

# Echocardiographic Evaluation of Elevated Left Ventricular Filling Pressures in Patients with Obstructive Coronary Artery Disease

Sy Van Hoang<sup>1,2</sup>, Kha Minh Nguyen<sup>1</sup>, Phuong Uyen Le Tran<sup>3</sup>, Luan Tri Mai<sup>3</sup>, Hai Phuong Nguyen Tran<sup>3\*</sup>

<sup>1</sup> Internal Medicine Department, Faculty of Medicine, University of Medicine and Pharmacy at Ho Chi Minh City, Vietnam. <sup>2</sup> Cardiovascular Department, Cho Ray Hospital, Ho Chi Minh City, Vietnam. <sup>3</sup> Interventional Cardiology Department, Cho Ray Hospital, Ho Chi Minh City, Vietnam.

## Abstract

**Objective:** To determine the efficacy of using echocardiography, compared with cardiac catheterization, to diagnose elevated left ventricular filling pressure (LVFP), according to the 2016 American Society of Echocardiography and the European Association of Cardiovascular Imaging (ASE/EACVI) recommendations, among patients with at least one coronary artery segment presenting stenosis of  $\geq 50\%$ . To compare the diagnostic accuracy of the 2009 and 2016 ASE/EACVI guidelines. **Methods:** Between January and May 2017, a descriptive cross-sectional study was carried out at Cho Ray Hospital in Ho Chi Minh City, Vietnam. The study recruited patients who were undergoing percutaneous coronary angiography. 2D echocardiography and Doppler echocardiography were conducted to estimate LVFP according to the 2009 and 2016 ASE/EACVI recommendations, before inserting a 6F pigtail catheter and undertaking coronary angiography. **Results:** 63 patients participated in this study. Their average age was  $66.9 \pm 11.4$  years. 39.7% of patients had LV contraction function of  $< 50\%$ , and the average LV ejection fraction was  $51.0\% \pm 14.8\%$ . The average LVFP was  $19.4 \pm 8.5$  mmHg, and 50.8% of patients were identified as having elevated LVFP. There was positive correlation between mitral E velocity ( $r = 0.29$ ), E/A ratio ( $r = 0.31$ ) and LAVI ( $r = 0.38$ ) with LVFP ( $P < 0.05$ ). The accuracy of the 2016 ASE/EACVI for diagnosing LVFP was greater than that of the 2009 version (68.5% and 62.5%, respectively) (Table 5). **Conclusions:** The 2016 ASE/EACVI recommendations for assessing LVFP are more predictable and clinically useful compared to the 2009 recommendations.

**Keywords:** left ventricular filling pressure, echocardiography, obstructive coronary artery disease

## INTRODUCTION

Coronary artery disease (CAD) - defined as a patient having at least one coronary artery segment presenting stenosis of  $\geq 50\%$  - is the leading cause of mortality in the United States, accounting for 48.3% of all cardiovascular disease cases [1-3]. CAD manifests in many ways, ranging from early manifestation with asymptomatic left ventricular filling pressure (LVFP) to heart failure with clinical symptoms [4]. Elevated LVFP is associated with long-term prognosis in CAD patients, and its clinical forms include stable CAD, myocardial infarction, or the necessity of coronary artery bypass graft surgery [5-7]. Data about elevated LVFP, not only provides valuable information for diagnoses and clinical practice guidelines but also contributes to the patient prognosis [8, 9].

Although cardiac catheterization is the gold standard for diagnosing elevated LVFP, it is invasive and not frequently available. Echocardiography is a non-invasive, repeatable, clinically simple procedure, which can estimate LVFP, according to the 2016 guidelines of the American Society of Echocardiography and the European Association of

Cardiovascular Imaging (ASE/EACVI) [10, 11]. These guidelines were based on the consensus of professional experts in the cardiology field [12].

The 2016 guidelines are highly accurate and uncomplicated compared to the 2009 guidelines [13-15]. Andersen et al. have shown that the echocardiographic assessment of LVFP is

**Address for correspondence:** Hai Phuong Nguyen Tran (PhD.), Interventional Cardiology Department, Cho Ray Hospital, Ho Chi Minh City, Vietnam.  
E-mail: diamondsaphia2108 @ gmail.com

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accurate and feasible, at a 91% success rate. However, only 20% of patients in the study population had CAD [13]. A multicenter EACVI Euro-Filling study has shown that the incidence of obstructive CAD is 53% [14]. However, the reliability and accuracy of indicators for elevated filling pressure were limited for patients with CAD, who were not fully assessed [16]. Therefore, it is necessary to determine whether a treatment regimen based on estimating elevated LVFP is plausible for different populations with separate underlying pathologies.

