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SHORT COMMUNICATION

The value of echocardiographic measurement of epicardial adipose tissue in heart failure patients

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Abstract

Aims Epicardial adipose tissue (EAT) is increasingly recognized as an important factor in the pathophysiology of heart failure (HF). Cardiac magnetic resonance (CMR) imaging is the gold-standard imaging modality to evaluate EAT size, but in contrast to echocardiography, CMR is costly and not widely available. We investigated EAT thickness on echocardiography in relation to EAT volume on CMR, and we assessed the agreement between observers for measuring echocardiographic EAT.

Methods and results Patients with HF and left ventricular ejection fraction >40% were enrolled. All patients underwent CMR imaging and transthoracic-echocardiography. EAT volume was quantified on CMR short-axis cine-stacks. Echocardiographic EAT thickness was measured on parasternal long-axis and short-axis views. Linear regression analyses were used to assess the association between EAT volume on CMR and EAT thickness on echocardiography. Intraclass correlation coefficient (ICC) was used to assess the interobserver agreement as well as the intraobserver agreement. EAT on CMR and echocardiography was evaluated in 117 patients (mean age 71 ± 10 years, 49% women and mean left ventricular ejection fraction 54 ± 7%). Mean EAT volume on CMR was 202 ± 64 mL and ranged from 80 to 373 mL. Mean EAT thickness on echocardiography was 3.8 ± 1.5 mm and ranged from 1.7 to 10.2 mm. EAT volume on CMR and EAT thickness on echocardiography were significantly correlated (junior-observer: r = 0.62, $P < 0.001$, senior-observer: r = 0.33, $P < 0.001$), and up to one-third of the variance in EAT volume was explained by EAT thickness (R^2 = 0.38, $P < 0.001$). The interobserver agreement between junior and senior observers for measuring echocardiographic EAT was modest [ICC, 0.65 (95% confidence interval (CI) 0.47–0.77], whereas the intraobserver agreement was good (ICC 0.98, 95% CI 0.84–0.99).

Conclusions There was a modest correlation between EAT volume on CMR and EAT thickness on echocardiography. Limited agreement between junior and senior observers for measuring echocardiographic EAT was observed. EAT thickness on echocardiography is limited in estimating EAT volume.

Keywords HFpEF; HFmrEF; Epicardial adipose tissue; Echocardiography; Cardiac magnetic resonance imaging

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Background

Epicardial adipose tissue (EAT) volume is associated with functional and structural cardiac impairment in heart failure (HF) with preserved ejection fraction (HFpEF) and is therefore increasingly recognized as an important factor in the pathophysiology of this condition.[1–4] The gold standard method for EAT volume quantification is cardiac magnetic resonance (CMR) imaging[5]; however, this imaging modality is costly and not widely available. It has been reported that EAT can also be measured with echocardiography, which is cheap and widely available.[6] While echocardiography could indeed

be used to assess EAT, the association of this measurement with EAT volume on CMR in patients with HF remains unknown. Furthermore, the agreement between observers for measuring echocardiographic EAT is unclear.

Aims

We aimed to investigate echocardiographic EAT thickness, in relation to EAT volume on CMR imaging and to assess the agreement between junior and senior observers for measuring echocardiographic EAT.

Methods

Study population

One hundred and one patients who participated in the Ventricular tachyarrhythmia detection by Implantable Loop-Recording in Patients with HFpEF (VIP-HF) registry were enrolled.[7] The remaining patients were collected from the VIP-HF screening database. All patients underwent a standard diagnostic protocol for HF with left ventricular ejection fraction (LVEF) $>$ 40%. Inclusion and exclusion criteria have been previously described.[1] The analysis was approved by the local ethics committee and conforms with the Declaration of Helsinki. Due to the retrospective nature of the study, the need for individual informed consent was waived.

