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ORIGINAL ARTICLE

Is Left Ventricular Dysfunction Reversed after Complete Alcohol Abstinence in Asymptomatic Alcoholics? A Tissue Doppler-Derived Strain and Two-Dimensional Strain Imaging Stress Echocardiography Study

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KEY WORDS: *alcoholic cardiomyopathy; left ventricular dysfunction; Tissue Doppler imaging; stress echocardiography*

ABBREVIATIONS
2D = two dimensional
CM = cardiomyopathy
DSE = dobutamine stress echocardiography
LV = left ventric-cle/-ular
TD = Tissue Doppler

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ABSTRACT

BACKGROUND: Long-term alcohol abuse exerts a deleterious effect on the myocardium, although clinical manifestations of alcoholic cardiomyopathy are not always present. In the present study we evaluate left ventricular (LV) dysfunction by means of tissue Doppler (TD) derived strain and two dimensional (2D) strain imaging stress echocardiography techniques in asymptomatic alcoholics and examine the reversibility of LV dysfunction after complete abstinence from alcohol.

METHODS AND RESULTS: In 13 chronic alcoholics (9 men, mean age 45±6 years) with mean alcohol consumption 207.7±98.3 g/day over 16.5±6.9 years, dobutamine stress echocardiography (DSE) was performed. Left ventricular deformation in 12 segments was assessed using TD velocity and strain and speckle tracking with 2D strain imaging, at baseline as well as at 5, 10, and 20 μg/kg/min stages of dobutamine infusion. The examinations were repeated one month after alcohol discontinuation. Left ventricular dimensions, wall thickness and ejection fraction were within normal limits. Grade I diastolic dysfunction was observed in 9 patients. During DSE, peak TD systolic velocity was increased significantly in all LV myocardial segments, whereas TD strain and 2D strain did not change significantly in the majority of the myocardial segments. Complete abstinence from alcohol for one month did not lead to any noticeable improvement, since baseline and peak DSE, TD and 2D strain did not progress significantly.

CONCLUSIONS: The lack of myocardial strain improvement during DSE may indicate early effects on the myocardium due to chronic alcohol abuse, before clinical manifestations are even present. No reversibility of LV dysfunction was observed after complete abstinence from alcohol for one month.

INTRODUCTION

Compromised cardiac function is regularly seen in patients with chronic alcohol consumption and is often manifested as cardiomegaly, reduced myocardial contractility with concomitant reductions in ejection fraction (EF) and stroke volume, myocardial fibrosis, enhanced risk of stroke and hypertension, and disruptions in the myofibrillatory structure.[1-3] In both genders and all races, long-term heavy alcohol consumption is the leading cause of a non-ischemic, dilated cardiomyopathy (CM), referred to as alcoholic CM[4] which shares similarities with idiopathic dilated CM.[5] However, mortality in patients with alcoholic CM is significantly lower than that in patients with idiopathic CM and similar degrees of heart failure.[6] Previous studies have shown that left ventricular (LV) systolic and diastolic dysfunction is relatively common even in asymptomatic alcoholics.[7-12]

The ability of heavy-drinking duration to affect LV volume and EF has become the focus of particular attention. The duration of alcoholism and the quantity of ethanol exposure were found to be a strong predictor of subsequent myocardial dysfunction by some,[10,11,13,14] but not all studies.[9,12] Previous studies have shown that abstinence from alcohol is associated with a more favorable clinical course in patients with alcoholic CM.[15,16] With the exception of a few case reports, improvement in LV function has been observed as early as 6 months after abstinence from alcohol, and complete recovery can be achieved in 18 months.[17]

The aim of the present study was to detect LV dysfunction by means of tissue Doppler (TD) derived strain and two-dimensional (2D) strain imaging stress echocardiography in asymptomatic alcoholics, and to examine the reversibility of LV dysfunction after complete abstinence from alcohol.

