 0.001 | 0.041 | 0.63 |
| Diastolic BP | -0.297 | 0.001 | -0.126 | 0.12 |
| LV mass index | 0.186 | 0.034 | 0.166 | 0.024 |
| LVESVI | -0.393 | <0.001 | -0.312 | <0.001 |
| Presence of coronary atherosclerosis | -0.115 | 0.19 | 0.051 | 0.47 |
| Epicardial adipose tissue volume | -0.546 | <0.001 | -0.422 | <0.001 |

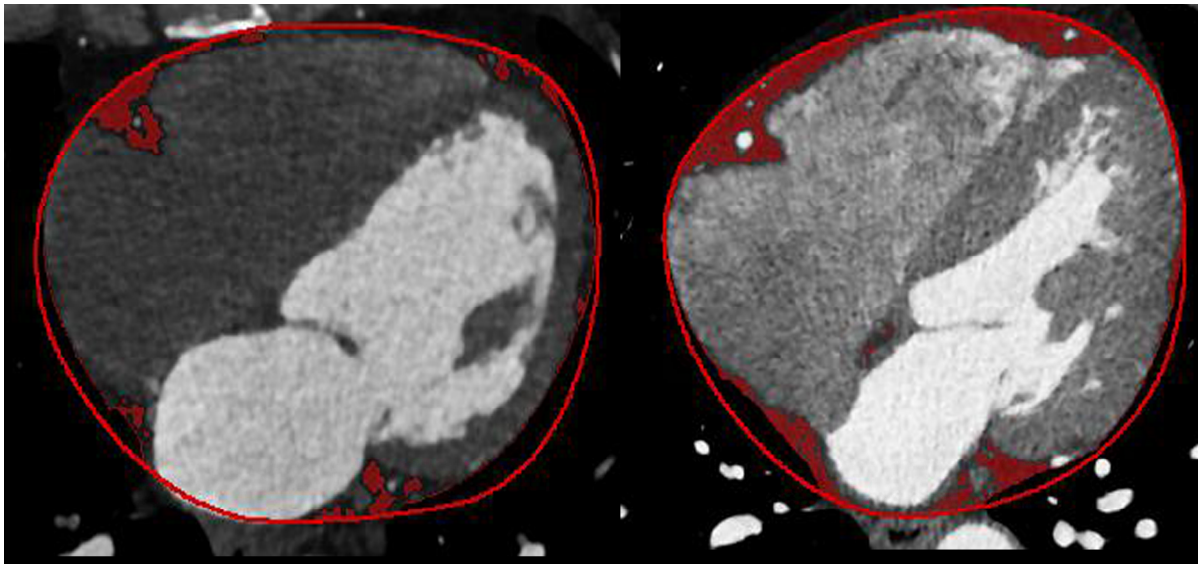
BP: blood pressure; ESVI: end-systolic volume index; LV: left ventricular.

Table 5. Univariable and multivariable linear regression models for 3-dimensional global area strain

| | Univariable | | Multivariable | |
|---|---|---|---|---|
| | Standardized β | p value | Standardized β | p value |
| Male gender | 0.209 | 0.017 | 0.006 | 0.95 |
| Hypertension | 0.252 | 0.004 | 0.179 | 0.022 |
| Diabetes | 0.221 | 0.011 | 0.087 | 0.23 |
| Body mass index | 0.308 | <0.001 | -0.053 | 0.52 |
| Waist/hip ratio | 0.341 | <0.001 | 0.116 | 0.20 |
| Systolic BP | 0.289 | 0.001 | -0.032 | 0.71 |
| Diastolic BP | 0.302 | <0.001 | 0.123 | 0.13 |
| LV mass index | -0.206 | 0.019 | -0.174 | 0.018 |
| LVESVI | 0.374 | <0.001 | 0.284 | <0.001 |
| Presence of coronary atherosclerosis | 0.133 | 0.13 | -0.027 | 0.70 |
| Epicardial adipose tissue volume | 0.558 | <0.001 | 0.428 | <0.001 |

BP: blood pressure; ESVI: end-systolic volume index; LV: left ventricular.

