

Association between diastolic stress test and H2FPEF score

Asociación entre prueba de estrés diastólico y puntuación H2FPEF

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Abstract

Objective: Heart failure with preserved ejection fraction is a highly prevalent disease; some advances for improving the diagnosis are the development of the H2FPEF score and the diastolic stress test for the evaluation of diastolic function. The objective is to describe the clinical and echocardiographic characteristics of patients referred for stress tests, and the association between the H2FPEF score and the results of the diastolic test. **Methods:** This is an analytical, observational, retrospective study. An exercise stress test was performed. The Chi-square test was used to establish an association between H2FpEF score and diastolic stress test results. Patients over the age of 18, in sinus rhythm, with the left ventricular ejection fraction > 54%, with no more than mild diastolic dysfunction on the baseline echocardiogram were included in the study. **Results:** A total of 99 patients met the eligibility criteria. About 49.5% were women, median age was 62.2 years. The H2FPEF score was low in 27.2%, intermediate 71.7%, and 1% in the high range. There was a high prevalence of hypertension 58.6%, diabetes 12.1%, and coronary disease 20.2%. The stress test was positive for diastolic dysfunction in 36.4% of the patients. A statistically significant association was found between the H2FPEF score and the diastolic stress test ($p = 0.02$). **Conclusions:** Although clinical scores such as H2FPEF help identify patients, a high percentage of patients are classified in the intermediate range. The diastolic stress test can help to make the diagnosis of diastolic function in this group of patients.

Keywords: Heart failure. Stress test. Diastolic function. Echocardiogram.

Resumen

Objetivo: La insuficiencia cardíaca con fracción de eyección preservada (FCFep) es una enfermedad de alta prevalencia, sin embargo, aún falta una estrategia de referencia para establecer el diagnóstico de FCFep. Algunos de los avances más importantes para mejorar el diagnóstico de FCFep son la puntuación H2FPEF y la prueba de esfuerzo para la evaluación de la función diastólica durante el ejercicio. El objetivo es describir las características clínicas y ecocardiográficas de los pacientes remitidos para pruebas de esfuerzo en un centro de referencia colombiano, y la asociación entre el puntaje H2FPEF con los resultados de la prueba de estrés diastólica. **Métodos:** Se trata de un estudio analítico, observacional y retrospectivo. Se realizó una ecocardiografía de esfuerzo solicitada por disnea o fatiga. La prueba Chi cuadrado se utilizó para establecer una asociación entre la puntuación H2FpEF y los resultados de la prueba diastólica. Se incluyeron pacientes mayores de 18 años, en ritmo sinusal, con fracción de eyección del ventrículo izquierdo igual o superior al 55%, con una disfunción diastólica no mayor de leve en el ecocardiograma basal. **Resultados:** Un total de 99 pacientes cumplieron los criterios de

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inclusión. El 49,5% de la población eran mujeres, la edad media fue de 62.2 años. La puntuación H2FPEF fue baja en 27.2%, intermedia 71,7% y 1% en el rango alto. Hubo una alta prevalencia de hipertensión 58.6%, diabetes 12.1% y enfermedad coronaria 20.2%. La prueba de esfuerzo fue positiva para disfunción diastólica en el 36,4% de los pacientes. Se encontró una asociación estadísticamente significativa entre la puntuación H2FPEF y la prueba de esfuerzo diastólico ($p = 0.02$).

Conclusiones: Aunque puntuaciones clínicas como H2FPEF ayudan a identificar a los pacientes, un alto porcentaje de pacientes se clasifican en el rango intermedio. La prueba de esfuerzo diastólico puede ayudar a realizar el diagnóstico de función diastólica en este grupo de pacientes.

Palabras clave: Insuficiencia cardíaca. Prueba de esfuerzo. Función diastólica. Ecocardiograma.

Introduction

Heart failure with preserved ejection fraction (HFpEF) is increasingly prevalent due to population aging and the growth of risk factors such as obesity. It is a challenging diagnosis and has been based on the findings of the resting echocardiogram^{1,2}. The problem is that a significant number of patients only have symptoms during physical activity; thus, only analyzing diastolic function at rest may not be sufficient to identify this group of patients³⁻⁵. Many studies have suggested the usefulness of diastolic stress test for showing diastolic function alterations with exercise⁶⁻⁸.

