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Impact of left ventricular function on health-related quality of life in coronary artery disease patients

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ABSTRACT

Objective: The aim of the study was to investigate the relation between health-related quality of life (HRQoL) and left ventricular systolic and diastolic function parameters in stable coronary artery disease (CAD) patients with mild and moderate heart failure.

Materials and methods: This study included 758 CAD patients. Left ventricular ejection fraction (LVEF) and ratio of peak velocities of early (E) and late (A) diastolic mitral inflow, ratio E/A, deceleration time, isovolumic relaxation time were assessed. Patients completed the SF-36 questionnaire.

Results: There were no strong and significant associations between echocardiographic measures and HRQoL in NYHA I-II class patients. In NYHA III class in univariate linear regression analyses significant associations were found between LVEF and physical functioning ($\beta = 0.230$, $P = 0.009$) and role limitations due to physical problems ($\beta = 0.230$, $P = 0.009$) and these associations remain significant after adjustment for age, gender, hypertension, angina pectoris class, nitrate, ACE inhibitors and diuretics use. E/A ratio was significantly associated only with mental health domain ($\beta = 0.188$, $P = 0.048$), and this association remains significant after all adjustments.

Conclusions: In stable CAD patients with NYHA I-II functional class HRQoL was not strongly associated with left ventricular function; in NYHA III functional class patients' greater systolic function mainly was associated with better physical health and better diastolic function, with better mental health.

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1. Introduction

Coronary artery disease (CAD) is a major cause of mortality and disability in developed countries and causes a negative impact on the physical, psychological, social, and occupational functioning of patients [1]. CAD is a major contributor to the progression of heart failure [2] and the most useful method for confirmation of the diagnosis of heart failure is echocardiography [3]. The most common echocardiographic abnormalities seen in patients with heart failure related to systolic function is reduced left ventricular ejection fraction (LVEF) and in cases with preserved LVEF related to diastolic dysfunction – abnormalities of the mitral inflow pattern. Left ventricular systolic and diastolic dysfunctions are important clinical prognostic factors for outcomes in stable CAD and heart failure and related with poor prognosis [4,5].

The primary outcome interest has traditionally been mortality, but now researchers are increasingly interested in health-related quality of life. Health-related quality of life (HRQoL) is a subjective and multidimensional concept composed from a range of domains, including physical, social, emotional, mental, and functional health [6]. HRQoL is an important outcome in the management of patients with chronic diseases, such as CAD, when the main treatment aim is not only to reduce mortality rates, but also to improve symptoms and ability to perform daily activities [7]. In extensive research, HRQoL in stable and unstable CAD patients was shown to be associated with clinical CAD severity [8], social support [9] and psychological factors, including symptoms of mental distress such as depression or anxiety [10]. However, to the best of our knowledge, limited data exist on the impact of left ventricular function on HRQoL in CAD patients and findings of these studies are controversial. Gorkin and colleagues in the SAVE study (184 acute myocardial infarction patients) found that HRQoL parameters were uncorrelated with LVEF [11]. Another study of 256 acute myocardial infarction patients showed, that LVEF was a determinant for HRQoL 2.5 years later [12]. It has been shown that in patients with systolic and diastolic heart failure, the impairment of HRQoL was similar in both its mental and physical components [13]. However, another study showed that impaired physical quality of life in patients with diastolic dysfunction associates more strongly with neurohumoral activation than with echocardiographic parameters [14]. Data regarding the association of left ventricular function with HRQoL remain mixed and warrants additional research.

Therefore, the main aim of this study was to investigate the relation between HRQoL and left ventricular systolic and diastolic function parameters in a large sample of stable CAD patients with mild and moderate heart failure.

2. Materials and methods

The study was a cross-sectional investigation of consecutive stable CAD patients attending the Clinic of Cardiovascular Rehabilitation, Behavioral Medicine Institute of the Lithuanian University of Health Sciences in Palanga, Lithuania, from January 2010 until September 2012 for routine cardiac examination. Patients were not included in the study if they had cognitive disorientation or communicative disabilities, had other severe diseases or were unable to understand and read Lithuanian. All patients were receiving standard treatment for secondary prevention of CAD and heart failure according to existing guidelines [3,15]. A total of 768 CAD patients were invited to participate in the study. However, 10 (1.3%) patients did not consent to participate in the study and our final study sample consisted of 758 CAD patients (64.6% men; mean age 60 ± 10 years). The study and its consent procedures were approved by the Ethics Committee for Biomedical Research at Lithuanian University of Health Sciences, Kaunas, Lithuania. Written informed consent was obtained from each study patient.

