THE NEW ARMENIAN MEDICAL JOURNAL
Vol.9 (2015), No 1 p. 27-30

PROGNOSTIC IMPORTANCE OF MYOCARDIAL REMODELING PARAMETERS IN PATIENTS WITH SEVERE CHRONIC HEART FAILURE AND ISCHEMIC CARDIOMYOPATHY

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Received 11/15/2014; accepted for printing 02/28/2015

Abstract

We aimed to assess whether the echocardiographic parameters as indicators of myocardial remodeling are of prognostic importance in patients with symptomatic chronic heart failure.

The study included 104 patients with systolic heart failure. The ejection fraction was less than 35% in all patients and the severity of their chronic heart failure under the New-York Heart Association's classification was III-IV class. All patients underwent clinical and laboratory examination, including transthoracic echocardiography performed in M-mode and 2D echocardiography from a left parasternal and apical window. They and were followed up for cardiac related death and non-fatal cardiac events including hospitalization. The median follow-up period was 13 months. Echocardiographic markers of prognostic assessment have several advantages taking into consideration availability, non-invasive approach and safety of this method.

The logistical regression analysis revealed the following effective predictors for both survival and event free survival: left ventricular ejection fraction, left atrial diameter and volume index and tricuspid annular plane systolic excursion. *Other parameters, such as pulmonary artery maximal systolic pressure, severity of mitral regurgitation, and left atrial area were moderately correlated with cardiovascular events.*

In our heart failure population we studied both left atrium size and volume as functional characteristics of left atrium and their prognostic role in cardiovascular mortality and found moderate correlation between left atrium structural parameters and cardiac events.

Thus, further prospective studies are needed for establishing precise levels of variable echocardiographic parameters associated with mortality. This would be of great prognostic importance for physicians during follow-up evaluation of cardiac functions.

The findings help conclude that the ejection fraction, left atrium diameter, left atrium volume index and tricuspid annular plane systolic excursion *represent significant predictors of survival and event free survival in patients with symptomatic heart failure.*

Keywords: *chronic heart failure, echocardiographic parameters, myocardial remodeling, survival, prognosis.*

Introduction

Chronic heart failure (CHF) under the New-York Heart Association's classification (NYHA) III-IV functional class patients with higher risk of cardiac events require more intensive therapy, surgery, and heart transplantation in some cases [*Roger VL et al., 2004*].

One of the important points in the management of heart failure (HF) is the availability of reliable prognostic factors that enable patients and physicians to determine expectation of prognosis and treatment options. In addition, insights into which factors relate to poor outcome may help to advance concepts for new therapeutic directions.

Echocardiographic markers of prognostic assessment have several advantages taking into consideration availability, non-invasive approach and safety of this method.

The objective of the study was to find out prognostic parameters of echocardiographic assessment in patients with NYHA III-IV CHF and LV dysfunction (LVD) in order to consider the influence of baseline remodeling characteristics on outcomes.

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Materials and Methods

The study included 104 patients with symptomatic CHF (class III-IV according to New York Heart Association), who were admitted to the department of general and invasive cardiology, YSMU Hospital No. 1, as outpatients for primary assessment with one of following factors: documented hospital admission within the previous 12 months with discharge diagnosis of CHF or documented left ventricle (LV) ejection fraction (EF) < 35% within the previous 6 months. The study was conducted in accordance with the WMA Declaration of Helsinki. The research protocol was approved by the YSMU research ethics committee. All patients with established symptomatic CHF were undergoing treatment according to institutional guidelines.

Follow-up. Clinical outcome included cardiovascular death, HF hospitalization, recurrent myocardial infarction, and resuscitated sudden death.

The patients were followed up for cardiac mortality for 13 months. Cardiac death was defined as death due to congestive HF, myocardial infarction, and malignant arrhythmias or cardiac arrest. In patients who died out of hospital and in whom autopsy was not performed, a sudden death (within 1 hour of the onset of symptoms) was attributed to a cardiac cause.

Echocardiography. Transthoracic echocardiography was performed using a HP 1000 and HP 5500 models (HP Corporation, USA) with 2.5 Mhz transducers. Patients were examined in the supine and left lateral positions. They underwent conventional M-mode and 2D echocardiography from a left parasternal and apical window. LV volume measurements for the calculation of LV EF were carried out in biplane projection from apical four- two- chamber views. LV volume was computed using the biapical Simpson rule [*Lang RM et al., 2005*]. Mitral regurgitation was determined by tracing the net area obtained with color Doppler imaging and was expressed as a proportion of left atrial area. The tricuspid regurgitation pressure gradient between the right ventricle (RV) and the right atrium (RA) was calculated by the simplified Bernoulli equation [*Lang RM et al., 2005*]. Lateral tricuspid annular plane systolic excursion (TAPSE) (*mm*) was determined by M-mode echocardiography as the distance between the basal, end diastolic position of the tricuspid annulus and its greatest apical long axis movement [*Kaul S et al., 1984; Ghio S et al., 2000*]

Statistics: A p value < 0.05 was taken as a universal indicative limit for statistical significance in all analyses. Both univariate and multivariate analyses were used to quantify predictive power of examined variables to the predefined study endpoints: cardiac related deaths and combined endpoint.

A logistic regression analysis was applied as a final model identifying significant predictors of survival. The odds ratio of different echocardiographic predictors was estimated within its 95% confidence limits and supported by the significance level.