Epicardial adipose tissue measurement on cardiac magnetic resonance imaging

Cardiac magnetic resonance studies were performed using a 1.5 Tesla scanner (Philips, Amsterdam, The Netherlands & Siemens, Erlangen, Germany). Total EAT volume was determined by manually delineating the outer wall of the myocardium and the visceral layer of the pericardium on end-diastolic short-axis slices, from the most basal slice around the atria towards the most apical slice around the ventricles (QMass 7.6 and 8.1, Medis, Leiden,The Netherlands).[1] EAT volume was calculated by summation of EAT volume of each slice using the modified Simpson's rule.[8] Measurements were performed by one investigator (G. v. W) and were visually checked in a random fashion by two other investigators (B. D. W and T. P. W.), all blinded for patient characteristics. The absence of pericardial effusion was verified on CMR using T1 mapping.

Epicardial adipose tissue measurement on echocardiography

Echocardiographic images were acquired on Vivid E95 (General Electric, Horton, Norway) and iE33 (Philips, Amsterdam, The Netherlands) systems using standard techniques. EAT measurements were performed by one blinded observer (G. v. W.) using GE EchoPAC version 203. EAT was measured as thickness over the free wall of the right ventricle (RV) using parasternal long-axis and short-axis views in end-systole (*Figure 1(A)* and *1(B)*).[6,9] EAT was measured twice on parasternal long-axis views and twice on short-axis views. These four measurements were then averaged.[9] As a sensitivity analysis, EAT was also measured in end-diastole. EAT was measured again, with at least 6 months between the first and second measurements. EAT was also measured by a blinded senior observer with extensive echocardiographic experience (H. S. O.).

Statistical analysis

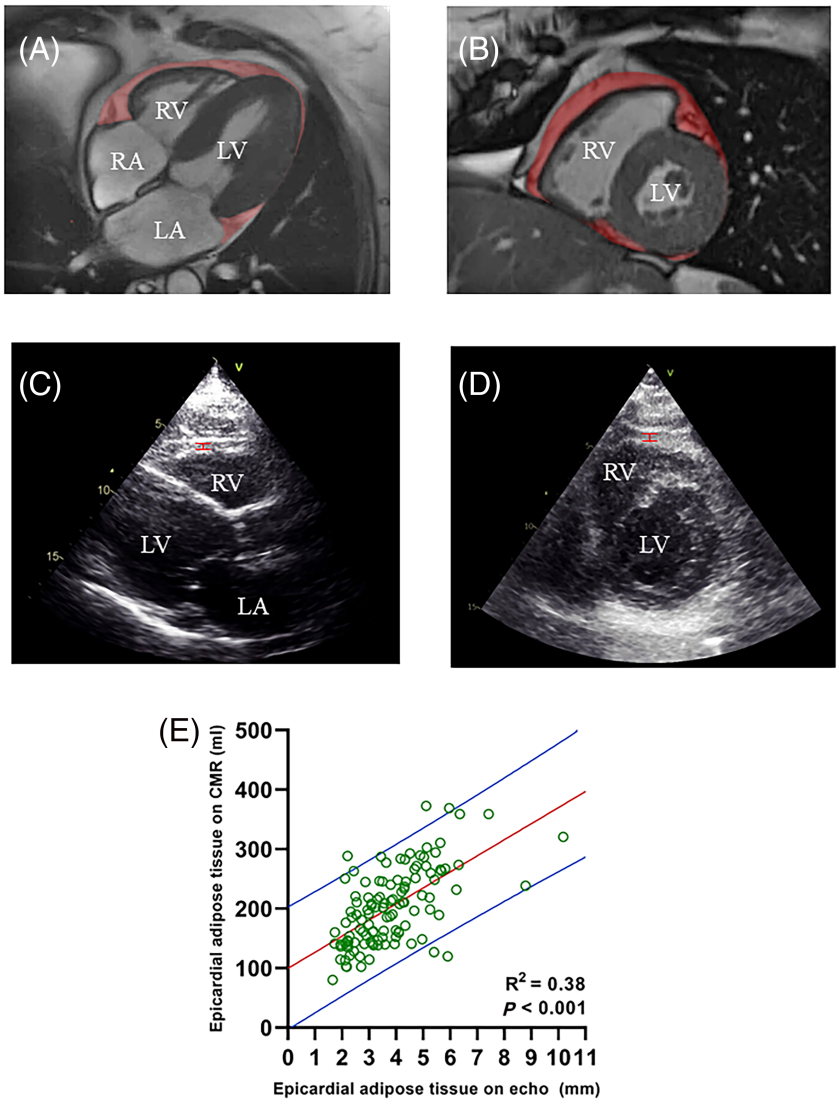
Data are presented as numbers (percentage), means ± standard deviations or medians with interquartile ranges, depending on the distribution. Linear regression was used to assess correlation between EAT volume on CMR and echocardiographic EAT thickness. A correlation coefficient $<$0.5 was considered poor, between 0.5 and 0.7 modest, and $>$0.7 strong.[10] A scatterplot with a regression line and 95% prediction intervals between EAT volume on CMR and echocardiographic EAT thickness was constructed, as described by Iacobellis *et al*.[6] The intraclass correlation coefficient (ICC) was used to assess interobserver and intraobserver agreement. Statistical analyses were performed using SPSS (Version 23, Chicago, Illinois) and R (Version 4.0.2, Vienna, Austria). A *P*-value of $<$0.05 was considered statistically significant.

