International Journal of Cardiology 286 (2019) 51–53

Contents lists available at ScienceDirect

International Journal of Cardiology

journal homepage: www.elsevier.com/locate/ijcard

Editorial

Epicardial adipose tissue in patients undergoing transcatheter aortic valve replacement: The not so innocent bystander?

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ARTICLE INFO

Article history:
Received 15 February 2019
Accepted 11 March 2019
Available online 14 March 2019

Epicardial adipose tissue (EAT) is a metabolically active adipose tissue located between the myocardium and visceral pericardium, and shares the same embryonic origin with omental and mesenteric fat [1]. There has been growing interest in EAT quantification in cardiovascular disease, including studies in coronary artery disease, arrhythmias, left atrial dysfunction and left ventricular diastolic dysfunction [2] (Fig. 1).

EAT can be assessed by transthoracic echocardiography, cardiac computed tomography (CT) and cardiac magnetic resonance imaging (CMR). Its ability to render the full volume of the heart and the higher spatial resolution make cardiac CT the first-choice imaging modality for EAT quantification. Pre-procedural assessment of EAT has been studied in electrophysiology, investigating the impact of EAT on the pathogenesis of arrhythmias, as well as post-ablation outcomes in atrial fibrillation and ventricular tachyarrhythmia [3]. In this issue of the *International Journal of Cardiology*, a single-center study reported the impact of EAT quantification from pre-procedural CT on early safety endpoint at 30 days, and 1, 2 and 3-year mortality in 503 patients undergoing transcatheter aortic valve replacement (TAVR) over a 7-year period [4]. Males had higher EAT volume than females (p: 0.003). Patients with higher EAT volumes were reported to have higher all-cause 1, 2 and 3-year mortality using several different binary cut-off values of EAT volume (cut-off of 100 mm^3: log-rank p: 0.002; hazard ratio (HR): 1.94, 95% confidence intervals (CI): 1.15–3.26; cut-off of 125 mm^3: log-rank p: 0.001; HR: 1.70, 95% CI: 1.06–2.68; cut-off of 130 mm^3: log-rank p: 0.001; HR: 1.69, 95% CI: 1.10–2.60) [4].

TAVR is an important treatment strategy not only for patients with symptomatic aortic stenosis (AS) at a prohibitive surgical risk, but also it is increasingly being considered a reasonable treatment option for intermediate surgical risk patients [5]. Taking the increasing applicability of TAVR in clinical practice into account, finding cost-effective ways of predicting outcomes without causing extra harm to the patient is paramount. Pre-procedural imaging with TAVR-protocol CT angiography is pivotal for procedural success and improving outcomes [6]. The authors deserve praise for extending the clinical investigation of EAT into the field of TAVR as a potential imaging marker to predict post-procedural outcomes. The large study cohort and the long follow-up period strengthen the study findings. Additionally, the authors have chosen EAT volumetric quantification by CT, which arguably is the current best imaging modality for this purpose. The patients in the study all underwent a pre-procedural contrast CT scan, therefore avoiding extra contrast or ionizing radiation.

Several issues must be considered when interpreting the study. First, different CT scanners with different scanning parameters and contrast protocols were used. The authors have already identified this as a study limitation. This highlights the current lack of standardized assessment of EAT quantification. The technical limitations include a lack of standardization on the contrast protocols, the threshold levels for epicardial fat quantification, and the cardiac phase used during image acquisition. Measured EAT volume has been shown to differ significantly between contrast enhanced and non-contrast CT studies. In order to prevent underestimation of EAT in contrast enhanced CT scans, adjusting the upper threshold for fatty tissue detection should be considered. Otherwise for a non-contrast CT, a typical fat attenuation range of −190 to −30 Hounsfield units (HU) has been used. Additionally, data are insufficient to determine the "normal" range of EAT volume in humans. Published EAT volume thresholds have varied from 100 mL to 125 mL [7].

Second, although the authors defined their fat definition threshold based on a previous study by Bucher et al. [8], the CT scanner and software used differed between the two studies. Therefore, a lack of standardized threshold values for EAT quantification limits the generalizability of the findings. Given this limitation, it should be noted that the authors commendably analysed several different cut-off values.