This study evaluated the echocardiographic diagnosis of elevated LVFP (following the 2016 ASE/EACVI recommendations) as compared to the gold standard of cardiac catheterization in patients with at least one coronary artery segment presenting stenosis at  $\geq 50\%$ , as determined by angiography. The study also compared the accuracy of diagnosing elevated LVFP between the 2009 and 2016 ASE/EACVI guidelines.

## METHODS

### Ethical approval

The research complied with the Declaration of Helsinki and was accepted by the Biomedical Research Ethics Committee of the University of Medicine and Pharmacy in Ho Chi Minh City, Vietnam. The participants, who were all aged 18 and older, were sufficiently conscious and agreed to sign the informed consent form.

### Sample size

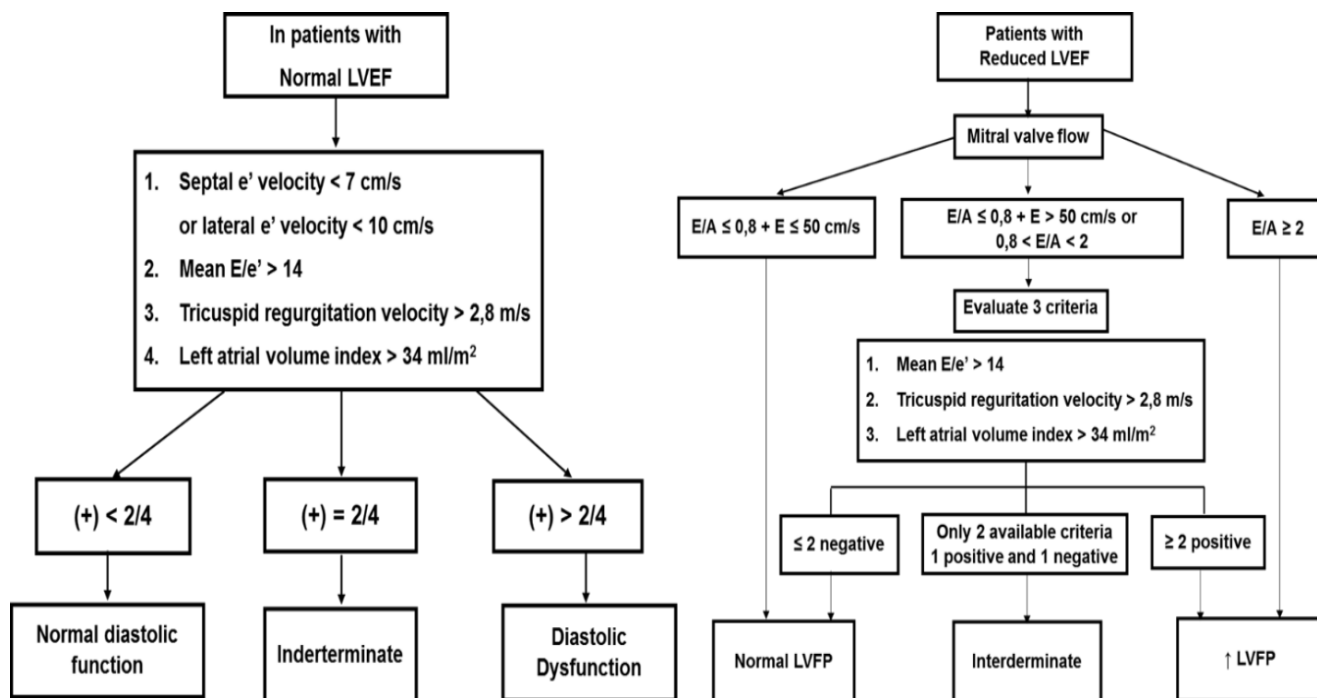
This was a descriptive cross-sectional study, conducted at Cho Ray Hospital in Ho Chi Minh City, Vietnam. It included patients who underwent percutaneous coronary angiography between January and May 2017.

