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ORIGINAL ARTICLE

Human Epicardial Adipose Tissue Activin A Expression Predicts Occurrence of Postoperative Atrial Fibrillation in Patients Receiving Cardiac Surgery

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Background Activin A secreted by epicardial adipose tissue (EAT) plays a major role in the progress of atrial fibrosis. However, the potential of Activin A in predicting the occurrence of postoperative atrial fibrillation (POAF) has yet to be elucidated. We aimed to investigate the predicable value of Activin A expression in EAT on POAF.

Methods A total of 89 patients receiving cardiac surgery without atrial fibrillation (AF) history were enrolled in this study, including 49 patients with valvular heart disease (VHD) and 40 patients with non-valvular heart disease (NVHD). Activin A expression in EAT was determined by quantitative polymerase chain reaction (qPCR), while the thickness of EAT (EATT) was estimated by echocardiography. New onset POAF before discharge was documented.

Results Eventually 32 patients (36.0%) developed POAF, including 20 patients with VHD (40.8%) and 12 patients with NVHD (30.0%). Activin A expression was higher in POAF than sinus rhythm (SR) patients, whether for VHD or NVHD group (All $p < 0.001$). In general, Activin A expression predicted the occurrence of POAF with a sensitivity of 65.6% and specificity of 91.2% (AUC: 0.795; 95%CI: 0.693–0.897, $p < 0.001$). Subgroup analysis showed that EATT was not significant for the VHD group in predicting POAF ($p = 0.07$), while Activin A expression demonstrated a sensitivity of 60.0% and specificity of 89.7% (AUC: 0.745; 95%CI: 0.601–0.889, $p < 0.001$). Multivariate regression analysis showed that Activin A expression in EAT was an independent risk factor for POAF (OR: OR = 1.067, 95%CI:1.002–1.136, $p = 0.042$).

Conclusions Activin A expression in EAT is an independent risk factor for POAF, which can be used for prediction of POAF, especially for patients with VHD.

Keywords Epicardial adipose tissue • Activin A • Postoperative atrial fibrillation • Cardiac surgery

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Introduction

Postoperative atrial fibrillation (POAF), occurring in 30% to 50% of all patients receiving cardiac surgery [1], increases in-hospital mortality by 70% [2]. POAF is also associated with more strokes, longer hospital stay and worse prognosis [3]. However, the underlying mechanism of POAF remains elusive.

Atrial fibrosis, as a fundamental process reacting to inflammation and metabolic disorder, is considered as a key part of structural remodelling of atrial fibrillation (AF) [4]. Increasing evidence from clinical or experimental studies has proven that epicardial adipose tissue (EAT) is strongly associated with the incidence, maintenance and recurrence of AF, as well as atrial fibrosis [5,6]. Indicators such as the EAT volume identified by magnetic resonance imaging (MRI) and EAT thickness (EATT) measured by echocardiography were reported associated with AF severity and ablation results [7,8].

Nevertheless, the different roles which EAT plays in valvular heart disease (VHD) and non-valvualr heart disease (NVHD) has seldom been investigated. Activin A, an emerging cytokine, plays multiple roles in inflammation, fibrosis, and tissue repair [9]. Epicardial adipose tissue can significantly induce atrial fibrosis by secreting adipo-fibrokines such as Activin A [6]. Although the relationship between Activin A and atrial fibrosis has been validated, there is no previous study focussing on the Activin A expression in EAT and POAF. In this study, we investigated and compared the feasibility of EATT and Activin A in predicting the occurrence of POAF after cardiac surgery. We also conducted a subgroup analysis of VHD patients and NVHD patients. A univariate and multivariate regression analysis were accomplished to identify risk factors for POAF.

Methods

Subjects

Patients with isolated valve disease or coronary heart disease (CAD) to receive cardiac surgery in our centre were recruited into this study. All patients meeting the following criteria were excluded: 1. Patients who were younger than 18 years old or older than 80 years old; 2. Patients who had received cardiothoracic surgery before; 3. Patients who were in a critical condition with multiple organ dysfunctions; 4. Patients with AF history, whether it was paroxysmal, persistent or permanent; 5. Patients with combined VHD and NVHD; 6. Patients whose condition was complicated by cardiomyopathy, congenital heart disease, infection, or tumour.

