DOI: 10.4274/jarem.galenos.2024.08870
J Acad Res Med 2024;14(2):72-6

The Relationship Between Normal-range Ejection Fraction and Diastolic Function

Mustafa Yılmaz[1], Mehmet Rasih Sonsöz[2]

[1]University of Health Sciences Türkiye, Gaziosmanpaşa Training and Research Hospital, Clinic of Cardiology, İstanbul, Türkiye
[2]University of Health Sciences Türkiye, Başakşehir Çam and Sakura City Hospital, Clinic of Cardiology, İstanbul, Türkiye

Cite this article as: Yılmaz M, Sonsöz MR. The Relationship Between Normal-range Ejection Fraction and Diastolic Function. J Acad Res Med. 2024;14(2):72-6

ABSTRACT

Objective: Understanding ejection fraction (EF) limits are crucial for the evaluation of diastolic function (DF). Therefore, in our study, we aimed to compare the DFs between patients with low-normal and high-normal EFs.

Methods: A total of 70 patients who were followed in our clinic were prospectively included in our study. Those with an EF of 55-62% were included in the low-normal EF group, and those with an EF >62% were included in the high-normal EF group. Subsequently, the relationship between DF and EF was analyzed.

Results: Both groups exhibited similarities in demographic characteristics, such as age, sex, and additional medical conditions, demonstrating homogeneous distribution among the groups. No statistically significant difference was observed between the groups in terms of diastolic and systolic parameters.

Conclusion: No relationship was found between normal EF and DF. Nonetheless, our work can serve as a model for more extensive research on this topic.

Keywords: Diastolic function, ejection fraction, diastolic parameters, echocardiography

INTRODUCTION

In patients with known or suspected heart disease, despite certain limitations, the most commonly used parameter for evaluating left ventricular systolic function is still the ejection fraction (EF). According to expert recommendations in clinical guidelines, the normal thresholds for EF are 54% or higher in women and 52% or higher in men (1). However, in some studies involving a large number of patients, individuals with EF levels of approximately 65% had the lowest mortality (2,3). Therefore, some argue that normal EF values should be redetermined. In the assessment of diastolic function (DF), as in many other fields, a defined threshold value for EF exists, thereby altering the DF evaluation algorithm. According to the 2016 DF guidelines, a threshold of 50% is considered normal for EF (4). Our study aimed to investigate the relationship between EF values above this threshold and DF.

METHODS

Study Population

Patients admitted to the outpatient clinic of our center between April and June 2022 were included in this cross-sectional, single center study. Comprehensive clinical histories were obtained from the hospital system and during assessment. Detailed physical examinations and electrocardiograms were conducted for the patients, followed by two-dimensional transthoracic echocardiography (TTE) using the Vivid S60 (GE Healthcare, USA) device at our center. TTE procedures were performed by an operator holding the European Association of Cardiovascular Imaging TTE certification.

Our study adhered to the standards of the Declaration of Helsinki and was conducted with the approval of the University of Health Sciences Türkiye, Gaziosmanpaşa Training and Research Hospital Clinical Research Ethics Committee (no: 387) on December 22, 2021.

Inclusion Criteria

Patients aged 18-80 years were eligible for the study. Individuals with an EF ranging from 55% to 62% were categorized as the low-normal EF group, whereas those with an EF value exceeding 62% were classified as the high-normal EF group.

ORCID IDs of the authors: M.Y. 0000-0002-2113-9891; M.R.S. 0000-0002-1535-5168.

Corresponding Author: Mustafa Yılmaz,
E-mail: drmustafayilmaz@outlook.com

Received Date: 17.05.2024 **Accepted Date:** 08.08.2024

J Acad Res Med 2024;14(2):72-6

Exclusion Criteria

The exclusion criteria included conditions hindering the assessment of DF, such as moderate to severe mitral insufficiency, advanced aortic insufficiency, and atrial fibrillation. Patients with wall motion abnormalities in regions where Doppler parameters were assessed were also excluded. Patients with a history of cardiac surgery, constrictive pericarditis, hypertrophic cardiomyopathy, or extreme tachy-bradyarrhythmia during TTE evaluation were excluded.