MATERIALS AND METHODS

STUDY POPULATION

The study sample comprised 13 asymptomatic alcoholics with normal ECG and cardiothoracic ratio (mean age 44.9±5.6 years, range 40-56 years, 9 males) attending the Drug and Alcohol Addiction Clinic of the Psychiatric Department at the Eginition Hospital. Participants were diagnosed by the Schedules for Clinical Assessment in Neuropsychiatry and assessed through the Composite International Diagnostic Interview (CIDI, World Health Organization 1990, Core Version 1.0. Geneva, Division of Mental Health, World Health Organization, section on alcohol consumption) for their pattern of alcohol abuse, potential major life problems related to alcohol consumption and the occurrence of withdrawal symptoms in the past.[18] The patient population was free of specific neurological medications. Patients with symptoms of coronary artery disease, heart failure, and more than mild valvular heart disease were excluded from the study. The study was approved by the Institutional Ethics Committee, and all subjects gave their written informed consent at enrollment.

STRESS ECHOCARDIOGRAPHY

Standard echocardiography and TD imaging with dobutamine stress echocardiography (DSE) were performed by an experienced cardiologist, using a commercially available GE Vivid 7 Dimension system (GE Vingment Ultrasound AS N-3190 Horten, Norway) with a 3.5 MHz transducer, in the echocardiography unit at the Department of Clinical Therapeutics of the “Alexandra” Hospital. In order to evaluate for possible reversible toxic effects of alcohol intake, a re-examination was performed one month after complete abstinence from alcohol. Complete abstinence was secured by the in-hospital stay of all patients, in accordance with the withdrawal protocol of the Drug and Alcohol Addiction Clinic. The repeat examination was carried out in 10 of the 13 patients. Of the remaining 3 patients, 1 had a non-cardiac death and 2 refused the follow-up examination.

M-mode parameters of LV dimensions and wall thickness were measured using the criteria of the American Society of Echocardiography.[19] Changes in LV volumes and EF were assessed by the modified bi-plane Simpson’s method. Conventional Doppler echocardiography was used to assess parameters of LV diastolic function, including the early filling (E) and atrial boost (A) velocities at the mitral valve. Tissue Doppler images were acquired from the apical 4-chamber view, and the diastolic indices of myocardial early (Em) and atrial (Am) velocity were measured at the level of the LV lateral mitral annulus; the ratio E/Em was also calculated. Right ventricular dimension and peak systolic velocity (St) at the level of the right ventricular lateral tricuspid annulus were also measured. Tissue Doppler images were acquired from the apical 2-, 3- and 4-chamber long-axis views to assess longitudinal myocardial systolic function.[20] Gain settings, filters, and pulse repetition frequency were adjusted to optimize color saturation, and sector size and depth were optimized for the highest possible frame rate (>130 frames/s). Three consecutive beats of TD images were saved for post-processing. After resting TD images had been recorded, DSE was performed using a standard 3-minute incremental protocol. Dobutamine was infused at a starting dose of 5 μg/kg/min for 5 min, and then increased by 5 μg/kg/min every 3 minutes to a maximum dosage of 20 μg/kg/min (peak dose). A twelve-lead ECG was monitored throughout, and arterial blood pressure was recorded at rest and at 3-minte intervals during infusion and recovery. Endpoints of the stress protocol were completion of the protocol, progressive or severe chest pain, serious ventricular arrhythmia, systolic hypertension (>240 mmHg), symptomatic hypotension or systolic blood pressure less than 100 mmHg, or intolerable side effects.

IMAGE ANALYSIS

Strain and 2D strain measurements from 3 cardiac cycles were performed offline with dedicated automated software (EchoPAC PC, version 7.0.0, GE Healthcare). At each stage of DSE, TD images were recorded and analyzed. Regional myocardial peak systolic velocity and strain curves from 12 myocardial segments of the LV walls were measured, namely the basal and mid-septum, basal and mid-lateral wall, basal and mid-anterior wall, basal and mid-inferior wall, basal and mid-anteroseptal wall, and basal and mid-posterior wall. The apical segments were ignored because tissue velocity in that area is close to 0. For 2D strain, images were obtained at a frame rate of 60-70/s. Each LV wall was divided into 3 segments, while basal and middle segments were used for strain measurements. A tracking-quality (TQ) score was obtained for each myocardial segment. The TQ scores were derived with a block-matching algorithm to define the quality of speckle-tracking, ranging between 1.0 (excellent tracking) and 3.0 (poor tracking). Segments with TQ persistently measured as 3 were excluded. The mean value from three measurements was calculated, thus there were 12 values for each patient. One investigator, who was unaware of the patients' clinical status, analyzed all data from the ultrasound examination. Comparisons between baseline and 20 μg/kg/min (peak dose) of dobutamine infusion were made, as well as between before and after alcohol discontinuation at both baseline and peak DSE. Acceptable measurements were obtained in 156/156 (100%) segments for TD velocity and strain, and in 155/156 (99.3%) for both at peak DSE, while for 2D strain measurements were satisfactory in 132/156 segments (84.6%) at baseline and peak DSE.

