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Mitral annular tissue velocity in the diagnosis of coronary artery disease

L. SUN, C. MA[1], S. LIU[1], L. ZOU, D. JIA

Department of Cardiology, First Affiliated Hospital of China Medical University, Shenyang, Liaoning, China
[1]Department of Cardiac Function, First Affiliated Hospital of China Medical University, Shenyang, Liaoning, China

Abstract. – OBJECTIVE: Non-invasive methods of coronary disease detection are immediately needed. Recent work suggested that mitral annular tissue velocity measurements could be helpful for assessing left ventricular function. We aim to determine the effect of coronary artery lesion on left ventricular function using tissue Doppler imaging (TDI), and to discuss the role of mitral annular tissue velocity in the diagnosis of coronary heart disease (CHD).

PATIENTS AND METHODS: Coronary angiographic examinations were conducted for 68 patients with suspected CHD. Left ventricular ejection fraction (LVEF), early diastolic mitral flow velocity E, late diastolic mitral flow velocity A, mean systolic (Sa) and mean early diastolic velocity (Ea) of the septal and lateral mitral annulus were measured before the angiographic examination. Patients were grouped according to the number of branches with ≥ 50% stenosis. The control group has 15 individuals. The remaining 53 patients with stenosis in 1, 2 and 3 branches were grouped into 1-Branch, 2-Branch, 3-Branch-Light-Condition and 3-Branch-Heavy-Condition groups, respectively. No significant differences in the other general health parameters of the patients were found.

RESULTS: There was no significant difference in LVEF and E/A but in Sa, Ea and E/Ea values between CHD and non-CHD patients. The E/Ea value was significantly elevated in CHD patients, aggravated by this pathological condition. The area bounded by the ROC (receiver operating characteristic) curve of E/Ea is the largest. The sensitivity and specificity of using E/Ea > 8.34 as the diagnostic criterion to pinpoint CHD were 77.4% and 100%, respectively.

CONCLUSIONS: E/Ea is a good indicator of diastolic function and can be useful to diagnose CHD.

Key Words:
Tissue Doppler imaging, Mitral annular velocity, Coronary disease, Diastolic function.

Introduction

Coronary angiography is widely recognized as the gold standard for the diagnosis of coronary heart disease (CHD)[1]. However, this technique is an invasive examination that requires advanced technology and operating conditions, limiting its application. Many researchers have focused on adapting other methods to diagnose coronary heart disease[2-6]. Echocardiography is a simple screening method with good reproducibility[7] that emphasizes the evaluation of cardiac function. Patients with coronary heart disease do not get adequate blood supply to the heart, which gradually leads to declined cardiac function. This is a significant difference between CHD and non-coronary heart disease[8]. In recent years, studies have shown that assessment of mitral annular velocity by tissue Doppler imaging (TDI) can be used to evaluate left ventricular function[9,10]. In this study we have observed the effect of coronary artery lesion on left ventricular function by mitral annular tissue velocity and assessed a variety of indicators for their effectiveness as diagnostic indicators of CHD.

Patients and Methods

Study Subjects

Study subjects included 68 patients who were hospitalized between January 2008 and December 2009 due to possible CHD at the Department of Cardiology of the First Affiliated Hospital of China Medical University. Among them, 43 were male and 25 were female. Ages ranged from 30 to 79 years old. Exclusion criteria used were: primary cardiomyopathy, heart valve disease, con-

Corresponding Author: Dalin Jia, MD; e-mail: jiadl2001@163.com

genital heart disease, persistent atrial fibrillation, severe heart failure, history of coronary intervention or coronary artery bypass surgery. Informed consent was obtained from all patients prior to administration of coronary angiography. The criteria for CHD used in this study was observation of coronary artery diameter stenosis ≥ 50%. After coronary angiographic examination, 15 cases of non-coronary heart disease were found and categorized as the control group. The remaining 53 cases had CHD. Patients with coronary disease were further divided into groups according to the number of branches with lesions: 13 cases with lesions in one branch (Group 1-Branch), 16 cases with lesions in two branches (Group 2-Branch) and 24 cases with lesions in 3 branches. Of those with lesions in 3 branches, 13 patients with stenosis greater than 75% in all 3 branches and without any collateral circulation were categorized as the 3-Branch-Heavy-Condition group, and the remaining 11 were categorized as the 3-Branch-Light-Condition group. All patients underwent two-dimensional and pulsed Doppler echocardiography and TDI inspection before angiography.