From January 2016 to June 2017, a total of 89 patients receiving cardiac surgery at Changzheng Hospital, Second Military Medical University were enrolled in this study, including 49 patients with valvular heart disease receiving a valve operation and 40 patients with CAD receiving a coronary artery bypass graft (CABG), who were classified into VHD group and NVHD group accordingly. Demographic data including age, gender, body mass index (BMI), and smoking status were collected. Baseline characteristics including New York Heart Association (NYHA) function class, echocardiography results, comorbidities, using drugs were also recorded.

This study was approved by the Committee on Ethics of Biomedicine of the Second Military Medical University. This study also complied with the Declaration of Helsinki, and signed, written informed consent was obtained from all subjects.

Surgical Protocol

Standard median sternotomy was performed on all patients. After the establishment of cardiopulmonary bypass (CPB), standard valve operations were completed on patients with valvular heart disease, including aortic valve replacement (AVR), mitral valve repair (MVP) or mitral valve replacement (MVR), tricuspid valve repair (TVP) or tricuspid valve replacement (TVR), or double valve replacement (DVR). Patients with CAD were given standard median sternotomy on-pump CABG or off-pump CABG (OPCABG). The left internal mammary artery was dissected to bypass the left anterior descending artery, while major saphenous vein grafts were used to anastomose the narrowed marginal, diagonal or right coronary artery (RCA).

Study Endpoint

All patients were transferred into the cardiac intensive care unit (CICU) after surgery, with a continuous monitor on heart rhythm. After the assessment, the patients were transferred into cardiothoracic wards until discharge. During the hospitalisation, every 4-hour assessment of heart rhythm was conducted routinely. Postoperative atrial fibrillation was defined as new onset AF validated by 12-lead electrocardiography (ECG) after cardiac surgery and before discharge. Any AF documented by ECG was considered as the study endpoint. When the patient developed AF, they were treated with amiodarone to make the cardioversion. Other treatments including correcting electrolyte and acid-base imbalance, controlling heart rate and adjusting haemodynamics were conducted depending on the situation.

Sample Acquisition and Test

Adipose tissue was acquired during surgery, before cardiopulmonary bypass establishment. Epicardial adipose tissue next to the right atrium (average 0.5 g each) was collected from each patient. The biopsy was frozen immediately at $-80\,^{\circ}C$ for RNA isolation. TRIzol® reagent (Invitrogen, Carlsbad, CA, USA) was used to extract total RNA. The purity of the isolated RNA was assessed by measuring optical density at 260 nm and 280 nm. Reverse transcription was performed using a High-Capacity cDNA Reverse Transcription Kit (Applied Biosystems, Foster City, CA, USA), according to the manufacturer's instructions. SYBR® Premix Ex

Taq™ (Takara Bio, Tokyo, Japan) was used to prepare samples for quantitative real-time PCR. An ABI Prism 7900 Detector System (Applied Biosystems, Foster City, CA, USA) was used to perform quantitative real-time PCR. Primers were designed using Primer Premier 6.0 software (Premier Biosoft, Palo Alto, CA, USA). Primer sequences used were listed as follows: Activin A (*INHBA*), forward 5′-ACGGGTATGTGGAGATAGAGGA-3′, reverse 5′-GGACTTTTAGGAAGAGCCAGACT-3′. β-actin (*ACTB*), forward 5′-CATGTACGTTGCTATCCAGGC-3′, reverse 5′-CTCCTTAATGTCACGCACGAT-3′. Relative gene expression was calculated using threshold cycle value (C_T) and formula $2^{-\Delta\Delta CT}$.

Transthoracic Echocardiography

All patients were given transthoracic echocardiography (TTE) before the surgery using a 3.5-MHz transducer (Vivid 9, GE-Vingmed Ultrasound AS, Horten, Norway). The criteria set by the American Society of Echocardiography guidelines was followed during the examination. Routine measurements of left atrium diameter (LAD) and left ventricular ejection fraction (LVEF) were performed. LAD referred to the distance from the leading edge of the posterior aortic wall to the leading edge of the posterior LA wall in end-systole at the parasternal long-axis view, while the LVEF was calculated by Simpson method. According to a previous report [8], EATT was defined as the width of the hypoechoic space between the right ventricle and the visceral layer of the pericardium from the parasternal long-axis view in end-systole (Figure 1). At least three measurements of EATT in different cardiac cycles were conducted to get the mean value.