The inclusion criteria required selected patients to have undergone coronary angiography and to have been diagnosed with at least one coronary artery segment with stenosis at  $\geq 50\%$ .

Patients were excluded if they had pacemakers, no sinus rhythms, slow rhythms ( $< 60$  beats/minute), fast rhythms ( $> 100$  beats/minute), ultrasound windows with poor image quality, hemodynamic disorders due to inotropes or vasopressors, moderate to severe mitral valve stenosis, or moderate to severe aortic stenosis.

### Echocardiography

To measure LVFP according to the recommendations of the 2009 and 2016 ASE/EACVI guidelines, two-dimensional and Doppler echocardiography methods were performed via commercial equipment (Philips CX50 ultrasound, S5-1 probe -5 MHz) before cardiac catheterization and coronary angiography. The parameters were evaluated independently and consistently by two cardiologists, who held certifications in echocardiography training. The study's results present the average of the two parameters as measured, independently, by two doctors. Techniques for measuring LV size, fractional shortening, and the LV ejection fraction were standardized according to current recommendations [17]. The LV ejection fraction was measured by Simpson's method on two planes—four chambers from the apex (tip) of the heart and two chambers from the apex of the heart—then presented as the average value. The left atrial volume index (LAVI) was measured at the surface on the end-systole four chambers from the apex of the heart and then calculated with skin surface area. Doppler echocardiography was employed to estimate LV diastolic function at four chambers from the apex of the heart. The Doppler parameters included peak velocity of the early diastole (E wave) and atrial contraction (A wave) through the mitral valve, the E/A ratio, the lateral and septal early diastolic mitral annular ( $e'$ ), the E/ $e'$  ratio, and the peak backflow velocity through the tricuspid aortic valve. Based on the LV contraction function, LVFP was estimated via echocardiography and was divided into three levels—normal, indeterminate, and elevated—according to the 2016 ASE/EACVI guidelines (Figure 1) [11]. LVFP was also estimated according to the recommendations of the 2009 ASE/EACVI guidelines and the corresponding echocardiography indicators [18].



**Figure 1.** Estimation of LVFP according to 2016 ASE/EACVI guidelines

### LVFP

LVFP was assessed before conducting coronary angiography (i.e., before injecting the contrast medicine). A technician inserted a 6F pigtail catheter was inserted from the femoral artery or the radial artery into the left chamber of the heart. LVFP was measured immediately after the bottom of A wave, before the rapid phase of LVFP pressure, and during three consecutive cardiac cycles. The result was the average value of the three cardiac cycles [19]. The parameters for determining LVFP via cardiac catheterization were performed blind, and the results of the evaluation were collected through echocardiography. LVFP was considered to be elevated when the pressure was  $\geq 15$  mmHg [19].

### Coronary Angiography

Percutaneous coronary angiography with contrast medicines was performed after measuring LVFP. Two cardiologists evaluated the coronary angiography results showing  $\geq 50\%$  stenosis in one or more coronary artery segments.

### Statistical analysis

Continuous variables were presented as mean  $\pm$  standard deviation for normal distribution or a median - quartile range for non-normal distribution. Categorical variables were presented as frequency and percentage. Regression analysis was used to determine the association between echocardiographic parameters and LVFP. A P-value of  $< 0.05$  was considered statistically significant. The accuracy of LV estimation based on both the 2009 and 2016 ASE/EACVI guidelines was determined by analyzing test sensitivity, test specificity, positive and negative predictive values, and

accuracy. Data were analyzed with Stata 13 software (StataCorp. 2013. *Stata Statistical Software: Release 13*. College Station, TX: StataCorp LP).

### RESULTS

The study recruited 63 patients who met the selection criteria. The clinical characteristics, echocardiographic results, and normal hemodynamic parameters of the sample are shown in Table 1. The average age of participants was  $66.9 \pm 11.4$  years, and 63.5% were male. The average LV ejection fraction was  $51.0\% \pm 14.8\%$ , and 39.7% of patients had LV contraction function of  $< 50\%$ . The percentage of people with stenosis in one coronary artery segment, two segments, and three segments or the left main coronary artery were nearly equal (31.8%, 22.8%, and 44.4%, respectively). The average LVFP was  $19.4 \pm 8.5$  mmHg, while elevated LVFP was recorded in 32 patients (50.8%). Statistically significant differences were found in the LVFP, left ventricular ejection fraction (Simpson), E/A, and LAVI ratios between the normal LVFP and elevated LVFP groups ( $P < 0.05$ ).

