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CASE REPORT

47 years old male, chronic alcoholic, drinking country made alcohol daily (25-30 drinks/week, 1 drink =60ml alcohol), came to OPD with dyspnoea and palpitations NYHA class II.

General physical examination revealed mild bilateral pedal oedema, no icterus, clubbing.

CVS: apical impulse in 6th intercostal space slightly lateral to mid-clavicular line. Normal heart sounds, no S3/S4, Soft systolic murmur grade III at apical region.

Electrocardiogram: sinus rhythm, poor R wave progression.

Echocardiography showed dilated cardiac chambers with global hypokinesia of left and right ventricle, eccentric LVH with moderate LV dysfunction and mild mitral regurgitation mildPAH (Figures 1 & 2).

Long-term heavy alcohol consumption (of any beverage type) is the leading cause of a non-ischemic, dilated cardiomyopathy, herein referred to as alcoholic cardiomyopathy (ACM)¹. ACM is a specific heart muscle disease of a known cause and is classified as a dilated cardiomyopathy,^{2,3} also frequently referred to as alcoholic heart muscle disease (AHMD).

ACM is characterized by a dilated left ventricle (LV), normal or reduced LV wall thickness, and increased LV mass. Unlike other cardiomyopathies, there are no

specific immuno-histochemical, immunologic, or other criteria for the diagnosis of ACM and the diagnosis is often considered presumptive usually one of exclusion. The key factor to consider is a long-term history of heavy alcohol abuse.

INCIDENCE, PREVALENCE, AND MORBIDITY

Prevalence of ACM is variable ranges from 23 to 40%.⁴⁻⁶ It represents about 3.8% of all cardiomyopathy cases¹. This statistic may seem rather insignificant; however, long-term heavy alcohol consumption is the second-leading cause of a dilated cardiomyopathy. Among ACM cases, men represent the larger percentage, whereas women represent approximately 14%^{1,7}. In all races, death rates due to ACM are greater in men compared to women, and are greater in African-American men and women compared to white men and women with ACM.

WHAT DURATION AND LEVEL OF ALCOHOL CONSUMPTION IS ASSOCIATED WITH ACM?

Alcoholics can present with either a preclinical (asymptomatic) or symptomatic ACM (the latter is primarily distinguished from the former by signs and symptoms of heart failure). The duration and amount of alcohol consumed by asymptomatic alcoholics does not correlate with changes in myocardial structure and functions except for study by Urbano-Ma'riquez and colleagues⁸, who found the total lifetime dose of alcohol was correlated to an increase in LV mass and a decrease in

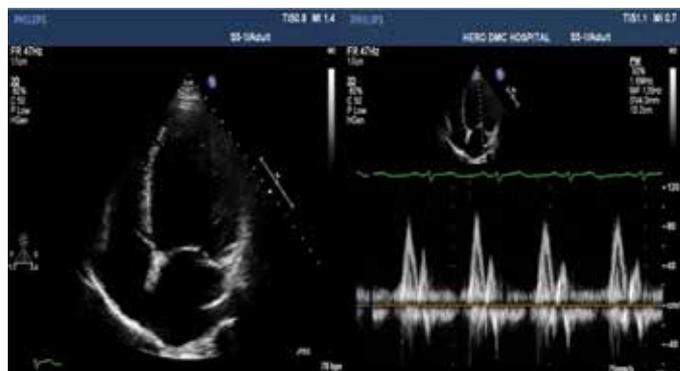


Fig. 1: A: Apical 4 chamber view showing dilated left atrium and left ventricle. B: Pulse wave Doppler at the level of mitral leaflet showing increased Left ventricle diastolic pressure (Type III diastolic dysfunction)



Fig. 2: Tissue Doppler Imaging at level of medial mitral annulus showing reduced systolic and diastolic velocities

Alcohol

Alcohol consumption $\downarrow > 90$ gms > 5 years

- Apoptosis (either directly via alcohol or indirectly via \uparrow NE levels)
- \downarrow synthesis and / or accelerated degradation of contractile proteins
- \downarrow myofilament Ca^{2+} sensitivity
- Intrinsic myocyte dysfunction due to mitochondrial and sarcoplasmic dysfunction (due to Ca^{2+} overload, fatty ethyl esters or NE)

