HEART RESEARCH

Openventio PUBLISHERS

ISSN 2377-164X Open Journal http://dx.doi.org/10.17140/HROJ-2-108

Research

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Volume 2 : Issue 1
Article Ref. #: 1000HROJ2108

Article History
Received: March 3rd, 2015
Accepted: April 10th, 2015
Published: April 13th, 2015

Citation
Xu Y, Tian B, Sharma D, Guo X, Wang X, Fu H. The related factors and clinical predictive value of left atrial spontaneous echo contrast in patient with nonvalvular chronic atrial fibrillation. *Heart Res Open J*. 2015; 2(1): 46-50. doi: 10.17140/HROJ-2-108

The Related Factors and Clinical Predictive Value of Left Atrial Spontaneous Echo Contrast in Patient with Nonvalvular Chronic Atrial Fibrillation

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ABSTRACT

Background: To investigate left atrial or left atrial appendage spontaneous echo by transesophageal echocardiography for clinical risk assessment, providing an important basis for guiding treatment and so on.
Methods: Select 113 atrial fibrillation patients who did not have formal warfarin treatment in 2011-2014 and did transesophageal echocardiography, after excluding substandard patients, 92 patients were divided into LASEC positive group (n=63) and negative group (n=29). Analyses the clinical features and echocardiographic parameters. Evaluate the diagnostic value with results of multivariate analysis.
Results: The study found a significant difference (P<0.05) between the two groups in the type of AF (permanent AF), hypertension, left atrial diameter, left ventricular diastolic function, among these factors, persistent atrial fibrillation, left atrial diameter >40 mm and hypertension have a extremely significant difference (P<0.01). CHA_2DS_2-VASC score, D-dimer in plasma have a predictive value for LASEC patients with atrial fibrillation.
Conclusion: Patients with persistent AF have a higher LASEC incidence, LASEC has clinical predictive value, there are certain guiding significance in clinical practice.

KEYWORDS: Left atrial spontaneous echo contrast; Atrial fibrillation; Transesophageal Echocardiography.

ABBREVIATIONS: AF: Atrial Fibrillation; LASEC: Left Atrial Spontaneous Echo Contrast; LA: Left Atrium; LAD: Left Atrial Diameter; LVEF: Left Ventricular Ejection Fraction; LAA: Left Atrial Appendage; ANOVA: Analysis of variance; CK: Creatinekinase; PTS: Prethrombotic state; AF: Atrial Fibrillation.

INTRODUCTION

Atrial Fibrillation (AF) is one of the most common arrhythmia encountered in clinical practice that has been associated with an increased mortality and morbidity from thromboembolic complications. Transesophageal echocardiography is frequently used to identify the presence of atrial thrombogenesis, which is a useful diagnostic method to exclude atrial thrombus in patients with atrial fibrillation before undergoing radiofrequency ablation.

Left Atrial Spontaneous Echo Contrast (LASEC), which is observed as a dynamic

ISSN 2377-164X Open Journal http://dx.doi.org/10.17140/HROJ-2-108

like-cloud echo signal by transthoracic and transesophageal echocardiography in the Left Atrium (LA) under the condition of non-radiography, has a varying density and morphological characters so it has no obvious contour.[1] Atrial fibrillation is the most common predisposing factor in the formation of LASEC, which is mainly related to a low left atrium blood flow velocity, blood stasis, the left atrium dysfunction and enlarged left atrium. In addition, it has been showed that AF has been associated with thromboembolic events. Some investigates showed that it was prone to LASEC when get atrial fibrillation means the change of hemodynamics and clotting mechanisms in the left atrium, which was considered prothrombotic state.[2] No doubt, the left atrial thrombus in AF patients by transesophageal echocardiography should be given anticoagulation therapy, however, some research showed that the cerebral embolism events likely up to 22% in AF patients with LASEC is an independent predictor of thromboembolic events,[3] but the formation mechanism of LASEC is not yet entirely clear, moreover, there is no an unified standard between the clinical laboratory indicators and anticoagulation therapy. This study was designed to investigate the relevance between the formation in AF patients with LASEC without formal anticoagulation therapy and multiple risk factors, and the clinical significance of the incidence of the left atrium or left atrial appendage thrombus in these patients, which could guide clinical anticoagulation therapy.

