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Assessment of left ventricular function in chronic alcoholics by real-time three-dimensional echocardiography

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Abstract

Chronic alcohol consumption may lead to progressive cardiac dysfunction. The aim of this study was to evaluate the feasibility of using real-time 3-dimensional echocardiography (3DE) on assessing left ventricular (LV) function in chronic alcoholics.

We classified 92 male alcoholics into mild, moderate, and severe groups; 30 age-matched controls were also recruited. LV end-diastolic volume (LVEDV), LV end-systolic volume (LVESV), LV ejection fraction (LVEF), LV mass (LVM), LV mass index (LVMI), and systolic dyssynchrony index (SDI) were measured by 3DE and 2-dimensional echocardiography (2DE).

Compared to the control group, LV volume and mass were higher in the moderate and severe alcoholic groups ($P < 0.05$). The severe alcoholic (symptomatic) group demonstrated decreased LVEF and increased SDI (detected by 3DE) ($P < 0.05$).

Real-time 3DE can detect the increases of LV volumes and mass in asymptomatic alcoholics, and the changes of LVEF and systolic synchrony index in symptomatic alcoholics.

Abbreviations: 2DE = 2-dimensional echocardiography, 3DE = 3-dimensional echocardiography, ACM = alcoholic cardiomyopathy, BSA = body surface area, CMR = cardiac magnetic resonance, ICC = intraclass correlation coefficient, LVEDV = left ventricular end-diastolic volume, LVEF = left ventricular ejection fraction, LVESV = left ventricular end-systolic volume, LVM = left ventricular mass, LVMI = left ventricular mass index, SD = standard deviation, SDI = systolic dyssynchrony index.

Keywords: alcoholic, echocardiography, left, 3-dimensional, ventricular function

1. Introduction

Alcohol consumption in moderation may offer protection against cardiovascular events,[1,2] but excessive alcohol intake may lead to cardiovascular diseases.[3,4] Chronic alcohol abuse can cause many toxic and metabolic disorders,[1,5] abnormalities in calcium homeostasis,[6] and increases norepinephrine,[7] which progressively lead to myocyte and cardiac dysfunction. Eventually, chronic alcohol abuse can develop alcoholic cardiomyopathy (ACM) and present congestive heart failure symptoms.[8] Therefore, early detection of the subtle cardiac abnormalities is essential to chronic drinkers who can benefit from early treatment.

Echocardiography is the primary imaging method used to monitor the cardiac function in clinical practice. Traditionally, clinical management and decisions regarding ACM have mostly relied on the echocardiographic left ventricular ejection fraction (LVEF). However, the LVEF is not sensitive to subtle myocardial dysfunction or asymptomatic alcoholic myocardial deterioration.[9]

Real-time 3-dimensional echocardiography (3DE) using a matrix array transducer enables the acquisition of the full 3D image of the heart and it provides unprecedented information for the quantification of cardiac function.[10] Real-time 3DE precludes the operator dependency and time-consuming acquisition associated with 2-dimensional echocardiography (2DE). It has also been reported to be able to provide accurate and reproducible volume and myocardial strain values comparable with cardiac magnetic resonance (CMR).[11,12] Furthermore, 3DE enables the visualization of cardiac structures from virtually any perspective, providing a more intuitive display, and offering advanced volume and segmental volume–time curves.[12]

Early detection of the subtle signs of cardiac abnormalities can lead to the early clinical treatment and better prognosis. Although 2DE has been used to explore the cardiac dysfunctions in chronic alcohol abusers, there has, however, been no report on 3DE cardiac evaluation in alcoholics, or a comparison of 3DE and 2DE assessment on ACM. Therefore, the aim of this study is to reveal the capability of 3DE in detecting the subtle changes of LV

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SZ: concept/design, data analysis/interpretation, critical revision of article; WB: recruiting patients, Image acquisition, statistics, data analysis/interpretation, proofreading;

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cardiac structure, function, and mechanical dyssynchrony in patients with varied consumption rates.