\downarrow

Cell drop out and weakly contracting myocytes

\downarrow

Decreased cardiac output

\downarrow

- LV dilation to increase EDV (preload) to compensate for \downarrow cardiac output, however this is may be accompanied by wall thinning due to cell drop out
 - Hypertrophy of normal myocytes to compensate for weakly contracting neighboring myocytes
- Continued drinking $\downarrow > 15$ years
- Progressive LV dilation and wall thinning
 - Activation of other neurohormonal systems
 - Signs and symptoms of heart failure

Fig. 3: Flowchart depicting pathogenesis of ACM. gms =grams, NE= Nor epinephrine. EDV- End Diastolic Volume

ejection fraction (EF). In general, asymptomatic alcoholic patients with changes in cardiac structure and function had a history of consuming > 90 g/d of alcohol (some studies report > 200 g/d) for > 5 years (average 15 years). 1 standard drink = 14 gram of alcohol = 250 ml of beer (7% alcohol) = 45 ml of whisky. The key variable linked to the development of heart failure appears to be the duration of heavy daily alcohol consumption.

MYOCARDIAL STRUCTURAL AND FUNCTIONAL CHANGES ASSOCIATED WITH ACM

How do clinicians distinguish asymptomatic from symptomatic ACM?

Symptomatic ACM is characterized by a greater degree of LV dilation and increased cardiac mass. LV EDD values and LV mass values were 40% and 60% greater, respectively, in symptomatic alcoholics compared to asymptomatic alcoholics, and LV ESD values were twice as large in the symptomatic patients.

Impaired early filling of the LV due to delayed relaxation is common in asymptomatic alcoholics and may in fact be the earliest functional sign of preclinical ACM. LV dilation is a very early finding that precedes changes in LV mass and diastolic dysfunction.

WOMEN WITH ACM?

There are very few studies that have examined the incidence, clinical characteristics, or outcomes of women

with ACM, and no study has considered the effects of oestrogen. However, similar to men, long term heavy alcohol consumption in women is associated with the development of a dilated cardiomyopathy.

Similar to men, ACM occurs in women of a relatively young age (45 to 50 years).⁷ The clinical features resemble those found in men, and include a dilated LV, modest degree of hypertrophy, and reduced systolic function.

BIOMARKERS FOR ALCOHOL ABUSE

Gamma glutamyl transferase (GGT) glycoprotein is neither a very sensitive marker, showing up in only 30–50 percent of excessive drinkers in the general population, nor is it a specific marker of chronic heavy alcohol use, because other digestive diseases, such as pancreatitis and prostate disease, also can raise GGT levels. Aspartate aminotransferase (AST) and Alanine aminotransferase (ALT) are enzymes that help metabolize amino acids, the building blocks of proteins. They are an even less sensitive measure of alcoholism than GGT. ALT is the more specific measure of alcohol-induced liver injury because it is found predominantly in the liver, whereas AST is found in several organs, including the liver, heart, muscle, kidney, and brain. Very high levels of these enzymes (e.g., 500 units per litre) may indicate alcoholic liver disease.

TREATMENT

Abstinence from alcohol is the cornerstone for treating ACM. Abstinence after development of milder HF can stop progression, or even reverse symptoms in some cases, otherwise severe HF ensues leading to a poor prognosis. Without complete abstinence, the 4 year mortality for ACM approaches 50%.

HYPERTENSION RELATED LEFT VENTRICULAR SYSTOLIC DYSFUNCTION

Case report 2

45 years old male, known hypertensive since past 2 years, compliant with medications now presented with chief complaints of weakness of right upper and lower limbs when he woke up in the morning. No past history of diabetes mellitus, heavy cigarette smoking or alcohol intake.

GPE was normal. Pulse: 70 beats/min.regular. BP: 170/100 mm Hg left arm supine. BMI: 27 kg/m²

Systemic examination:

CNS: Broca's aphasia present. Facial deviation towards left side. Grade 3/5 Power in Right upper and lower limbs.

CVS: Apex beat in 5th ICS. Normal heart sounds, no murmur.

ECG : LVH with LV strain

2D Echocardiography showed moderate eccentric LVH with global hypokinesia of left ventricle with moderate LV systolic dysfunction and Type I Diastolic dysfunction (Figures 3, 4 and 5).

NCCT brain left MCA infarct.