Two-dimensional Transthoracic Echocardiography

All patients underwent detailed TTE using the parasternal long-axis, parasternal short-axis, apical 2-, 3-, and 4-chamber views, and subcostal windows. EF was measured using the biplane Simpson method. DF was evaluated using the parameters outlined in Nagueh et al.'s (4) 2016 guidelines. Assessment included left atrial volume index, E/e', mitral E/A, tricuspid regurgitation peak velocity, mitral septal and lateral e' velocities, tricuspid E/A, tricuspid lateral e', as well as tricuspid annular plane systolic excursion (TAPSE), tricuspid lateral S wave velocity, inferior vena cava diameter, and right atrial pressure evaluations. Additionally, indexed echocardiographic data were obtained from the patient's height, weight, and body surface area. Cardiac output and stroke volumes were calculated for all patients.

Assessment and Grading of the Diastolic Function

Patients were initially evaluated for the presence of diastolic dysfunction (DD). The criteria outlined by Nagueh et al. (4) were taken into consideration. Those with low EF or left ventricular hypertrophy were considered to have DD, and staging was performed. In the other patient groups, the presence of DD was initially assessed, followed by staging. DD was staged as grade 0 (no dysfunction), grade I (impaired relaxation), grade II (pseudonormalization), or grade III (restrictive pattern).

Consent to Publish the Report

Informed consent was obtained from the patients.

Artificial Intelligence

Artificial intelligence was not used in this study.

Statistical Analysis

Continuous data was expressed as the mean ± standard deviation or median (interquartile range) values, whereas categorical data was described as proportions and was evaluated using the chi-square test or Fisher's Exact test. Kolmogorov-Smirnov test was used to evaluate the distribution of the data. Student's t-test or Mann-Whitney U test was used to compare continuous variables. The correlation between left ventricular ejection fraction (LVEF) and the degree of DD was assessed using Spearman's correlation test. Data were analyzed using SPSS version 29.0 (SPSS Inc., Chicago, IL, USA). A two-sided p-value <0.05 was considered statistically significant.

RESULTS

Demographic Characteristics

The study included a total of 70 patients, further divided into two groups based on LVEF: 55-62% (n=40) and LVEF >62% (n=30). The mean age of the entire cohort was 50±14 years, and there was no significant difference between the two LVEF groups (p=0.146). Female proportion was 40%, with a non-significant distribution between LVEF categories (p=0.338). Other baseline characteristics, including body surface area, hypertension, diabetes mellitus, coronary artery disease, heart rate, and blood pressure, showed no statistically significant differences between the groups (Table 1).

Left ventricular end-systolic diameter was significantly lower in the high-normal EF group (p=0.005). The left ventricular wall thickness, left atrium size, stroke volume, and TAPSE [were similar between the groups (Table 2)].

Table 1. Demographic characteristics of the patients

	All patients (n=70)	LVEF 55-62% (n=40)	LVEF >62% (n=30)	p-value
Age, years	50±14	47±14	52±14	0.146
Female, n (%)	28 (40)	14 (35)	14 (47)	0.338
BSA, m^2	1.9±0.2	1.9±0.2	2.0±0.3	0.305
HT, n (%)	30 (43)	17 (43)	13 (43)	0.944
DM, n (%)	5 (7)	4 (10)	1 (3)	0.284
CAD, n (%)	11 (16)	5 (13)	6 (20)	0.394
Heart rate, bpm	75±13	74±15	75±11	0.713
SAP, mmHg	128±22	128±27	127±15	0.911
DAP, mmHg	76±12	78±13	75±10	0.421

LVEF: left ventricular ejection fraction, BSA: body surface area, HT: hypertension, DM: diabetes mellitus, CAD: coronary artery disease, SAP: systolic arterial pressure, DAP: diastolic arterial pressure

Two-dimensional Transthoracic Echocardiography Parameters

Diastolic Function Parameters

Parameters such as the mitral E-wave, mitral A-wave, E/A ratio, deceleration time, and E' velocities did not differ significantly between the LVEF groups. Similarly, the tricuspid regurgitation velocity and the parameters related to the tricuspid inflow and E' velocities did not differ significantly (Table 3).