Statistics and Data Analysis

All data were analysed with SPSS 22.0 software (IBM, Armonk, NY, USA). Differences were considered significant when $p < 0.05$. Continuous data, when distributed normally, were expressed as mean ± standard deviation, while the categorical data were expressed as percentages. The demographical data and baseline characteristics of the POAF group and SR group were compared with Student's t-test and the chi-square test. EATT and Activin A expression were compared between POAF group and SR group by using Student's t-test. Receiver operating characteristic (ROC) curve analysis was used to evaluate the value of EATT and Activin A expression in predicting the occurrence the POAF. Cut-off value was determined when the Youden Index was highest. Univariate and multivariate logistic regression analysis was conducted to specify the risk factor for POAF. Variables with p value <0.3 in the univariate analysis or reported to be associated with AF would be included in multivariate analysis, when a "forward" pattern was chosen to select the variates. A p value <0.05 was considered as statistical significant.

Results

Patient Characteristics

A total of 32 patients (36.0%) developed POAF verified by ECG, including 20 patients with VHD (40.8%) and 12 patients with NVHD (30.0%). For the VHD group, the age of POAF patients was significantly higher than SR patients ($p = 0.0442$), and the LAD of POAF patients was much higher than SR patients ($p < 0.001$). There was no statistical difference between POAF patients and SR patients in other demographical data and baseline characteristics ($p > 0.05$), which is shown in Table 1. For the NVHD group, BMI appeared to be different between POAF patients and SR patients without statistical significance ($p = 0.08$). Similarly, the LAD of POAF patients was significantly higher than SR patients ($p < 0.001$). Also, other indicators showed no significant difference between two groups ($p > 0.05$). The results of the NVHD group are shown in Table 2.

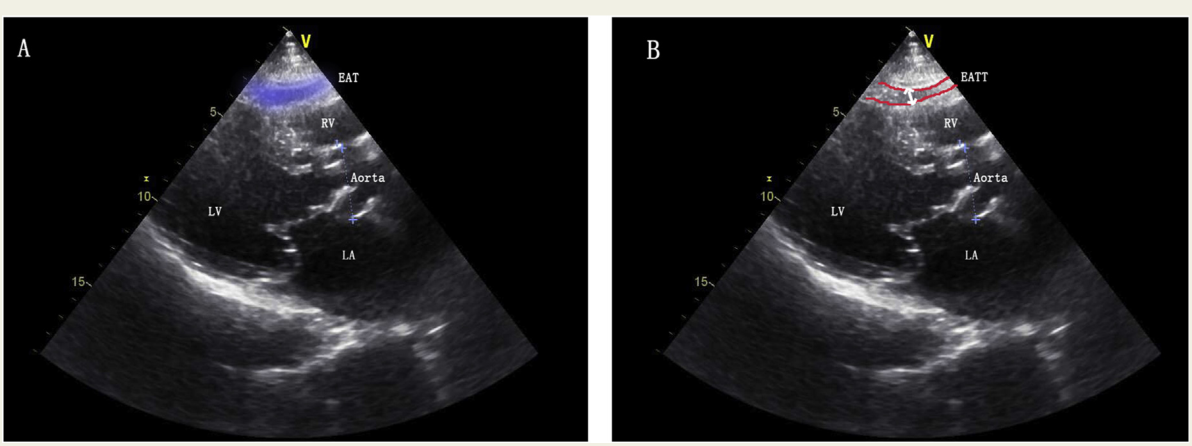

Figure 1 Typical examples of TTE measurement of EATT. A) EAT was tinted blue between the right ventricle and the visceral layer of the pericardium in parasternal long-axis view. B) EATT was defined as the distance between white lines. Abbreviations: TTE, transthoracic echocardiography; EATT, thickness of EAT; EAT, epicardial adipose tissue

Table 1 Patient characteristics of POAF and SR patients in VHD group.

