Review Article

Hemodynamic Assessment In Exercise Stress Echocardiography

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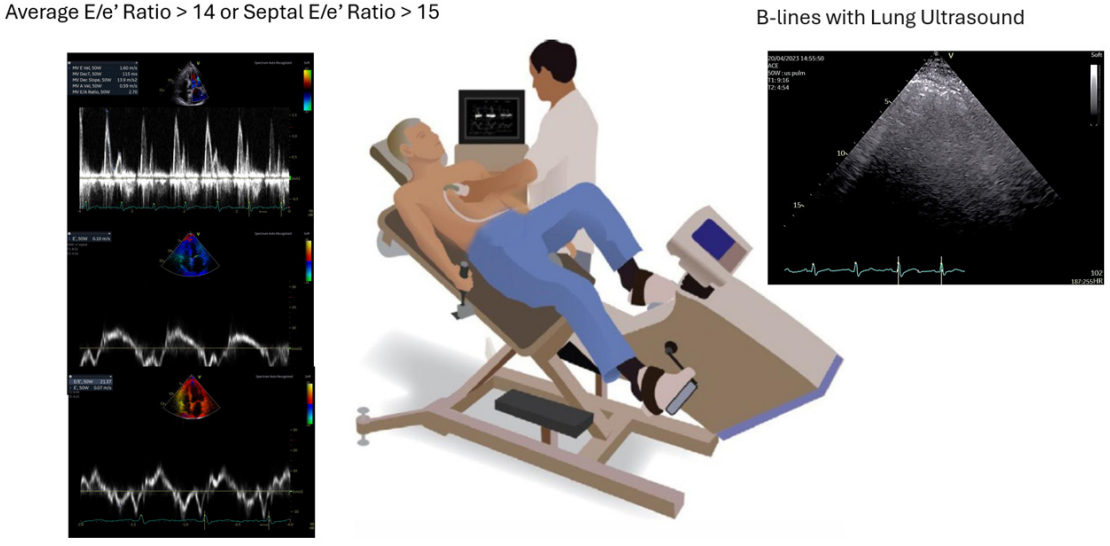
Central Illustration: Hemodynamic Assessment In Exercise Stress Echocardiography



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Abstract

Cycle ergometer stress echocardiography is an important technique to provides information of cardiac chambers dynamics and cardiovascular hemodynamics during exercise. This method identifies patients who present hemodynamic congestion during exertion, assessment of different causes of dyspnea, through the analysis of diastolic filling pressures and pulmonary artery systolic pressure. Recently, with the incorporation of lung ultrasound, it was possible to add the pulmonary congestion parameter with the identification of the appearance of "B" lines during the exam, increasing the sensivity of the protocol.

However, Cycle ergometer stress echocardiography is still little used in our country. This reality is probably due, in part, to the need for appropriate training of the medical and nursing staff; in addition to the lack of knowledge of the method among the medical community, which rarely requests this test for hemodynamic assessment and research into exertional dyspnea. Therefore, the objective of this document is not only to disseminate the method, but also to describe in a practical and didactic way the step-by-step hemodynamic evaluation of the echocardiogram with physical stress on a Cycle ergometer. We suggest a protocol that is easy to apply and capable of distinguishing between the findings of patients with normal hemodynamics and those with an inappropriate hemodynamic response to physical effort. Additionally, two clinical cases are reported with multiple images and hemodynamic changes,

Keywords

Diastolic stress; Exercise stress echocardiography; Hemodynamics; Echocardiopraphy

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with a description of the correct interpretation of the findings to better understand the method and its diagnostic capacity.

Introduction

Among the many indications for exercise echocardiography in nonischemic heart disease, hemodynamic assessment has emerged as a fundamental part of the examination, providing both diagnostic and prognostic information. Currently, one of the primary scenarios in which exercise echocardiography is highly applicable is in the evaluation of heart failure with preserved ejection fraction (HFpEF), in which the main complaint is exertional dyspnea. Hemodynamic assessment is part of the study protocol, evaluating the presence or absence of signs of hemodynamic and/or pulmonary congestion during exercise.

Cycle ergometer stress echocardiography (CESE) has an advantage over treadmill stress echocardiography. CESE allows for real-time detection of the pathological increase in the E/e' ratio, which is indicative of hemodynamic congestion, as well as the moment when B-lines appear on lung ultrasound (LUS), which is indicative of pulmonary congestion.

In the present study, we will describe the echocardiography findings of hemodynamic congestion, the ultrasound findings of pulmonary congestion, and the step-by-step process of hemodynamic assessment by using CESE. We also aim to suggest an examination protocol for the evaluation of exertional dyspnea using clinical cases. We will not discuss hemodynamic assessment in valvular heart disease.