MATERIALS AND METHODS

General Information of Study Population

92 cases of patients with atrial fibrillation had no formal warfarin anticoagulation therapy, and they were all examined by transesophageal echocardiography. These selected patients were diagnosed atrial fibrillation by 24 hours dynamic electro-cardiogram, simultaneously; rheumatic valvular heart disease, congenital heart disease and prosthetic heart valve had been excluded. Among them, there are 50 males and 42 females, and mean age was 60.89±8.94 years old. According to whether LASEC existed or not, the two groups included positive and negative groups, and negative group patients had no thrombosis.

Study Protocol

Characteristics of patients were age, gender, type of atrial fibrillation, BMI, coronary heart disease, hypertension, diabetes, clinical laboratory indication and so on. CHA_2DS_2-VASC score was calculated based on risk factors. Philips iE color Doppler ultrasonography (Siemens Company, Bavaria, Germany) was used with multi-plane TEE probe, and the frequency was at 3.5~7.0 MHz. All patients signed informed consent, then TEE were performed after at least six hours of fasting, using oropharynx 2% lidocaine gel posterior pharyngeal anesthesia. In left lateral position, patients were checked by the probe to enter into a deep of 30~40 cm in esophagus, with a adjustable rear section in the left atrium to obtain the horizontal section images in pulmonary artery bifurcation levels of the Left Atrium (LA) and Left Atrial Appendage (LAA), including longitudinal section, aortic short axis section, atrial septal level and four-chamber section. The presence of SEC was diagnosed when dynamic and swirling intracavitary smoke-like echoes were detected, which were differentiated from white noise artifact by their characteristic swirling pattern and by careful attention to the gain settings.[4] At the same time 12-lead ECG was recording. All these patients underwent transthoracic echocardiography before TEE was performed.

Observed Indicators

Left Atrial Diameter (LAD), Left Ventricular Ejection Fraction (LVEF) blood velocity by mitral valve, mitral regurgitation, and diastolic function underwent transthoracic echocardiography before TEE was performed.

Statistical analysis

The statistical analyses were performed using SPSS 18.0. Metric variable were presented as mean±SD. Measurement data were analyzed by independent-samples T test. The comparisons of means between groups used Analysis of variance (ANOVA). Categorical data were analyzed using the chi-square (χ^2), and relation of data were evaluated using linear regression analysis. A p value <0.05 was considered statistically significant, and a p value <0.01 had extremely statistically significant.

RESULTS

Relation between CHA_2DS_2VASC score with risk of SEC

As summarized in Table 1, no statistically significant interaction by participant some variables, including age, BMI, abdominal girth, were detected. Also, some laboratory indicators were obtained with non significant, like Creatinekinase (CK), CK-MB, fibrinogen, blood lipid spectrum, etc, (Table 2). On the other hand, there were significant differences between the two groups in levels of D-dimer, LAD, CHA_2DS_2VASC, of which, the LAD had a extremely statistically significant (P<0.01), and a higher CHA_2DS_2VASC score was associated with higher risk of SEC (2.32±1,255 *vs.* 1.69±1.1, P=0.023).

The Possibility of the Presence of LA or LAA Thrombus in AF Patients

In the SEC group analysis, 44% patients had thrombogenesis (28/63) with a high morbidity that means the possibility of the presence of LA or LAA thrombus in AF patients was great. The association was stronger in patients with a decline of LV diastolic function than comparison group, which means that the decline of LV diastolic function might be one of risk factors. However, there was no statistically significant in some risk factors, like gender, CHD, DM and mitral regurgitation.

ISSN 2377-164X Open Journal http://dx.doi.org/10.17140/HROJ-2-108

Presence of SEC had a Positive Correlation with Hypertension

As summarized in Table 3, there was an extremely significant difference of hypertension between two groups (P=0.007), moreover, atrial fibrillation with hypertension classification was associated with higher risk of SEC, compared with no SEC patients, the presence of SEC had a positive correlation to hypertension classification (P<0.005).