Variables	SR (n = 29)	POAF (n = 20)	χ^2/t	P
Demographics				
Age(y)	55.8 ± 11.2	61.7 ± 6.8	2.092	0.042
Gender(%male)	13(44.8%)	10(50.0%)	0.127	0.721
BMI(kg/m^{-2})	22.4 ± 5.7	22.2 ± 4.2	0.150	0.881
Smoking	8(27.6%)	5(25.0%)	0.041	0.840
NYHA functional class			2.103	0.551
I	0(0)	1(5.0%)		
II	4(13.8%)	2(10.0%)		
III	16(55.2%)	9(45.0%)		
IV	9(31.0%)	8(40.0%)		
Echocardiography				
LVEF(%)	55.2 ± 5.9	55.0 ± 5.9	0.140	0.889
LAD (mm)	36.3 ± 3.1	41.7 ± 4.2	5.201	<0.001
Comorbidities				
Hypertension	6(20.7%)	4(20.0%)	0.003	0.953
Type 2 diabetes	5(17.2%)	4(20.0%)	0.060	0.806
Stroke	2 (6.9%)	1(5.0%)	0.074	0.785
COPD	4(13.8%)	2(10.0%)	0.158	0.691
Valve disease				
Mitral valve	23(79.3%)	16(80.0%)	0.003	0.953
Aortic valve	11(37.9%)	8(40.0%)	0.021	0.884
Tricuspid valve	21(72.4%)	13(65.0%)	0.306	0.580
Operation			1.463	0.833
AVR	5(17.2%)	3(15.0%)		
MVP/MVR	3(10.3%)	4(20.0%)		
TVP/TVR	1(3.4%)	1(5.0%)		
MVP/MVR + TVP	14(48.3%)	7(35.0%)		
DVR+ TVP	6(20.7%)	5(25.0%)		
Cause			2.084	0.353
Rheumatic	14(48.3%)	7(35.0%)		
Degenerative	15(51.7%)	12(60.0%)		
Congenital	0(0)	1(5.0%)		
Drugs				
β-blockers	19(65.5%)	14(70.0%)	0.108	0.742
ACEIs	4(13.8%)	2(10.0%)	0.158	0.691
CCBs	16(55.2%)	12(60.0%)	0.113	0.737

Abbreviations: BMI, body mass index; NYHA, New York Heart Association; LVEF, left ventricle ejection fraction; LAD, left atrial diameter; COPD, chronic obstructive pulmonary disease; MVR, mitral valve replacement; MVP, mitral valve repair; TVR, tricuspid valve replacement; TVP, tricuspid valve repair; DVR, double valve replacement; ACEIs, angiotensin converting enzyme inhibitors; CCBs, calcium channel blockers.

Table 2 Patient characteristics of POAF and SR patients in NVHD group.

Variables	SR (n = 28)	POAF (n = 12)	χ^2/t	P
Demographics				
Age(y)	56.2 ± 10.4	60.1 ± 5.19	1.203	0.237
Gender(%male)	15(53.6%)	7(58.3%)	0.077	0.781
BMI(kg/m^{-2})	20.6 ± 2.8	22.3 ± 2.7	1.799	0.080
Smoking	8(28.6%)	4 (33.3%)	0.091	0.763
NYHA functional class			0.469	0.926
I	6(21.4%)	3(25.0%)		
II	17(60.7%)	6(50.0%)		
III	3(10.7%)	2(16.7%)		
IV	2(7.1%)	1(8.3%)		
Echocardiography				
LVEF(%)	59.2 ± 5.9	57.8 ± 5.6	0.729	0.471
LAD (mm)	34.4 ± 4.2	42.5 ± 3.9	5.657	<0.001
Comorbidities				
Hypertension	8(28.6%)	4(33.3%)	0.091	0.763
Type 2 diabetes	6(21.4%)	3(25.0%)	0.061	0.804
Stroke	2(7.1%)	1(8.3%)	0.017	0.896
COPD	4(14.3%)	1(8.3%)	0.272	0.602
History				
Recent MI	5(17.9%)	2(16.7%)	0.008	0.928
RCA disease	11(39.3%)	6(50.0%)	0.395	0.530
Drugs				
β-blockers	19(67.9%)	8(66.7%)	0.005	0.941
ACEIs	9(32.1%)	5(41.7%)	0.335	0.563
CCBs	8(28.6%)	4(33.3%)	0.091	0.763
CABG				
Number of bypass grafts	2.2 ± 0.7	2.2 ± 0.8	0.048	0.962
OPCABG	13(46.4%)	6(50.0%)	0.043	0.836

Abbreviations: BMI, body mass index; NYHA, New York Heart Association; LVEF, left ventricle ejection fraction; LAD, left atrial diameter; COPD, chronic obstructive pulmonary disease; MI, myocardial infarction; RCA, right coronary artery; ACEIs, angiotensin converting enzyme inhibitors;

EATT and Activin A Expression

Thickness of EAT and Activin A expression of the VHD group and NVHD group are shown in Figure 2. For the VHD group, the EATT was 7.14 ± 1.14 mm of SR patients, while it was 7.62 ± 0.69 mm of POAF patients. There was no significant difference between POAF and SR patients in EATT ($p = 0.101$). The Activin A expression of the POAF group was significantly higher than SR patients (35.11 ± 15.57 vs 21.85 ± 11.26, $p = 0.034$). For NVHD group, EATT of POAF patients was higher than that of SR patients (7.61 ± 1.01 vs 6.11 ± 0.91, $p < 0.001$). Activin A expression was higher in POAF group than SR group (37.77 ± 15.00 vs 18.46 ± 8.60, $p = 0.018$).

