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Short Communication

Relationship of left ventricular diastolic dysfunction with quality of life in heart failure patients with reduced ejection fraction (HFrEF)

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Abstract

Heart failure is a complex clinical manifestation due to diastolic dysfunction and systolic dysfunction of the left ventricle (LV). Diastolic dysfunction of the LV plays an important role in worsening the quality of life (QoL) in heart failure patients. The aim of this study was to assess the relationship between the severity or grade of LV diastolic dysfunction and QoL in heart failure with reduced ejection fraction (HFrEF) patients. A retrospective cohort study was conducted at the Cardiac Center of H. Adam Malik Hospital, Medan, Indonesia, from January 2022 to December 2022. This study included inpatients and outpatients aged above 18 years who were diagnosed with HFrEF, identified by echocardiography with an ejection fraction of ≤40%. Echocardiography was performed to evaluate left ventricular diastolic dysfunction, and QoL was assessed using the Minnesota Living with Heart Failure Questionnaire (MLHFQ) 6–12 months after the severity of LV diastolic dysfunction was confirmed. The MLHFQ was classified into good and poor QoL. The severity of LV diastolic function was measured using the E/A ratio, mean E/e' ratio, tricuspid regurgitation velocity (TR Vmax), and left atrial volume index (LAVI), and was classified into grades I, II, and III. The relationships between the severity of diastolic dysfunction and other factors with QoL were measured using Chi-squared, Fisher's exact test, or Mann-Whitney test, as appropriate. A total of 96 patients were included in the study, of which 56 (58.3%) patients had grade I, 12 (12.5%) had grade II, and 28 (29.2%) patients had grade III of LV diastolic dysfunction. There were 77 (80.2%) and 19 (19.8%) patients with good and poor QoL, respectively. This study revealed a significant relationship between the severity of LV diastolic dysfunction and QoL in HFrEF patients with p=0.040. In conclusion, the degree of LV diastolic dysfunction is related to the QoL of HFrEF patients and therefore better comprehensive management strategies should be considered in HFrEF cases to address the impact of LV diastolic dysfunction on QoL.

Keywords: HFrEF, LV diastolic dysfunction, quality of life, MLHFQ, echocardiography

Introduction

Heart failure (HF) is a complex clinical syndrome caused by a decrease in the structural and functional abilities of ventricular filling or blood ejection. Clinical diagnosis of HF is based on typical symptoms (e.g., shortness of breath, fatigue, and ankle swelling) and signs (e.g., tachycardia, third heart sound, rales) as well as objective evidence of heart structural or functional

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Received: February 7, 2024 - Accepted: June 3, 2024 - Published online: June 19, 2024

abnormality leading to elevated intracardiac pressures or inadequate cardiac output at rest or during exercise [1,2]. In Indonesia, based on the data from the Basic Health Research (Riskesdas) in 2018, there were over one million HF cases [2,3]. The number of HF cases is increasing, as well as the incidence of re-hospitalization and death [4].

HF is due to diastolic dysfunction and systolic dysfunction of the left ventricle (LV). LV diastolic dysfunction occurs due to impaired LV relaxation, potentially accompanied by decreased restoring forces and increased LV space stiffness, resulting in increased left ventricular filling pressure. LV diastolic pressure can be measured by invasive procedures or non-invasive techniques such as echocardiography [5,6]. A comprehensive evaluation of LV diastolic function can be achieved by assessing a combination of parameters, including E velocity, A velocity, E/A ratio, deceleration time (DT), isovolumic relaxation time (IVRT), tissue Doppler imaging (TDI), tricuspid regurgitation velocity (TR Vmax) and left atrial volume index (LAVI) [6]. The parameter e' obtained from TDI examination and E/e' ratio >15 are predictors of increased LV diastolic pressure [7].

A study found that the patients diagnosed with HF following acute myocardial infarction (AMI) were often reported with poor quality of life (QoL) and it was independently associated with a higher mortality rate within one year post-AMI [7]. Another study found no difference in QoL, clinical symptoms, frequency of remission, and six-month mortality between HF patients with systolic dysfunction and those with pure diastolic dysfunction [8]. The aim of this study was to evaluate the relationship between the degree of left ventricular diastolic dysfunction and QoL in HF with reduced ejection fraction (HFrEF) patients.