Echocardiography evidence of hemodynamic congestion in CESE

Left ventricular (LV) filling pressures may be estimated from the ratio of the peak velocity of the E wave of mitral valve diastolic flow (estimated by pulsed Doppler) to the velocity of the e' wave of the mitral annulus (estimated by tissue Doppler).[1,2] During exercise, the velocities of the E and e' waves typically increase proportionally with increasing transmitral gradient (Figure 1). In healthy hearts, despite the shortening of the diastolic period (because of the increase in heart rate during exercise), diastolic filling pressures remain unchanged or increase minimally. This is due to increased LV suction at the beginning of diastole, which allows for more efficient atrial emptying and an increase in stroke volume.[3] Individuals with HFpEF have an increase in the velocity of the E wave while the velocity of the e' wave remains unchanged, leading to a peak in the E/e' ratio. In these patients, there is an increase in afterload with slowed myocardial relaxation and reduced ventricular suction during exercise; there is also an increase in heart rate, which, in the presence of a less compliant myocardium, leads to increased LV diastolic pressure and left atrial (LA) pressure, leading to increased pulmonary capillary pressure (PCP) with pulmonary congestion and dyspnea (Figure 2).[4]

Diastolic stress testing refers to the use of Doppler echocardiography to detect reduced LV diastolic functional reserve and the resulting increase in LV filling pressures during exercise in patients with dyspnea of unknown origin or subclinical diastolic dysfunction (a common finding in diabetic cardiomyopathy, obesity, and hypertension).[5-8] Studies have shown Doppler echocardiography is a viable technique for noninvasive detection of pathologic increases in exercise-induced diastolic filling pressures (Table 1), allowing the differentiation between dyspnea of cardiac and noncardiac origin.[4]

Ultrasound signs of pulmonary congestion in CESE

LUS was introduced in intensive care units and emergency departments more than 20 years ago, primarily as an assessment tool for patients with acute dyspnea.[9-11] Over the past decade,

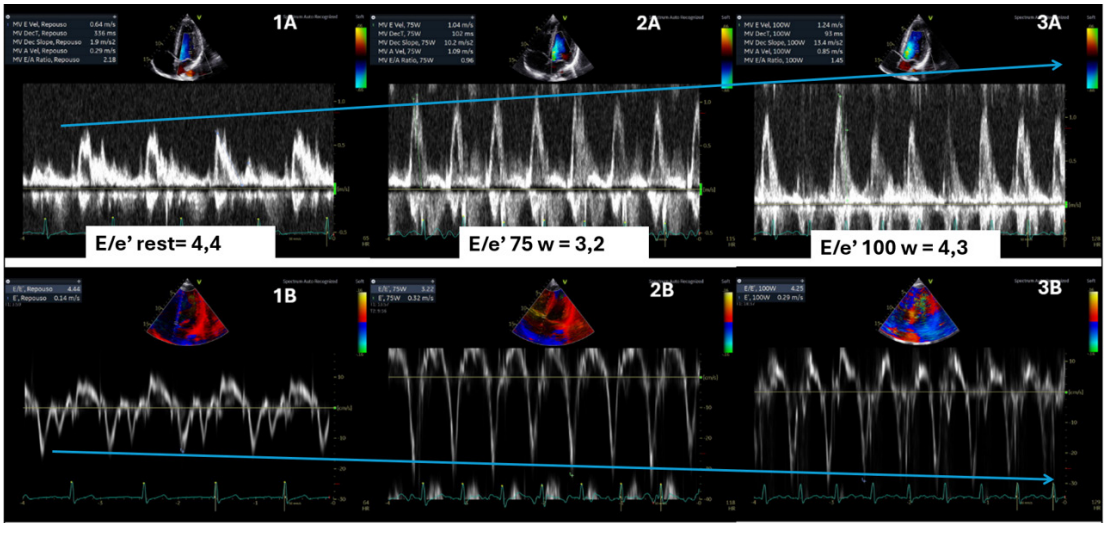

Figure 1 – *Increase in E and e' velocities in individuals with normal filling pressure response to exercise (source: image bank of the Dante Pazzanese Institute of Cardiology [IDPC]). E: mitral inflow velocity during the rapid filling phase; e': tissue Doppler velocity during the rapid filling phase.*