All patients were evaluated for demographic characteristics (age and gender), clinical characteristics, including New York Heart Association (NYHA) functional class [16], angina pectoris class [17], heart failure stages [18], hypertension grades [19], previous coronary interventions, history of diabetes mellitus and use of medications. During consultation of cardiologists patients were asked if they had symptoms of dyspnea, orthopnea or dependent edema. They were also examined for the presence of a tachycardia, lung crepitations, peripheral edema and response to treatment directed toward heart failure symptoms. Heart failure clinical status was ascertained according to clinical scores based on the NYHA classification of functional status [16] and criteria for the clinical diagnosis of CHF [18]. The mean exercise capacity, evaluated using a standardized computer-driven bicycle ergometer, was 73.6 W (SD, 36.0).

Health-related quality of life was evaluated using the 36-item Short Form Medical Outcome Questionnaire (SF-36) [20]. It is a 36-item questionnaire that measures 8 multi-item dimensions of health: physical functioning, social functioning, role limitations due to physical problems, role limitations due to emotional problems, mental health, energy/vitality, pain, and general health perception. For each dimension item scores are coded, summed, and transformed on to a scale from 0 (worst possible health state) to 100 (best possible health state).

Echocardiography characteristics were evaluated using 2D and M-mode and Doppler echocardiographic examinations by means of an ultrasound scanner, Mylab 50 Xvision LA 523 (Esaote Biomedica, Genoa, Italy). LVEF was quantified by the biplane disk summation method (using the modified biplane Simpson method) on the two-dimensional echocardiographic images from the apical four- and two-chamber views according to the recommendations of the American Society of Echocardiography [21]. We include patients with systolic and diastolic HF. Patients with diastolic HF were with symptoms and signs of HF and with normal or only mildly reduced LVEF. The mean of LVEF was $48.4\% \pm 8.7\%$. LV systolic function was categorized according to EF (<40%, 40%–50%, >50%). LV diastolic function was measured by ratio of peak velocities of early (E) and late (A) diastolic mitral inflow (E/A), and E-wave deceleration time (DT), isovolumic relaxation time (IVRT) using Doppler echocardiography [21]. E/A ratio <1 and DT >240 ms, IVRT >90 ms indicated impaired relaxation; E/A >2, DT <160 ms, IVRT <70 ms, restrictive diastolic dysfunction; E/A ratio of 1–1.5 and DT >240 ms, IVRT <90 ms, as pseudonormal diastolic dysfunction.

2.1. Statistical analysis

Descriptive statistic was presented as means ± standard deviation (M ± SD) or numbers of cases (percentage). Univariate linear regression analyses were performed to assess the associations between scores of SF-36 domains and left ventricular function echocardiographic parameters in NYHA I–II and in NYHA III patients. Next, we employed multivariate linear regression analyses (enter method) to evaluate same associations adjusting for gender and age (Model 1) and adjusting for gender, age, hypertension, angina pectoris class, nitrate, ACE inhibitors and diuretics use (Model 2). A probability of 0.05 or less was used as a criterion to include an independent variable into the multivariate model. A probability level of $P < 0.05$ was considered as statistically significant. Data were analyzed with the SPSS 17.0 for Windows (SPSS Inc., Chicago, IL, USA).

3. Results

Demographic and clinical characteristics of all patients and stratified by the NYHA class are summarized in Table 1. Patients (490 men and 268 women) had a mean age of 60 years (SD, 10), the majority of them had heart failure stage B (57.4%) and C (28.9%), angina pectoris (51.1%), previous myocardial infarction (48.9%), coronary artery bypass graft surgery (4.2%), more than 6 months after acute interventions, and had grade 2 arterial hypertension (44.1%), ACE inhibitors, diuretics use. The mean LVEF was 48.4% (SD, 8.73). More than half of the patients (58.4%) had left ventricular systolic dysfunction (LVEF < 50%) and 15% of the patients, LVEF below 40%. The mean left ventricular diastolic function parameter E/A ratio was 0.95 (SD 0.28), E/A <1 was in 512 (67.5%) patients, E/A ≥1 but <2 was in 241 (31.8%) patients and E/A ≥2 was in 5 (0.7%) patients. NYHA III class patients were significantly older, more female; had more severe hypertension, lower LVEF and angina pectoris; used more nitrates, ACE inhibitors, diuretics (48%) and had worse health-related quality of life. Therefore, we conducted a separate analysis in patients with heart failure mild (NYHA class I–II) and moderate symptoms (NYHA class III).