Methods

Study design and setting

A prospective cohort study was conducted at the Cardiac Center of H. Adam Malik Hospital, Medan, Indonesia, from January 2022 to December 2022. The echocardiography examination was conducted among HF patients to assess the diastolic dysfunction severity (grade). After 6–12 months, the QoL of the patients was measured using the Minnesota Living with Heart Failure Questionnaire (MLHFQ).

Sample and criteria

The Cochran's sample size formula was used to calculate the minimum sample size, resulting in 88 participants. The total sampling strategy was used to recruit the samples. This study included inpatient and outpatient HFrEF cases identified by echocardiography with ejection fraction (EF) of ≤40% aged above 18 years old. Patients with poor-quality echocardiography features, heart disease with valvular and congenital abnormalities, arrhythmia, and using permanent pacemakers were all excluded from the study.

Data collection

Demographic data, such as age, gender, body mass index (BMI), comorbidity, medications, and a follow-up on rehospitalization, were collected. An echocardiography examination was carried out with the GE Healthcare VIVID S60N and GE Healthcare VIVID e9 BT13 devices, and the diastolic functions were measured, and the results were confirmed by two cardiologists. LV diastolic function was measured using the E/A ratio, mean E/e' ratio, TR Vmax, and LAVI. Subsequently, the degree of LV diastolic dysfunction was determined using the American Society of Echocardiography (ASE) guideline 2016 LV Diastolic Function Evaluation [5] and categorized into grade I, II, and III (**Figure 1**).

The QoL of each patient was measured using MLHFQ [9] through a telephone interview conducted 6–12 months after the degree of LV diastolic dysfunction was confirmed. The Indonesian version of MLHFQ has been validated by a previous study [10] and used in this study. The questionnaire comprises 21 questions rated on a 6-point Likert scale, ranging from 0 (disagree) to 5 (strongly agree); therefore, the higher MLHFQ score suggests a lower QoL of patients [10]. A study proposed a cut-off score for the MLHFQ as follows: less than 24 indicates good QoL, 24–45 suggests moderate QoL, and more than 45 reflects poor QoL [11]. Another study

combined the MLHFQ and SF-36 questionnaires to evaluate the QoL in HF patients [12]. The study defined the good QoL as an MLHFQ score below 24 or an MLHFQ score under 45 with an SF-36 score of at least 60 [12]. Based on that, we decided to adopt an MLHFQ score of <24 for good QoL and an MLHFQ score of ≥24 for poor QoL.