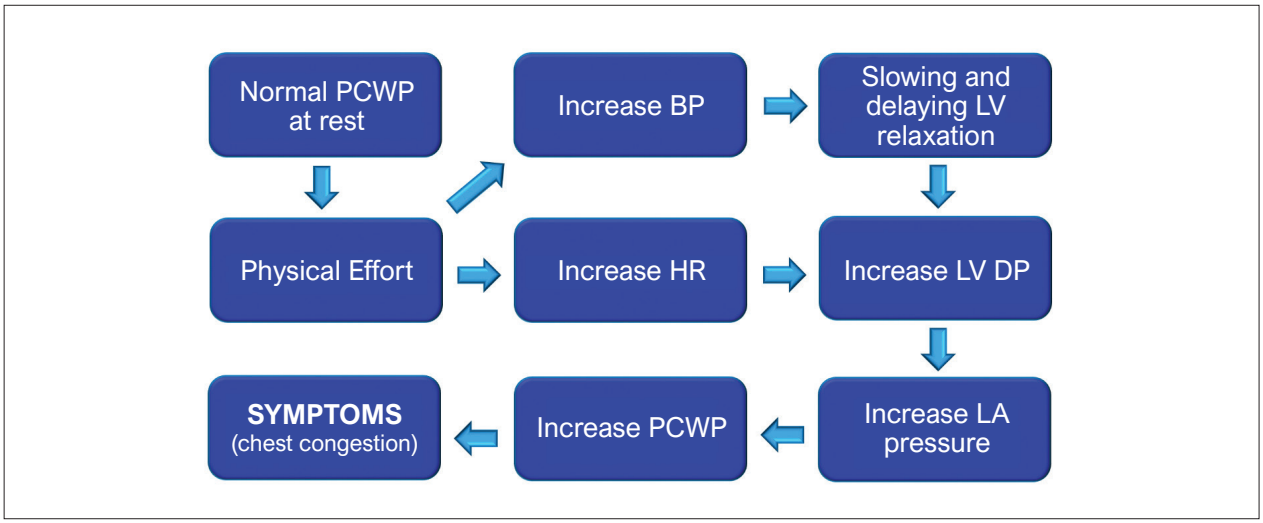

Figure 2 – *Algorithm of the pathophysiology of stress-induced congestion (source: personal collection of the author Assef JE). PCWP: pulmonary capillary wedge pressure; PA: arterial pressure; LV: left ventricle; HR: heart rate; DP: diastolic pressure; LA: left atrium.*

Table 1 – Studies validating stress echocardiography for evaluation of dyspnea of undetermined origin, correlating E/e' parameter with invasive measures of diastolic filling pressures (adapted from Ha et al.[4])

	Burgess et al., 2006[7]	Talreja et al., 2007[8]	Obokata et al., 2017[9]	Hong et al., 2018[10]
Study design	Prospective	Prospective	Prospective	Prospective
Casuistry	37	12	74	21
Effort mode	Cycle ergometer	Cycle ergometer	Cycle ergometer	Cycle ergometer
Invasive measure to assess LV filling pressure	Mean LVEDP	PCP	PCP	Mean LVEDP
Noninvasive parameter to assess LV filling pressure	Average E/e' ratio	Average E/e' ratio	Average E/e' ratio	Average E/e' ratio
Sensitivity/Specificity	73/96	89/100	-----	----
Correlation coefficient	0.59	-----	0.57	0.51

LVEDP: LV end-diastolic pressure; PCP: pulmonary capillary pressure

the cardiology community has recognized the potential of LUS to detect pulmonary congestion and has expanded its use in the diagnosis and management of patients with heart failure.[12]

LUS is a versatile examination with high sensitivity for detecting pulmonary deaeration due to increased extravascular water in the pulmonary interstitium. Its integration with echocardiography allows for a comprehensive analysis, facilitating better management of patients with exertional dyspnea suspected of having heart failure.[13,14]

In a fully aerated lung, the pleura is the only anatomical structure that can be visualized, appearing as a smooth, hyperechoic horizontal plane moving synchronously with respiration. This line is called the pleural line, and its movement is known as lung sliding, which allows assessment of lung excursion during ventilation. The ultrasound pattern of a ventilated lung also includes horizontal, parallel, hyperechoic lines that are seen at regular intervals from the pleural line (A-lines, Figure 3).

As the air content in the lungs decreases and lung density increases, vertical reverberation artifacts (B-lines, Figure 3) appear. B-lines originate from the pleural line and move in sync with respiration, appearing as laser-like lines extending toward the bottom of the ultrasound image sector. These lines are present in patients with heart failure (cardiogenic pulmonary edema) and lung disease (noncardiogenic pulmonary edema).[13] Otto and Andrioli describe in detail the technique for image acquisition and interpretation of LUS for congestion.[15]

By integrating LUS with stress echocardiography, a simplified approach can be performed by evaluating four zones by placing the sector transducer in the third intercostal space along the anterior and midaxillary lines.[16;17]

This simplified protocol has shown a good correlation between practicality and accuracy when performed at rest, at peak exercise, and immediately after exercise is completed.[16]