Methods

Philips IE33 Ultrasound Machine was used to perform the examinations. S 5-1 probes were used and the probe frequency was 1-5 MHz. Two-dimensional echocardiography was performed under the left lateral decubitus position. Via the apical four-chamber view method, early diastolic mitral flow velocity E and late diastolic mitral flow velocity A were measured. Left ventricular ejection fraction (LVEF) was obtained by the biplane Simpson's method. We switched to the TDI process with a frame rate of 124-142 fps. The myocardial motion direction was made as parallel as possible to the beam direction. In the apical four-chamber view, peak systolic velocity S and peak early diastolic velocity E of septal and lateral mitral annulus were measured. Mean systolic and mean early diastolic velocities of the septal and lateral mitral annulus were denoted as Sa and Ea. All the ultrasound data were sampled from 3 cardiac cycles and the mean value was calculated.

Statistical Analysis

All statistical analysis of the data was performed using the SPSS15.0 software (SPSS Inc., Chicago, IL, USA). Quantitative data were presented as mean ± standard deviation (± s). Comparison of means between multiple groups was conducted by analysis of variance and F test. Comparison of means between two groups was performed by independent sample t-test. Count data were compared using χ^2 test. $p < 0.05$ was considered to be statistically significant.

Results

Gender, age, hypertension and history of diabetes were compared between the groups and no significant differences were found. Heart rate and the functional indicators LVEF and E/A value, which were obtained by two-dimensional echocardiography, were not statistically different between the groups. There was no significant discrepancy in the number of cases with an E/A < 1 between these groups. The results are shown in Table I.

Table I. Comparison of general information and examination results from 2D echocardiography.

	Control	1-Branch	2-Branch	3-Branch-light-condition	3-Branch-heavy-condition	p value
Number of cases	15	13	16	11	13	——
Sex (Male/Female)	6/9	10/3	12/4	7/4	8/5	>0.05
Age (years)	59 ± 8	59 ± 13	60 ± 11	63 ± 7	66 ± 10	>0.05
Heart rate (beats/min)	72 ± 10	68 ± 13	74 ± 10	70 ± 10	70 ± 9	>0.05
Hypertension (number of cases)	4	3	7	6	9	>0.05
Diabetes (Number of cases)	2	2	4	1	4	>0.05
LVEF (%)	62 ± 5	57 ± 7	57 ± 6	58 ± 7	61 ± 8	>0.05
E/A value	0.88 ± 0.23	0.88 ± 0.37	0.79 ± 0.23	0.90 ± 0.30	0.93 ± 0.39	>0.05
E/A<1 (number of cases)	8	9	13	8	9	>0.05

Table II. Comparison of mitral annular tissue velocity ($\bar{x} \pm s$, cm/s).

	Sa	Ea	E/Ea
Control	9.76 ± 1.72	8.46 ± 1.15	7.67 ± 0.63
CHD	8.38 ± 1.91*	7.11 ± 1.69**	10.61 ± 3.08***
1-Branch	8.87 ± 1.93	7.29 ± 2.31	9.68 ± 1.82**
2-Branch	7.99 ± 1.28**	7.10 ± 1.61*	10.32 ± 3.19**
3-Branch-Light-Condition	8.22 ± 1.60*	7.14 ± 1.45*	10.86 ± 3.28**
3-Branch-Heavy-Condition	8.52 ± 2.69	6.91 ± 1.42**	11.67 ± 3.69**

Note: All pathological groups were compared to the control group, $^{*}p < 0.05$, $^{**}p < 0.01$, $^{***}p < 0.001$.

Evaluation of Left Ventricular Systolic and Diastolic Function by Mitral Annular Tissue Velocity

As compared to the control group, the CHD group had a significantly lower Sa and Ea, and the E/Ea was significantly elevated. Elevated E/Ea was consistent even in the least severely affected CHD patients with stenosis in 1 branch (Table II). Based on the subgrouping of the CHD patients, the E/Ea value positively correlated with a more aggravated disease state (Figure 1).

The Role of Mitral Annular Tissue Velocity in the Diagnosis of Coronary Artery Disease

Using coronary angiography as the gold standard, receiver operating characteristic (ROC) curves of Sa, Ea and E/Ea were plotted to diagnose the CHD. The largest area bounded by the E/Ea curve was 0.858. The optimal boundary point on the upper left corner of this curve indicated that the sensitivity and specificity of using a value of E/Ea > 8.34 to diagnose CHD were 77.4% and 100%, respectively (Figure 2).