Table 1: Markers of alcohol consumption with respective sensitivity and specificity

Summary of State Markers for Alcohol Consumption				
Marker	Sensitivity (percent)	Diagnostic Specificity (percent)	Possible or Current Use	Used Clinically in U.S.?
Gamma-glutamyl-transferase (GGT)	61 ¹	n/a	Chronic alcohol abuse	Yes
Alanine aminotransferase (ALT)	Method-dependent	n/a	Chronic alcohol abuse	Yes
Aspartate aminotransferase (AST)	56 ¹	N/A	Chronic alcohol abuse	Yes
Carbohydrate-deficient transferrin (CDT)	26-83 ²⁺	92 ³	Heavy alcohol use**	Yes
N-acetyl- β -hexosaminidase	94 ²	91 ²	Heavy alcohol use	No
Whole blood-associated acetaldehyde (WBAA)	100 ⁴	95 ⁴	Recent alcohol consumption as all levels; monitoring abstinence	Yes
Mean corpuscular volume (MCV)	42 ¹	n/a	Heavy alcohol use	Yes
Apolipoprotein J	n/a	n/a	Heavy alcohol use	No
5-hydroxytryptophol (5-HTOL)	n/a	n/a	Monitoring sobriety	No
Salsolinol	n/a	n/a	Chronic alcohol consumption	No
Fatty acid ethyl esters (FAEE)	100 ⁵	90 ⁵	Recent heavy alcohol use	No
Ethyl glucuronide (EIG)	n/a	Method-dependent	Monitoring sobriety. Torenics	No

*Depending on method and gender; **More than 60 grams per day (4-5 standard drinks); n/a – data not available; ¹Anitla et al 2004;

²Stowel et al. 1997.; ³Jevona and Johnson 2003; ⁴Bean et al 2001; ⁵Wurst et al 2004

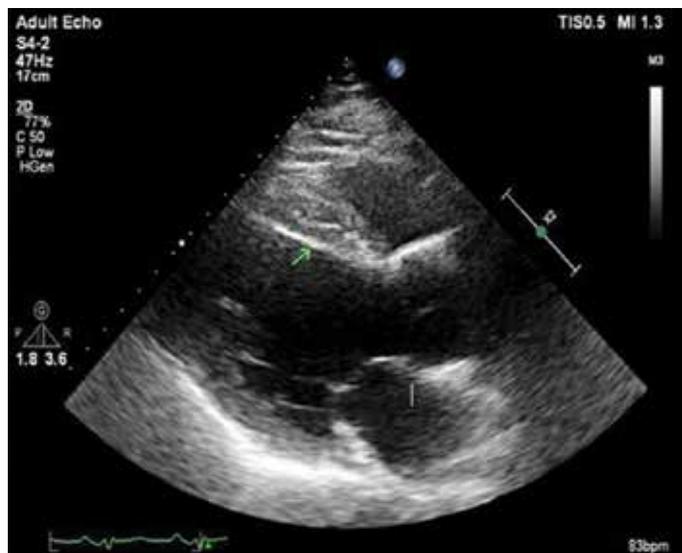


Fig. 3 : Dilated ventricle with hypertrophied walls and mildly dilated aorta

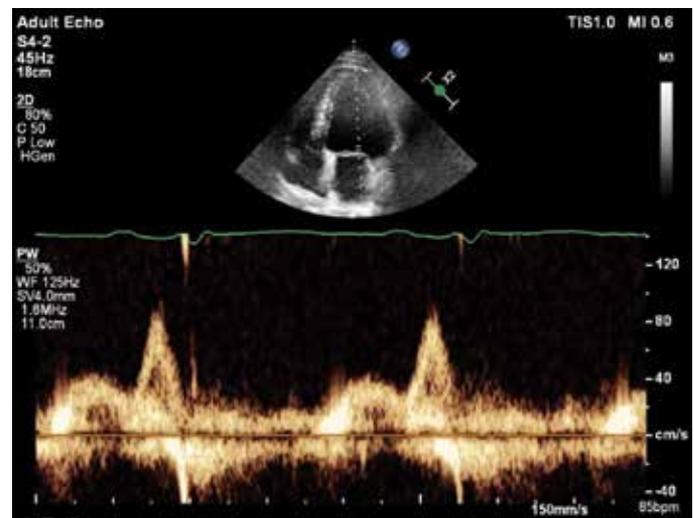


Fig. 4: Pulse wave Doppler at mitral valve level showing diastolic dysfunction type I pattern