Results

Patient characteristics

We identified 117 eligible patients who underwent CMR and echocardiography. Supporting Information, *Table S1* details patient characteristics: mean age 71 ± 10 years, 49% women, and mean BMI 30 ± 6 kg/m^2. Fifty-two patients (44%) experienced a previous hospitalization for HF. Seventy-seven patients were classified as HFpEF, and 40 patients were classified as HF with mid-range ejection fraction (HFmrEF). Typical examples of EAT on CMR and echocardiography are depicted in *Figure 1(A)–(D)*. Median time between CMR and echocardiography was 57 [21–105] days. Mean EAT volume on CMR was 202 ± 64 mL and ranged from 80 to 373 mL.

Figure 1 (A) Typical example of epicardial adipose tissue (EAT) on cardiac magnetic resonance (CMR) imaging on long-axis 4 chamber-view and (B) short-axis view. (C) Typical example of echocardiographic EAT thickness on parasternal long-axis view and (D) short-axis view. (E) Scatterplot with a regression line (red) and 95% prediction intervals (blue) showing the relationship between EAT volume on CMR imaging and EAT thickness on transthoracic echocardiography. This method is used to assess not only correlation but also individual variation. Prediction intervals provide the range that contains the value of the dependent variable (EAT volume on CMR) for a single new observation of the independent variable (echocardiographic EAT thickness). LA, left atrium; LV, left ventricle; RA, right atrium; RV, right ventricle.



Mean echocardiographic EAT thickness was 3.8 ± 1.5 mm and ranged from 1.7 to 10.2 mm.

Correlation between epicardial adipose tissue on cardiac magnetic resonance and echocardiography

Epicardial adipose tissue volume on CMR was significantly correlated with echocardiographic EAT thickness (junior observer: r = 0.62, $P < 0.001$, senior observer: r = 0.33, $P < 0.001$). Up to one third of the variance in EAT volume was explained by EAT thickness (R^2 = 0.38). No difference was observed between echocardiographic EAT measured in end-systole and end-diastole for the association with EAT volume on CMR (r = 0.33 vs. r = 0.35, respectively). *Figure 1(E)* depicts the relation between EAT on CMR and echocardiography, showing a wide range of possible values for EAT volume, for a given individual value of EAT thickness.

Agreement between observers for measuring echocardiographic epicardial adipose tissue

Interobserver agreement between junior and senior observers for measuring echocardiographic EAT was modest (ICC 0.65, 95% CI 0.47–0.77), whereas the intraobserver agreement for measuring echocardiographic EAT was good (ICC 0.98, 95% CI 0.84–0.99).