Table 2 shows significant differences in associations between HRQoL and left ventricular systolic and diastolic function parameters. After adjusting for possible confounders there were no strong and significant associations in NYHA I–II class patients and several strong and significant associations were found in NYHA III class patients. In NYHA III functional class in univariate linear regression analyses significant associations were found between LVEF and physical functioning ($\beta = 0.230$, $P = 0.009$) and role limitations due to physical problems ($\beta = 0.230$, $P = 0.009$), and these associations remained significant after adjustment for age, gender, hypertension, angina pectoris class, nitrate and ACE inhibitors, diuretics use. E/A ratio was significantly associated only with mental health domain ($\beta = 0.188$, $P = 0.048$), and this association remains significant after all adjustments.

4. Discussion

Our study revealed significant differences in the associations between HRQoL and left ventricular systolic and diastolic function parameters in patients with stable CAD in different NYHA functional classes. In NYHA I-II functional classes HRQoL was not strongly associated with left ventricular function; in NYHA III functional class greater systolic function mainly was associated with better physical health and better diastolic function, with better mental health.

Our results indicate that objective parameters, such as LV systolic and diastolic function, are important determinants of HRQoL in stable CAD patients with more expressed heart failure symptoms and these associations are independent from demographic and clinical characteristics.

There may be several explanations how the LVEF affects HRQoL. Patients with reduced LVEF may experience symptoms of fatigue, dyspnea and reduced activity. These symptoms can affect the patients' quality of life. In previous our study, we found that fatigue strongly correlated with HRQoL [22]. On the other hand, a reduced EF may not have any symptoms; this condition frequently is referred to as asymptomatic LV dysfunction. The association between LVEF and HRQoL increased with decline in functional class, suggesting that, in early CAD phase, other factors might play a major role in HRQoL and, with progression of functional decline, cardiovascular factors may be more important in HRQoL. Our findings that LVEF is associated with HRQoL correspond to the study by Coyne et al. [23]. In a large sample of post myocardial infarction patients (1848 patients) they found that LVEF was significantly related to physical and social function, psychological well-being and perceived health status after adjustment for demographic and clinical characteristics. Ecochard et al. [24] in 671 patients analyzed correlations between myocardial dysfunction assessed within the first month after myocardial infarction and HRQoL perceived one year later. The main result of this study indicates that low LVEF, high number of abnormally contracting segments, as well as high number of diseased vessels during the first month after myocardial infarction are independent predictors of discomfort perception in one year later.

Previous studies that failed to show relationships between LVEF and HRQoL in cardiac patients were performed mostly on patients without significant deterioration of LVEF. For example, Sjoland et al. [25] analyzed patients who underwent coronary artery bypass grafting (CABG) without concomitant valvular surgery. In their sample HRQoL scores did not differ significantly between patients with normal and depressed LVEF in any of the dimensions, neither before nor 2 years after the operation. The authors explained the absence of differences regarding HRQoL by the lower proportion of patients with significant depressed LVEF less than 40% (9%). One of the biggest study was performed by Mattera et al. [26]. The authors conclude that in CAD patients resting LVEF was not associated with HRQoL in their population. However it also must be mentioned that only a small percentage of patients had an abnormal LVEF. Ruo et al. [27] performed the cross-sectional Heart and Soul Study of 1024 adults with stable CAD. They found that depressive symptoms were strongly associated

Table 1 – Demographic, clinical characteristics and health-related quality of life in NYHA I–II and NYHA III class patients with stable coronary artery disease.