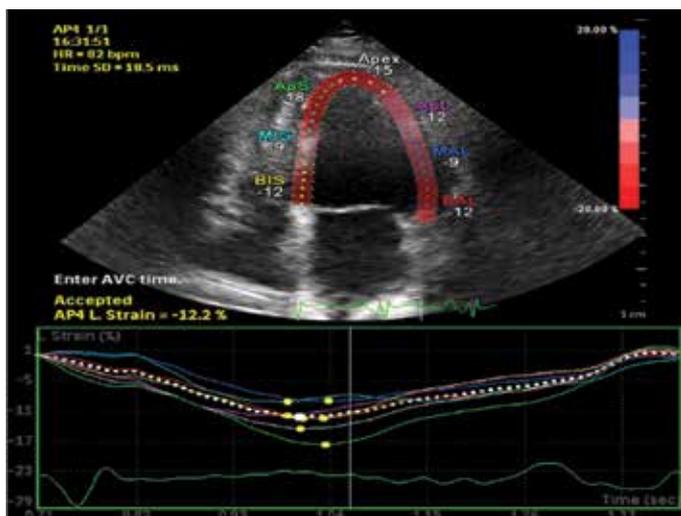


Fig. 5 : Reduced left ventricular longitudinal functions using speckle tracking based strain measurement in this case value of GLS is =-12%(normal >-20%)

Hypertension is a potent risk factor for left ventricular systolic dysfunction. All hypertensive subjects without symptoms of CHF and without structural heart disease should be classified as belonging to stage A, which denotes a high risk for CHF, whereas those without symptoms of CHF but with left ventricular (LV) hypertrophy, should be classified as belonging to stage B.

Development of overt CHF may be preceded by a phase of asymptomatic LV systolic dysfunction (ALVSD). Diagnosis of ALVSD is important because treatment with angiotensin-converting enzyme (ACE) inhibitors may delay progression toward overt CHF in these subjects.

PREVALENCE OF ASYMPTOMATIC LEFT VENTRICULAR SYSTOLIC DYSFUNCTION

In general population, prevalence of ALVSD has been estimated at 2% in most studies. In the PIUMA study prevalence of ALVSD in hypertensive subjects was 3.6%, EF was 40% to 49% in 87% of subjects, 30% to 39% in 9% of subjects and 30% in 4% of subjects. According to the Framingham Heart Study, severe LVSD developed in 3% to 6% among hypertensive patients and the risk of heart failure is increased by 2-fold in men and by 3-fold in women.⁹

PATIENT CHARACTERISTICS

Compared with the subjects without ALVSD, those with ALVSD are more frequently men and current smokers. Office and 24-hour ambulatory BP levels and heart rate were significantly higher in the subset with than without ALVSD.

INCIDENCE OF HEART FAILURE HOSPITALIZATIONS

Hospitalizations for symptomatic CHF are 1.48 per 100 subjects per year in most of the studies. Age, LV mass on echocardiography and reduced systolic functions LVEF <45% are independent predictors of overt CHF with a 9-fold higher risk of hospital admission for CHF over a mean follow-up period of 6 years compared with those

with normal EF. The excess risk persists after simultaneous adjustment for age and LV mass.

ROLE OF ELECTROCARDIOGRAM

Development of LVH or its persistence during antihypertensive therapy is associated with an increased risk of left ventricular systolic dysfunction after 3 years follow-up.

BIOMARKERS INDICATIVE OF INCIPIENT HEART FAILURE IN HYPERTENSIVE SUBJECTS

N-terminal propeptide of procollagen type III (PIIINP) - one of the biomarkers of extracellular matrix remodelling is the first early biomarker for the development of HF in patients with hypertension and normal resting echocardiography Unlike traditionally used biomarkers for overt heart failure BNP, NT pro BNP which lack specificity and sensitivity this new biomarker holds promise for clinical use in hypertensive patients with mild left ventricular systolic dysfunction.

LV SYSTOLIC FUNCTION PARAMETERS FROM LINEAR MEASUREMENTS IN HYPERTENSION

LV linear dimensions for the calculation of FS and EF by Teichholz or Quinones methods are widely used in hypertensive patients. The use of these measurements has been superseded by more accurate and reliable measures as these linear measurements are dependent on geometric assumptions so are not recommended for clinical use. [10]

Mid-wall fractional shortening (MFS) is relatively independent of afterload and hypertensive patients with left ventricular hypertrophy and normal ejection fraction have abnormal MFS.