Discussion

The two-dimensional echocardiogram is a basic method used to effectively evaluate cardiac function. Two indicators, LVEF and E/A, were used in the 2D echocardiogram to evaluate systolic and diastolic function of the left ventricle. However, precise reproducibility of LVEF is difficult to achieve. LVEF is determined by measuring the end systolic and end diastolic vol-

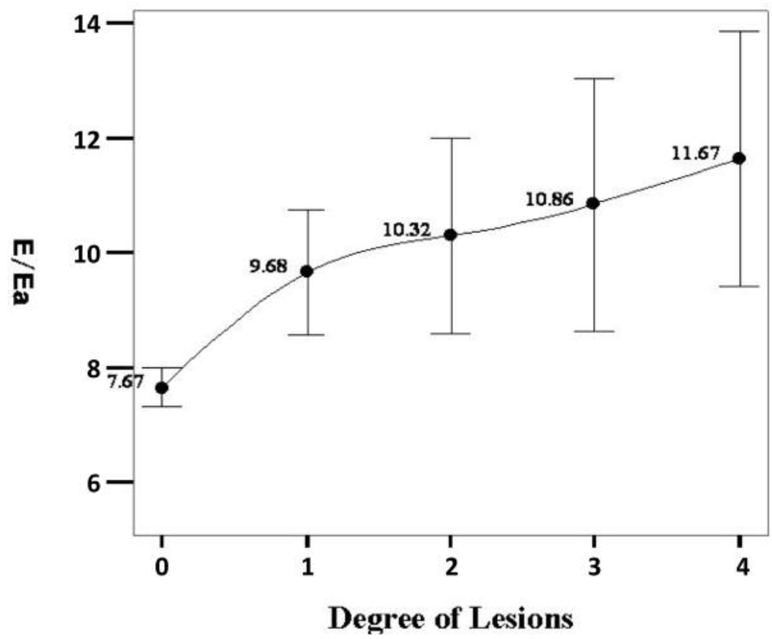

Figure 1. Comparison of E/Ea in different coronary artery lesions. 0, 1, 2, 3, 4 represented the control group, 1-Branch, 2-Branch, 3-Branch-Light-Condition, 3-Branch-Heavy-Condition, respectively. The error bars show a 95% confidence interval.

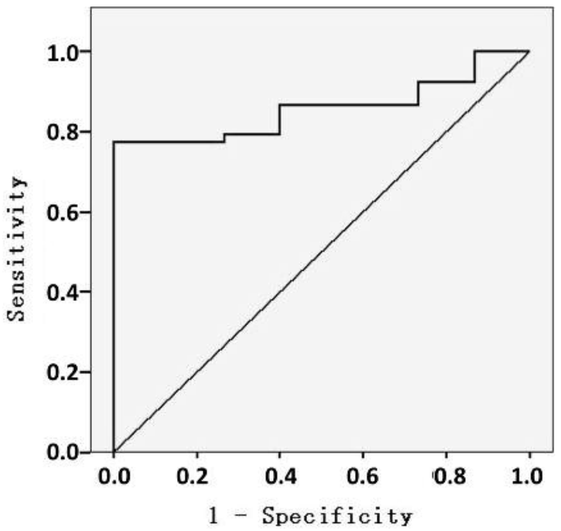

Figure 2. Receiver operating characteristic curve of E/Ea. The area bounded by the curve was the largest as shown. The optimal boundary point on the upper left corner of this curve indicated that the sensitivity and specificity of using a value of E/Ea > 8.34 to diagnose CHD were 77.4% and 100%, respectively.

umes on an artificial 2D plane. This procedure is hard to repeat and a flat plane does not sufficiently represent a 3D structure. Even using the biplane method, in the presence of irregularities in shape such as ventricular aneurysm, measurement results are not very accurate. Normally, ventricular diastolic filling was completed actively by relying mainly on the pressure gradient between the atrium and the ventricle, which was formed in the early diastolic phrase. At this moment E/A > 1. When the ventricular diastolic function undergoes a mild fall, left ventricular relaxation is delayed and the atrioventricular pressure gradient that forms during the early ventricular diastolic phase will decrease. Such a reduction leads to an increase in atrial pressure, which will be reflected by a decreased peak E resulting in an E/A < 1. When ventricular diastolic function declines further, the ventricular muscle becomes stiff and compliance reduces. This will produce a sharp increase in E and a value for E/A > 1 will be observed, which is a phenomenon called pseudo-normalization[11]. For patients with persistent atrial fibrillation, the peak A will disappear and thus this method is not applicable. Moreover, mitral annular blood flow is subject to the influence of multiple factors such as age, preload and cardiac contractile function[12-14]. Therefore, it is occasionally difficult to appropriately assess diastolic function by analyzing E/A values as greater than or less than 1. In this study, we were unable to differentiate CHD patients from the control group using the LVEF and E/A indicators.