**Table 1.** Clinical characteristics, echocardiography, and normal hemodynamic parameters of patients with obstructive CAD

Variables	N = 63	Normal LVFP n = 31	Elevated LVFP n = 32	P value
Age, years	66.9 ± 11.4	68.3 ± 11.0	65.6 ± 11.8	0.36
Male, %	40 (63.5%)	21 (67.7)	19 (59.4)	0.48
BSA, m <sup>2</sup>	1.57 ± 0.16	1.56 ± 0.16	1.57 ± 0.16	0.64
CAD				
- 1 segment, n (%)	20 (31.8)	13 (41.9)	7 (21.9)	0.23
- 2 segments, n (%)	15 (23.8)	6 (19.4)	9 (28.1)	
- 3 segments or left main, n (%)	28 (44.4)	12 (38.7)	16 (50.0)	
LVEDd, mm	47.8 ± 7.2	46.3 ± 7.6	49.4 ± 6.6	0.08
Fractional shortening, %	31.2 ± 12.8	32.9 ± 12.7	29.5 ± 12.8	0.28
LVEF Simpson, %	51.0 ± 14.8	58.2 ± 12.1	44.1 ± 14.0	<b>0.0001</b>
Mitral E velocity, m/s	66.0 ± 21.1	62.1 ± 17.1	69.8 ± 18.6	0.09
Mitral A velocity, m/s	73.0 ± 25.5	74.7 ± 20.7	71.3 ± 29.7	0.60
E/A ratio	1.00 ± 0.63	0.80 ± 0.71	1.19 ± 0.80	<b>0.012</b>
Deceleration time of mitral E velocity, ms	156.6 ± 53.9	167.3 ± 48.1	146.3 ± 57.8	0.12
e' lateral	12.0 ± 9.8	11.9 ± 12.7	12.1 ± 6.1	0.95
e' septal	14.3 ± 8.5	12.6 ± 9.8	15.8 ± 6.7	0.12
E/e' ratio	12.8 ± 8.7	11.7 ± 10.9	14.0 ± 5.7	0.29
TR Vmax, m/s	2.22 ± 0.70	2.10 ± 0.62	2.31 ± 0.76	0.27
LAVI, ml/m <sup>2</sup>	28.7 ± 12.7	24.4 ± 12.3	32.9 ± 11.9	<b>0.007</b>
Isovolumic relaxation time, ms	109.5 ± 32.7	113.1 ± 31.6	106.1 ± 33.9	0.40
S/D	1.62 ± 0.90	1.57 ± 0.44	1.67 ± 1.20	0.67
Ar-A, ms	13.1 ± 28.8	11.3 ± 34.8	14.8 ± 21.2	0.64
Pulmonary vein atrial reversal, ms	143.2 ± 27.2	148.9 ± 30.4	137.2 ± 22.3	0.09
LVFP, mmHg	19.4 ± 8.5	12.4 ± 3.5	26.2 ± 5.9	<b>&lt;0.001</b>