2. Methods

2.1. Study subjects

Ninety-two male alcoholics (mean age 55 ±8 years; age range, 36–65) were recruited at the Second Affiliated Hospital of Dalian Medical University from June 2009 to March 2012. Exclusion criteria included a history of hypertension, diabetes mellitus, ischemic cardiac diseases, atrial fibrillation, congenital cardiovascular diseases, systemic and metabolic conditions which could adversely affect the cardiac structure and function. A group of age-matched (mean age 54±7 years, age range from 40 to 65) healthy volunteers (30 healthy male subjects) who did not exhibit any cardiovascular abnormalities were also recruited. The alcohol users were divided into 3 groups according to the duration and amount of alcohol consumed:[13] mild (consumed >90 mg ethanol (2–3 beers) 3–5 days per week for 5–8 years), moderate (consumed 90 mg to 140 mg ethanol 3–5 days per week for 9–20 years), and severe (consumed >150 mg ethanol (>4 beers) 6–7 days per week for more than 10 years). In the alcoholic groups, the mild and moderate groups were asymptomatic patients with preserved LVEF, and without clinical evidence of heart failure, the severe group included symptomatic patients with decreased LVEF, and/or clinical heart failure signs. All subjects were given written informed consent for participation in the study. The study design, manner of data collection, and analysis were approved by the ethics committee of the Second Affiliated Hospital of Dalian Medical University in China.

2.2. Image acquisition and analysis

A GE Vivid 7 color Doppler ultrasonic diagnostic apparatus, equipped with an M3S transducer (the frequency of 1.7–3.4 MHz), and a 3 V transducer (the frequency of 2–4.3 MHz) were used for image acquisition. The standard echocardiographic assessment was performed according to the American Society of Echocardiography Guidelines.[14,15] During acquisition, all subjects were in the left lateral decubitus position, with electrocardiogram recorded simultaneously. Standard 2DE image loops were taken by the M3S transducer, and full-volume 3DE was acquired by the 3 V transducer.

2DE variables were measured from apical views by Simpson's biplane method, including left ventricular end-diastolic volume (LVEDV), left ventricular end-systolic volume (LVESV), left ventricular ejection fraction (LVEF), and left ventricular end diastolic epicardial volume (LVEDVepi). Left ventricular mass (LVM) and left ventricular mass index (LVMI) were calculated according to the formula: (1) LVM = 1.05 × (LVEDVepi−LVEDV), 1.05 for myocardial density; (2) LVMI = LVM/BSA, (BSA: body surface area).[14,15]

The 3DE images were performed offline using the commercially available software package (4D LV Analysis, TomTec Imaging Systems GmbH, Unterschleissheim, Germany) which would automatically generate values after the observer manually traces the left ventricular end-diastolic endocardial borders and end-systolic endocardial borders, including (Fig. 1): left ventricular end-diastolic volume (LVEDV), left ventricular end-systolic volume (LVESV), left ventricular ejection fraction (LVEF), and systolic dyssynchrony index (SDI). SDI is the standard deviation (SD) of the time-to-minimum systolic volume computed at each of the 16 segments.[16] Higher SDI denotes increasing intraventricular dyssynchrony.[17] The 4D Auto LVQ software [18] can calculate LVM and LVMI by subtracting the endocardial volumes from epicardial volumes after the observer manually traces the left ventricular epicardial border. All the image acquisition and analyses were performed by the same cardiologist (WYZ) and same sonographer (SGX) who were blinded to the patients' clinical information. Intra-observer analysis was performed 4 months after completion of the initial measurement, and a second observer (SJQ) analyzed 20% of all the images for interobserver evaluation.