Discussion

We found a modest correlation between EAT volume on CMR imaging and EAT thickness on echocardiography. Indeed, there is a substantial variability in EAT volume measured on CMR when estimated with echocardiographic EAT thickness. Limited agreement between junior and senior observers for measuring echocardiographic EAT was observed. Therefore, estimating EAT volume on CMR with echocardiographic EAT thickness is limited.

Other studies in patients without HF have also described an association between EAT on CMR and echocardiography.[11,12] However, the strength of the associations was variable and correlation-coefficients ranged from 0.61 to 0.90.[11,12] This variance may in part be a consequence of estimating a three-dimensional structure using two-dimensional measurements.[13] To put into context: the association between EAT volume and EAT thickness in our study is comparable with the association between ventricular volume and ventricular diameter (RV: $r = 0.58$, LV: $r = 0.74$).[13,14] The use of two-dimensional measurements of EAT is therefore limited and should be used with caution.

The techniques used to measure EAT thickness differ slightly between the literature.[11,12] We and Malavazos *et al*. have measured EAT over the RV using standard echocardiographic views.[11] Alternatively, Parisi *et al*. measured EAT at the Rindfleisch fold using a non-standard view.[12] For this approach, ultrasound settings were adjusted to obtain images of diagnostic resolution. The use of different techniques to assess echocardiographic EAT may lead to different correlations to EAT volume.

One study did not find a relationship between EAT on CMR and echocardiography.[15] In that study, EAT was measured on one long-axis view, and EAT was expressed in area, rather than volume. This approach is different from quantifying EAT volume on short-axis views and may not accurately reflect total EAT volume.

One important limitation of echocardiographic EAT is that it does not inform on the distribution of EAT, as can be carried out with CMR, but also computed tomography (CT).[5,16] This is important, as EAT volume is asymmetrically distributed around the heart and location of EAT may even be of greater relevance to HF than overall EAT volume.[5] In addition, CT also allows for EAT attenuation assessment which has been associated with coronary inflammation.[16]

Clinical implications

If one is interested in the amount of EAT in a patient, use of EAT thickness should be used with caution, because actual EAT volume may still vary considerably when estimated with EAT thickness. The modest correlation between EAT on echocardiography and EAT on CMR is also of limited value from a cost-effectiveness point of view, as this would mean that for precise quantification of EAT, individual patients should undergo expensive CMR imaging.

However, although the association between EAT on echocardiography and CMR was modest, it was still significant, meaning that measuring echocardiographic EAT thickness may still be useful as a research tool in larger datasets to investigate associations with cardiovascular disease.[9,17–19]

Because echocardiographic EAT is related to visceral fat,[6] which in turn is associated with worse outcomes in HFpEF, EAT thickness may also be used to estimate visceral adiposity. However, we did not specifically investigate the association between EAT thickness and visceral fat. This suggestion is therefore speculative in nature and further research is warranted.

Limitations

First, EAT on echocardiography may be difficult to assess and may lead to incorrect results. However, we verified the absence of pericardial effusion on CMR using T1 mapping but does represent a critical limitation in a clinical setting where CMR has not recently been performed. Second, the present study was performed in HF patients with LVEF $>40\%$, and the findings may not be applicable to other patient groups with a different amount of EAT. Third, it was not possible to compare our method of EAT measurement with the one proposed by Parisi *et al*., as this method requires non-standard views that were not available.[12] Fourth, the association between EAT and waist-circumference and visceral abdominal fat would have added to this manuscript. However, we did not have these measurements at our disposal.

Conclusions

There was a modest correlation between EAT volume on CMR and EAT thickness on echocardiography. Limited agreement between junior and senior observers for measuring echocardiographic EAT was observed. EAT thickness on echocardiography is limited in estimating EAT volume.

Conflict of interest

None declared.

Funding

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Supporting information

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

Table S1. Patient characteristics.

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