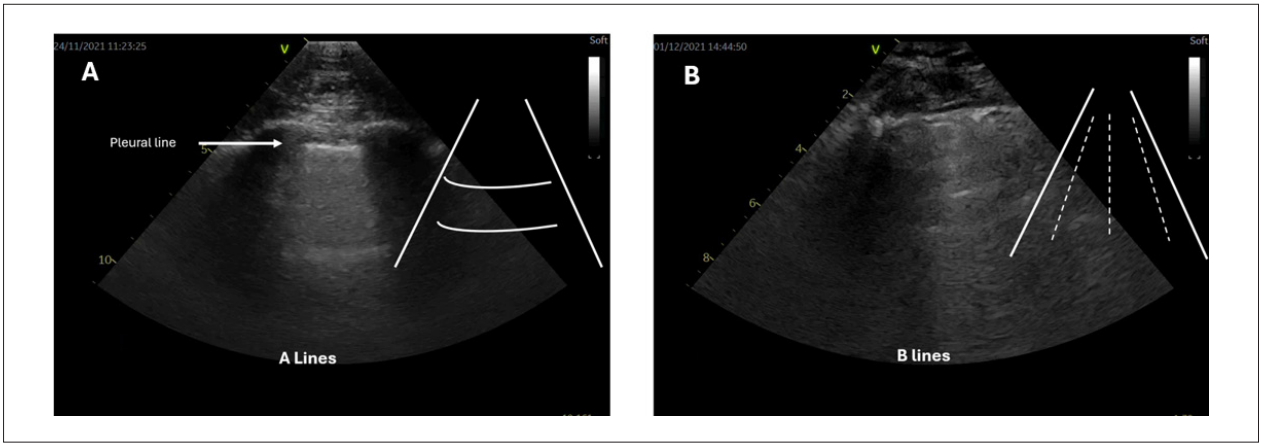

Figure 3 – *A) Lung ultrasound image with A lines. B) Lung ultrasound image with B lines (arrow) (source: personal collection of the author Otto ME).*

In patients with HFpEF, the appearance of B-lines on LUS is because of pulmonary congestion and correlates with worsening diastolic function induced by exercise, as assessed by peak E/e' ratio and reduced global strain rate values at the end of diastole.[18] Based on an invasive hemodynamic study (using high-fidelity micromanometers), acute pulmonary congestion during exercise is because of both increased pulmonary capillary hydrostatic pressure and systemic venous hypertension, which can be assessed by the decoupling between right ventricular function and pulmonary artery (RV-PA) pressure.[19] Assessment of RV-PA decoupling during CESE, calculated by the ratio of tricuspid annular plane systolic excursion (TAPSE) to peak tricuspid regurgitation velocity (TRV), is a parameter that can help identify the cause of exertional pulmonary congestion with a normal E/e' ratio, likely indicating systemic venous hypertension, often associated with pulmonary disease. According to the literature, values below 0.36 mm.cm/s correlate with greater RV-PA uncoupling in patients with postcapillary pulmonary hypertension (PH)[20] and values below 0.31 mm.cm/s are associated with greater RV-PA uncoupling in individuals with precapillary PH due to idiopathic and thromboembolic pulmonary disease.[21]

The appearance of B-lines on CESE, even if there is only one per field evaluated, should be taken seriously. The number of B-lines at peak exercise is directly related to rehospitalization and death from heart failure in patients with preserved or reduced ejection fraction.[22]

Protocol for physical stress test

The expected normal response to exercise on a treadmill or cycle is a two- to threefold increase in heart rate, a three- to fourfold increase in contractility, an increase in systolic blood pressure of at least 50%, and a decrease in systemic vascular resistance with maintenance or reduction of diastolic blood pressure.[23] In terms of cardiac volume, there is initially an increase in end-diastolic volume because of the increased venous return, resulting in an increase in stroke volume, initially because of the Frank-Starling mechanism and subsequently because of the increased heart rate.

If the objective of the test is the hemodynamic assessment of filling pressures during exercise, the cycle ergometer is more sensitive to the increase in these pressures than the upright bicycle because diastolic volume and mean arterial pressure are greater in the supine position because of the increased venous return. Thus, the supine position contributes to greater wall stress, increased myocardial oxygen demand, and higher filling pressures compared to the upright bicycle test.[23,24]

The profile of patients undergoing hemodynamic assessment on the cycle ergometer is often complex and accompanied by multiple comorbidities. The evaluation of dyspnea includes various pathologies such as ischemic cardiomyopathy, hypertrophic cardiomyopathy, diastolic dysfunction and pulmonary disease. Therefore, the evaluation protocol must include all the necessary information for a wide variety of diagnoses. Figure 4 shows an example of the protocol used in our service. In the initial views, corresponding to the baseline examination, it is necessary to obtain data on increased filling pressures and pulmonary congestion: pulsed Doppler of the mitral valve to estimate the E wave velocity, septal and lateral tissue Doppler of the mitral annulus to estimate the e' wave, continuous Doppler of the tricuspid regurgitation (TR) to estimate the peak velocity, LUS to assess pulmonary congestion, and in the final views, at least three LV views to analyze segmental contractility of the 17 segments and to study ischemia. In the central figure, we have an image showing the arrangement of the cycle ergometer/patient and the echocardiography machine as well as images with criteria defining hemodynamic congestion and pulmonary congestion.