Diastolic Dysfunction

The study assessed DD, and the distributions across grades (none, grade I, grade II, grade III, indetermined) was comparable between the LVEF groups (p=0.837) (Table 4). There was no significant correlation between LVEF and the degree of DD (r=0.004, p=0.837) (Table 4).

Correlation Analysis

A scatterplot demonstrated no significant relationship between LVEF and DD in the study population (r=0.004, p=0.978), emphasizing the independence of these parameters (Figure 1).

DISCUSSION

DF assessment is a critical component of echocardiography (4). This is because distinguishing between normal and abnormal DF is crucial for diagnosing diastolic heart failure (HF), which accounts for half of all heart failure (HF) cases and has a mortality rate of least as high as that of HF with reduced EF (5). Therefore, addressing uncertainties in this area through research could contribute to a more accurate evaluation of DF and to advancements in the diagnosis and treatment of diastolic HF.

In our study, we tested the hypothesis that 'if the lower limit of normal EF is in the range of 60-65%, patients with EF below this range should have worse DF and diastolic parameters'. DF and diastolic parameters were compared between patients with low-normal (55-62%) and high-normal (>62%) EF, aiming to investigate the relationship between normal-range EF and DF and diastolic parameters. Although numerical differences were observed for various diastolic parameters, our study did not identify statistically significant distinctions between the two groups.

EF is a crucial metric for assessing cardiac systolic function and is often considered a cornerstone in clinical decision-making.

Table 2. TTE parameters of patients

	All patients (n=70)	LVEF 55-62% (n=40)	LVEF >62% (n=30)	p-value
LVEDD, mm	46±4	47±4	45±4	0.083
LVESD, mm	30±4	32±5	29±3	0.005
IVSD, mm	11±2	10±2	11±2	0.488
PWD, mm	9±2	9±1	9±2	0.358
RWT	0.39±0.08	0.37±0.07	0.40±0.08	0.137
LV mass index	81±20	83±23	80±17	0.491
LA, mm	37±6	37±7	37±7	0.735
LAVI, mL/m^2	26±8	25±9	27±8	0.337
SV, mL	83±20	80±20	87±20	0.182
TAPSE, mm	22±4	22±4	23±5	0.281

TTE: two-dimensional transthoracic echocardiography, LVEF: left ventricular ejection fraction, LVEDD: left ventricular end-diastolic diameter, LVESD: left ventricular end-systolic diameter, IVSD: interventricular septal diameter, PWD: pulse wave Doppler, RWT: relative wall thickness, LV: left ventricular, LA: left atrial, LAVI: left atrial volume index, SV: stroke volume, TAPSE: tricuspid annular plane systolic excursion

Table 3. Diastolic parameters of patients

	All patients (n=70)	LVEF 55-62% (n=40)	LVEF >62% (n=30)	p-value
Mitral E-wave (cm/s)	72±19	71±21	76±17	0.296
Mitral A-wave (cm/s)	65±11	69±15	69±15	0.998
Mitral E/A	1.1±0.3	1.1±0.4	1.1±0.3	0.643
DT, ms	170±45	188±57	170±42	0.134
Mitral septal E' wave (cm/s)	8±3	8±3	9±3	0.938
Mitral septal E/E' joints	9±4	9±4	10±3	0.503
Mitral lateral E/E' joints	7±3	6±2	7±3	0.398
Peak TRV m/sc	2.2±0.4	2.2±0.4	2.3±0.5	0.610

