Epicardial fat thickness assessment by multi-slice computed tomography for predicting cardiac outcomes in patients undergoing transcatheter aortic valve implantation

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Abstract

Introduction: Chronic inflammation promotes aortic valve calcification. It is known that epicardial fat is a source of inflammation. The aim of this study was to investigate the relationship between epicardial fat thickness, cardiac conduction disorders and outcomes in patients undergoing transcatheter aortic valve implantation (TAVI).

Methods: During a three-year period, 45 patients with severe aortic stenosis who underwent TAVI were recruited to the study. Data were collected retrospectively. Epicardial fat was defined as the adipose tissue between the epicardium and the visceral pericardium. Mean epicardial fat thickness was determined by multi-slice computed tomography, which was performed before the procedure.

Results: The average thickness of epicardial fat was 13.06 ± 3.29 mm. This study failed to reveal a significant correlation between epicardial fat thickness and post-procedural left bundle branch block, right bundle branch block, paravalvular aortic regurgitation and pacemaker implantation rates (p > 0.05).

Conclusion: The results of this study failed to show a significant relationship between epicardial fat thickness, cardiac conduction disorders and outcomes, however further studies with larger sample numbers are required to explore the relationship.

Keywords: epicardial fat thickness, calcific aortic stenosis, transcatheter aortic valve implantation, multi-slice computed tomography

Epicardial fat is a metabolically active visceral fat that has paracrine and endocrine functions. It surrounds the heart between the pericardium and myocardium and can be found in highest concentration in the atrioventricular and interventricular grooves and in direct contact with the major coronary arteries and their branches. Epicardial fat may also act as an endocrine organ due to its adipocytokine production. Epicardial fat thicknesses and volumes can be accurately evaluated by non-invasive imaging modalities such as echocardiography, computed tomography (CT) or magnetic resonance imaging (MRI).

Recent studies indicate that epicardial fat may contribute to the progression of coronary atherosclerosis due to its proximity to the coronary arteries. Epicardial fat is independently associated with coronary atherosclerosis, adverse cardiovascular events and myocardial ischaemia. However, the exact underlying mechanisms are still not fully understood. The association between epicardial fat and atrial fibrillation has been demonstrated. Interestingly, an association between epicardial fat thickness and valvular heart disease has been found. The authors revealed that epicardial adipose tissue has an increased thickness in patients with calcific aortic stenosis.

The aim of this study was to evaluate the epicardial fat thickness for predicting cardiac conduction disorders and outcomes in patients undergoing transcatheter aortic valve implantation (TAVI). As far as we know, this is the first study to address the potential association between epicardial fat thickness and outcomes in patients undergoing TAVI.
Methods
We performed a retrospective analysis of 45 consecutive patients with severe symptomatic calcific aortic stenosis who underwent TAVI at Siyami Ersek Hospital from 2013 to 2015. Pre-procedural coronary angiography was performed to assess the need for revascularisation. Pre-TAVI assessment was initially done with transthoracic echocardiography, followed by an electrocardiography-gated, multi-slice CT study.

Severe aortic stenosis was defined as: peak transvalvular gradient of \( \geq 40 \) mmHg on transthoracic echocardiography or transoesophageal echocardiography or dobutamine stress echocardiography (DSE), and an aortic valve area \( \leq 1.0 \) cm\(^2\). Each case was considered by a multidisciplinary cardiovascular team. The patient was accepted for TAVI if he/she was deemed unable to undergo open-heart surgery due to excessive risk [Society of Thoracic Surgeons (STS) score \( \geq 10 \) or logistic EuroSCORE \( \geq 20 \)] or was unsuitable for surgical aortic valve replacement because of medical co-morbidities or because of technical considerations (for example if the patient had a calcified aorta or scarring from previous cardiac surgery).

TAVI was performed under general anaesthetic, or under local anaesthetic with sedation. The procedure was performed via the transfemoral approach. A temporary pacemaker was placed in the right ventricular apex, and a balloon valvuloplasty was performed under rapid ventricular pacing, followed by implantation of the valve. Electrocardiographic and echocardiographic parameters after TAVI were recorded.

The study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki as reflected in a priori approval by our institution's human research committee.

All CT examinations were performed with a 64-slice CT scanner (Toshiba Aquilion 64, Otawara, Japan). Image acquisition occurred using a detector collimation of \( 64 \times 0.5 \) mm, tube current of 120 kVp and rotation time of 400 msn. Scanning time varied between 5.7 and 8.4 seconds. Retrospective ECG gating was used for data reconstruction. Image reconstructions were performed at 70–80% RR intervals.

An intravenous dose of 100 ml non-ionic contrast agent Iopromide (Schering AG, Berlin, Germany) was administered at an infusion rate of 4 ml/s, followed by 30 ml saline infusion. Post-processing was performed on an Aquarius workstation (TeraRecon, Inc). All images were read by two experienced physicians. Intra- and inter-observer reproducibility for quantification of epicardial fat was greater than 0.95.