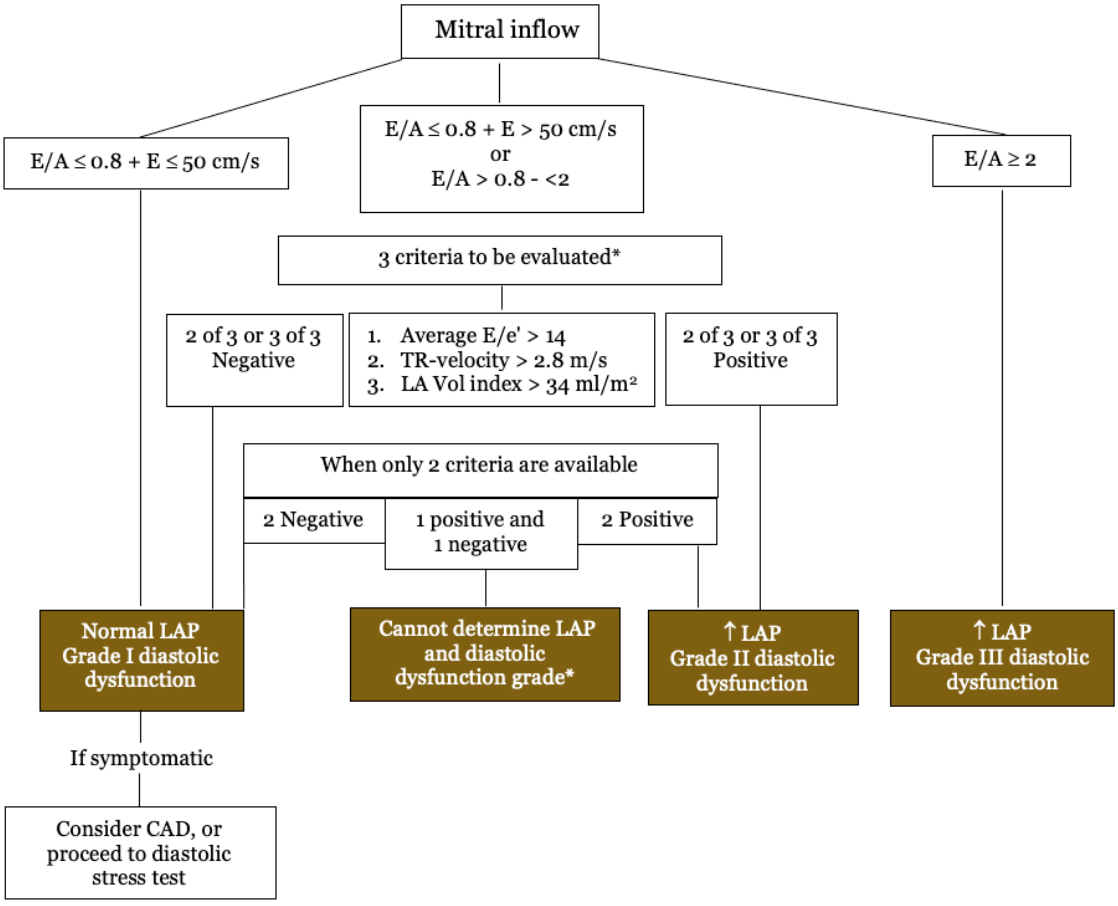

Figure 1. Evaluation of LV diastolic dysfunction used in this study. *: LAP is indeterminate if only 1 of 3 parameters is available. Pulmonary vein S/D ratio <1 applicable to conclude elevated LAP in patients with depressed LV EF.

Statistical analysis

Categorical data were presented in frequency (n) and percentages (%). Numerical data were presented with mean (average) and standard deviation (SD) for data with normal distributions, while the non-normal distribution of numerical data used median (minimum-maximum). The relationships between the patients' characteristics and diastolic dysfunction grades with QoL (measured using the MLHFQ scoring system) were measured using Chi-squared, Fisher's exact test or Mann-Whitney test, as appropriate based on the data. A *p*-value of <0.05 was considered statistically significant. All analysis was performed using SPSS version 24 software (IBM SPSS, Chicago, USA).

Results

Characteristics of heart failure patients

A total of 96 HFrEF patients were included in this study and their characteristics are presented in **Table 1**. The majority of the patients were male (83.3%) and coronary artery disease (89.6%) was the most common comorbidity. The mean values of diastolic function parameters were recorded as follows: mitral inflow (E/A) 1.54±0.99; TDI (E/e') 15.32±7.37; TR Vmax 15.32±7.37 m/s, and LAVI 37.35±15.26 mL/m². Based on the degree of LV diastolic dysfunction, there were 56 patients (58.3%) with grade I, 12 patients (12.5%) with grade II, and 28 patients (29.2%) with grade III. We found 71 patients (74%) on diuretics, 54 patients (56.3%) on angiotensin-converting

enzyme inhibitors (ACE-I) and angiotensin II receptor blockers (ARBs), 78 patients (81.3%) on beta-blockers, 51 patients (53.1%) on mineralocorticoid receptor antagonists (MRA), 22 patients (22.9%) on angiotensin receptor-neprilysin inhibitor (ARNI), and 13 patients (13.5%) on sodium/glucose cotransporter 2 inhibitors (SGLT2-I). No patients were hospitalized within 30 days after echocardiography; however, 12 patients (12.5%) were hospitalized within six months after the echocardiography examination. According to the MLHFQ questionnaire, we found 77 patients (80.2%) with a good QoL and 19 patients (19.8%) with a poor QoL.

Table 1. Characteristics of patients with heart failure with reduced ejection fraction (HFrEF) included in the study (n=96)