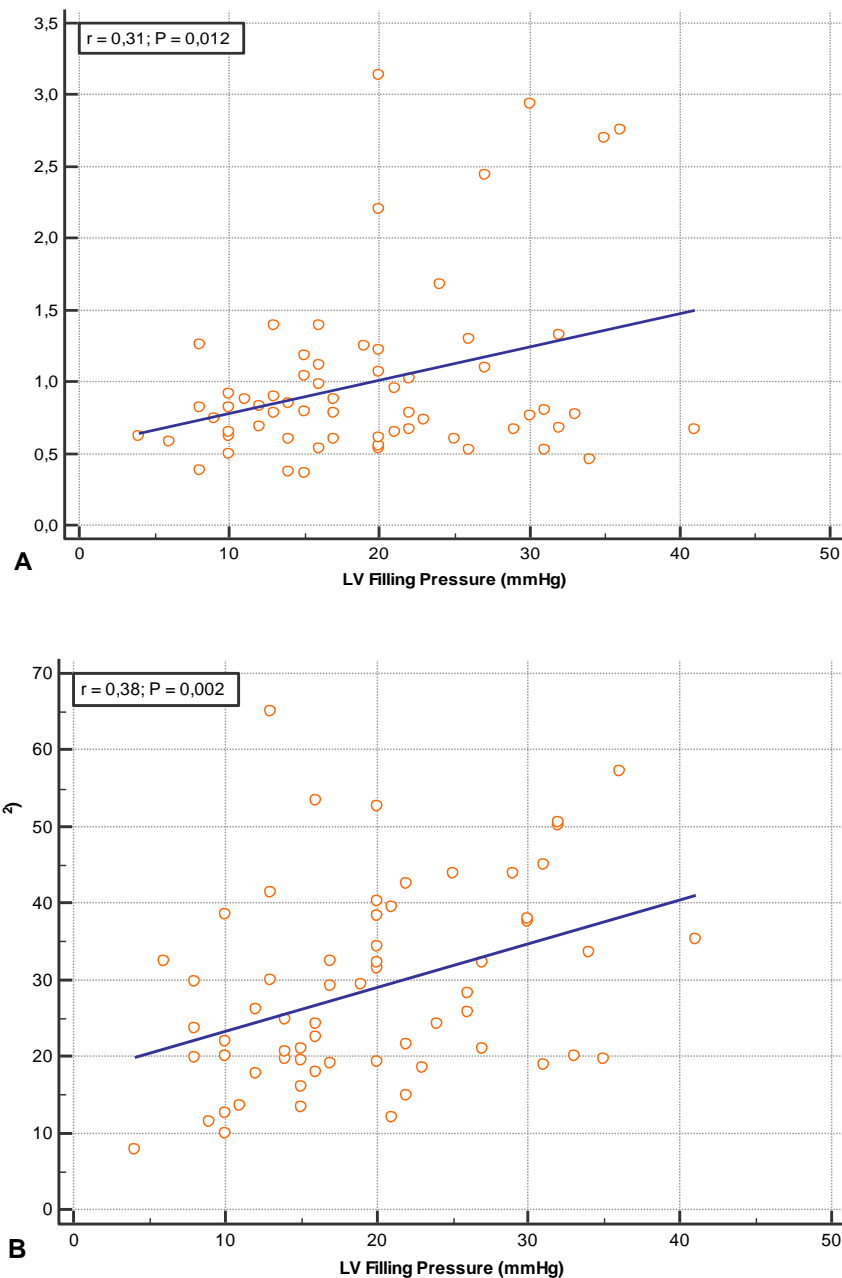
LVEDd: Left ventricular end-diastolic diameter; TR Vmax: Tricuspid regurgitation velocity; LAVI: Left atrial maximal volume index; S/D: Pulmonary veins: systolic velocity/diastolic velocity ratio; Ar-A: Pulmonary veins: atrial reversal duration-mitral A duration; LVFP: Left ventricular filling pressure.

**Table 2.** Correlation between 2D echocardiography, Doppler parameters, and LVFP

Parameters	r	P-value
Mitral E velocity	0.29	<b>0.02</b>
Mitral A velocity	0.04	0.72
E/A ratio	0.31	<b>0.01</b>
Deceleration time of mitral E velocity	-0.24	0.05
Isovolumic relaxation time	-0.18	0.15
E/e' lateral	0.08	0.55
E/e' septal	0.28	0.03
Mean E/e'	0.22	0.08
TR Vmax	0.26	0.06
LAVI	0.38	<b>0.002</b>
Pulmonary artery: S/D	-0.04	0.78
Ar-A	0.01	0.94
Pulmonary veins atrial reversal	-0.26	<b>0.04</b>

Table 2 depicts the parameter relationships between echocardiography values and LVFP. A positive correlation was observed in mitral E velocity, E/A ratio, LAVI, and

LVFP (P <0.05). LAVI was the most significant parameter correlating with LVFP (r = 0.38, P = 0.002 [Figure 2B]), followed by the E/A (r = 0.31, P 0.01 [Figure 2A]).



**Figure 2.** Regression Plot: LVFP. **2A:** Correlation between E/A ratio and LVFP. **2B:** Correlation between LAVI and LVFP.