Interpretation of hemodynamic data

For the correct interpretation of hemodynamic data during exercise, it is important to consider the workload (generated in watts by the calculation in the ergometry module coupled to the ergometer bed) and the age of the patient, since there is an increase in pulmonary artery systolic pressure (PSAP) with advancing age both at rest and during exercise, a finding also observed in athletes.[24] In patients aged ≥ 70 years, the increase in pulmonary systolic pressure is associated with decreased transpulmonary flow and increased systemic pulse

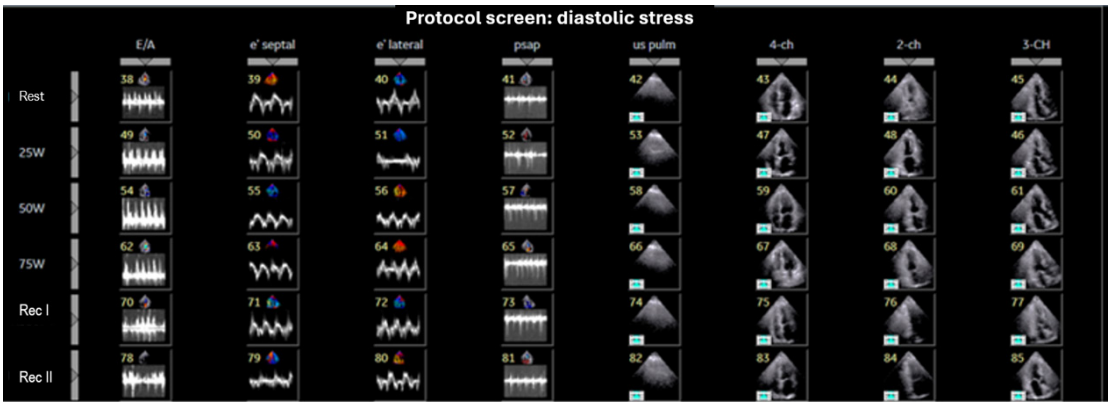

Figure 4 – *Example of an ergometric bed protocol with assessment of filling pressures, pulmonary congestion, and segmental contraction analysis (source: IDPC image bank).*

pressure, which is explained by increased arterial stiffness in older people[24]. A higher stroke volume compared to normal subjects justifies the increase in PSAP during exercise in athletes.[25]

In healthy individuals, exercise increases cardiac output and decreases pulmonary vascular resistance (PVR). A PSAP value of < 43 mmHg during exercise is considered normal.[26] Pathologically, based on the fundamental flow equation (flow [F] = pressure change [ΔP] / resistance [R]), the abnormal increase in pulmonary artery pressure during exercise can be attributed to supranormal cardiac output (e.g., in athletes) or an increase in resistance because of the limited capacity of the pulmonary vascular bed (as occurs in chronic obstructive pulmonary disease or congenital heart disease). In this context, the relationship between pressure change (estimated by the TR velocity) and flow (estimated by the right ventricular outflow tract [RVOT] velocity time integral [VTI]) can help differentiate whether the pressure increase is due to increased flow or resistance. The PVR is calculated by the formula: (maximum TR velocity/RVOT VTI) X 10 + 0.16. Calculation of PVR also helps to identify patients with postcapillary pulmonary hypertension (PVR < 3 WU) and patients with precapillary or mixed pulmonary hypertension (PVR > 3 WU).

Shim CY et al.[28] followed 498 patients who underwent diastolic stress echocardiography for 41 months and found patients with exercise-induced PH had a worse prognosis. Patients with a pathological increase in the E/e' ratio and exercise-induced PH had a significantly worse outcome compared with the normal diastolic stress group and the group with only exercise-induced PH.[28]

Case reports

Case report 1: A 45-year-old woman with nonobstructive hypertrophic cardiomyopathy presents with complaints of fatigue and moderate exertional dyspnea. The purpose of the requested study was to evaluate the intraventricular gradient during exercise (resting study: Figure 5).

She underwent CESE. The following hemodynamic data were assessed: E/e' ratio, peak TRV, LUS, and LV outflow tract gradient (Figure 6).

As observed in the analysis of the study described in Figure 6, patient did not have LV outflow tract obstruction during exercise. However, there was a pathological increase in the E/e' ratio during low-load exercise (E/e' ratio = 15.2 at 25W) associated with PH and the appearance of B-lines on LUS, consistent with HFpEF. In this case, the patient had hemodynamic and pulmonary congestion during exercise. At 50 W, we observed fusion of the E and A waves at a heart rate of 100 bpm, a common finding that prevents evaluation of the E/e' ratio. However, the acquisition of pulsed Doppler of the mitral flow during immediate recovery, when the E and A waves separate, allows an accurate assessment of the filling pressures modified by exercise.

Case report 2: A 62-year-old hypertensive, diabetic, former smoker man presents with complaints of moderate exertional dyspnea. Clinically, he was classified as obese grade I. In addition, B-type natriuretic peptide level was normal, estimated at 65 pg/ml. A transthoracic echocardiography (Figure 7) and CESE (Figure 8) were performed.