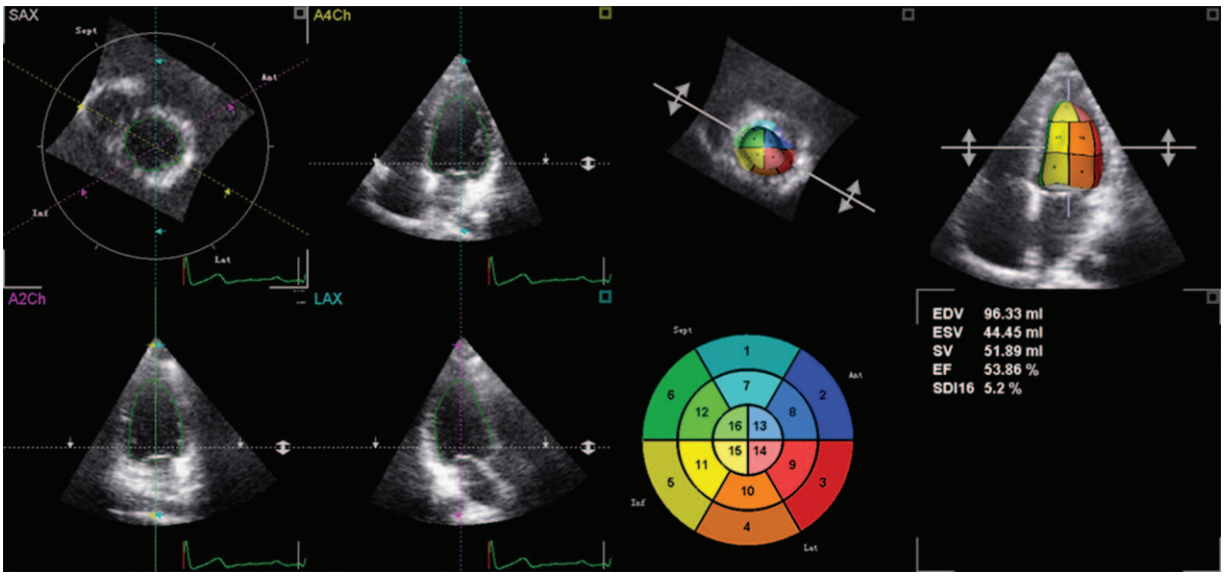

Figure 1. Real-time 3-dimensional echocardiography analysis. Manually tracing the left ventricular end-diastolic endorcardial borders and end-systolic endorcardial borders in apical 4-chamber, 2-chamber, and LV long-axis views, the software automatically draws: left ventricular end-diastolic volume (LVEDV), left ventricular end-systolic volume (LVESV), left ventricular ejection fraction (LVEF), and the systolic dyssynchrony index (SDI). LV = left ventricular, LVEDV = left ventricular end-diastolic volume, LVEF = left ventricular ejection fraction, LVESV = left ventricular end-systolic volume, SDI = systolic dyssynchrony index.

Table 1

Comparison of patients' characteristics, LV parameters measured by 2DE.

Variable	Control	Mild	Moderate	Severe
Age, y	55 ± 8	56 ± 7	58 ± 6	54 ± 7
HR, beats/min	68 ± 7	67 ± 8	68 ± 11	67 ± 9
BSA, m^2	1.98 ± 0.21	2.01 ± 0.12	2.13 ± 0.17	2.09 ± 0.15
EDV, mL	124.52 ± 15.34	126.43 ± 17.28	135.42 ± 17.62*,†	144.71 ± 19.22*,†,‡
ESV, mL	46.29 ± 12.21	47.31 ± 15.72	77.28 ± 19.33*,†	81.23 ± 23.23*,†,‡
LVEF, %	64.50 ± 12.11	63.37 ± 10.89	60.87 ± 7.15	44.50 ± 6.59*,†,‡
LVM, g	130.10 ± 27.19	138.72 ± 19.83*	158.72 ± 22.43*,†	163.70 ± 28.74*,†,‡
LVMI, g/m^2	67.58 ± 17.67	78.28 ± 16.25*	82.52 ± 13.58*,†	86.21 ± 11.94*,†,‡

2DE = 2-dimensional echocardiography, BSA = body surface area, EDV = end-diastolic volume, ESV = end-systolic volume, HR = heart rate, LV = left ventricular, LVEF = left ventricular ejection fraction, LVM = left ventricular mass, LVMI = left ventricular mass index.

Group mild: alcoholic patients with short duration of heavy drinking; Group moderate: alcoholic patients with intermediate duration of heavy drinking; Group severe: alcoholic patients with long duration of heavy drinking. Data presented are mean value ± SD.

* $P < 0.05$ vs controls

† $P < 0.05$ vs mild alcoholics

‡ $P < 0.05$ vs moderate alcoholics.