At the same time, a clinical score has been developed to identify patients with HFpEF: the H2FPEF⁹. This score confirms HFpEF with high scores or rules it out with low scores. However, intermediate scores require additional studies to confirm or rule out the diagnosis.

The objective of this study is to determine the association between diastolic dysfunction after exercise, clinical variables, and H2FPEF score in a population of patients referred for exercise stress test at a Colombian reference center.

Methods

The researchers retrospectively analyzed exercise stress test performed between January 2018 and December 2019 which had been ordered due to dyspnea or fatigue, from which images were extracted to evaluate diastolic function as well as contractility parameters.

A convenience sample was taken and patients who met the eligibility criteria were included in the study.

Inclusion criteria

Patients over the age of 18, in sinus rhythm, with a left ventricular ejection fraction (LVEF) equal to or > 55%, with no more than mild diastolic dysfunction

(grade 1) on the baseline echocardiogram, according to guidelines of the American Society of Echocardiography and the European Association of Cardiovascular Imaging¹⁰, were included in the study.

Exclusion criteria

Studies which were read as positive for myocardial ischemia were discarded, as well as those which did not fully report the diastolic function parameters. Patients with atrial fibrillation, significant mitral valve disease; at least moderate mitral annular calcification, any mitral stenosis or mitral regurgitation of more than moderate severity, mitral valve repair or prosthetic mitral valve, LV assist devices, left bundle branch block, and ventricular paced rhythms¹⁰, were excluded from the study.

Resting echocardiogram

A conventional resting echocardiogram was performed according to the American Society of Echocardiography's recommendations¹¹. The LVEF was evaluated using the modified Simpson's method measured from the apical four-chamber view; the left ventricular filling pressure was calculated by the ratio of early mitral inflow velocity to early diastolic mitral annular tissue velocity (E/e'); and pulmonary artery systolic pressure (PASP) was evaluated by the peak velocity of the tricuspid regurgitant jet, using Bernoulli's equation, plus the estimated right atrial pressure.

Post-exercise echocardiography stress protocol

Patients were evaluated using the Bruce protocol immediately after exercising on a treadmill, measuring the tricuspid regurgitant velocity before the 1st min and the E/e' ratio once mitral wave separation was observed. A septal E/e' ratio equal to or > 15 was used to

establish the presence of post-exercise diastolic dysfunction, accord of the most recent guideline of stress echocardiography¹²⁻¹⁴. The H2FPEF score was calculated for all patients and an association was sought with the diastolic stress test results.

Statistical analysis

Categorical variables were summarized in absolute and relative frequencies. The normal distribution of continuous variables was evaluated with the Kolmogorov–Smirnov test. They were normally distributed and therefore were expressed as mean \pm standard deviation (SD). For the bivariate analysis, the dependent variable was the result of the diastolic test (positive/negative); Pearson's Chi-square test was used to measure the association with the categorical independent variables and Student's t-test was performed for quantitative independent variables. Chi-square was used to determine the association between the H2FPEF score and the diastolic test results. Demographic and clinical data processing was performed using the SPSS® version 21.0 statistical package.

The study was conducted according to the rules of the Declaration of Helsinki and was approved by relevant ethical committees and/or regulatory bodies in participating hospitals. All patients gave written informed consent to participate, in accordance with national and local regulations.

Results

A total of 99 patients who met the eligibility criteria were included for data analysis (Fig. 1), the average age of the population was 62.2 years (SD 12.3), 49.5% were women. Altogether, 58.6% had a history of arterial hypertension, 12.1% had diabetes mellitus, and 20.2% had a prior diagnosis of coronary disease (Table 1).

The following echocardiographic parameters were obtained: LVEF 59.7% (SD 3.1); resting septal e' 7.5 cm/s (SD 1.1) and post-exercise septal e' 7.3 cm/s (SD 1.8); resting tricuspid regurgitant velocity 2, 4 mt/s (SD 21.0) with 2.8 mt/s (SD 37.0) post-exercise; and resting E/e' 9.7 cm/s (SD 1.6) with 12.6 cm/s (SD 4.6) after exercise.

Regarding to the terms included in the H2FPEF score, 13.1% of patients had a body mass index > 30 , 58.6% of patients with hypertension were treated with 2 or more medications, 6.1% had a history of paroxysmal atrial fibrillation, 27.3% had pulmonary hypertension, 56.5% were older than 65 years, and 63.6% had an $E/e' > 9$ (Table 2).