Analyses of clinical and echocardiographic parameters are performed by Stata 6 software.

Results

Table 1 demonstrates the clinical, echocardiographic variables in chronic heart failure population.

104 patients with chronic heart failure were included in the study. Of 104 patients studied there were 38 cardiac related deaths. No patient underwent myocardial revascularization.

All the followed up echocardiographic variables listed in table 2 were studied as potential pre-

Table 1.

Clinical characteristics of the HF patients

All patients	104
Cardiac related deaths during follow up period	38
Mean age (year)	65.15
Time from diagnosis (year)	7.1
Diabetes mellitus (patients)	35
Renal failure (patients)	50
Atrial fibrillation (patients)	27
Arterial hypertension (patients)	77
Mean left ventricular ejection fraction (%)	29% ±7.6%
left atrial diameter (cm)	4.42±1.2
tricuspid annular plane systolic excursion (cm)	1.77±0.84
left atrial area (cm^2)	22.87±11.2
left atrial volume index (ml/m^2)	52.12±36.6
pulmonary artery. hypertension stage	1.14

dictors of survival study end-points in logistic regression analysis.

The strongest echocardiographic predictors of mortality from all the causes were TAPSE (strongly related to mortality; r=-34.25; p=0.0001; CI 95%= 0.005-0.215), LA diameter and volume index (r=-48.9; p= 0.047; CI 95% = 1.2-5.17) and LVEF (r= -59.17, p=0.0001; CI 95% = 0.83-0.94), whereas other parameters such as pulmonary artery maximal systolic pressure, mitral regurgitation, LA area and RV diastolic diameter were not associated with mortality (are not statistically significant p>0.05 in our study).

Discussion.

There are several studies about the clinical and prognostic role of different parameters in patients with chronic heart failure. However data on the importance of ventricular systolic and hemodynamic parameters are rare. Reasons for determination of RV function in patients with left ventricular dysfunction may include secondary pulmonary hypertension or myocardial diseases [*Ghio S et al., 2000*]. The present study was aimed to evaluate echocardiographic remodeling parameters in an unselected population of hospitalized CHF patients.

Thus, the objective of our study was to assess the prognostic significance of noninvasively obtained parameters derived from echocardiography [*Lang RM et al., 2005*]. In most studies of the assessment of RV prognostic role in heart failure the right ventricular ejection fraction was obtained by radioisotope ventriculography or thermodilution technique was used [*DiSalvo TG et al., 1995; Juilliere Y et al., 1997; De Groote et al., 1998*]. Minority of authors measured the TAPSE, which is simple, noninvasive method of RV function assessment. The feasibility of TAPSE measurement is likely to be higher than for parameters which are dependent on clear endocardial definition, which has been reported as a limited factor in studies using fractional shortening change or 3- dimensional echocardiography [*Kaul S et al., 1984; Karatasakis GT et al., 1998; Zornoff LA et al., 2002*].

The MUSIC study showed that LA size is the predictor for both total and cardiovascular mortality in ambulatory HF patients with both preserved and reduced EF. We studied in our HF population both LA size and LA volume as functional characteristics of LA and their prognostic role in cardiovascular mortality and found moderate correlation between LA structural parameters and cardiac events [*Vazques R et al., 2009*]. We suppose that high compliance of LA to pressure and volume hemodynamic changes makes its structural monitoring parameters important for clinical and prognostic assessments.

The present study showed that LVEF and TAPSE are considered as significant predictors of one year mortality.

Several studies found controversy in the assessment of prognostic role of LV systolic dysfunction in patients with CHF [*Bhatia RS et al., 2006, Tsuchihashi-Makaya M et al., 2009*]. New remodeling echocardiographic parameters of adverse survival in HF are needed.

This study has several limitations. It did not include relationship between clinical data such as

Table 2.

Logistic regression analyses of different echocardiographic parameters association with 1 year mortality.

	Odds Ratio	Std. err	z	P > |z|
Ejection fraction	0.89	0.28	-3.86	0.0001
Left atrial diameter	2.28	0.95	1.98	0.047
Left atrial area	1.08	0.05	1.72	0.085
Right ventricle diameter	1.10	0.43	0.24	0.81
TAPSE	0.03	0.30	-3.53	0.0001
Pulmonary artery pressure (stage)	2.44	1.62	1.40	0.16
Mitral Regurgitation	1.61	0.78	0.22	0.82
Left atrial volume index	1.2	0.08	2.0	0.04

NYHA functional class, comorbidities, and BNP which are important prognostic factors. We did not evaluate the influence of treatment on the outcome and echocardiographic parameters.

Finally, this was a single cardiac study and included limited number of patients which could act on the statistical power and fail to reveal the statistical significant impact of other echocardiographic parameters on long-term mortality.

Conclusion

Several myocardial remodeling parameters such as decreased left ventricular ejection fraction, left atrial diameter, left atrial volume index and right ventricular systolic dysfunction as measured by TAPSE are independently associated with mortality in an unselected population of chronic heart failure patients. The obligatory assessment of mentioned noninvasive simple rapid assessment echocardiographic parameters may be applied as part of work-up in patients hospitalized for CHF.

Further prospective studies are needed for establishing precise levels of variable echocardiographic parameters associated with mortality. This would be of great prognostic importance for physicians during follow-up evaluation of cardiac functions.

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