Variable	All patients (n = 758)	NYHA I-II (n = 630)	NYHA III (n = 128)	P*
Age, years, mean ± SD	60 ± 10	59 ± 10	66 ± 10	<0.001
Men, n (%)	490 (64.6)	419 (66.5)	71 (55.5)	0.017
History of diabetes mellitus, n (%)	78 (10.3)	61 (9.7)	17 (13.3)	0.222
Diagnosis, n (%)				0.218
Angina pectoris	387 (51.1)	328 (52.1)	59 (46.1)	
Previous myocardial infarction	371 (48.9)	302 (47.9)	69 (53.9)	
Previous interventions, n (%)				
Percutaneous coronary intervention	595 (78.5)	486 (77.1)	109 (85.1)	0.066
Coronary artery bypass graft surgery	32 (4.2)	27 (4.3)	5 (3.9)	0.968
Hypertension grades, n (%)				<0.001
1	44 (5.8)	41 (9.4)	3 (3.1)	
2	334 (44.1)	285 (65.4)	49 (51.0)	
3	154 (20.3)	110 (25.2)	44 (45.8)	
Heart failure stages, n (%)				<0.001
A	104 (13.7)	98 (15.6)	6 (4.7)	
B	435 (57.4)	398 (63.2)	37 (28.9)	
C	219 (28.9)	134 (21.3)	85 (66.4)	
Angina pectoris class, n (%)				<0.001
1	190 (25.1)	183 (29)	7 (5.5)	
2	364 (48.0)	291 (46.2)	73 (57.0)	
3	31 (4.1)	9 (1.4)	22 (17.2)	
Medications use, n (%)				
Nitrate	432 (57.0)	336 (53.3)	96 (75.0)	<0.001
Beta-blockers	381 (50.3)	317 (50.3)	64 (50.0)	0.965
ACE inhibitors	577 (76.1)	464 (73.7)	113 (88.3)	<0.001
Diuretics	167 (22.0)	106 (16.8)	61 (47.7)	<0.001
SF-36 domains, score, mean ± SD				
Physical functioning	63 ± 23	66 ± 22	46 ± 22	<0.001
Role limitation due to physical problems	36 ± 40	39 ± 39	20 ± 31	<0.001
Role limitation due to emotional problems	50 ± 42	54 ± 41	33 ± 39	<0.001
Social functioning	63 ± 25	65 ± 25	54 ± 23	<0.001
Mental health	63 ± 18	65 ± 18	58 ± 19	<0.001
Energy/vitality	56 ± 25	58 ± 18	47 ± 20	<0.001
Pain	58 ± 25	60 ± 25	47 ± 26	<0.001
General health perception	43 ± 16	44 ± 16	35 ± 15	<0.001
Echocardiography, mean ± SD				
LVEF, %	48.4 ± 8.7	49.2 ± 8.3	44.5 ± 9.7	<0.001
E/A	0.95 ± 0.28	0.95 ± 0.27	0.98 ± 0.33	0.299
Deceleration time, ms	214.3 ± 44.0	212.4 ± 41.8	224.4 ± 53.4	0.008
Isovolumic relaxation time, ms	96.4 ± 10.7	95.9 ± 10.4	98.8 ± 12.1	0.015
LVEF, n (%)				
>50%	315 (41.6)	279 (44.3)	36 (28.1)	<0.001
40%–50%	333 (43.9)	280 (44.4)	53 (41.4)	0.528
<40%	110 (14.5)	71 (11.3)	39 (30.5)	<0.001
E/A ratio, n (%)				0.212
<1	512 (67.5)	410 (68.3)	70 (63.1)	
≥1 but <2	241 (31.8)	187 (31.2)	39 (35.1)	
≥2	5 (0.7)	3 (0.2)	2 (1.8)	

NYHA, New York Heart Association; SF-36, 36-item Short Form Medical Outcome Questionnaire (higher score reflect better-perceived health); LVEF, left ventricular ejection fraction; E, peak velocity of early diastolic mitral inflow; A, peak velocity of late diastolic mitral inflow.
* Differences between NYHA I-II class and NYHA III class were tested using independent-sample t tests and the Pearson χ^2 test.

with health status outcomes; in contrast, two physiological measures of disease severity – LVEF and ischemia – were not. Authors concluded that mood disturbance is a primary variable influencing HRQL and that the two traditional measures of cardiac function, LVEF and ischemia, had a minimal influence on patient reported health status. Despite a large sample of this study, the prevalence of systolic dysfunction was very low (12%). In our sample more than 58.4% of the patients had left ventricular systolic dysfunction that is why we think our sample is more informative in this case.