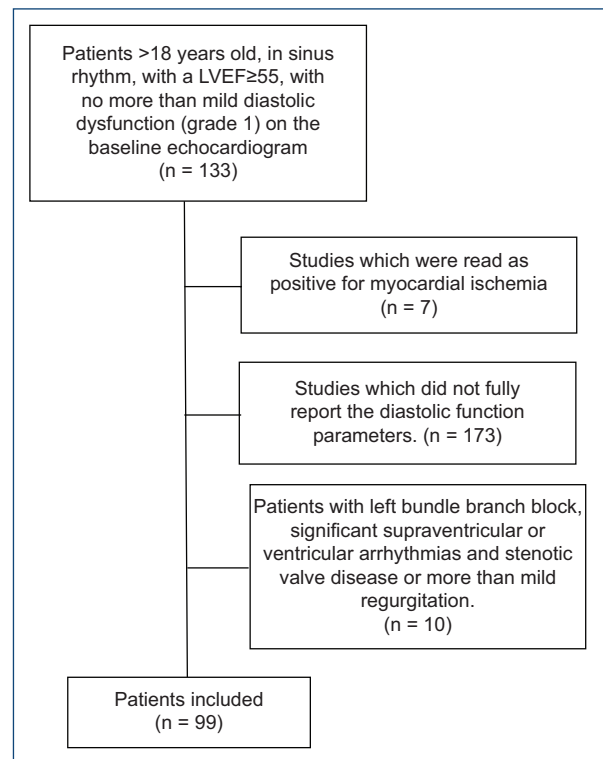


Figure 1. Patient's flow chart.

The average H2FPEF score was 2.3 (SD 1.4): 27.2% of the patients had a low H2FPEF score (0-1), 71.7% an intermediate score (2-5), and 1% a high score (≥ 6). About 12.5% of the patients with a low H2FPEF score had a positive stress test for diastolic dysfunction, in the intermediate range, the positivity was 45%.

The stress test was positive for diastolic dysfunction in 36.4% of the patients.

A statistically significant association was found between the H2FPEF score and the diastolic stress test ($p = 0.02$) (Table 3).

The use of the post-exercise tricuspid regurgitant velocity more than 3,4 mt/s as a parameter for the diagnosis of diastolic dysfunction was present in only one patient without $E/e' > 15$ and in 10 patients with $E/e' > 15$, all of these patients were classified as intermediate probability of having the disease according to the H2FPEF score.

Discussion

This study found a high frequency of diastolic dysfunction diagnosed by stress test in a population of symptomatic patients with a medium to high probability

Table 1. Clinical and echocardiographic characteristics of the study population, by diastolic stress test results

	Negative DST (n (%) = 36)	Positive DST (n (%) = 63)	p-value
Males	34 (54.0%)	16 (44.4%)	0,4*
Age (year, DS)	58.5 (± 11.74)	68.1 (± 10.5)	< 0.01 ⁺
BMI (DS)	25.7(± 3.1)	26.2 (± 3.6)	0.55 ⁺
BMI > 30	7 (11.1%)	6 (16.7%)	0.54*
Hypertension	30 (47.6%)	28 (77.8%)	0.01*
Paroxysmal AF	5 (7.9%)	1 (2.8%)	0.41*
DM	5 (7.9%)	7(19.4%)	0.11*
Coronary disease	8 (12.7%)	12 (33.3%)	0.19*
Dyslipidemia	20 (31.7%)	20 (55.6%)	0.33*
LVEF% (DS)	59.9 (± 2.1)	58.8 (± 4.4)	0.57 ⁺
Baseline TRV mt/s (DS)	2.3 (± 0.18)	2.5 (± 0.2)	< 0.01 ⁺
PASP mmHg (DS)	30.5 (± 3.5)	34.3 (± 4.1)	< 0.01 ⁺
Baseline E/e (DS)	9.3 (± 1.7)	10.3 (± 1.4)	< 0.01 ⁺
Post-exercise TRV mt/seg (DS)	2.6 (± 0.2)	3.2 (± 0.3)	< 0.01 ⁺
Post-exercise E/e' cm/seg (DS)	9.6 (± 2.2)	17.8 (± 2.6)	< 0.01 ⁺
Mets reached	9.8 (± 1.8)	8.4 (± 2.4)	< 0.01 ⁺

*Pearson's Chi-square.

⁺Student's t.

