

The Prognostic Value of Left Bundle Branch Block and Biochemical Parameters in Alcoholic Dilated Cardiomyopathy

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Alcoholic cardiomyopathy is one of the main causes of dilated cardiomyopathy. The aim of this study was to review biochemical and electrocardiographic parameters on a group of patients diagnosed with alcoholic cardiomyopathy in order to see which correlates with a poor outcome. The analysis showed different degrees of hyponatremia, without a statistically significant correlation to outcome. We did not find a positive connection between the impaired renal function and severe evolution. On the other hand, LBBB presence was strongly correlated with the poor outcome ($p < 0.00001$). We emphasize the importance of alcoholic dilated cardiomyopathy proportions in the study group and the prognostic value of LBBB presence for negative outcome.

Keywords: left bundle branch block, biochemical parameters, alcoholic dilated cardiomyopathy, prognostic

Dilated cardiomyopathies (DCM) are a heterogeneous group of myocardial dysfunctions consisting of ventricular dilation and depressed myocardial contractility in the absence of a preloaded condition (hypertension, valvular disease). For clinical purposes, the pathogenesis of DCM and heart failure manifestation has been divided in ischemic and non-ischemic cardiomyopathy [1-4].

Alcoholic dilated cardiomyopathy (ACM) represents one of the main causes of non-ischemic cardiomyopathy, and it is an exclusion diagnosis, being established in a patient with a history of long excessive alcohol consumption (>80 g/day for a minimum of 5 years). The methods of diagnosis and the histological analysis are unspecific in ACM. The value of gamma-glutamyl transpeptidase (GGT), associated with the mean corpuscular volume (MCV) and the co-existence of hepatic disorder can suggest the alcoholic etiology and also monitor the abstinence [4-5].

There is a debate among specialists regarding the role of moderate alcohol consumption, which has been noted to reduce the mortality risk (2 standard drinks/day for men and 1 standard drink/day for female) and excessive one (which leads to hypertension, atherosclerosis, arrhythmias, dilated cardiomyopathy) [5].

If the acute and occasionally consumption of alcohol, the so called holiday heart syndrome, leads to tachyarrhythmia (the most frequent - atrial fibrillation, but also ventricular tachycardia, torsade de pointes, sudden cardiac death), the chronic and excessive one determines ultrastructure changes leading to ACM [5].

Alcohol has direct and indirect toxic myocardium effects. Experimental studies have noted the decrease of intracellular calcium concentration and reduce ATP levels which lead to decreased contractility in rats fed with alcohol [5]. Acetaldehyde and ethyl-ester are the main toxic metabolites of alcohol that determine the uncoupling of excitation-contraction and an increase in oxidative stress. Also, alcohol produces nutritional deficit of group B vitamins, electrolyte imbalance, induces mitochondrial disorder and cardiomyocytes' apoptosis. As a

compensatory mechanism, the sympathetic nervous system is stimulated, and the activation of RAA system, that determine in time left ventricular dilation, decreased cardiac output and increased preload. Another important factor to be considered is that not all the heavy drinkers develop ACM, the genetic determinants having an important role [5-7].

The treatment of ACM focuses on heart failure treatment and the results of DANISH trial emphasized the idea that the use of ICD (implantable cardioverter defibrillator) wasn't associated with a better mortality outcome in patients with non-ischemic cardiomyopathy compared to optimal medical treatment [5].

Literature data shows a better prognosis for ACM than idiopathic dilated cardiomyopathy, with an important role of alcohol abstinence; though the exact limit between reversible and irreversible myocardial damage in ACM hasn't been well defined [7-8]. Also, the prognostic elements for ACM have not fully been established.

In the light of these ideas, the present study proposes to analyze clinical, biochemical and electrocardiographic findings that can easily be revised by any specialist, in order to see if there are prognostic elements for patients with alcoholic cardiomyopathy.

Experimental part

Material and methods

A number of 100 patients diagnosed with dilated cardiomyopathy and admitted in the Cardiology Department of Sf. Spiridon Emergency Hospital in Iasi, Romania were analyzed in the study.

The epidemiological data (age, sex), the type of cardiomyopathy and the *New York Heart Association* (NYHA) functional class, along with the medical treatment of the patients (beta-blockers, diuretics, ACE inhibitors, antiarrhythmics), biochemical parameters (the value of Na, K, creatinine in the serum of the patients, eGFR calculated by MDRD formula - *Modification of Diet in Renal Disease*), and the electrocardiographic patterns (LBBB, the prolonged QT interval) were registered.