Variable	Frequency (percentage)
Age, mean±SD	54.65±10.75 years
Gender	
Male	80 (83.3)
Female	16 (16.7)
Body mass index (BMI), mean±SD	24.5±21 kg/m²
Comorbidity	
Coronary artery disease (CAD)	86 (89.6)
Hypertensive heart disease (HHD)	29 (30.2)
Type 2 diabetes mellitus (T2DM)	36 (37.5)
Chronic kidney disease (CKD)	16 (16.7)
Cardiomyopathy	12 (12.5)
Diastolic function, mean±SD	
Left ventricular ejection fraction (LVEF)	31.57±6.02%
Mitral inflow (E/A)	1.54±0.99
Tissue doppler imaging (TDI)	15.32±7.37
tricuspid regurgitation velocity (TR Vmax)	2.54±0.77 m/s
Left atrial volume index (LAVI)	37.35±15.26 mL/m²
Tricuspid annular plane systolic excursion (TAPSE)	17.65±4.03 mm
Diastolic dysfunction	
Grade I	56 (58.3)
Grade II	12 (12.5)
Grade III	28 (29.2)
Medications	
Diuretic	71 (74)
Angiotensin-converting enzyme inhibitors (ACE-I)/angiotensin II receptor blockers (ARB)	54 (56.3)
Beta-blocker	78 (81.3)
Mineralocorticoid receptor antagonists (MRA)	51 (53.1)
Angiotensin receptor-neprilysin inhibitor (ARNI)	22 (22.9)
SGLT2-I	13 (13.5)
Rehospitalization follow-up	
30 days	0
6 months	12 (12.5)
MLHFQ score	
Good quality of life	77 (80.2)
Poor quality of life	19 (19.8)

Characteristic factors associated with quality of life

Our data indicated that the LVEF, E/A ratio, and E/e' ratio were associated with the QoL of HFrEF patients, which showed *p*-values of 0.026, 0.018, and 0.006, respectively (**Table 2**). LVEF was significantly higher in patients with good QoL than in those with poor QoL. The values of E/A, E/e' ratio, and LAVE were significantly lower in HFrEF patients with good QoL than those with poor QoL.

Table 2. Factors associated with quality of life (QoL) in heart failure with reduced ejection fraction (HFrEF) patients (n=96)

Characteristics	Quality of life based on MLHFQ		*p*-value
	Good	Poor	
Gender			
Male	62 (80.5%)	18 (94.7%)	0.182[a]
Female	15 (19.5%)	1 (5.3%)	
Coronary artery disease (CAD)			
Yes	68 (88.3%)	18 (94.7%)	0.681[a]

Characteristics	Quality of life based on MLHFQ		*p*-value
	Good	Poor	
No	9 (11.7%)	1 (5.3%)	
Hypertensive heart disease (HHD)			
Yes	23 (29.9%)	6 (31.6%)	1.000[a]
No	54 (70.1%)	13 (68.4%)	
Type 2 diabetes mellitus (T2DM)			
Yes	30 (39%)	6 (31.6%)	0.741[a]
No	47 (61%)	13 (68.4%)	
Chronic kidney disease (CKD)			
Yes	11 (14.3%)	5 (26.3%)	0.299[a]
No	66 (85.7%)	14 (73.7%)	
Cardiomyopathy			
Yes	11 (14.3%)	1 (5.3%)	0.449[a]
No	66 (85.7%)	18 (94.7%)	
Rehospitalization (6 months)			0.246[a]
Yes	8 (10.4%)	4 (21.1%)	
No	69 (89.6%)	15 (78.9%)	
Age	56 (18–83)	59 (30–71)	0.387[b]
Body mass index (BMI)	24.44 (16.53–63.54)	22.89 (15.15–29.38)	0.327[b]
Left ventricular ejection fraction (LVEF)	34 (15–40)	28 (17–39)	0.026[b*]
Mitral inflow (E/A)	1.01 (0.28–6.25)	2.04 (0.72–4.71)	0.018[b*]
E/e' ratio	12.6 (5.9–38.24)	17 (9.13–45.35)	0.006[b*]
Left atrial volume index (LAVI)	34 (12.03–101.22)	37.65 (18–61)	0.532[b]

[a] Analyzed with Fisher exact test
[b] Analyzed with Mann-Whitney test
* Statistically significant at $p<0.05$

Association between diastolic dysfunction degree with quality of life (QoL)

Most HF patients with grade I diastolic dysfunction had a good QoL (63.6%) and 52.6% of HF patients with grade III diastolic dysfunction had poor QoL. There was a significant relationship between the degree of LV diastolic dysfunction and the QoL in HFrEF patients (p=0.040) (**Table 3**).