DET: diastolic stress test; SD: standard deviation BMI: body mass index; AF: atrial fibrillation; DM: diabetes mellitus; LVEF: left ventricular ejection fraction; TRV: tricuspid regurgitation velocity; PASP: pulmonary artery systolic pressure; Mets: metabolic equivalent of task.

of having the disease according to the H2FPEF score. These data are congruent with the prevalence reports of the disease, which have increased over the past decades; HFpEF constitutes up to 56% of all heart failure cases¹⁵. Despite the high prevalence of the disease, the ideal strategy for diagnosing it is still unclear, and thus, it is important to use other tools such as the exercise stress test and scores like H2FPEF. Some of the diagnostic difficulties have been the existence of multiple predisposing phenotypes such as diabetes, obesity, or kidney disease^{16,17}, along with the fact that, unlike patients with heart failure with reduced ejection fraction, in these patients, biomarkers such as natriuretic peptides may be within normal limits or only slightly elevated¹⁸.

Table 2. Positivity of the H2FPEF items by diastolic stress test results

	Clinical variable	Definition	Patients with a positive parameter	
			Negative DST (n = 6)	Positive DST (n = 36)
H	Heavy	BMI > 30 kg/mt ²	14 (22%)	13 (36%)
	Hypertension	Treatment with ≥ 2 antihypertensives	20 (32%)	13 (36%)
F	Atrial fibrillation	Paroxysmal or persistent	5 (8%)	1 (3%)
P	Pulmonary hypertension	PSAP > 35 mmHg	9 (14%)	17 (47%)
E	Elderly	> 60 years	27 (42.8%)	28 (77%)
F	Elevated filling pressures	E/e' > 9	39 (62%)	23 (64%)
	H2FPEF score		1.8 (sd 1.3)	3.2 (sd 1.3)

DST: diastolic stress test.

Table 3. Association of the total H2FPEF score and the diastolic stress test result

H2FPEF score (n = 99)	H2FPEF score	Positive DST (n = 36)	Negative DST (n = 63)	Association
Low 0-1 (n = 27)	0	1 (2.8%)	13 (20.6%)	p = 0.02*
	1	2 (5.6%)	11 (17.5%)	
Intermediate 2-5 (n = 71)	2	12 (33.3%)	21 (33.3%)	
	3	9 (25.0%)	9 (14.3%)	
	4	7 (19.4%)	8 (12.7%)	
High ≥ 6 (n = 1)	5	4 (11.1%)	1 (1.6%)	
	6	1 (2.8%)	0	

*Pearson's Chi-square test. DST: diastolic stress test.

This study found a high prevalence of a history of coronary disease with post-exercise diastolic dysfunction, it may have resulted from a selection bias in the referral for the exercise test. It has been reported relatively recently that the development of diastolic dysfunction during stress studies could, theoretically, be an early marker of myocardial ischemia and allow an

earlier diagnosis of coronary disease^{19,20}. Furthermore, Gimelli study, using nuclear medicine, suggests that post-stress diastolic function testing could help identify patients with non-obstructive coronary disease²¹.

Evaluation of the variables used for the H2FPEF score showed that, in general, they were more frequently positive in the population with a positive diastolic dysfunction stress test, except for age and atrial fibrillation. However, approximately 70% of the patients had intermediate scores which require further testing to be able to determine the presence or absence of HFpEF. Furthermore, there were patients with low scores and a positive test. The clinical characteristics of patients with HFpEF vary among population groups and the discrimination capacity of the clinical scores may also vary according to the population to which they are applied. It would be important to validate these scores in our population.

Although atrial fibrillation has been documented as a marker of diastolic dysfunction^{22,23}, in this study, this disease was more frequently found in the group of patients with normal diastolic function in response to exercise (1% vs. 5%). This could be due to the sample size and to the fact that the stress test was not performed on patients who had fibrillation at the time of the study, which constitutes a selection bias. Diastolic dysfunction increases with age; however, the lack of age-adjusted and standardized references may lead to overestimating its importance in the development of HFpEF²⁴.

Elevated baseline filling pressures, defined as $E/e' > 9$, were found in a high percentage of patients in both groups, although they were more prevalent in those with a positive diastolic dysfunction test. The E/e' ratio increases with age, from 7.8 at 35 years to 10.9 in individuals at or above the age of 75²⁵. Antonello study found that 48% of healthy individuals between the ages of 55 and 64 had an E/e' ratio > 10 , and in patients between 65 and 74 years old, this percentage increased to 63% of asymptomatic patients, suggesting that the cutoff points for this population should be modified²⁶. In our study, we found a total of 55 patients over the age of 60, 67% of whom had an E/e' ratio ≥ 10 ; the average E/e' ratio was 10.1, with no significant differences between those with post-exercise diastolic dysfunction and those without (10.2 and 10.0, respectively).