LVEF: left ventricular ejection fraction, DT: deseleration time, TRV: tricuspid regurgitation velocity

Table 4. Diastolic function of patients

DD	All patients	EF 55-62% n (40)	EF >62% n (30)	p-value: 0.837
None	31 (44)	17 (45)	14 (47)	
Grade I	31 (44)	17 (45)	14 (47)	
Grade II	5 (7)	3 (8)	2 (7)	
Grade III	1 (2)	1 (3)	0 (0)	
Indetermined	2 (3)	2 (5)	0 (0)	

EF: ejection fraction, DD: diastolic dysfunction

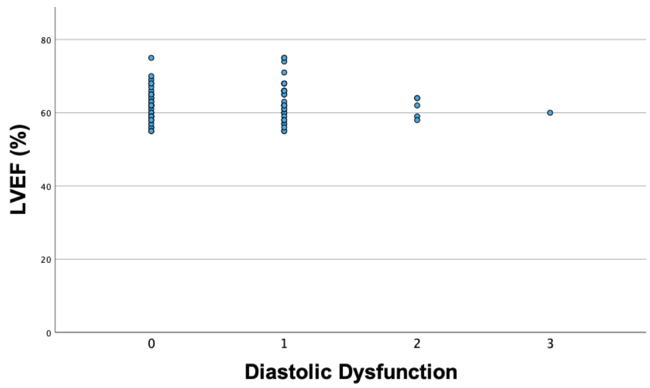

Figure 1. The scatterplot demonstrates no relationship between left ventricular ejection fraction and DD in the study population
DD: diastolic dysfunction, LVEF: left ventricular ejection fraction

The conventional normal range for EF is generally regarded as 50-55%. However, recent research has introduced nuances to this understanding, revealing potential variations in mortality and morbidity outcomes associated with different EF ranges (6). A landmark study by Wehner et al. (3) (2020), which included a substantial cohort of 400,000 patients, challenged the traditional norm by identifying an EF range of 60-65% as associated with the lowest mortality rate. These findings hinted at a potential shift in the definition of normal EF. Similarly, Tsao et al. (7) demonstrated increased morbidity and mortality in patients with EF values 50%, emphasizing the clinical significance of variations within the normal range. The PARAGON-HF trial further nuanced this understanding by highlighting therapeutic benefits for women with an EF of up to 57% (8).

In guidelines related to DF, it is generally accepted that patients with impaired systolic function will have also impaired DF. For example, in the guidelines published in 2016, an EF value of 50% was considered a threshold value (4). The notion that the work performed during the systolic and diastolic phases of the heart may not be independent is not new. This occurs because the energy of external work performed during systole is restored by internal work performed during diastole (9). Therefore, if there is a disturbance in either of these phases, there should be a disturbance in the other as well. In a study conducted by de Simone (10), it was emphasized that systolic functions calculated from the midwall level and DFs show parallelism, and changes in both phases could occur concomitantly.

Study Limitations

In this study, we did not find the expected result, and there were limitations that could have contributed to this outcome. The most important limitation was the restriction in the number of patients and the inability to use strain echocardiography to evaluate left ventricular systolic function (11,12). Additionally, the single-center nature of the study and the inclusion of relatively healthy patients were other study limitations. However, we believe that elucidating the relationship between EF and DF is crucial, and conducting studies in this regard is essential. Therefore, we believe that the current study could pave the way for research in this area, as we could not identify any study directly evaluating the relationship in the literature.

CONCLUSION

In our study, no relationship was found between EF within the normal range and DF and parameters. To provide a clearer understanding of the relationship between EF within the normal range and DF, more extensive studies are required. Our study provides a nucleus for future studies in the field of normal-range LVEF and DD.