In contrast to clinical case 1, he did not show increased filling pressures during exercise (normal E/e' ratio). However, at 75W he experienced dyspnea with a slight decrease in O_2 saturation (initially 98% on room air, dropping to 93% at 75W) associated with pulmonary congestion. Based on these findings, the TAPSE/TRV ratio was evaluated and found to be decreased (Figure 9). The conclusion from these changes in saturation and right ventricular function was pulmonary congestion was likely because of systemic venous hypertension associated with ventriculo-arterial uncoupling. In addition, the patient's history of smoking with chronic obstructive pulmonary disease supports the findings of decreased saturation and "hidden" right ventricular dysfunction.

Conclusion

Exercise stress echocardiography using a cycle ergometer allows detailed assessment of several parameters beyond segmental contraction of the LV. This method allows the

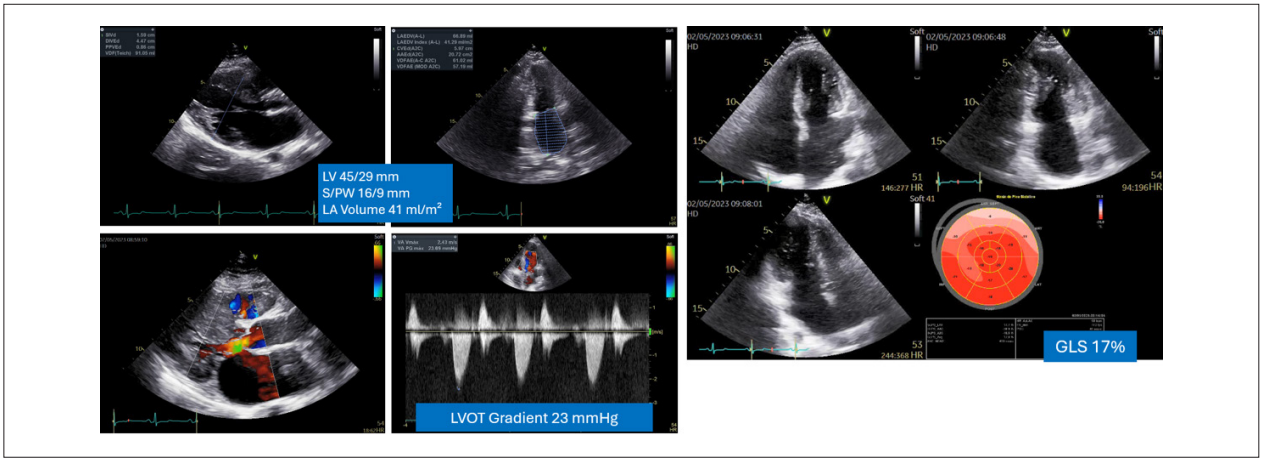

Figure 5 – *Resting assessment of a patient with hypertrophic cardiomyopathy with septal predominance. For Review Only: Left images: resting gradient and right images: assessment of global longitudinal strain with reduction of the septal wall (source: IDPC image bank).*