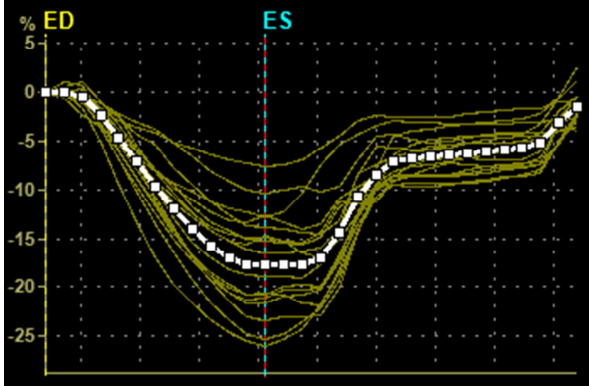


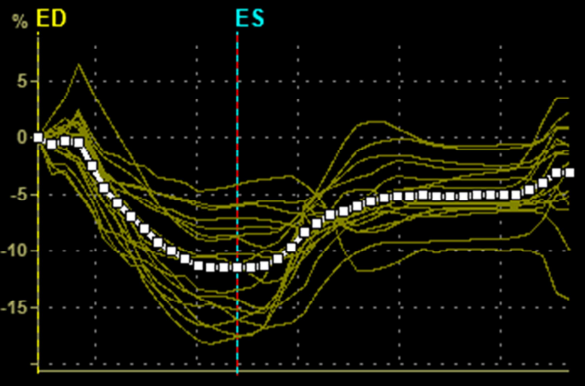


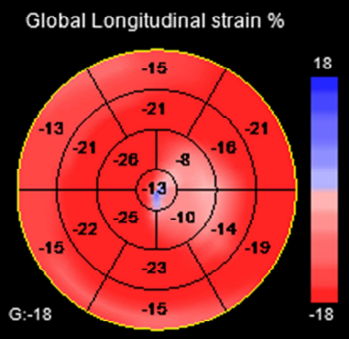
EAT volume 54.3 $cm^3$

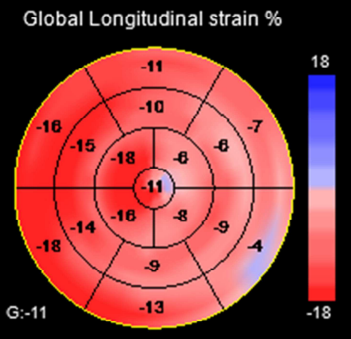


EAT volume 129.0 $cm^3$



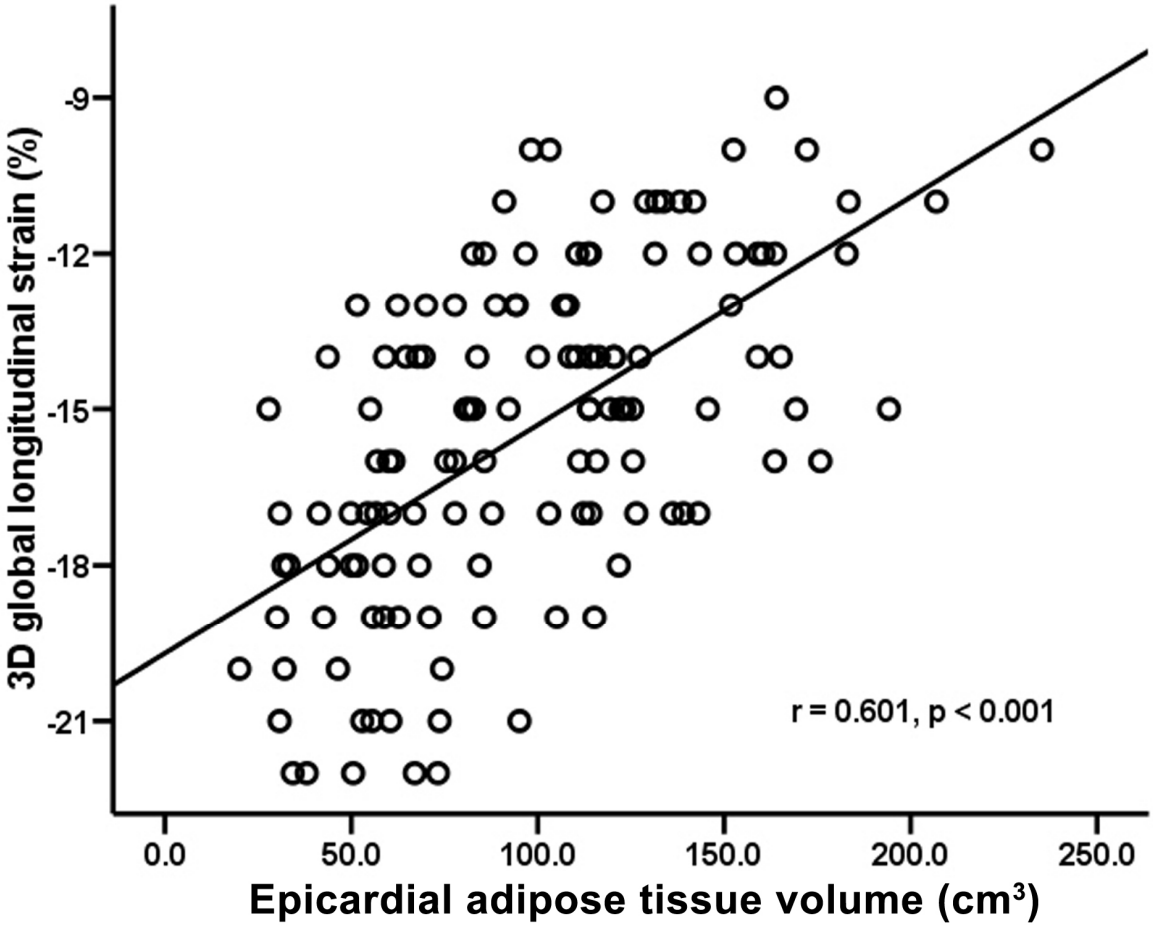




| | |
|---|---|
| LVEDVI_3D | 61 mL/$m^2$ |
| LVESVI_3D | 24 mL/$m^2$ |
| LVEF_3D | 60 % |
| LVMI_3D | 72 g/$m^2$ |
| GLS_3D | -18 % |

| | |
|---|---|
| LVEDVI_3D | 61 mL/$m^2$ |
| LVESVI_3D | 25 mL/$m^2$ |
| LVEF_3D | 59 % |
| LVMI_3D | 70 g/$m^2$ |
| GLS_3D | -11 % |


3D global longitudinal strain (%)
-9
-12
-15
-18
-21
r = 0.601, p < 0.001
0.0
50.0
100.0
150.0
200.0
250.0
Epicardial adipose tissue volume (cm³)