The tricuspid regurgitation velocity is usually used in the assessment of diastolic function, although its normal values at rest are well standardized, the same does not happen with the values during exercise, the

European guide suggests values for the diagnosis of diastolic dysfunction > 3.4 m/s¹⁴, while some authors such as Belyavsiy suggest a cutoff point of > 2.8 m/s²⁷. In our work, with the cutoff point of > 3.4 m/s, only one patient was found who did not meet the criteria of presenting an $E/e' > 15$, and this had a low pre-test probability. In addition, this parameter is the one with the lowest reproducibility with an intraoperative correlation of 65%, for which we decided not to use it in our work as a diagnostic criterion for diastolic dysfunction²⁸.

Limitations

This study's limitation includes its retrospective nature, the small sample size, and the NT pro-BNP or BNP levels which were not available. The elevated filling pressure findings were not validated by invasive measurements, which are the gold standard. This study's finding should be validated through prospective studies with a larger sample.

Conclusions

Although clinical scores such as H2FPEF help identify patients, a high percentage of patients are classified in the intermediate range. The diastolic stress test can help to make the diagnosis of diastolic function in this group of patients.

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Conflicts of interest

The authors declare no conflicts of interest.

Ethical disclosures

Protection of people and animals. The authors declare that no experiments were performed on humans or animals for this research.

Confidentiality of the data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors declare that no patient data appear in this article.