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Statistical analysis was performed using Microsoft Excel 2010 and SPSS Statistics version 17.0 for Windows 7. The value of $p < 0.05$ was considered statistically significant.

Results and discussions

49% of the patients were diagnosed with alcoholic dilated cardiomyopathy and included in the study. The rest of 51% had different types of dilated dilated cardiomyopathy (22% - ischemic, 15% - valvular and 14% - another form (fig. 1) and were excluded from the analysis.

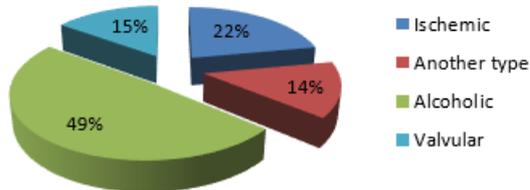


Fig. 1 Distribution of dilated cardiomyopathy etiology

All the patients included were male. 30 (61.2%) were younger than 65 years, 18 (36.7%) were between 65 and 74 years and 1 patient (2.04%) was older than 75 years, with an average age of 62.75 years.

The NYHA functional class distribution was: 43 patients (87.75%) in functional class III and 6 (12.25%) in functional class IV. We noticed that all the patients with alcoholic dilated cardiomyopathy included in this study received beta-blockers, ACE inhibitors and diuretics, 87.75% had digoxin treatment and just 12.25% needed amiodarone in their therapeutic approach.

We reviewed some of the biochemical parameters to establish their prognostic value in ACM. The statistical analyze of eGFR (estimated glomerular filtration rate) calculated by MDRD formula showed an average value of 56.57 mL/min/1.73m². 26 patients (53%) had an eGFR < 60 mL/min/1.73m², and 23 patients (47%) an eGFR e+ 60 mL/min/1.73m². The ionogram data revealed that just 6.12% had severe hyponatremia (serum Na < 125 mmol/L), and 4.08 % hypokalemia (serum K < 3.5 mmol/l), 28.57% had moderate hyponatremia (serum Na 125-129 mmol/L) and 65.3% had mild hyponatremia (serum Na 130-135 mmol/L), while 93% had hyperkalemia (serum K > 5.1 mmol/L) (fig. 2).

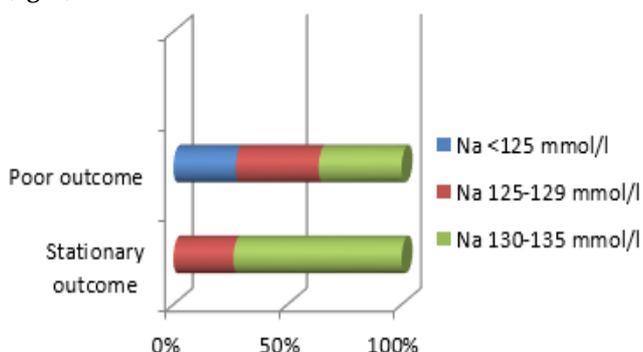


Fig. 2 Association between serum Na level and patients outcome

The electrocardiogram analyses showed 10 patients (20.4%) with morphology of LBBB (left bundle branch block), an 11 patients (22.4%) with severe evolution and poor outcome (fig. 3). None of the patients included in study had long QT interval.

We tried to determine whether or not there is a connection between the presence of LBBB and the poor outcome of patients using statistical analyzes. Based on Pearson correlation result of 0.94 between the two variables, these indicates that there is a positive linear,

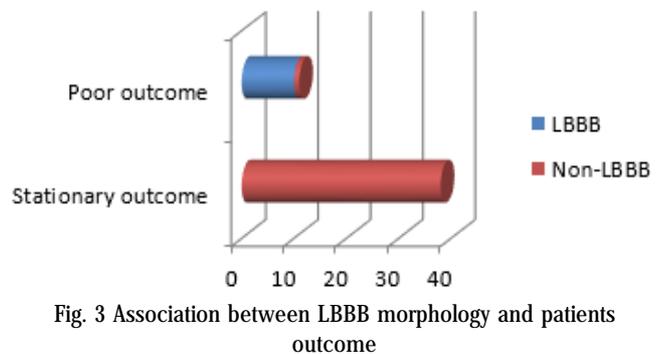


Fig. 3 Association between LBBB morphology and patients outcome

strong correlation between LBBB and the severe evolution ($p < 0.00001$).

A wide range of parameters have been proposed to have prognostic values in heart failure and dilated cardiomyopathy. The predictors for severe outcome and mortality remain a complex issue nowadays. Numerous recent studies have tried to demonstrate the value of biochemical, electrocardiographic and echocardiographic parameters in predicting the outcome of patient with non-ischemic dilated cardiomyopathy.