**Table 3.** Echocardiography results for estimating LVFP according to the 2016 ASE/EACVI guidelines

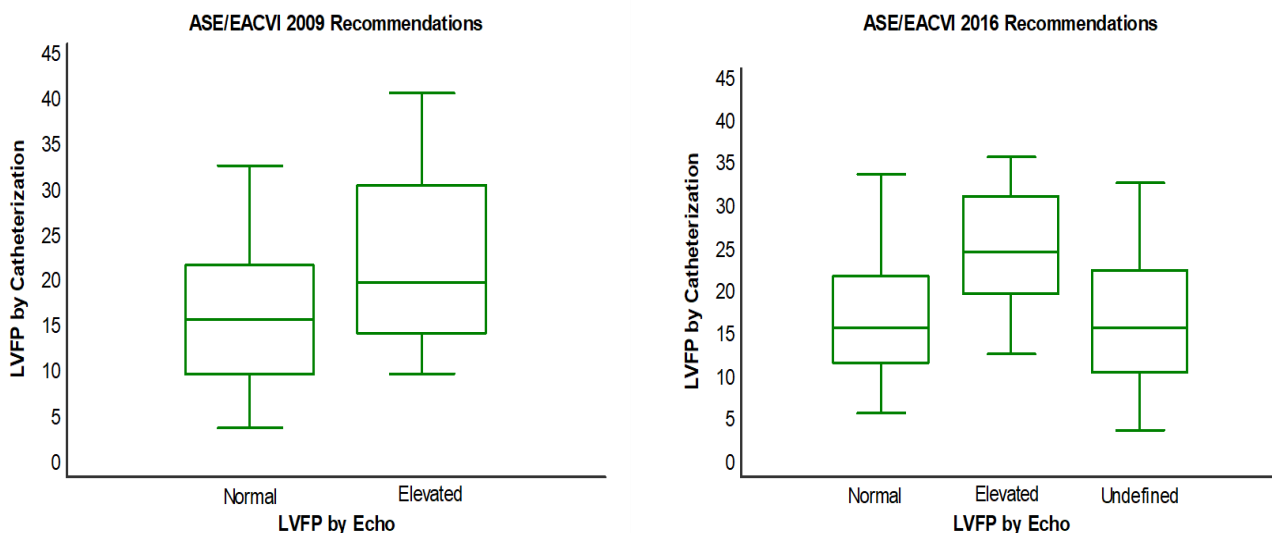
Parameters	Echo Normal LVFP (N = 39)	Echo Elevated LVFP (n = 15)	Echo Indeterminate (n = 9)
Invasive LVFP < 15, mmHg	24 (61.5%)	2 (13.3%)	5 (55.6%)
Invasive LVFP ≥ 15, mmHg	15 (38.5%)	13 (86.7%)	4 (44.4%)

39 patients (61.9%) had normal LVFP; 15 (23.8%) had elevated LVFP; and 9 (14.3%) were indeterminate, as classified by the 2016 ASE/EACVI guidelines (Table 3). Approximately two-thirds (61.5%) of the patients with normal LVFP had normal invasive LVFP (< 15 mmHg), while 86.7% of patients with abnormal non-invasive LVFP had elevated invasive LVFP (≥ 15 mmHg). The LVFP in 44.4% of patients with elevated invasive LVFP could not be determined by the non-invasive method.

**Table 4.** Echocardiography results for estimating LVFP according to the 2009 ASE/EACVI guidelines

Parameters	Echo Normal LVFP n = 36	Echo Elevated LVFP n = 27
Invasive LVFP < 15, mmHg	22 (61.1%)	9 (33.3%)
Invasive LVFP ≥ 15, mmHg	15 (38.9%)	18 (66.7%)

Using the 2009 ASE/EACVI guidelines, LVFP was normal in 36 patients (57.1%) and elevated in 27 patients (42.9%) (Table 4). 61.1% of patients with non-invasive LVFP at normal levels had normal invasive LVFP (< 15 mmHg), which was similar to the results collected when applying the 2016 recommendations. However, the proportion of patients with elevated non-invasive LVFP having elevated invasive LVFP was only 66.7%, which was lower than the results obtained with the 2016 recommendations. The relationship between the LV filling grades in non-invasive assessment (echocardiography) and invasive assessment (catheterization), according to the 2009 and 2016 recommendations, is illustrated in Figure 3.



**Figure 3.** Relationship between LV filling grades by echo and by catheterization.\*  
\*“Undefined” corresponds to the “indeterminate” category.