STATISTICS

Results are expressed as mean values ± SD. Descriptive statistics were applied in order to evaluate differences in TD velocities, strain and 2D strain in each of the 12 LV segments separately, as well as total LV segments, between baseline and peak DSE, as well as any changes following alcohol discontinuation (paired t-test). Linear correlations were analyzed by Pearson's method. Data were analyzed using the SPSS statistical software package (version 11.5). A p-value of <0.05 was considered statistically significant.

RESULTS

CLINICAL AND ECHOCARDIOGRAPHIC CHARACTERISTICS

Clinical and laboratory characteristics of the study patient population are shown in Table 1. The asymptomatic, heavy-drinking (207.7±98.3 g/day for 16.5±6.9 years) alcoholics were evaluated initially with conventional echocardiography (Table 2). Left ventricular dimensions and EF were within normal limits, whereas 2 of the 13 patients had mild LV hypertrophy. Right ventricular systolic function as assessed with tissue Doppler and tricuspid annular plane systolic excursion (TAPSE) was within normal limits. Grade I diastolic dysfunction was observed in 9 patients, with an E/Em ratio of 7.9±2.2. In all subjects, DSE was completed successfully without any complications. None of the patients revealed any segmental wall motion abnormality during DSE. Age, gender, alcohol intake duration and quantity of alcohol consumption were not found

TABLE 1. Clinical and laboratory characteristics of 13 alcoholics.

Age (mean±SD) (years)	45±6
Gender (M/F)	9/4
Alcohol consumption (g/day)	207.7±98.3
Alcohol intake duration (years)	16.5±6.9
Arterial hypertension (number of patients)	0
Hyperlipidemia (number of patients)	8
Diabetes mellitus (number of patients)	3
Smokers (number of patients)	5
Renal dysfunction (number of patients)	0
Liver dysfunction (number of patients)	7

F = female; M = male; SD = standard deviation

TABLE 2. Baseline echocardiographic findings during alcohol consumption and after abstinence from alcohol.

	Alcohol consumption	Alcohol abstinence	P value (<)
LV-EDD (mm)	47.3±3.5	46.7±4.4	0.3
LV-ESD (mm)	28.9±3.5	29 ±3.1	0.8
IVS (mm)	9.4±1.1	9.4±1.2	1.0
PW (mm)	9.6±1.1	9.3±1.2	0.3
LA (mm)	38.5±3.6	39.2±5.2	0.3
LV-EF (%)	67.5±4.9	66.8±5.24	0.4
Ratio E/Em	8.4±2.2	7.7±2.2	0.5
RV-EDD (mm)	21.7±3.7	21.9±3.2	0.7
St (cm/s)	13.1±1.3	13.4±1.7	0.4

E/Em = early transmitral flow velocity/Tissue Doppler mitral annular peak early velocity; IVS = interventricular septum (end-diastolic thickness); LA = left atrium (dimension); LV-EDD = left ventricular end-diastolic dimension; LV-EF = left ventricular ejection fraction; LV-ESD = left ventricular end-systolic dimension; PW = (left ventricular) posterior wall (end-diastolic thickness); RV-EDD = right ventricular end-diastolic dimension; St = Tissue Doppler tricuspid annular peak systolic velocity.

to correlate with systolic or diastolic dysfunction parameters in our patient population (p>0.05 in all).

TD-DERIVED STRAIN AND 2D STRAIN IMAGING OF STRESS ECHOCARDIOGRAPHY

Tissue Doppler peak velocities increased significantly in all myocardial segments from baseline to peak of DSE in our 13 patients before they discontinued alcohol intake (Table 3). Three of the 12 segments by TD and 1 by 2D showed a remarkable strain increase from baseline to peak DSE. Right ventricular systolic function indexes were found to remain normal.