2.3. Statistical analysis

Statistical analysis was performed by using SPSS17.0 (SPSS Inc., Chicago, IL), whereas all quantitative variables were presented as mean ± standard deviation (SD). One-way ANOVA was performed to test the differences among groups. Intraobserver and interobserver variabilities were assessed using the intraclass correlation coefficient (ICC). All statistical tests were 2-sided, and $P < 0.05$ was set for statistical significance.

3. Results

3.1. Clinical characteristics and 2DE measurements

There were no statistical differences in age, heart rate, and body surface area (BSA) among the 3 alcoholic groups and the control group (Table 1). The left ventricular volume and mass measurements derived from 2DE in the alcoholic groups were higher than in the control group (Table 1). The EDV and ESV in the moderate and severe alcoholic groups were both significantly increased when compared to the control and mild groups ($P < 0.05$). In addition, the severe group showed the most significant increase in left ventricular volume ($P < 0.05$). The 3 alcoholic groups all demonstrated significant LVM and LVMI increase when compared to the normal control ($P < 0.05$), the moderate group, and the severe group showed a further increase when compared to the mild group (with greater increase in the severe alcoholic consumption group).

Despite the significant LV volume and mass increase in the alcoholic groups, only the severe group showed decreased LVEF ($P < 0.05$), whereas the mild and moderate groups demonstrated preserved LV function (Table 1).

3.2. Real-time 3DE measurements among the alcoholic groups and the control group

The LV volume and mass measurements derived from the 3DE demonstrated significant increases compared to the 2DE in the alcoholic groups and the normal control group (Table 2). The EDV and ESV in the moderate and severe alcoholic group showed significant increases when analyzed with the normal control and mild alcoholic groups; the severe group demonstrated further increases than the moderate group. The LVM and LVMI in all 3 alcoholic groups increased when compared to the control group. The absolute increase values were related to the severity of alcohol consumption.

Similar to the 2DE, 3DE also showed the decrease of LVEF in the severe group, and the mild and moderate groups showed preserved LV systolic function.

Table 2

Comparison of LV volumes, systolic function, and LV mass and SDI measured by RT3DE.

Variable	control	mild	moderate	severe
EDV, mL	101.14 ± 8.79	107.28 ± 10.30	121.47 ± 12.37*,†	129.24 ± 16.17*,†,‡
ESV, mL	35.28 ± 5.18	42.93 ± 9.76	53.60 ± 15.42*,†	67.06 ± 21.33*,†,‡
LVEF, %	62.49 ± 5.27	63.50 ± 8.76	58.47 ± 9.33	47.85 ± 8.12*,†,‡
LVM, g	108.15 ± 20.03	119.23 ± 18.40*	135.72 ± 21.95*,†	139.40 ± 21.67*,†,‡
LVMI, g/m^2	53.08 ± 12.67	65.39 ± 10.42*	70.88 ± 12.24*,†	73.16 ± 13.39*,†,‡
SDI, %	3.61 ± 1.03	3.03 ± 1.18	2.96 ± 1.21	9.49 ± 2.31*,†,‡

BSA = body surface area, EDV = end-diastolic volume, ESV = end-systolic volume, HR = heart rate, LVEF = left ventricular ejection fraction, LVM = left ventricular mass, LVMI = left ventricular mass index, RT3DE = real-time 3-dimensional echocardiography, SDI = systolic dyssynchrony index.

Group mild: alcoholic patients with short duration of heavy drinking; Group moderate: alcoholic patients with intermediate duration of heavy drinking; Group severe: alcoholic patients with long duration of heavy drinking. Data presented are mean value ± SD.

* $P < 0.05$ vs controls.

† $P < 0.05$ vs mild alcoholics.

‡ $P < 0.05$ vs moderate alcoholics.

The left ventricular segmental volume-time curves in the control group demonstrated highly synchronization during the cardiac cycle; each section reached the minimum volume at the same time (Fig. 2, left) with an SDI value of 3.61±1.03%. According to Kapetanakis et al[17] SDI >3SD is considered as significant dyssynchrony; in our study, a value of 6.30% was set as the cutoff value. The SDI derived from 3DE demonstrated significant increase in the severe group when compared to all other groups. The mild and the moderate group showed preserved synchronization. Additionally, the segmental minimum volume peak time points were widely dispersed during the cardiac cycle in the alcoholic groups, especially the severe group (Fig. 2, right).