Epicardial fat was defined as the adipose tissue between the epicardium and the visceral pericardium. Epicardial fat tissue was identified with voxels between \(-30\) and \(-190\) Hounsfield units. Measurement was performed at the basal level of the short-axis images. Three measurements were performed at the superior, mid and inferior levels (75, 50 and 25% level of full length, respectively) of the right ventricle. The average of three separate measurements was used for the analysis\(^{10}\) (Fig. 1).

Results
The patient demographics and clinical characteristics are shown in Table 1. A total of 45 patients, including 37.8\% (\( n = 17 \)) male and 62.2\% (\( n = 28 \)) female were included in the study. The mean age of the study population was 79.07 ± 6.18 years (age range 60–89).

Baseline laboratory data characteristics are shown in Table 2. Two patients died during the procedure prior to valve implantation (4.4\%). The overall in-hospital mortality rate was 11.4\% (five patients).

Pre-procedural echocardiographic and CT data are shown in Table 3. The mean valve area was 0.78 ± 0.15 cm\(^2\). The mean STS score was 5.15 ± 3.54, and the mean logistic EuroSCORE was 11.91 ± 9.14. Seven patients (18.9\%) underwent permanent pacemaker implantation after the TAVI procedure, mostly due to high-degree atrioventricular block. The rate of stroke was 9.3\% (four patients).

Twelve patients (27.3\%) had minor vascular complications, according to the VARC definition.\(^{11}\) The average thickness of epicardial fat was 13.06 ± 3.29 mm. We did not find a significant correlation between epicardial fat thickness and post-procedural left bundle branch block (LBBB), right bundle branch block (RBBB), paravalvular aortic regurgitation and pacemaker implantation rates (\( p > 0.05 \)) (Tables 4, 5).

Statistical analysis
Statistical analyses were performed with NCSS (Number Cruncher statistical system) 2007 (NCSS, LLC Kaysville, Utah, USA). Data were analysed using descriptive statistical methods (mean, standard deviation, median, frequency and rate). The Kruskal–Wallis test was used for the comparison of normally distributed variables and two-group assessment was done with the Mann–Whitney U-test. Comparison of numerical data for before and after measurements was performed with the paired-samples test. The McNemar test was used for comparison of qualitative data. A \( p \)-value of < 0.05 was considered statistically significant. A 95\% confidence interval reflected a significance level of 0.05.
Discussion

This study is the first clinical study that evaluated the potential association between epicardial fat thickness and outcomes in patients undergoing TAVI. Our results failed to show a significant correlation between epicardial fat thickness and post-procedural LBBB, RBBB, paravalvular aortic regurgitation and pacemaker implantation rates.

Obesity is an important determinant of cardiovascular disease. Previous studies have revealed that epicardial fat is strongly correlated with other visceral fat deposits. Higher epicardial fat volumes independently predicted major adverse cardiac events in a healthy population. Epidemic fat thickness has also been...
found to be significantly correlated with the severity of coronary artery disease in patients with known coronary artery disease.\textsuperscript{14} Epicardial adipose tissue has been shown to be a source of inflammatory mediators such as interleukin (IL)-1β, IL-6 and tumour necrosis factor.\textsuperscript{15} Inflammatory mediators have been shown to play a role in the pathogenesis of calcific aortic stenosis as well.\textsuperscript{16,17}

A significant correlation between epicardial fat thickness and levels of pro-inflammatory cytokines and calcific aortic stenosis has been described.\textsuperscript{18} The authors indicated a strong association between epicardial fat thickness and aortic stenosis.\textsuperscript{9} Epicardial adipose tissue is an important source of several pro-inflammatory mediators and it may play a role in promoting aortic valve degeneration and calcification.

Mancio et al. reported that low body mass index (BMI) was paradoxically associated with aortic valve calcification and mortality in elderly aortic stenosis patients submitted for TAVI.\textsuperscript{20} Koifman et al. also concluded that patients with BMI < 20 kg/m\textsuperscript{2} were associated with a higher risk of mortality.\textsuperscript{19} Interestingly, in another study, the authors revealed that patients with larger epicardial adipose tissue volume had an increased all-cause one-, two- and three-year mortality rate after TAVI.\textsuperscript{21}

In our study, we aimed to evaluate the association of epicardial fat thickness with post-procedural outcomes of TAVI. To the best of our knowledge, our study is the first report to focus on the relationship between epicardial fat thickness and outcomes of patients who underwent TAVI. Our results failed to reveal any significant relationship.

The limitations of this study are the small sample size and retrospective design. There is no consensus on the gold standard of an in vivo quantification of epicardial adipose tissue. Volume measurement could be more accurate in the assessment of epicardial adipose tissue, however, epicardial fat thickness measurement is less time consuming and easier.

Conclusion
Larger trials are needed to evaluate whether epicardial fat thickness might have predictive properties and become a routine way of assessing cardiovascular risk in a clinical setting of TAVI.

References