Parameter	Group with SEC(n=63)	Group without SEC(n=29)	t	P
Age	61.41±8.998	60.65±8.975	-0.379	0.706
BMI	26.43±3.78	24.92±3.29	-1.848	0.068
Abdominal Girth	84.52±10.4	84.31±7.865	-0.098	0.922
Serum creatinine	72.74±17.75	69.71±14.71	-0.802	0.425
CK	81±52.85	63.68±26.63	-1.667	0.099
CKMB	11.876±5.11	10.57±4.3	-1.19	0.237
D-dimer	0.43±0.47	0.22±0.157	-2.28	0.025▲
Fobrinogen	2.87±0.65	2.99±0.76	0.806	0.422
WBC	5.95±1.28	6.21±1.28	0.896	0.372
RBC	4.46±0.47	4.59±0.46	1.275	0.206
PLT	207.05±31.27	219.69±47.2	1.524	0.131
HCT	0.412±0.043	0.419±0.037	0.724	0.471
A/G	1.69±0.25	1.62±0.2	-1.376	0.172
TC	4.57±1.03	4.84±1.44	1.031	0.305
TG	1.7±0.848	1.72±1.22	0.07	0.945
LDL	2.87±0.817	2.98±0.911	0.568	0.571
HDL	1.05±0.28	1.13±0.28	1.166	0.247
LAD	43.73±6	37.7±5.38	-4.57	0.000▲
LVEF	59.24±6.27	59.99±5.93	0.543	0.589
MV-velocity	96.72±22.18	89.02±15.7	-1.68	0.096
CHA_2DS_2-VASC	2.32±1,255	1.69±1.1	-2.31	0.023▲

Table 1: General Characteristics of study population in two groups ($\bar{\chi}$±s, T test).

Parameter	0 class (n=27)	1 class (n=5)	2 class (n=29)	3 class (n=31)	P
Positive group (n=63)	13(48.15%)	1(20%)	26(89.6%)	23(74.19%)	P<0.005▲
Negative (n-29)	14(51.85%)	4(80%)	3(10.34%)	8 (25.8%)	

Table 2: Correlation analysis between severity of hypertension and SEC.

Parameter	Group with SEC (n=63)	Group without SEC (n=29)	chi-square value	P
Gender(femal)	26 (41.2%)	16 (55%)	1.547	0.214
CHD	29 (46%)	10 (34.4%)	1.085	0.298
Hypertension	50 (79.3%)	15 (51.7%)	7.317	0.007▲
Diabetes mellitus	14 (22.2%)	7 (24%)	0.041	0.839
LAD>40 mm	45 (73%)	7 (24%)	18.07	0.000▲
permanent AF	21 (33%)	1 (3.4 %)	9.748	0.002▲
mitral regurgitation	17 (26.9%)	7 (24.1%)	0.083	0.773
decline of LVDF	24 (38%)	18 (62%)	4.6	0.032▲

Table 3: The comparison of risk factors between two groups (χ^2 test).

DISCUSSION

In the present study, patients with SEC had thrombogenesis with a high morbidity in LA or LAA by TEE examination. There were statistical significance in presence of SEC with respect to permanent AF, hypertension, LAD >40 mm, decline of LV diastolic function. While CHA_2DS_2-VASC score and D-dimer had a predictive value to the formation of SEC.

Numerous clinical and animal experiments show that the formation of SEC was usual accompanied by thrombus and thrombogenesis almost corresponded with blood stasis. Previous studies showed that SEC could reflect hypercoagulability in LA blood,[5] which was called Prethrombotic state (PTS). PTS is a pathological process about blood coagulation fibrinolytic system involved in many factors and it is prone to cause hematological change to have a high risk for thromboembolism which increases blood coagulation, and tiny thrombosis that can increase the occurrence of thromboembolism has formed virtually with no positive presence by imageological examination. If intervention and identification are taken earlier, it may avoid thromboembolic events. However, currently, there is no uniform diagnostic criteria for PTS. D-dimer, as a maker of fibrin that has a procedure of product and degradation reflected PTS by someone, which has already reflected a slightly pathological change in blood coagulation fibrinolytic system, is quite sensitive and specificity.[6] The level of D-dimer changes has already signed thrombogenesis or thrombolysis.[7] In this study, D-dimer was found a certain predictive value to support above views, but there were no other PTS specific molecular markers, which cannot be assessed a higher predictive value of clinical laboratory indicators.