3.3. Comparison of 2DE and 3DE measurements

The LV volume and mass values derived from 3DE were smaller than those derived from 2DE (Tables 1 and 2) in all groups; however, the LVEF values derived from 3DE and 2DE were similar in the control group, and the mild and moderate alcoholic groups. The severe alcoholic group demonstrated higher LVEF in 3DE measurement compared to the 2DE measurements.

3.4. Intra- and interobserver analysis

EDV, ESV, LVM, LVMI, and LVEF values derived from both 2DE and 3DE were used for intra- and interobserver analysis. The intraclass correlation coefficients (ICCs) for all 2DE measurements were between 0.81 and 0.88; the ICCs for all 3DE measurements were between 0.85 and 0.94. The intra- and interobserver ICC for SDI were 0.91 and 0.89, respectively.

4. Discussion

Excessive alcohol consumption is a main cause of nonischemic dilated cardiomyopathy, which is indistinguishable from other types of dilated non-ischemic cardiomyopathy.[19] In recent years, with the increase of alcohol consumption, the incidence of alcoholic cardiomyopathy (ACM) rate is increasing. The clinical manifestation of ACM is heart enlargement, arrhythmia, and symptoms of congestive heart failure. There are no specific diagnostic methods or standards for ACM, and it can be easily misdiagnosed as other types of cardiomyopathy. Therefore, in order to improve the diagnosis and the prognosis of the ACM, an effective method is needed for clinical practice.

Echocardiography is the primary method to evaluate heart anatomy and function.[14,15] There are many echocardiographic technologies available for the evaluation. Speckle tracking echocardiography is an angle-independent method for myocardial strain measurements that has been used to estimate deformation and quantitatively characterize cardiac function. It provides a powerful means of unmasking subtle LV dysfunction that is not detected by LVEF in the early stages of myocardial dysfunction[20–24]; hence, speckle tracking echocardiography can detect subtle myocardial dysfunction or asymptomatic alcoholic myocardial deterioration. Assessment of cardiac dimension and function using echocardiography depends on the experiences of the operator, which can greatly impact the image quality, and the accuracy of measurements.[25] Contrast 3DE showed the greatest accuracy in patients with poor ultrasound image quality and outperformed 2DE and 3DE when compared to MRI.[26] Moreover, contrast echocardiography can also demonstrate perfusion deficits in alcoholic cardiomyopathy which would significantly increase the evaluation of ventricular function.[26,27] The reproducibility of longitudinal strain was reported higher than the other strain measurements,[28] but the values derived from 2D, triplane 3D, and real-time 3D are not interchangeable.[29] We hypothesize that 3DE is more superior than 2DE in evaluating ACM because it can demonstrate the structural changes of the LV in real time, including dimensional (volume) and contracting (function) changes throughout the cardiac cycle; however, 2DE can only estimate dimensions and contraction of the heart-based geometric assumptions of the 2-dimensional sliced images. In conjunction with the LV volumes and function, the analyses of left atrial volumes and function are equally important,[30] which would lead to better understanding of the impact of alcohol on atrial fibrillation, a very common condition that patients with alcoholic cardiomyopathy often suffer with.[31–33]

In this study, we demonstrated that chronic asymptomatic alcoholics (mild and moderate alcoholic groups) had increased LV mass and LV dilation. The results were in accordance with the previous study.[34] Several echocardiographic studies also have demonstrated increased LV mass and LV dilation in chronic alcohol abusers.[35,36] Moreover, we found that LV mass demonstrated earlier changes before LV volume. The LVM and LVMI were significantly increased in the mild group, whereas the EDV and ESV from the mild group remained insignificant with the control group. In our study, the LV mass was a sensitive index for finding early changes of cardiac structure. Other