EFFECT OF ABSTINENCE FROM ALCOHOL

The baseline echocardiographic study did not reveal any significant change following one month's abstinence from alcohol (Table 2); nor was there any significant progression in the DSE parameters (Tables 3 & 4). Thus, a comparison of baseline and

TABLE 3. Changes of TD peak velocity, TD and 2D strain values in 12 LV segments from baseline to peak DSE during alcohol consumption and after alcohol abstinence (n=13).

	DSE during alcohol consumption								
	Velocity			TD Strain			2D Strain		
LV segments	**Baseline**	**Peak**	**p<**	**Baseline**	**Peak**	**p<**	**Baseline**	**Peak**	**p<**
Basal anterior	5.2±1.6	9.1±3.1	0.001	-16.4±5.5	-16.9±7.7	0.84	-22.8±11.7	-20.1±11.5	0.43
Basal inferior	6.5±1.0	10.6±2.5	0.001	-15.1±4.8	-19.8±7.2	0.04	-15.0±12.2	-22.0±6.4	0.12
Basal IVS	6.0±1.0	9.4±2.4	0.001	-17.8±5.5	-22.2±10.7	0.18	-16.4±2.9	-18.3±3.5	0.17
Basal lateral	5.5±1.2	9.0±3.6	0.008	-17.7±7.6	-19.9±7.5	0.18	-16.1±8.8	-17.1±7.6	0.73
Mid-anterior	3.4±1.5	6.8±2.2	0.001	-14.0±4.7	-16.4±6.8	0.35	-13.9±7.5	-18.3±11.4	0.07
Mid-inferior	4.2±1.0	7.6±2.6	0.001	-17.1±4.9	-22.2±5.9	0.03	-17.6±4.3	-19.6±4.6	0.25
Mid IVS	4.3±1.0	6.8±2.2	0.005	-19.8±7.3	-24.6±55.5	0.01	-18.9±2.3	-20.7±4.3	0.23
Basal posteroseptal	4.8±1.3	8.8±4.0	0.002	-15.2±8.0	-17.4±5.3	0.18	-14.3±7.3	-21.8±11.6	0.02
Mid-posteroseptal	3.3±1.2	6.2±3.8	0.017	-13.1±4.3	-14.1±6.1	0.62	-14.6±5.5	-17.0±8.5	0.42
Basal posterior	6.2±0.7	10.4±2.5	0.001	-15.5±5.4	-19.2±7.2	0.07	-20.0±6.1	-18.0±6.3	0.52
Mid-posterior	3.8±0.7	6.7±2.2	0.001	-19.1±4.3	-18.7±6.6	0.85	-19.6±3.1	-19.7±5.9	0.95
Mid-lateral	4.0±1.2	7.6±3.7	0.002	-12.6±4.5	-15.6±8.0	0.14	-16.1±5.6	-17.2±8.3	0.70
DSE after alcohol abstinence									
Basal anterior	5.0±1.2	7.2±2.8	0.02	-19.5±6.5	-18.1±7.1	0.60	-14.6±7.3	-17.4±7.2	0.51
Basal inferior	6.8±1.3	10.0±1.8	0.001	-14.2±6.5	-17.7±6.5	0.37	-9.9±5.2	-24.2±13.1	0.37
Basal IVS	6.4±1.0	9.9±2.8	0.002	-18.6±2.6	-20.6±7.0	0.52	-16.1±6.2	-19.9±4.9	0.10
Basal lateral	5.2±1.1	8.8±3.7	0.006	-13.0±7.2	-16.6±9.3	0.25	-15.02±6.3	-15.0±8.0	0.99
Mid-anterior	3.7±1.5	5.7±3.3	0.05	-12.8±3.2	-15.1±7.7	0.37	-8.2±5.6	-13.0±4.4	0.004
Mid-inferior	4.5±0.7	6.5±0.9	0.001	-17.6±9.2	-18.1±10.5	0.87	-19.1±4.3	-20.1±4.4	0.40
Mid IVS	4.8±1.1	6.6±1.8	0.007	-15.9±17.8	-20.5±7.9	0.42	-17.8±5.3	-22.1±3.5	0.04
Basal posteroseptal	4.4±0.6	9.4±3.4	0.003	-16.5±6.3	-16.8±8.5	0.91	-11.8±7.9	-14.2±5.7	0.48
Mid-posteroseptal	3.8±1.2	6.2±3.5	0.04	-17.4±4.8	-17.0±7.1	0.81	-12.9±5.8	-14.3±6.1	0.47
Basal posterior	6.3±1.0	6.4±1.4	0.81	-14.6±4.4	-18.8±7.3	0.20	-16.0±5.1	-14.9±12.6	0.75
Mid-posterior	4.3±0.5	9.9±2.6	0.001	-18.2±8.9	-16.4±7.8	0.54	-16.4±5.2	-22.1±6.0	0.08
Mid-lateral	4.2±1.5	7.3±3.2	0.01	-13.3±3.4	-17.2±6.2	0.11	-9.1±5.5	-11.1±5.4	0.33