Diastolic dysfunction is often unaccompanied by overt congestive heart failure. Despite the lack of symptoms, advanced diastolic dysfunction with normal EF is associated with reduced quality of life and structural abnormalities that reflect increased cardiovascular risk [28]. It was shown that subjects with LV diastolic dysfunction had a tendency to be female and older [29]; therefore, in our analysis, we adjusted for these factors. Also it was shown that abnormalities of left ventricular diastolic function were independently associated with the impairment of exercise capacity [30]. So, this may

Table 2 – Significant determinants of SF-36 domains in univariate and in multivariate models of 758 patients with CAD.

SF-36 domains	Model	Significant β (P)			
		NYHA I-II (n = 630)		NYHA III (n = 128)	
		LVEF	E/A	LVEF	E/A
Physical functioning	Univariate		0.090 (0.028)	0.230 (0.009)	
	Model 1			0.240 (0.006)	
	Model 2			0.225 (0.011)	
Role limitation due to physical problems	Univariate		0.147 (0.000)	0.230 (0.009)	
	Model 1		0.108 (0.010)	0.220 (0.014)	
	Model 2		0.090 (0.032)	0.217 (0.018)	
Role limitation due to emotional problems	Univariate		0.101 (0.013)		
	Model 1				
	Model 2				
Social functioning	Univariate				
	Model 1				
	Model 2				
Mental health	Univariate		0.092 (0.024)		0.188 (0.048)
	Model 1		0.099 (0.020)		0.214 (0.029)
	Model 2				0.205 (0.049)
Energy/vitality	Univariate		0.116 (0.004)		
	Model 1		0.103 (0.015)		
	Model 2				
Pain	Univariate				
	Model 1				
	Model 2				
General health perception	Univariate		0.105 (0.010)		
	Model 1		0.091 (0.031)		
	Model 2				

Model 1, adjusted for gender and age; Model 2, adjusted for gender, age, hypertension, angina pectoris class, nitrate and diuretics, ACE inhibitors use.
NYHA, New York Heart Association; LVEF, left ventricular ejection fraction; E, peak velocity of early diastolic mitral inflow; A, peak velocity of late diastolic mitral inflow.

affect lower physical functioning, but in our study we found that in NYHA III class diastolic function parameter was mainly associated with mental health. On the other hand, it is not improbable, as has been recently published, that LV diastolic function parameters, such as the E/A ratio, were progressively altered across the levels of depression ($P = 0.007$) [31]. It should be noted that this study was conducted on participants without known cardiovascular disease. Do these findings fit for CAD patients, additional studies are needed. Many prior prospective studies with the aim of investigating the association between depression and LV function have reported controversial results. Some of them have found the associations between depression and lower LVEF and/or higher Killip class [32,33], but many others [34–36] found no relationship between depression and echocardiographic measures. This may be due to several reasons. Barth et al. in a recent meta-analysis [37] have noted that studies in this area varied considerably. Moreover, prior studies that found a relationship between depression and cardiac disease severity parameters have sampled patients after acute coronary events such as acute myocardial infarction [38] or coronary artery bypass surgery [39]. It must be mentioned that rates of elevated depressive symptoms are particularly high at the time of hospitalization and tend to decrease within the subsequent months [40], so this could be transient distress rather than true clinical depression. In the Heart and Soul study in a sample of 1020 patients with stable CAD, the investigators found no evidence that major depression was associated with systolic dysfunction, diastolic dysfunction, inducible ischemia, or cardiac wall motion abnormalities [34].

We highlight several limitations of this study. Left ventricular diastolic function was measured by E/A ratio and deceleration time. There is, therefore, a risk that E/A ratio, deceleration time underestimates LV diastolic dysfunction and for precisely evaluation there is a need for more comprehensive echocardiographic evaluation. There are no data on natriuretic peptide BNP or NT pro-BNP for confirming the heart failure level. On the other hand, the major strengths of our study include a large sample size of stable CAD patients and evaluation associations between patient-reported outcomes and objective measures of disease severity.

5. Conclusions

In stable CAD patients with NYHA I-II functional class HRQoL was not strongly associated with left ventricular function parameters; in NYHA III functional class greater systolic function mainly was associated with better physical health and better diastolic function, with better mental health.

Conflict of interest

The authors state no conflict of interest.

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