ROC Curve

Receiver operating characteristic curve and its related results are demonstrated in Figure 3. For the VHD group, using a cut-off value of 6.54 mm, EATT predicted the occurrence of POAF with a sensitivity of 100% and specificity of 58.6%, and the area under the curve (AUC) was 0.653 (95%CI 0.498–

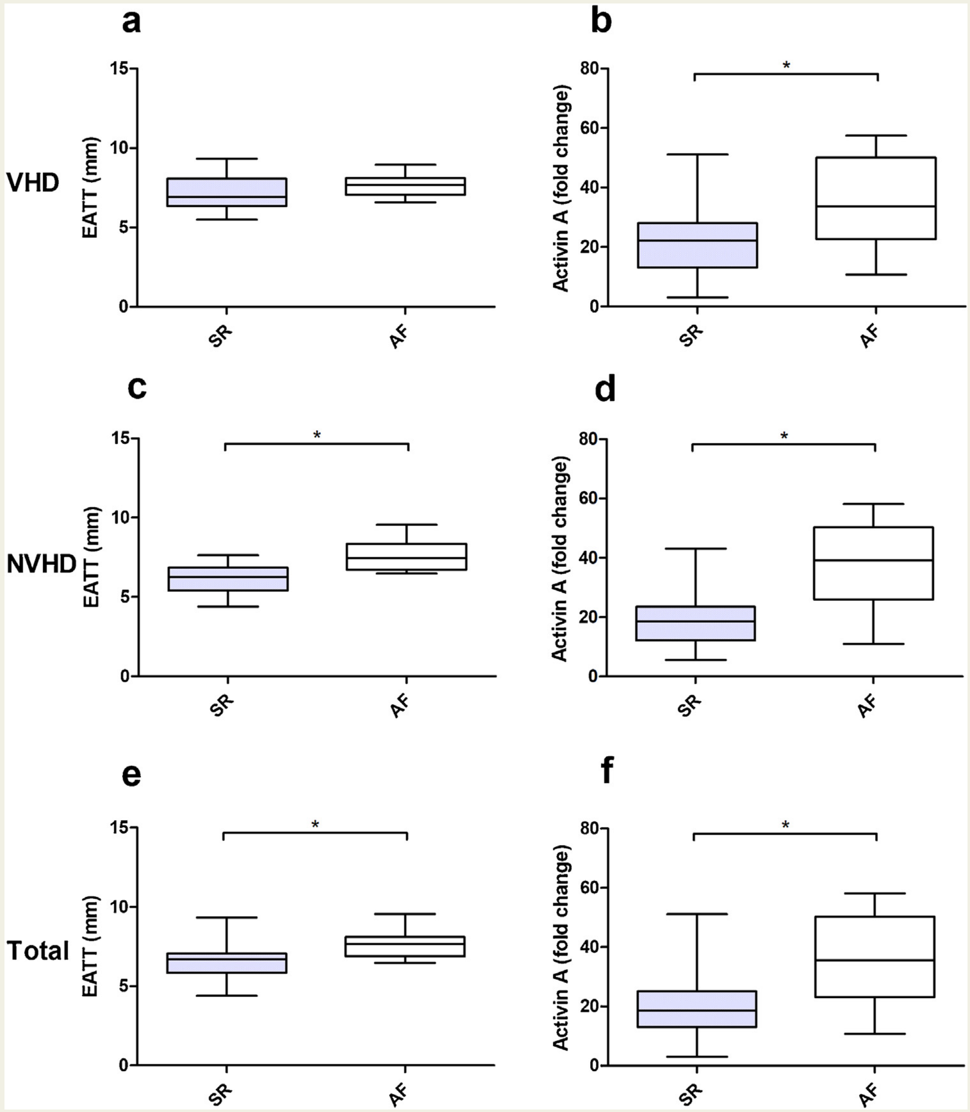

Figure 2 EATT and Activin A of POAF and SR patients in VHD, NVHD and total group, * $P < 0.05$.
Abbreviations: EATT, thickness of EAT; POAF, postoperative atrial fibrillation; SR, sinus rhythm; VHD, valvular heart disease; NVHD, non-valvular heart disease