References

- Obokata M, Kane GC, Reddy YN, Olson TP, Melenovsky V, Borlaug BA. Role of diastolic stress testing in the evaluation for heart failure with preserved ejection fraction: a simultaneous invasive-echocardiographic study. *Circulation*. 2017;135:825-38.
- Paulus WJ, Tschöpe C, Sanderson JE, Rusconi C, Flachskampf FA, Rademakers FE, et al. How to diagnose diastolic heart failure: a consensus statement on the diagnosis of heart failure with normal left ventricular ejection fraction by the heart failure and echocardiography associations of the European society of cardiology. *Eur Heart J*. 2007;28:2539-50.
- Park JH, Marwick TH. Use and limitations of E/e' to assess left ventricular filling pressure by echocardiography. *J Cardiovasc Ultrasound*. 2011;19:169-73.
- Tschöpe C, Lam CS. Diastolic heart failure: what we still don't know. Looking for new concepts, diagnostic approaches, and the role of comorbidities. *Herz*. 2012;37:875-9.
- Santos M, Rivero J, McCullough SD, West E, Opotowsky AR, Waxman AB, et al. E/e' ratio in patients with unexplained dyspnea: lack of accuracy in estimating left ventricular filling pressure. *Circ Heart Fail*. 2015;8:749-56.
- Holland DJ, Prasad SB, Marwick TH. Contribution of exercise echocardiography to the diagnosis of heart failure with preserved ejection fraction (HFPEF). *Heart*. 2010;96:1024-8.
- Erdei T, Smiseth OA, Marino P, Fraser AG. A systematic review of diastolic stress test in heart failure with preserved ejection fraction, with proposals from EU-FP7 MEDIA study group. *Eur J Heart Fail*. 2014;16:1345-61.
- Takagi T. Diastolic stress echocardiography. *Echocardiography*. 2017;15:99-109.
- Reddy YN, Carter RE, Obokata M, Redfield MM, Borlaug BA. A simple, evidence-based approach to help guide diagnosis of heart failure with preserved ejection fraction. *Circulation*. 2018;138:861-70.
- 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.
- Haude M. Management of valvular heart disease: ESC/EACTS guidelines 2017. *Herz*. 2017;42:715-20.
- Burgess MI, Jenkins C, Sharman JE, Marwick TH. Diastolic stress echocardiography: hemodynamic validation and clinical significance of estimation of ventricular filling pressure with exercise. *J Am Coll Cardiol*. 2006;47:1891-900.
- Pellikka PA, Arruda-Olson A, Chaudhry FA, Chen MH, Marshall JE, Porter TR, et al. Guidelines for performance, interpretation, and application of stress echocardiography in ischemic heart disease: from the American society of echocardiography. *J Am Soc Echocardiogr*. 2020;33:1-41.e8.
- Pieske B, Tschöpe C, de Boer RA, Fraser AG, Anker SD, Donal E, et al. How to diagnose heart failure with preserved ejection fraction: the HFA-PEFF diagnostic algorithm: a consensus recommendation from the heart failure association (HFA) of the European society of cardiology (ESC). *Eur Heart J*. 2019;40:3297-317.
- Vasan RS, Xanthakis V, Lyass A, Andersson C, Tsao C, Larson MG, et al. Epidemiology of left ventricular systolic dysfunction and heart failure in the Framingham study: an echocardiographic study over 3 decades. *JACC Cardiovasc Imaging*. 2018;11:1-11.
- Shah SJ, Kitzman DW, Borlaug BA, van Heerebeek L, Zile MR, Paulus WJ, et al. Phenotype-specific treatment of heart failure with preserved ejection fraction: a multiorgan roadmap. *Circulation*. 2016;134:73-90.
- Obokata M, Reddy YN, Pislaru SV, Melenovsky V, Borlaug BA. Evidence supporting the existence of a distinct obese phenotype of heart failure with preserved ejection fraction. *Circulation*. 2017;136:6-19.
- Anjan VY, Loftus TM, Burke MA, Akhter N, Fonarow GC, Shah SJ, et al. Prevalence, clinical phenotype, and outcomes associated with normal B-type natriuretic peptide levels in heart failure with preserved ejection fraction. *Am J Cardiol*. 2012;110:870-6.
- Gimelli A, Liga R, Bottai M, Pasanisi EM, Giorgetti A, Fucci S, et al. Diastolic dysfunction assessed by ultra-fast cadmium-zinc-telluride cardiac imaging: impact on the evaluation of ischaemia. *Eur Heart J Cardiovasc Imaging*. 2015;16:68-73.
- Ishii K, Imai M, Suyama T, Maenaka M, Nagai T, Kawanami M, et al. Exercise-induced postischemic left ventricular delayed relaxation or diastolic stunning: is it a reliable marker in detect in coronary artery disease? *J Am Coll Cardiol*. 2009;53:698-705.
- Gimelli A, Liga R, Pasanisi EM, Casagrande M, Marzullo P. Myocardial ischemia in the absence of obstructive coronary lesion: the role of post-stress diastolic dysfunction in detecting early coronary atherosclerosis. *J Nucl Cardiol*. 2017;24:1542-50.
- Reddy YN, Obokata M, Gersh BJ, Borlaug BA. High prevalence of occult heart failure with preserved ejection fraction among patients with atrial fibrillation and dyspnea. *Circulation*. 2018;137:534-5.
- Lam CS, Rienstra M, Tay WT, Liu LC, Hummel YM, van der Meer P, et al. Atrial fibrillation in heart failure with preserved ejection fraction: association with exercise capacity, left ventricular filling pressures, natriuretic peptides, and left atrial volume. *JACC Heart Fail*. 2017;5:92-8.
- Wan SH, Vogel MW, Chen HH. Pre-clinical diastolic dysfunction. *J Am Coll Cardiol*. 2014;63:407-16.
- de Sutter J, de Backer J, van de Veire N, Velghe A, de Buyzere M, Gillet TC, et al. Effects of age, gender, and left ventricular mass on septal mitral annulus velocity (e') and the ratio of transmitral early peak velocity to e' (E/e'). *Am J Cardiol*. 2005;95:1020-3.
- D'Andrea A, Vriz O, Ferrara F, Cocchia R, Conte M, Golino P, et al. Reference ranges and physiologic variations of left E/e' ratio in healthy adults: clinical and echocardiographic correlates. *J Cardiovasc Echogr*. 2018;28:101-8.
- Bahrami HS, Pedersen FH, Myhr KA, Møgelvang R, Hassager C. Feasibility, repeatability, and reproducibility of contemporary diastolic parameters and classification. *Int J Cardiovasc Imaging*. 2021;37:931-44.
- Belyavskiy E, Morris DA, Uri-Michitsch M, Verheyen N, Meinitzer A, Radhakrishnan AK, et al. Diastolic stress test echocardiography in patients with suspected heart failure with preserved ejection fraction: a pilot study. *ESC Heart Fail*. 2019;6:146-53.