Ethics Committee Approval: Our study adhered to the tenets of the Declaration of Helsinki and was conducted with the approval of the University of Health Sciences Türkiye, Gaziosmanpaşa Training and Research Hospital Clinical Research Ethics Committee with 387 number on December 22, 2021.

Informed Consent: Informed consent was obtained from the patients.

Author Contributions: Concept - M.Y., M.R.S.; Design - M.Y., M.R.S.; Data Collection and/or Processing - M.Y.; Analysis and/or Interpretation - M.Y., M.R.S.; Literature Search - M.Y., M.R.S.; Writing - M.Y.

Conflict of Interest: The authors have no conflict of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

REFERENCES

1. Lang RM, Badano LP, Mor-Avi V, Afilalo J, Armstrong A, Ernande L, et al. Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. J Am Soc Echocardiogr. 2015; 28: 1-39.e14.
2. Stewart S, Playford D, Scalia GM, Currie P, Celermajer DS, Prior D, et al. Ejection fraction and mortality: a nationwide register-based cohort study of 499 153 women and men. Eur J Heart Fail. 2021; 23: 406-16.
3. Wehner GJ, Jing L, Haggerty CM, Suever JD, Leader JB, Hartzel DN, et al. Routinely reported ejection fraction and mortality in clinical practice: where does the nadir of risk lie? Eur Heart J. 2020; 41: 1249-57.
4. Nagueh SF, Smiseth OA, Appleton CP, Byrd BF 3rd, Dokainish H, Edvardsen T, et al. Recommendations for the Evaluation of Left Ventricular Diastolic Function by Echocardiography: An Update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. Eur Heart J Cardiovasc Imaging. 2016; 17: 1321-60.
5. Kittleson MM, Panjrath GS, Amancherla K, Davis LL, Deswal A, Dixon DL, et al. 2023 ACC Expert Consensus Decision Pathway on Management of Heart Failure With Preserved Ejection Fraction: A Report of the American College of Cardiology Solution Set Oversight Committee. J Am Coll Cardiol. 2023; 81: 1835-78.
6. Yeboah J, Rodriguez CJ, Qureshi W, Liu S, Carr JJ, Lima JA, et al. Prognosis of Low Normal Left Ventricular Ejection Fraction in an Asymptomatic Population-Based Adult Cohort: The Multiethnic Study of Atherosclerosis. J Card Fail. 2016; 22: 763-8.

7. Tsao CW, Lyass A, Larson MG, Cheng S, Lam CS, Aragam JR, et al. Prognosis of Adults With Borderline Left Ventricular Ejection Fraction. JACC Heart Fail. 2016; 4: 502-10.
8. Solomon SD, McMurray JJV, Anand IS, Ge J, Lam CSP, Maggioni AP, et al. Angiotensin-Neprilysin Inhibition in Heart Failure with Preserved Ejection Fraction. N Engl J Med. 2019; 381: 1609-20.
9. Cesarman E, Brachfeld N. Thermodynamics of the myocardial cell. A redefinition of its active and resting states. Chest. 1977; 72: 269-71.
10. de Simone G, Greco R, Mureddu G, Romano C, Guida R, Celentano A, et al. Relation of left ventricular diastolic properties to systolic function in arterial hypertension. Circulation. 2000; 101: 152-7.
11. Voigt JU, Pedrizzetti G, Lysyansky P, Marwick TH, Houle H, Baumann R, et al. Definitions for a common standard for 2D speckle tracking echocardiography: consensus document of the EACVI/ASE/Industry Task Force to standardize deformation imaging. Eur Heart J Cardiovasc Imaging. 2015; 16: 1-11.
12. Potter E, Marwick TH. Assessment of Left Ventricular Function by Echocardiography: The Case for Routinely Adding Global Longitudinal Strain to Ejection Fraction. JACC Cardiovasc Imaging. 2018; 11(2 Pt 1): 260-74.