0.809, $p = 0.070$). Activin A showed better results than EATT, with a sensitivity of 60.0% and specificity of 89.7% (cut-off value = 29.45, AUC = 0.745, 95%CI 0.601–0.889, $p = 0.004$). For the NVHD group, the sensitivity of EATT was 66.7%, while the specificity was 89.3% (cut-off value = 7.05 mm, AUC = 0.851, 95%CI 0.724–0.979, $p < 0.001$). Similarly, Activin A in NVHD group presented with a sensitivity of 75.0% and specificity of 92.9% (cut-off value = 30.20, AUC = 0.845, 95%CI 0.694–0.996, $p < 0.001$). When combining the two groups together, EATT showed a sensitivity of 68.8% and specificity of 78.9% (cut-off value = 7.21 mm, AUC = 0.762, 95%CI 0.663–0.860, $p < 0.001$), while Activin A showed a sensitivity of 65.6% and specificity of 91.2% (cut-off value = 29.45, AUC = 0.795, 95%CI 0.693–0.897, $p < 0.001$).

Logistic Regression Analysis

The risk factors for POAF were investigated using univariate and multivariate logistic regression models, which are presented in Table 3. Univariate analysis showed only LAD (OR = 1.152, 95%CI[1.276–1.790], $p < 0.001$), EATT (OR = 1.040,95%CI[1.003–1.077], $p = 0.032$), Acitvin A (OR = 1.076, 95%CI[1.023–1.131], $p = 0.004$) were risk factors for POAF. Further multivariate analysis included all variates with p value less than 0.3 (age, LAD, tricuspid valve disease, cause, EATT, Activin A) and all reported related risk factors (BMI, smoking, T2DM), when only LAD (OR = 1.542, 95%CI [1.171–2.030], $p = 0.002$), EATT(OR = 2.521,95%CI[1.060–5.999], $p = 0.037$), Activin A(OR = 1.067, 95%CI[1.002–1.136], $p = 0.042$) were left in the last model.