TDI can quantify myocardial velocities and times, and its use has increased widely in recent years. Analysis of mitral annulus movement is being considered as a novel method to assess overall cardiac function[15,16]. Since Sa is positively correlated with LVEF, it can be used as a new indicator of ventricular systolic function[17]. Ea reflects left ventricular relaxation: it decreases as left ventricular diastolic function declines, and is not heavily affected by cardiac preload or systolic function. Using Ea, there is the added advantage that there is no issue of pseudo-normalization, making the Ea parameter a more accurate indicator than the traditionally used parameter E[18,19]. Some research studies concluded that use of the E/Ea ratio would be superior to Ea alone due to findings showing that this value correlates closely with left atrial pressure, left ventricular filling pressure and pulmonary wedge pressure[20-22]. E/Ea>15 not only reflects decreased diastolic function, but also suggests poor prognosis for patients with CHD[23,24].

The exact location of myocardial injury is difficult to ascertain due to the variety of coronary myocardial lesions involving different cardiac muscles. In order to be able to apply this diagnostic method to all different cardiac conditions, taking measurements of the mitral annular velocity at multiple sites as a means to assess the whole heart is a better approach than taking a single measurement at a specific site[25]. The quality of diagnostic data obtained using TDI relies on the angle at which the measurement is taken. The velocity of myocardial motion measured should be the vector parallel to the beam direction[26]. We chose the apical four-chamber view in which the angle between the direction of the beam and the myocardial motion is minimized, so that the velocity measured is closest to the true value.

Our results show that the Sa and Ea values of CHD patients were significantly reduced while the E/Ea value was elevated, suggesting that there was a decrease in both ventricular systolic and diastolic functions, diastolic function being more markedly affected. This is probably due to weakening diastolic function, an early sign of CHD[27]. Compared to systolic function, diastolic function is more vulnerable in CHD. Calcium recycling from the cytosol back into ER during the cardiac diastolic phrase requires energy consumption because this calcium transport occurs against the concentration gradient, from the low-concentration cytosol to a higher concentration compartment[28]. In the ischemic conditions associated with CHD, this energy requirement may not be met in the myocardium. Inadequate oxygen supply to the myocardium, and the resulting inability to produce the required energy significantly slows and prolongs the motion of relaxation. This leads to further, slow decline in ventricular pressure and subsequent attenuated rapid ventricular filling[29].

It is crucial to have a reliable diastolic function indicator for the early identification and diagnosis of CHD. In this study, we used E/A, E and E/Ea to evaluate the patients' diastolic function. E/A values smaller than 1 can present in patients with or without coronary lesions. Therefore, the E/A value cannot be used to specifically identify CHD. In contrast, the E value or E/Ea can distinguish CHD from non-CHD[30]. Both of these two indicators have clinical importance for assessing left ventricular diastolic function. In particular, E/Ea value seems to be the more sensitive marker of diastolic function, and is positively correlated with the degree of CHD. E/Ea has the sensitivity to distinguish patients with lesions in a single coronary artery from non-CHD patients. In this study we employed ROC curves to demonstrate the usefulness of mitral annular tissue velocity in the diagnosis of CHD, and our results confirmed that E/Ea is the best indicator to help determine whether patients with suspected CHD have coronary artery lesions. The optimal cutoff values on the upper left corner of the ROC curve showed, using coronary angiography as the standard, that the CHD detection rate using E/Ea > 8.34 can reach 85.8%, with 77.4% sensitivity and 100% specificity.

Coronary artery lesion is certainly not the only cause of abnormal ventricular diastolic function. Common CHD risk factors such as diabetes and high blood pressure can also increase myocardial stiffness[31,32], eventually resulting in diastolic dysfunction. Moreover, age and heart rate can also alter diastolic function. In order to control for these factors, patients participating were selected and matched according to these factors. It is important to note that vascular stenosis detected via the angiography may not represent an actual myocardial ischemia, and would not show the degree of decline in cardiac function[33]. In the current study, the sample number was limited and a larger patient population should be studied to confirm these findings.

Conclusions

CHD is a serious, life-threatening disease and it is of great importance that clinicians have a powerful diagnostic indicator in order to detect CHD at earlier stages. In this study, we showed that E/Ea is the optimal indicator of whether patients with suspected CHD have coronary lesions and impaired diastolic function. These findings provide an effective method to assess cardiac function and diagnose CHD.

Conflict of Interest

The Authors declare that there are no conflicts of interest.

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