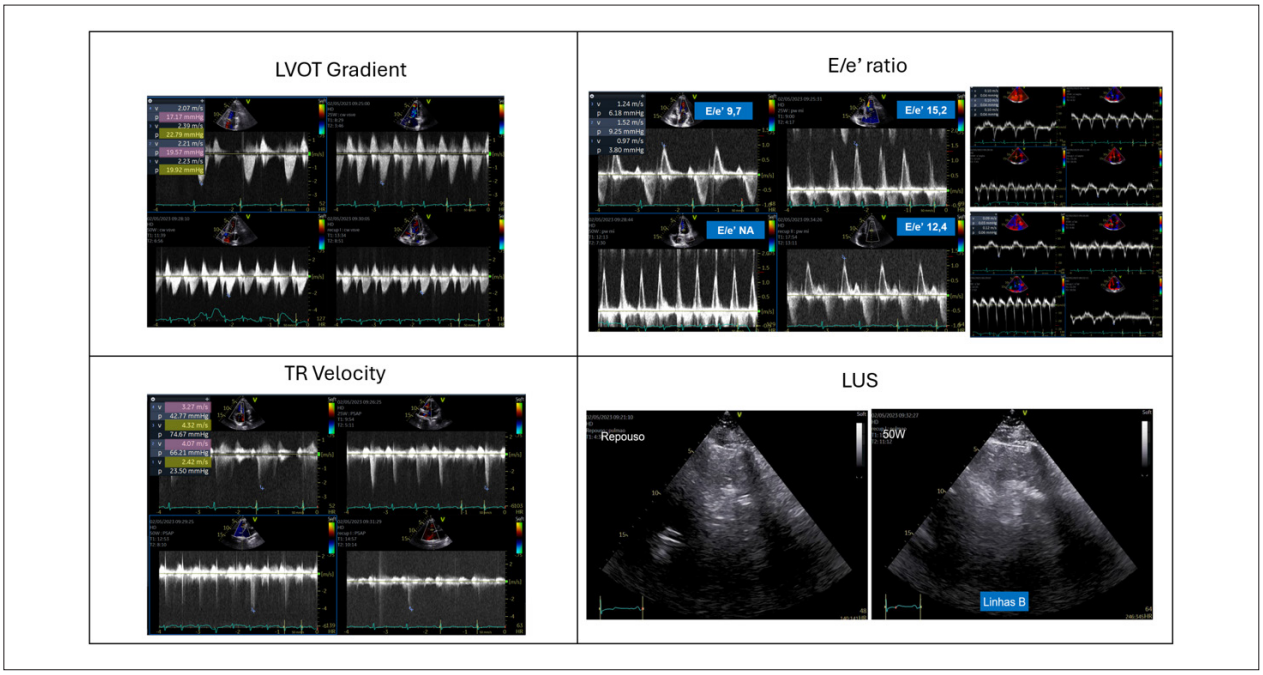

Figure 6 – *Exercise evaluation of a patient with hypertrophic cardiomyopathy with septal predominance. Upper left images: gradients measured in the LV outflow tract at rest: 17.1 mmHg; at 25W: 22.8 mmHg; at 50W: 19.6 mmHg; and during recovery: 19.9 mmHg. Upper right images: Resting E/e' ratio: 9.7; E/e' at 25W: 15.2; E/e' at 50W: not evaluated because of fusion of E and A waves, and E/e' during recovery: 12.4. Bottom left images: Peak TRV at rest: 3.27 m/s; at 25W: 4.32 mmHg; at 50W: 4.07 mmHg, and during recovery: 2.32 mmHg. Bottom right images: LUS analysis at rest and at 50W (source: IDPC image bank).*

investigation of the cause of dyspnea by describing the ventricular hemodynamic behavior during exercise by detecting dynamic intraventricular gradients, the evaluation of increased filling pressures by analyzing the E/e' ratio during exercise, the increased PSAP in the presence of TR, and the appearance of B-lines on lung ultrasound (pulmonary congestion). Although financially accessible, this method requires extensive training of the involved team and the development of specific protocols on the echocardiography equipment, as well as knowledge of the use of a specific ergometry system to apply the appropriate protocol with progressive loads on the cycle ergometer. Thus, although the cycle ergometer offers a wide range of possibilities for the study of dyspnea, it remains underutilized in our setting.

Author Contributions

Conception and design of the research and acquisition of data: Vilela AA; writing of the manuscript: Vilela AA, Otto ME; critical revision of the manuscript for intellectual content: Vilela AA, Otto ME, Assef JE; organization of references: Nishida G.

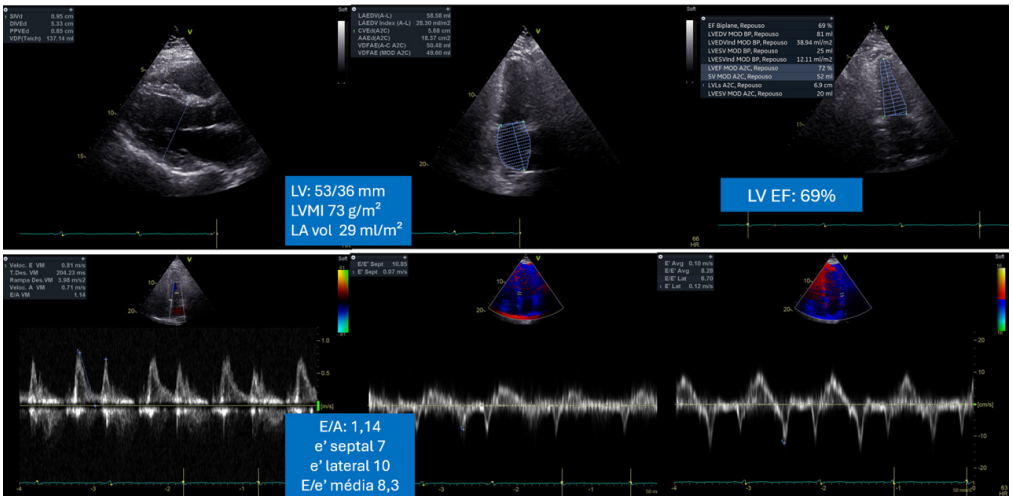

Figure 7 – *Resting echocardiogram of a hypertensive, diabetic, ex-smoker patient complaining of moderate exertional dyspnea (source: IDPC image bank).*