2D = two-dimensional; DSE = dobutamine stress echocardiography; IVS = interventricular septum; LV = left ventricular; n = number of patients; TD = Tissue Doppler

TABLE 4. Differences in baseline and peak DSE velocity, TD and 2D strain values between before and after alcohol discontinuation (n=10).

	PD-Velocity				PD-TD Strain				PD-2D strain			
LV segments	**DSE baseline**	**p<**	**DSE peak**	**p<**	**DSE baseline**	**p<**	**DSE peak**	**p<**	**DSE baseline**	**p<**	**DSE peak**	**p<**
Basal anterior	-0.29±1.8	0.62	2.0±2.7	0.04	2.83±8.1	0.32	-1.25±8.5	0.69	-1.05±9.2	0.79	-0.71±15.2	0.91
Basal inferior	-0.49±1.1	0.22	1.04±2.1	0.16	-2.40±3.1	0.05	-5.51±8.8	0.15	3.85±3.3	0.04	1.30±7.2	0.67
Basal IVS	-0.54±0.7	0.06	0.31±1.8	0.60	-1.36±3.9	0.32	-1.56±7.9	0.59	2.94±2.6	0.04	1.22±6.2	0.65
Basal lateral	-0.09±1.5	0.84	0.71±3.5	0.53	-6.64±8.6	0.05	-6.36±6.4	0.03	3.60±11.8	0.48	2.1±12.5	0.69
Mid-anterior	-0.69±1.5	0.19	1.15±2.8	0.23	2.43±7.2	0.34	-2.70±7.6	0.35	-4.38±12.3	0.42	-6.64±15.1	0.33
Mid-inferior	-0.46±0.64	0.05	1.15±2.9	0.25	-1.30±9.6	0.69	-3.97±10.1	0.30	3.24±5.5	0.20	0.59±4.4	0.75
Mid-IVS	-0.76±0.59	0.003	0.91±1.8	0.15	-6.68±13.3	0.17	-5.03±7.9	0.11	1.44±2.5	0.21	0.17±5.0	0.93
Basal posteroseptal	0.32±0.79	0.23	-0.09±3.1	0.92	-0.96±9.9	0.77	-0.96±9.6	0.78	-1.51±7.1	0.62	-5.64±12.6	0.32
Mid-posteroseptal	-0.68±1.6	0.20	0.21±3.6	0.86	-3.84±8.17	0.19	4.06±10.2	0.29	2.79±5.0	0.23	0.07±6.5	0.97
Basal posterior	0.15±0.8	0.58	4.28±1.8	0.001	-0.99±11.4	0.80	-4.50±12.8	0.35	-3.12±2.0	0.14	1.94±11.2	0.69
Mid-posterior	0.50±0.7	0.05	-3.4±2.49	0.003	-6.43±5.2	0.006	1.34±9.0	0.68	-1.02±6.2	0.70	-2.11±3.7	0.22
Mid-lateral	0.14±1.6	0.78	0.99±3.1	0.34	-0.33±4.9	0.84	-0.52±10.8	0.89	6.01±9.1	0.16	-7.51±15.9	0.30

PD-Velocity = paired differences of baseline and peak DSE velocities between before and after alcohol discontinuation; PD-TD strain = paired differences of baseline and peak DSE TD strain between before and after alcohol discontinuation; PD-2D strain = paired differences of baseline and peak DSE 2D strain between before and after alcohol discontinuation. Other abbreviations as in Table 2.

peak DSE before and after alcohol discontinuation showed that TD velocity improved significantly at baseline in only 1 segment (mid-posterior), but deteriorated in 2 segments (mid-inferior and mid-septal), whereas at peak DSE, improvement was observed in 2 segments (basal-anterior, basal-posterior), while there was deterioration in 1 segment (mid-posterior). Tissue Doppler strain deteriorated in 3 LV segments (basal-inferior, basal-lateral, mid-posterior) and 1 segment (basal-lateral) at baseline and peak, respectively, after alcohol discontinuation. 2D strain improved in 2 LV segments (basal-inferior, basal-septum) at baseline after abstaining from alcohol, whereas no change was observed at peak DSE (Table 4).