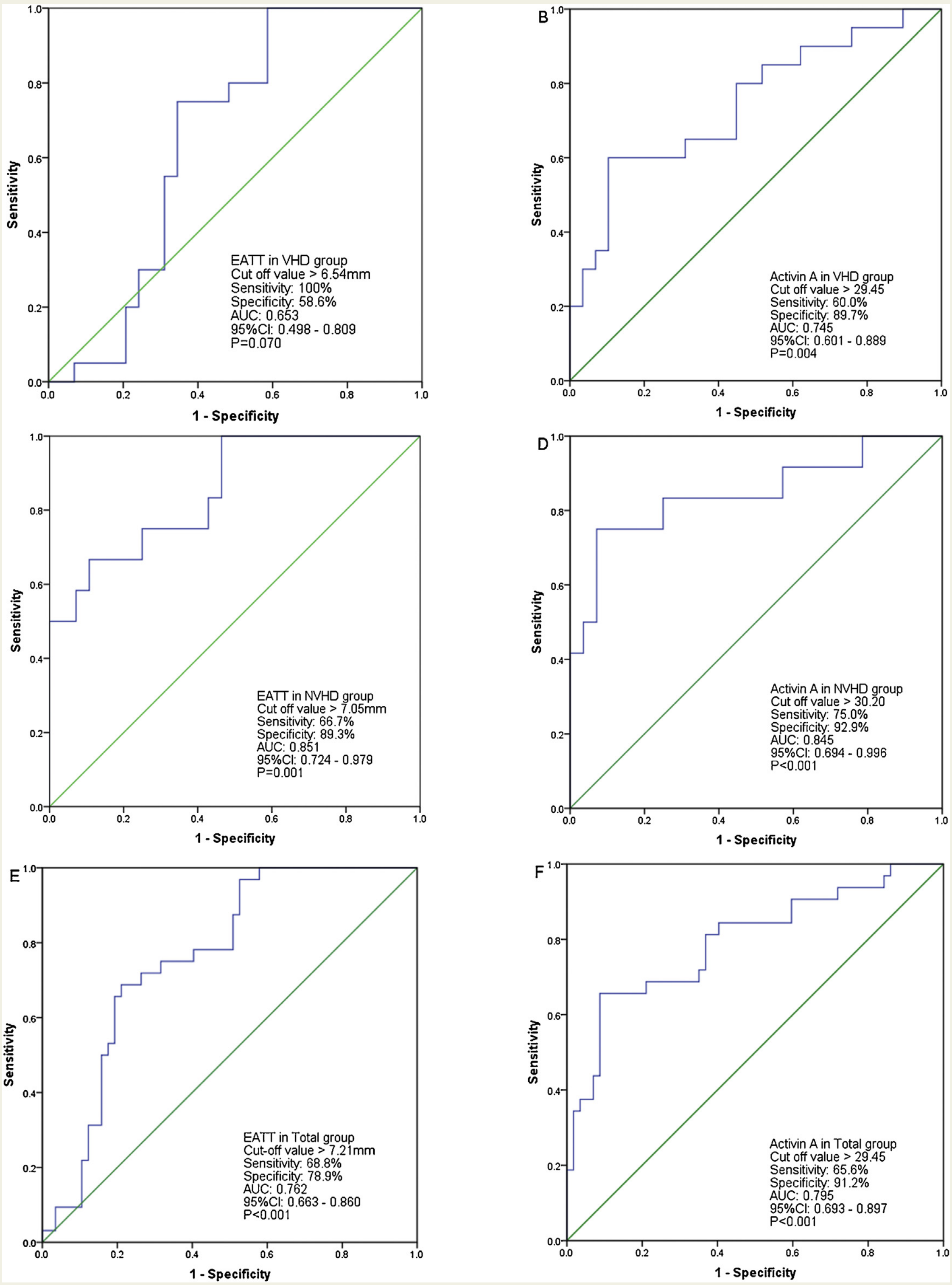

Figure 3 ROC curve and related results of EATT and Activin A in VHD, NVHD and total group.
Abbreviations: ROC, receiver operating characteristic; EATT, thickness of EAT; VHD, valvular heart disease; NVHD, non-valvular heart disease

Discussion

In this study, we investigated the EATT and Activin A expression in EAT of VHD patients and NVHD patients receiving cardiac surgery, and explored their potential in predicting POAF, with multivariate regression analysis conducted to study the risk factors for POAF. We found that EATT was significantly higher for POAF patients of the

Table 3 Univariate and multivariate logistic regression of POAF risk factors for overall patients.

Variables	Univariate Model			Multivariate Model		
	OR	95%CI	*P*	OR	95%CI	*P*
Demographics						
Age	1.029	0.984–1.077	0.214			
Gender(male/female)	1.174	0.493–2.793	0.717			
BMI	1.041	0.939–1.155	0.444			
Smoking	1.003	0.383–2.627	0.996			
NYHA functional class	1.157	0.737–1.815	0.527			
Echocardiography						
LVEF	0.968	0.901–1.041	0.385			
LAD	1.152	1.276–1.790	<0.001	1.542	1.171–2.030	0.002
Comorbidities						
Hypertension	1.024	0.376–2.789	0.963			
Type 2 diabetes	1.171	0.403–3.398	0.772			
Stroke	0.883	1.153–5.111	0.890			
COPD	0.634	0.156–2.580	0.524			
Valve disease						
Mitral valve	1.332	0.558–3.180	0.519			
Aortic valve	1.237	2.979	0.635			
Tricuspid valve	0.775	0.482–1.245	0.292			
Operation	1.084	0.853–1.378	0.508			
Cause	1.580	0.820–3.046	0.172			
Drugs						
β-blockers	1.429	0.598–3.412	0.422			
ACEIs	0.994	0.865–1.144	0.938			
CCBs	0.948	2.686	0.919			
EATT	1.040	1.003–1.077	0.032	2.521	1.060–5.999	0.037
Activin A	1.076	1.023–1.131	0.004	1.067	1.002–1.136	0.042

Abbreviations: BMI, body mass index; NYHA, New York Heart Association; LVEF, left ventricle ejection fraction; LAD, left atrial diameter; COPD, chronic obstructive pulmonary disease; ACEIs, angiotensin converting enzyme inhibitors; CCBs, calcium channel blockers.