In idiopathic cardiomyopathy, the value of new-onset LBBB has proved to be an independent predictor of long-term mortality requiring a more aggressive therapy [9], similar to ischemic dilated cardiomyopathy [10].

Guzzo-Merello G et al showed in their study that LBBB was an independent predictor of ventricular arrhythmias for patients with ACM and decreased left ventricle ejection fraction (LVEF d+40%). LBBB identified patients with a higher risk of sudden cardiac death. Also, compared with idiopathic dilated cardiomyopathy (IDCM) malignant ventricular arrhythmias were found to be more frequent in the ACM group which associated LBBB [7].

It is well known that a LVEF $\leq 40\%$ is associated with an important prognostic impact, and a low systolic function is a predictor of mortality. A study conducted in Germany on patients with non-ischemic dilated cardiomyopathy emphasized the idea that a LVEF $\leq 35\%$, QTc interval > 440 ms, and impaired renal function with an eGFR < 60 mL/min/1.73m² (as was also showed in CHARM trial). On the other hand, LBBB morphology, presence of atrial fibrillation, mild mitral regurgitation and the need for digitalis treatment had no effects on patients' outcome. It is important to note that they excluded from the study those with ACM, valvular heart disease and hypertension [11].

Literature data has shown some electrocardiographic differences between LBBB morphology in ischemic and non-ischemic dilated cardiomyopathy. Bayes-Genes et al. concluded in their study that there is a statistically significant correlation between S wave voltage in precordial leads and etiology of DCM. V3 voltage > 2100 iV represented the most specific and sensitive parameter from their analysis for non-ischemic etiology [12].

We determined a strong, linear correlation between the presence of LBBB and the poor outcome of patients with ACM, similar to the one noted in literature data. A QRS width > 120 ms was associated in literature with severe evolution, along with the absence of beta-blocker treatment, the need of digitalis and the presence of atrial fibrillation [5, 8, 13]. All the patients included in our study with ACM had beta-blocker treatment. We could not find any statistical correlation between the digitalis treatment, neither with the decreased eGFR and the poor outcome. Also, severe hiponatremia was associated with a poorer outcome, without a statistical significance level.

Guzzo-Merello G et al showed a better prognostic for patients with ACM compared to IDCM, probably based on

a degree of recovered systolic function in patients with abstinence or decreased to moderate alcohol consumption. These two were associated with the same outcome in the study. The mean age was 49.6 years in the Spanish study compared to 62.75 years in our study. Similar, the majority of patients included were male (99%), versus 100% in our study [8]. Similar studies reported an incidence of approximately 40% ACM from the total of DCM (in our study -49 %), comparative with the incidence reported in European Society of Cardiology statement position from 2016 of 21-32% ACM from the total group of DCM [2,5,8].

In our opinion, LBBB impact on the prognostic of patients with DCM is mainly determined by the asynchronies of contraction and ventricular relaxation [14]. Recent studies, using magnetic resonance imaging (MRI) showed that not all patients with LBBB that could benefit from CRT (cardiac resynchronization therapy) improve their heart failure symptoms, based on the difference of left ventricle filling morphology and the origin of the conductance delay [15-17].

Also, LBBB has a great impact on myocardial contractile reserve and coronary flow in non-ischemic dilated cardiomyopathy. This leads to microvascular dysfunction, and the need for optimizing medical and interventional treatment [18, 19].

The prognostic of patients with DCM and heart failure manifestations is influenced by renal function impairment and electrolyte imbalance. We did not find any statistical evidence between the parameters analyzed and the patient's outcome, but hyponatremia was an independent negative prognostic factor especially in patients enrolled in the NYHA IV functional class.

Study limits

The limits of our study are represented by the small amount of patient included in the study that could cause some biases in statistical analyses. There were no female patients included and it is known that the percentage affected by ACM is much lower (approximately 14% [4]) but they are more vulnerable, developing the disease at a lower exposing period to alcohol than men. We didn't assess the prognostic value of echocardiographic parameters or the impact of natriuretic atrial peptides in patient with ACM. This study opens the perspective for larger, multivariate analyses on dilated non-ischemic cardiomyopathy.

Conclusions

Our study results confirmed that alcoholic dilated cardiomyopathy represents approximately one half of the total dilated cardiomyopathy analyzed and it mostly affects male patients. Left bundle branch block presence was strongly associated with a poor outcome and severe prognostic in patient with ACM. The association between LBBB and other negative prognostic factors as electrolyte imbalance especially hyponatremia greatly darkens the prognosis and evolution of these patients.

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