Table 3. Relationship of degree of diastolic dysfunction with quality of life using MLHFQ questionnaire

Diastolic dysfunction	Quality of life based on MLHFQ		Total	*p*-value
	Good	Poor		
Grade I	49 (63.6%)	7 (36.8%)	56 (58.3%)	0.040
Grade II	10 (13.0%)	2 (10.5%)	12 (12.5%)	
Grade III	18 (23.4%)	10 (52.6%)	28 (29.2%)	

Discussion

Our findings showed that the average age of the patients was 54.65±10.75 years, with 83.3% being male and 16.7% female. According to the Framingham study, the annual incidence in men with HF (per 1000 events) increased from 3 at ages 50 to 59 to 27 at ages 80 to 89, while women had a relatively one-third lower incidence of HF than men [1-3]. Another study similarly reported that HF incidence in developed countries increases with age, rising from around 1% in individuals under 55 to more than 10% in those aged 70 or older [1]. A previous study reported that although the incidence of HF in women is lower than in men, women have a longer life expectancy than men, so the prevalence of HF in women is higher in the age group >80 years [13]. This is attributed to the presence of estrogen in women's bodies, which provides a protective effect against cardiovascular disease—an advantage not found in men. Consequently, men are more vulnerable to cardiovascular conditions such as HF [14].

We found some comorbidities such as CAD (89.6%), HHD (30.2%), and DM (37.5%) in this study. CAD and hypertension are the most common comorbidities found in HF patients from developing countries [1]. Another study found that CAD was the most prevalent comorbidity in HF in Asia, Australia, and the Middle East, while in Africa, HF was commonly associated with HHD and cardiomyopathy [15]. CAD can lead to increased left ventricular wall stress, causing ventricular enlargement and persistent restrictive LV filling. This, in turn, raises the LV filling pressure [16]. LV diastolic dysfunction can be evaluated through an echocardiography

examination, which classifies the condition into three grades. Grade III, the most severe, is identified by a mitral inflow E/A ratio greater than 2 and an increase in LV filling pressure [5,17].

This study found a significant relationship between the degree of LV diastolic dysfunction and the QoL of HFrEF assessed using the MLHFQ questionnaire (p=0.040). This is consistent with other studies that reported diastolic dysfunction has an important role in worsening the QoL of HFrEF patients assessed by the MLHFQ questionnaire [18,19]. In support, a study also states diastolic dysfunction is a significant predictor of QoL and physical capacity [20]. A previous study showed that QoL, clinical symptoms, frequency of hospital admission, and six-month mortality were similar in kidney failure patients with systolic dysfunction and those with pure diastolic dysfunction [8,21]. Grade III of LV dysfunction is associated with an increase in LV filling pressure, which can lead to signs of congestion. This congestion negatively affects the QoL in HF patients [20].

This study reported the average value of the E/e' ratio of 15.32±7.37 showed an increase in left ventricular diastolic pressure. A study revealed that an E/e' ratio of >15 indicates an increase in left ventricular filling pressure, while an E/e' ratio of <8 indicates a normal left ventricular filling pressure [6]. Elevated E/e' ratios are also predictors of prognosis worsening in patients with HF [5,8].

Our study found a statistically significant relationship between LVEF, E/A ratio, and E/e' ratio and QoL of HFrEF patients, as evaluated using MLHFQ questionnaires. An increase in E/A ratio and E/e' ratio will increase the left atrial pressure, pulmonary capillary pressure (PCWP) and left ventricular filling pressure, therefore can worsen the QoL of HF patients [16,22].

There are some limitations of this study. The patients' QoL was assessed via telephone interview and this could be associated with bias. During the study, some patients were unable to be contacted, resulting in some patients being excluded.

Conclusion

This study revealed a significant relationship between the degree of left ventricular diastolic dysfunction and the QoL of HFrEF patients assessed through the MLHFQ questionnaire (p-value 0.04). Further studies with larger sample sizes are necessary to evaluate the QoL of HFrEF patients, possibly employing the same questionnaire system with a shorter interval between echocardiography examination and QoL assessment.

Ethics approval

This study has received ethical approval from the Research Ethics Committee of the Faculty of Medicine, University of Sumatera Utara, with a registration number of 1229/KEPK/USU/2023.

Acknowledgments

None to declare.

Competing interests

All the authors declare that there are no conflicts of interest.

Funding

This study received no external funding.

Underlying data

Derived data supporting the findings of this study are available from the corresponding author on request.

How to cite

Khaidirman SK, Hasan H, Andra CA, *et al.* Relationship of left ventricular diastolic dysfunction with quality of life in heart failure patients with reduced ejection fraction (HFrEF). Narra J 2024; 4 (2): e707 - http://doi.org/10.52225/ narra.v4i2.707.

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