The study found that there was an extremely significant difference of hypertension between two groups (P=0.007), moreover, the presence of SEC had a positive correlation to hypertension classification. Hypertension was the most important risk factor in Nonvalvular atrial fibrillation patients,[8] and the chronic hypertension impairs myocardial contractility, then the increased left ventricular diastolic pressure overload leads to elevation of the left atrial pressure, which causes decompensated LA enlargement, thus bloodstream slows down to result in blood stasis, sequentially Red Blood Cell (RBC) makes conglutination and aggregation to form local hypercoagulable state. Blood stasis in LA or LAA is one of the important mechanisms of LASEC formation. Our study found that incidence rate of LASEC had a positive correlation to hypertension classification that means hypertension was same as the main risk factor in LASEC patients.

The CHA_2DS_2-VASc score was calculated from the sum of risk predictors of congestive heart failure; hypertension; age ≥75 years; type 2 diabetes; previous stroke, TIA, or thromboembolism ; vascular disease; and sex category. Score of ≥2 means high-risk, score of 1 means moderate risk, low risk score is 0. The $CHADS_2$ and CHA_2DS_2-VASc scores are originally formulated for risk assessment of stroke in patients with

non-valvular Atrial Fibrillation (AF). A recent study found that CHA_2DS_2-VASC had better discrimination than $CHADS_2$ for predicting risk for thromboembolism in atrial fibrillation,[9] and the CHA_2DS_2-VASc score is believed to have better prognostic predictive value for thrombotic events in low-risk patients. In this study, there was statistical significant difference of two groups assessed by CHA_2DS_2-VASc score, which means the higher risk of stroke in the group with LASEC, indicating CHA_2DS_2-VASc score that could apply to AF patients with LASEC, and it perhaps was regarded as a routine evalution system to predict stroke. CHA_2DS_2-VASC score is also a risk index for predicting stroke in patients with SEC, and not only it contributes to identify PTS timely, but also it guides valid anticoagulation therapy to prevent serious thromboembolism complication.

In this study, the indices to diagnose left ventricular diastolic function was spectral tissue doppler imaging of the lateral mitral annulus early diastolic velocity (e) / late diastolic velocity (a) [e/a], or pulsed-wave doppler recording of early diastolic mitral inflow velocity (E) / e [E/e], which was significantly different (P =0.032). Doukky R, et al.[10] found that the diastolic function indices E:e' and e' velocity were independently associated with LAAT in Nonvalvular AF patients and might help identify patients at risk for LAAT, which was coincided with this study that the diastolic function indicate also predicted SEC independently.

It has been reported that 85% patients with thromboembolism had LASEC or AF. The earliest study was Daniel, et al.[11] that they found LA thrombogenesis usually existed with LASEC, and a low thrombotic incidence in patients without SEC through the study of 52 patients with severe mitral stenosis, thus SEC was considered as a predictive index before MS or prosthetic heart valve surgery. Takayuki, et al.[12] divided 84 AF patients with SEC from anticoagulant group and non- anticoagulant group, after 8~14 weeks follow-up, there was a statistical significant difference that the former incidence of cerebral embolism was 0%, the latter was 11.9%, which suggested that LASEC patients were high risk group. In addition, fresh LA thrombus is easy to fall off or dissolve by fibrinolysin without visualized place or size by ultrasonic probe, therefore, LASEC could get a long-time existence to have a higher prediction of stroke, and it also prompts clinicists to take anticoagulation therapy to prevent thrombogenesis.

CONCLUSION

LASEC could get a long-time existence to have a higher prediction of stroke, and it also prompts clinicists to take anticoagulation therapy to prevent thrombogenesis.

ACKNOWLEDGEMENTS

Dr. Xu is the guarantor for this article, and takes responsibility for the integrity of the work as a whole.

FUNDING

Supported in part by grants from foundation and ministry of health of Tian Jin.

CONFLICTS OF INTEREST: None declared.

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