Taking the relationship of EAT with metabolic syndrome into account, the study could have been strengthened by including serum biomarkers, such as lipid levels, as this may potentially alter the results of logistic regression analyses. It has been previously shown that increased indexed visceral adipose tissue in obese patients was related with increased mortality after TAVR [9], whereas in the current study, non-indexed EAT values, rather than indexed EAT values were found

DOI of original article: https://doi.org/10.1016/j.ijcard.2019.01.068.
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https://doi.org/10.1016/j.ijcard.2019.03.019
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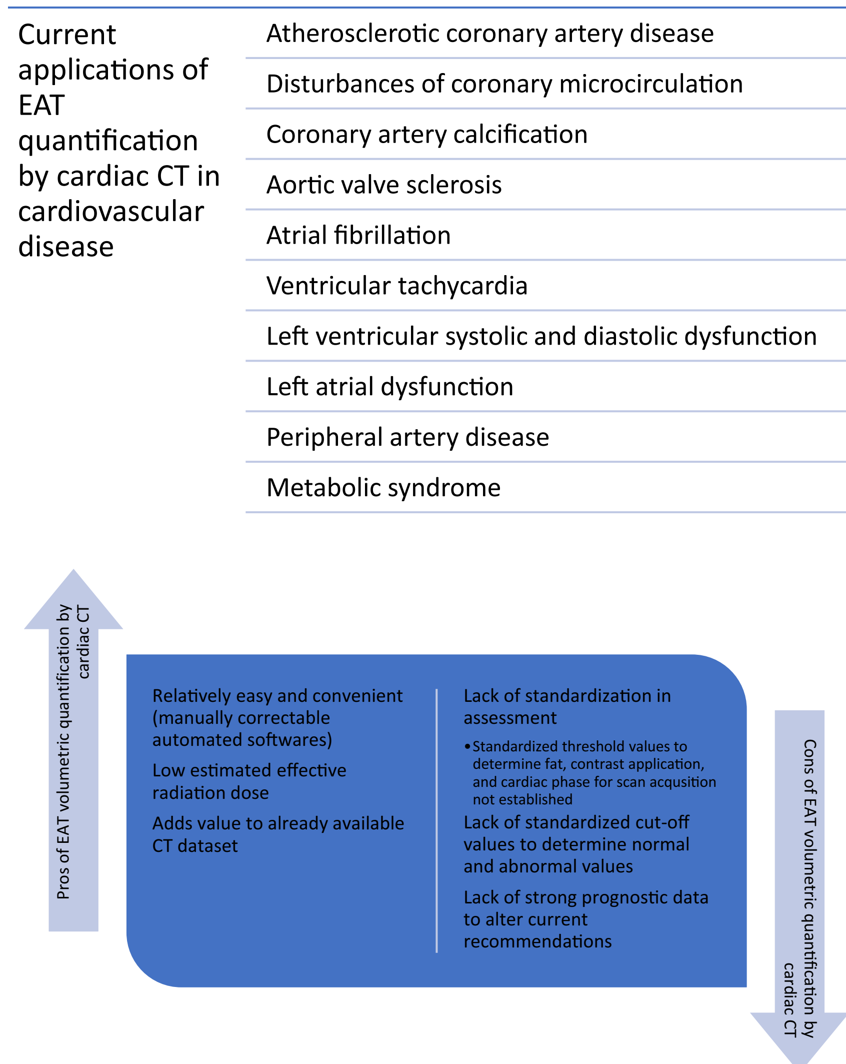

Fig. 1. Current applications of EAT assessment by cardiac CT in cardiovascular disease, as well as strengths and limitations of EAT volumetric quantification by cardiac CT.

to significantly predict adverse outcomes [4]. Clearly, discrepancies exist in the currently limited data. The authors proposed that patients with higher EAT volumes at baseline should be followed up more closely due to increased mortality post TAVR, however, it was unclear whether mortality at follow-up was due to cardiovascular, or non-cardiovascular causes.

Patients with severe AS undergoing surgical and medical treatments were not included in the study. It was therefore not possible to assess whether TAVR would still be a recommended treatment option in patients with severe AS and high EAT volumes, compared to surgery or medical therapy. The central clinical message of this study is therefore limited to potentially following up patients with higher EAT volumes after TAVR more closely in the post-procedural period. Future studies may investigate the impact of EAT volume in patients with severe AS undergoing surgical, transcatheter and medical treatments. Additionally, it would be interesting to assess if certain medical therapies may impact on EAT volume, and subsequently affect outcomes after TAVR.

Although some encouraging findings have been reported in terms of EAT quantification in risk stratification of coronary artery disease [10], there is still a long way to go before implementing routine EAT quantification into clinical practice. The data on EAT quantification in patients with severe AS are even more scarce. Should EAT be routinely quantified and reported in pre-procedural TAVR CT examinations, simply because it is part of the pre-procedural CT data? What are the mechanisms through which EAT exerts its impact on patient outcomes in the TAVR population? Clearly, further data are needed to clarify these questions.

Conflict of interest

The authors report no relationships that could be construed as a conflict of interest.

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