**Table 5.** Accuracy diagnosing elevated LVFP according to the 2009 and 2016 guidelines

Variables	2009 ASE/EACVI diagnostic algorithm	2016 ASE/EACVI diagnostic algorithm
Sensitivity (95% CI)	54.6 (36.4 - 71.9)	46.4 (27.5 - 66.1)
Specificity (95% CI)	71.0 (52.0 - 85.8)	92.3 (74.9 - 99.1)
PPV (95% CI)	66.7 (51.5 - 79.0)	86.7 (61.8 - 96.3)
NPV (95% CI)	59.5 (48.7 - 69.4)	61.5 (52.7 - 69.7)
Overall Accuracy	62.5 (49.5 - 74.3)	68.5 (54.5 - 80.5)

Values are %.  
CI: confidence interval; NPV: negative predictive value; PPV: positive predictive value.

Using the 2016 recommendations to identify patients with elevated LVFP was more accurate than using the 2009 recommendations, at 68.5% and 62.5%, respectively (Table 5).

## DISCUSSION

This cross-sectional study evaluated LVFP by echocardiography, according to the 2016 ASE/EACVI guidelines, before performing cardiac catheterization (the gold standard) on patients with at least one coronary artery segment having stenosis (≥ 50%). The findings showed high sensitivity and specificity when following the 2016 ASE/EACVI guidelines, and the accuracy of the 2016 recommendations was greater than that of the 2009 recommendations. This result was consistent with several previous studies [14, 20]. Also, the correlation between several parameters measured by 2D echocardiography and Doppler echocardiography (including LVFP) was found through regression analysis.

The study population included patients with obstructive CAD with at least one coronary artery presenting stenosis (≥ 50%) (Table 1). LVFP is an indicator of dilated cardiomyopathy, which indirectly reflects the diastolic function of the left ventricle. Elevated LVFP may manifest during the first stage of myocardial ischemia [4, 21]. In the present study, LVFP was considered elevated when it was ≥ 15 mmHg [19].

## Parameters of echocardiography to estimate elevated LVFP

The 2009 and 2016 ASE/EACVI recommendations offered different parameters, each of which could have separate values and present distinct results. This research has shown that there was a correlation between the valve index (E/A ratio), the tissue Doppler index (E/e' septal), the LAVI or PAVR index, and LVFP. These results were consistent with LVFP diagnosis when the 2016 ASE/EACVI guidelines (Figure 1) were chosen as the parameters for the echocardiography flowchart. LAVI and the E/A index were most significantly correlated with elevated LVFP, at r values of 0.38 and 0.31, respectively (Figure 2). This has also been reported in other recent studies [13-15].

## Comparison between the 2009 and 2016 recommendations

The 2016 algorithm seems simpler and easier for clinicians to use. It also identifies patients with elevated LVFP at a greater level of accuracy than the 2009 approach. Some previous studies have suggested that clinicians have a higher probability of diagnosing elevated LVFP when using the 2016 ASE/EACVI guidelines as opposed to the 2009 version [14, 20]. Such studies have been conducted among different populations, with the incidence of CAD ranging from 20% to 53% [13, 14].

The present study—which only assessed a homogeneous group of patients, having at least one coronary artery segment with stenosis of  $\geq 50\%$ , through percutaneous coronary angiography—has also confirmed the higher accuracy of the 2016 algorithm compared to the 2009 version. Wan *et al.* emphasize that the 2016 protocol offers a high specificity for estimating the LVFP among patients with diabetes [15]. Flowcharts of the 2016 ASE/EACVI recommendations also indicate a great proportion of true negative determinations, which has resulted in this higher specificity over the 2009 recommendations. Therefore, the 2016 guidelines may help clinicians make better decisions when diagnosing elevated LVFP through echocardiography in CAD patients.

## Limitations

The study had several limitations. First, the number of patients was relatively small, and the research was carried out in only one hospital. Furthermore, the authors did not investigate the clinical characteristics of CAD patients. Acute or chronic ischemia could affect the probability of identifying patients with elevated LVFP through echocardiography. Therefore, further, multicenter research should be conducted with larger samples, including analysis of myocardial ischemia clinical presentations.

## CONCLUSIONS

This study has revealed that using echocardiography to evaluate elevated LVFP, following the 2016 ASE/EACVI recommendations for patients with obstructive CAD, was considerably more feasible and accurate than the approach

proposed by the 2009 recommendations. The 2016 guidelines also have higher specificity and lower sensitivity than the 2009 version.

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## Conflict of interest

The authors have no conflicts of interest to declare.

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