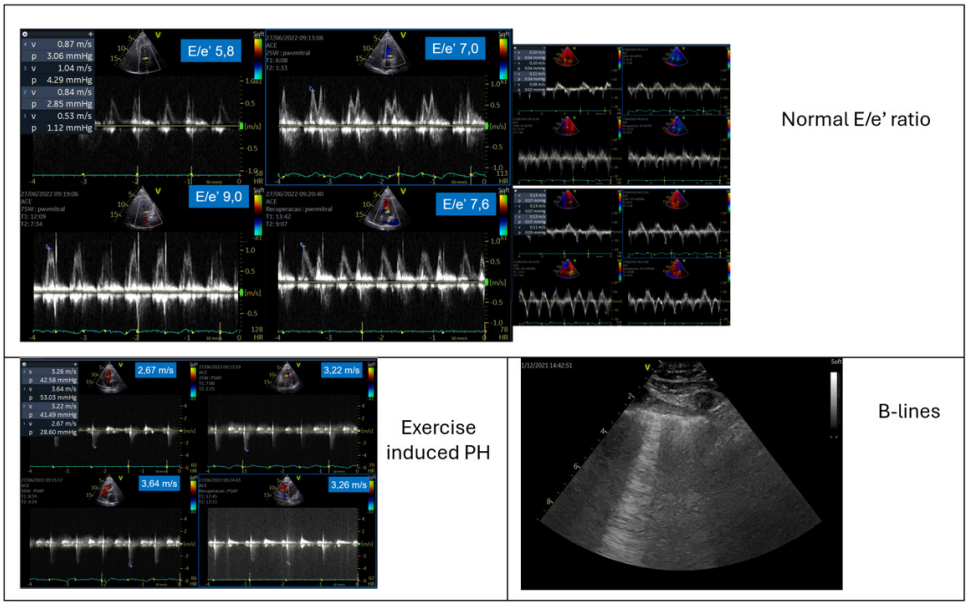

Figure 8 – *Exertional assessment of a hypertensive, diabetic, former smoker with complaints of moderate exertional dyspnea. Upper half images: Normal E/e' ratio during exercise. Lower left images: Peak TRV at rest: 2.67 m/s; at 25 W: 3.22 m/s; at 75 W: 3.64 m/s, and during recovery: 3.26 m/s, respectively. Bottom right images: LUS analysis at 75W (source: IDPC image bank).*

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Study Association

This study is not associated with any thesis or dissertation work.

Ethics Approval and Consent to Participate

This article does not contain any studies with human participants or animals performed by any of the authors.

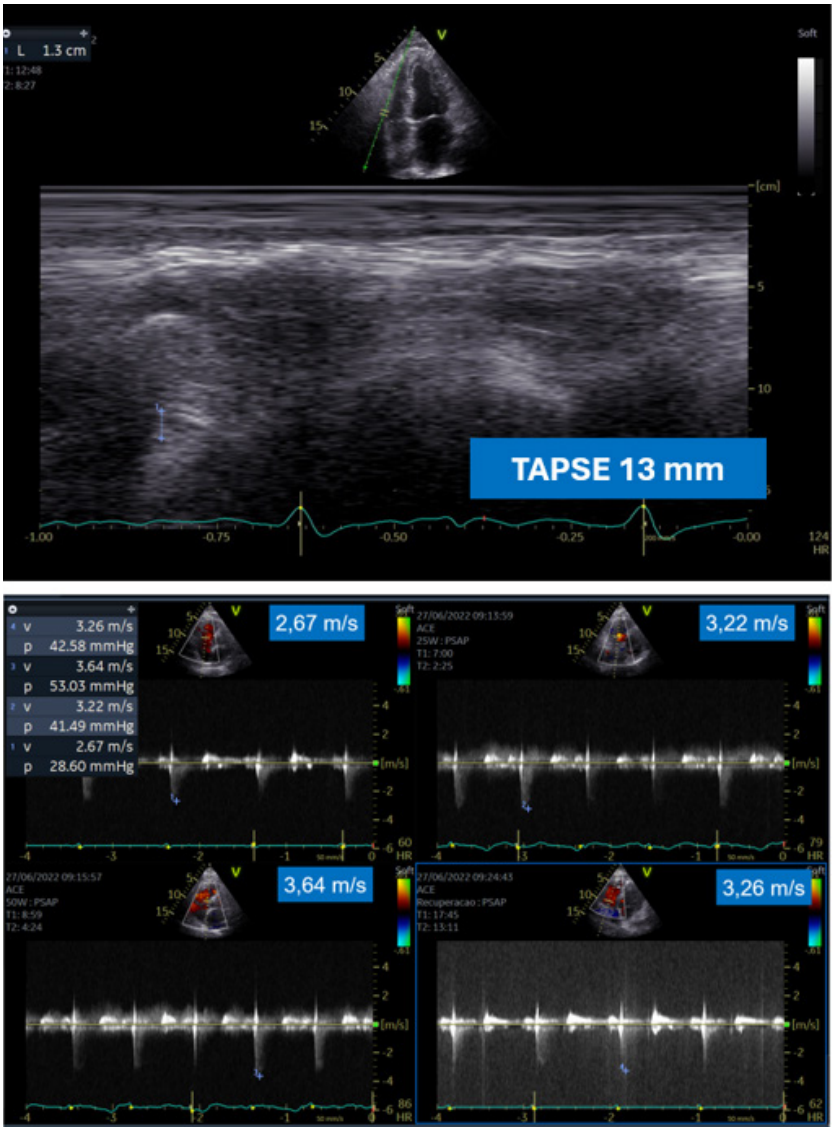

Figure 9 – *Assessment of right ventricle-pulmonary artery uncoupling. TAPSE/TR velocity ratio estimated at 0.35 mm.cm/s*

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