A study of all LV segments taken together showed that TD velocity was significantly improved at baseline after alcohol discontinuation but was decreased at peak DSE. TD strain was not changed at baseline but decreased significantly at the peak of DSE after alcohol discontinuation, while 2D strain did not change significantly (Table 5).

TABLE 5. The effect of alcohol discontinuation on LV systolic function, assessed by DSE examining all segments as a whole.

		n	During alcohol intake	After alcohol discontinuation	p<
Velocity	DSE baseline	120	4.64±1.47	5.0±1.49	0.002
	DSE peak	116	8.70±3.51	7.88±3.10	0.009
TD strain	DSE baseline	108	-16.77±5.92	-15.27±7.92	0.07
	DSE peak	95	-20.02±7.16	-17.81±7.58	0.01
2D strain	DSE baseline	72	-15.58±6.11	-15.65±6.11	0.94
	DSE peak	72	-19.01±9.46	-17.75±6.68	0.30

2D = two dimensional; DSE = dobutamine stress echocardiography; LV = left ventricular; n = number of total LV segments; TD = Tissue Doppler.

REPRODUCIBILITY

The intraobserver and interobserver variability (as a percentage of mean values) were 10% ± 6% and 15% ± 8% for TD velocity, 15% ± 8% and 12% ± 7% for TD strain, and 10%±3% and 11%±6% for 2D strain analysis.

DISCUSSION

The main findings of the present study are suggestive of subclinical myocardial involvement due to chronic alcohol abuse, which does not reverse after one month of complete abstinence from alcohol.

To be able to detect subclinical LV dysfunction is a cornerstone of echocardiography in many situations, and stress echocardiography is well recognized as playing a role in the uncovering of subclinical dysfunction when conventional echocardiography is normal, in patients with cardiomyopathy and other diseases. Dobutamine stress echocardiography (DSE) is a well established diagnostic modality for detecting myocardial systolic dysfunction[21-23] and low dose dobutamine (up to 20 μg/kg/min) has been used for assessment of contractile reserve.[24,25] Doppler evaluation of global systolic function using tissue Doppler assessment of velocity, strain, and 2D strain have shown promise as clinically useful quantitative methods for the detection of myocardial ischemia in various diseases.[26-29] To our knowledge, the present study is the first to examine the use of tissue Doppler in combination with DSE in heavy-drinking, asymptomatic patients for the evaluation of LV systolic function.

This study demonstrates the limitations of conventional echocardiography for detecting early abnormalities in cardiac function and the value of newer echocardiographic modalities. Numerous clinical studies examining the effect of chronic alcohol consumption on LV systolic and diastolic function have yielded conflicting results.[6-17] Some authors[14] found an impaired ejection fraction, but others found well preserved LV systolic function in heavy as well as moderate drinkers.[30-32] Similarly, normal[32] and impaired LV filling were reported.[9,12] These disparate findings are in part due to different diagnostic criteria, failure to exclude other forms of heart diseases, different age, gender, and differences in drinking histories.[33,34] In the present study, to overcome these drawbacks, particular care was taken to include a homogeneous patient population with respect to age, quantity and duration of alcoholism, and past medical history. All the clinically asymptomatic alcoholics had normal cardiac structure and ejection fraction, except that some had mild diastolic dysfunction. In contrast to conventional echocardiography, TD and 2D strain at DSE were able to demonstrate a significant effect on systolic function that may have been the result of heavy alcohol consumption. TD and 2D strain at DSE revealed decreased regional contractile reserve during the period of alcohol intake as well as after alcohol discontinuation, although TD velocities showed a normal response (Table 3). In contrast with previous studies, in our study, the change of 2D strain in basal posteroseptum from -14.3±7.3 to -21.8±11.6, p=0.02) and of all other LV segments (50% change from baseline for the majority of the segments), indicates the presence of an adequate inotropic reserve and the lack of a clinically significant cardiotoxic effect of alcohol in this small cohort of patients with normal LV ejection fraction (mean of 60%).