NVHD group, while Activin A was higher for POAF patients of both the VHD and NVHD groups. Receiver operating characteristic curve also showed that Activin A expression in EAT was capable of predicting POAF, with superiority over EATT for VHD group. Regression analysis also validated the strong link between Activin A expression in EAT and the incidence of POAF. To our knowledge, this study firstly reported the relationship between Activin A expression in EAT and POAF.

Occurring in about 35% of cardiac surgery cases, POAF greatly increases treatment costs, hospital stay, incidence of complications as well as short-term mortality [10]. We reported a total rate of 36.0%, which conformed to previous reports. Notably, a subgroup analysis was conducted for VHD patients and NVHD patients, due to their disparity in AF mechanism. Within VHD patients, 20 out of 49 (40.8%) patients developed POAF, which was higher than that of NVHD patients (30.0%). The existence of valvular disease changes the haemodynamics, stretches the atrium, activates a variety of signalling pathways, and eventually leads to AF [11]. However, AF patients with or without VHD share a common pathological transformation of atrial remodelling, including changes in electrical, contractile, and structural properties [12].

Recent clinical and experimental studies indicated that EAT participated significantly in atrial remodelling. The association between AF and EAT was firstly reported by Chekakie et al. in 2010 [13], followed by sequential studies focussing on the clinical relevance of EAT and the role of EAT in AF. Postoperative AF and EAT has been investigated before by Villareal et al., who found that EAT volume estimated by computed tomographic (CT) scan can predicts the occurrence of POAF [14], with a sensitivity of 86% and specificity of 56%. However, VHD patients were not considered in his study and the CT scan was harmful and rather expensive for most of the patients. We adopted the EATT measured by TTE instead as the variable for both VHD and NVHD patients, when its effectiveness in predicting POAF within NVHD patients was confirmed in this study. The cutoff value was about 7 mm, with a sensitivity of 66.7% and specificity of 89.3%. Even though EATT wasn't applicable for VHD patients, the multivariate regression analysis showed than EATT was an independent risk factor for POAF, indicating the positive role of EAT in the development of POAF.

Activin A, an inflammation cytokine, was previously studied for its role in cancer [15], tissue repair [16] and heart failure [17]. It was reported that EAT induces atrial fibrosis through paracrine secretes of Activin A [6], which could activate the proliferation of cardiac fibroblasts and the production of collagen [18]. Atrial fibrosis is the fundamental process of AF, and an important risk factor for AF [4]. However, there are few studies focussing on AF and Activin A. We tried to associate Activin A expression in EAT with the incidence of POAF, and the results were promising, which showed that Activin A expression was significantly higher for POAF patients than SR patients in both the VHD and NVHD groups. Receiver operating characteristic curve also validated its feasibility in predicting POAF with AUC of 0.745 for the VHD group and 0.845 for the NVHD group. Univariate and multivariate regression showed that Activin A expression was independently associated with the incidence of POAF. Compared with EATT, Activin A expression was more significant in predicting POAF for VHD patients. We inferred that EATT was less efficient in VHD patients because the haemodynamic change caused by valve disease mitigated the role of EAT, while Activin A expression was not affected. Other reported risk factors were also considered in the regression model. However, some variables such as smoking, T2DM, and LVEF were not significant for POAF because of the relatively limited sample size, while variables such as age, LAD, and BMI remained significant.

Limitations

Some limitations of this study must be noted. First, the EAT samples must be acquired during an operation to examine the Activin A expression. Compared with non-invasive examinations such as CT or echocardiography, the test of Activin A can be time-consuming and sometimes risky for the patients. Also, the preservation of the EAT sample is critical for qPCR examination, which may affect the results. Second, despite the convenience and low cost of TTE, the two dimensional measurement of thickness may not be as accurate as the three dimensional estimation of EAT volume. Further study aiming to compare difference validity and accuracy between CT, MRI and TTE is needed. Last, in order to simplify the design, we only included valve disease and CAD, without congenital heart disease or cardiac tumour. The disease spectrum should be expanded in further studies.

Conclusions

In summary, a strong association between Activin A and POAF was first reported in this study, making it a promising biomarker in predicting POAF. A difference between VHD and NVHD patients in the relationship between EATT and POAF was also noted. This study found more evidence on the role of EAT and Acitvin A in the development of AF. However, the underlying mechanism of EAT and the generalisation of Activin A as a biomarker requires further investigation.

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Disclosure

None.

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

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