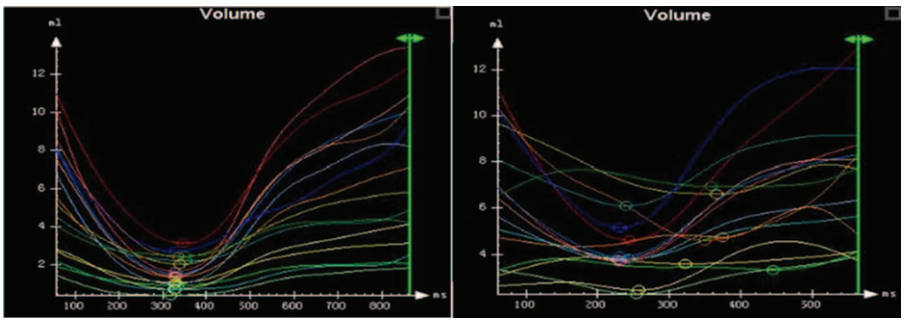

Figure 2. The left ventricular volume-time curves of 16 segments. Left: the volume-time-curves of 16 segments were synchronized during the cardiac cycle, all the sections reached to the minimum volume almost at the same time, which reflecting the synchronous contraction of the left ventricle. Right: the volume-time-curves of 16 segments were desynchronized during the cardiac cycle. The peak time points of all the segments reached the minimum volume were widely dispersed.

reports[37,38] also suggested that hypertrophy, exemplified by either an increase in posterior and/or septal wall thickness and LV mass, rather than LV dilation, are early findings in asymptomatic alcoholics. The left ventricular hypertrophy is an independent risk factor for cardiovascular diseases, so the accurate measurement of patients with LV mass is conducive to judging the degree of myocardial damage.[39,40] Recent studies showed that 3DE measurements of myocardial mass had a good correlation and consistency with the actual value .[41,42] With 3DE, the left ventricular wall hypertrophy can be viewed comprehensively with more intuitiveness, so that a better understanding of the structural changes of the heart would be obtained. The LVM and LVMI values derived from 3DE were smaller than those from 2DE in our study. The difference may be due to the 2DE geometry assumption which was based on 1 measurement of the sampled wall thickness, which can cause overestimation due to the intention of measuring the thick section of the septum and posterior wall (below the tip of the mitral valve). Additionally, the potential asymmetrical left ventricular hypertrophy of alcoholics can cause overestimation as well. Real-time 3DE showed better correlation with cardiac magnetic resonance imaging (CMR) measurements in evaluating left ventricular volume and mass.[43,44]

In our study, the EDV and ESV values derived from 3DE were smaller than those from the 2DE, and previous studies [45,46] have also shown that 3DE can accurately evaluate the left ventricular volume and ejection fraction consistent with CMR. The 2DE Simpson biplane method was based on the geometry assumption of left ventricular chamber as an ellipse, which limited its accuracy in volume calculation.

Real-time 3DE is feasible to assess the LV mechanical dyssynchrony.[47,48] It was reported that LV systolic synchrony will disappear when heart failure is presented.[47,48] Left ventricular systolic dyssynchrony was presented in the severe alcoholic group, and lower LVEF is correlated with higher SDI values.

Cardiac remodeling is critical to the prognosis and management of ACM and dilated cardiomyopathy (DCM). Similar to DCM, the LV size and EF are intrinsic in the diagnosis, risk stratification, and treatment for patients with ACM. Therefore, a full clinical investigation with ECG, echocardiography, and CMR would be recommended to assess the remodeling of the ACM.[49] Without CMR as the reference standard to validate LV measurement for 2DE and 3DE, our results and conclusions are limited. Furthermore, tissue Doppler imaging (TDI) [50–53] and speckle tracking echocardiography [24,54] are beneficial in revealing the subtle changes of LV, via detecting global and regional cardiac functions in systole and diastole. The present study demonstrated the significant changes of cardiac volume and function in alcoholic patients. The TDI and strain evaluation of alcoholic patients are worthy to investigate for future studies.

In summary, we found that real-time 3DE can detect the increases of LV volumes and mass in asymptomatic alcoholics, and the changes of LVEF and systolic synchrony index in symptomatic alcoholics.

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