Midwall Fractional Shortening is based on too many assumptions using M-mode and has a cumbersome formula.¹¹

$$\text{Inner shell} = \left[\left(\frac{\text{LVIDd} + \text{SWTd}}{2} + \frac{\text{PWTd}}{2} \right)^3 - \text{LVIDd}^3 + \text{LVIDs}^3 \right] / \left[\frac{1}{3} - \text{LVIDs} \right]$$

$$\text{MWFS} = \left(\frac{\text{LVIDd} + \text{SWTd}}{2} + \frac{\text{PWTd}}{d} \right) - \left[\text{LVIDs} + \text{inner shell} \right] / \left(\text{LVIDd} = \frac{\text{SWTd}}{2} + \frac{\text{PWTd}}{2} \right) \times 100$$

TWO-DIMENSIONAL MEASUREMENTS

Biplane method of discs (modified Simpson's rule obtained from apical four- and two-chamber views) is the most accurate in abnormally shaped ventricles and combined with harmonic imaging it improves the reproducibility of LV volumes used in EF calculation.

Whether observed LV pump function is representative of actual myocardial contractile performance is determined by measurement of end systolic stress (σ_m)

$$\sigma_m \text{ (dynes/cm}^2\text{)} = 1.35 \times P(\text{LVID}) / 4h(1+h/\text{LVID})$$

σ_m = end-systolic meridional wall stress. P = pressure in the LV at the end of systole (may substitute SBP) LVID=LV internal diameter h=end-systolic posterior wall thickness

OR

$$\sigma_m \text{ (dynes/cm}^2\text{)} = 1.33 \times \{ \text{BP}_{\text{sys}}(\text{A}_m) / \text{A}_c \} \times 103$$

σ_m = end-systolic meridional wall stress, A_c = LV cavity

626 area in the short axis view, Am = myocardial area BPsys = systolic blood pressure

To eliminate the effects of LV afterload on FSmw, stress corrected FSmw is calculated through the following formula:

$cESS \frac{1}{4} \{ [SBP \times (LVIDs/2)^2] \times [1 + (LVIDs/2 + LV \ 2 \ PWs)/2 / (LVIDs/2 + LV \ 2 \ PWs/2)] \} / \{ (LVIDs/2 + LV \ 2 \ PWs)^2 / (LVIDs/2)^2 \}$, where SBP represents systolic blood pressure. This correction has shown to discriminate hypertensive from physiological LV hypertrophy in athletes.¹²

THREE-DIMENSIONAL MEASUREMENTS

Transthoracic 3DE provides a rapid and accurate method for quantifying LV volumes and EF (LVEF) It showed a superior reproducibility to 2DE, with a closer correlation to CMR-derived volumes in previous studies.¹³

A recent meta-analysis of validation studies comparing 3DE and CMR demonstrated that considerable variability still exists in the measurement of LV volumes (+34 mL for EDV, +30 mL for ESV, and +12% for EF), although it is less than that observed between 2DE and CMR.¹³

Several sources of 3D volume acquisition and measurement error are difficulty in imaging the anterior and lateral walls because of interference from ribs, low line density (and therefore lower spatial resolution—which may be partly readdressed with the use of LV opacification), low temporal resolution (which may be addressed by using multiple subvolumes—but at the risk of stitching artefacts), and time-consuming off-line analysis.¹⁴

TISSUE DOPPLER ASSESSMENT OF SYSTOLIC FUNCTION

In hypertensive heart disease, main parameter for systolic performance by tissue Doppler evaluation is s' with measurements at six sites from the apical four-chamber, two-chamber and long-axis views (six-site average s' . 5.4 cm/s has 88% sensitivity and 97% specificity for LVEF >50%). main limitation is reliability on detection of cardiac motion which may hamper correct estimation.

ASSESSMENT OF MYOCARDIAL FUNCTION BY STRAIN

Longitudinal strain corresponds to the function of the endocardial layer of myocardium, where longitudinal fibres are subjected to the negative impact of early development of fibrosis in hypertensive heart disease. It is useful in identifying sub clinical left ventricular systolic dysfunction.¹⁵

KEY MESSAGE

Echocardiography plays an important role in detecting complications related to hypertension and alcohol. LV systolic dysfunction can be earlier identified by simple reproducible measures of longitudinal LV function using advanced echocardiographic techniques like tissue Doppler and strain.

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