In healthy adults, both peak TD velocities and strain increase in response to low dobutamine stress.[35] Galderisi et al[36] examined the use of strain rate imaging in patients with diabetic cardiomyopathy during DSE and found a blunted response to dobutamine for both strain and strain rate (but not tissue velocities) compared with controls. This discrepancy between TD velocities and strain, which we also observed in our population, has been attributed to the inability of TD velocities to differentiate between tissue movement due to active contraction and passive motion. This motion results either from translational motion of the whole heart, or from "tethering" of normal surrounding tissue on a segment of diseased myocardium.[28] This observation supports the hypothesis of an altered myocardial biochemistry in chronic alcoholics. It has been shown that chronic alcohol intake may impair the transport of calcium ions from the sarcoplasm into the sarcoplasmic reticulum. Consequently, this biochemical abnormality may lead to the delay of the inactivation of the actomyosin interaction and could be responsible for delayed myocardial relaxation.[3,37]

Previous studies focusing on the ability of heavy-drinking duration or quantity of ethanol exposure to predict further myocardial dysfunction have yielded conflicting results. Lazarević et al[10] reported that LV systolic function was not affected by the duration of heavy drinking, while Urbano-Marquez et al[14] reported that alcohol is toxic to the cardiac muscle in a dose-dependent manner. In our heavy-drinking patient population, duration or quantity of alcohol consumption were not found to be correlated with LV systolic dysfunction. The findings of the present study agree with data from previous studies indicating that diastolic dysfunction precedes systolic dysfunction.[8,9,12]

Although the natural course of chronic alcoholic cardiomyopathy is not precisely defined, abstinence from alcohol has been reported to improve cardiac function, or at least halt its deterioration, in particular 6 to 12 months after alcohol discontinuation. Demakis and colleagues[15] showed that abstaining from alcohol is associated with a more favorable clinical course in patients with alcoholic cardiomyopathy. In a more recent study, Guillo and associates[16] concluded that LV EF improves in alcoholics with NYHA class IV heart failure if complete abstinence is accomplished. In the present study, we examined the possible reversibility of the toxic effects of alcohol on the myocardium one month after complete abstinence from alcohol. At re-evaluation of our patients early after alcohol intake discontinuation, EF had remained stable, but TD and 2D strain showed no significant improvement in the majority of segments in all patients who controlled their drinking, either at baseline or at peak DSE (Table 4 and 5).

The limitations of the current study should be acknowledged. Our patient population sample was small. The reversibility and prognostic significance of changes following the discontinuation of alcohol intake also require further study. Our results need to be confirmed by prospective studies, which should include a large number of alcoholics with various levels of alcohol intake and possibly longer duration of abstinence. On the other hand, open issues in the quantitative analysis remain to be resolved: which technique should be employed among systolic velocities, strain and strain rate; the assessment of normality criteria of myocardial velocities and how to interpret their values; the management of patients with regional and global LV dysfunction; the analysis of the apical segments; the complexity of the analysis in a real clinical environment; the applicability to unselected populations; its unsuitability to exercise, the most widely used stressor in clinical practice. TD-derived strain is limited by the inherent Doppler angle dependence and signal noise, which could potentially affect its routine clinical application. On the other hand, the lower frame rates of 2D strain entail reduced temporal resolution, but its angle independency and the increased averaging capability improve the signal-to-noise ratio. In the present study, feasibility was 99-100% for TD strain and 85% for 2D strain in the LV segment analysis. Leitman et al[38] showed that in normal patients TD strain is correlated with 2D strain.

The lack of myocardial strain improvement during dobutamine administration may indicate an early effect on the myocardium due to chronic alcohol abuse, before any clinical manifestations are even present. The findings of the present study are suggestive of subclinical myocardial involvement due to chronic alcohol abuse, which did not improve after short period of complete alcohol abstinence. TD-derived strain and 2D strain imaging techniques during DSE may prove a useful method of screening for myocardial involvement in asymptomatic alcoholics, monitoring its progression, and potentially evaluating the effects of therapeutic intervention.

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