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Role of Left Atrial Functions for The Assessment of Left Ventricular Filling Pressure in Patients with Acute Coronary Syndrome.

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ORIGINAL ARTICLE

Role of Left Atrial Functions for the Assessment of Left Ventricular Filling Pressure in Patients with Acute Coronary Syndrome

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Abstract

Background: **The significance of evaluation of the hemodynamic status of patients with acute coronary syndromes is well established. The approach for noninvasive evaluation of Left ventricular filling pressure (LVFP) and the role of left atrium phasic functional assessment is not well studied in ACS patients.**

Aim: **1) Evaluation of the significance of the diagnostic algorithm recommended by the ESC for evaluation of LVFP in patients with ACS. 2) Assessment of correlation between left atrium parameters assessed by different echocardiography modalities and the invasively measured LVFP.**

Patients and methods: **A cross sectional analytical study enrolled 54 patients with ACS admitted at Al-Azhar University Hospitals for PCI. LVFP was measured invasively after PCI. Full Echocardiography study including left atrium functions assessment by (volumetric, speckle and Doppler techniques) was done within 24 h after PCI. LVFP was noninvasively estimated according to last ASE/EACVI recommendations.**

Results: **Invasively measured LVFP showed significant correlation with LA reservoir function either measured by volumetric method ($r = 0.567$, P value < 0.001) or two dimensional-speckle tracking ($r = 0.590$, P value < 0.001) and total LA ejection fraction ($r = 0.567$, P value < 0.001). The 2016 ESC recommended approach showed high false negative value (73.1%).**

Conclusion: **Our results indicate that currently recommended AHA/EACVI approach has limited value in ACS patients. The assessment of left atrium reservoir function may provide an adequate surrogate for elevated LVFP.**

Keywords: ACS, Left atrium functions, Left ventricular filling pressure

1. Introduction

Multiple invasive studies revealed that raised Left ventricular filling pressure (LVFP) is associated with adverse outcome.[1] Direct measurement of intra-cardiac pressures requires invasive procedures with potential risks, there have been various attempts to develop noninvasive alternatives.[2] ASE/EACVI recommended an algorithm for assessment of LVFP in 2009 and 2016.[3,4] Validation of this approaches has been studied by multicenter EUROFILLING study[5] which include patient with chronic heart diseases and exclude Patients with acute Coronary syndrome.

The role of left atrium volume as a predictor of prognosis has been well established in chronic CV diseases.[6,7] However, the role of the left atrium assessment in the acute CV situations is still unclear and the assessment of the phasic left atrium functions may show earlier response to the acute rise of the LVFP than LA volume.

This study aimed to (1) evaluate of the significance of the diagnostic algorithm recommended by current guidelines for evaluation of LVFP in patients with ACS; (2) assessment of correlation between left atrium parameters assessed by different echocardiography modalities (2D-Doppler-speckle tracking) and the invasively measured LVFP.

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2. Patients and methods

This was a cross-sectional analytical study, enrolled 54 consecutive patients who were presented by ACS for PCI either STEMI or NSTE-ACS at cardiac catheterization laboratory at Al-Azhar university hospitals from September 2021 to May 2022. AMI diagnosis was defined using the fourth universal definition of AMI.[8]

2.1. Inclusion criteria

All patients presented by ACS for PCI either STEMI or NSTE-ACS from both genders.

2.2. Exclusion criteria

Patients with poor echocardiographic window, significant arrhythmia during assessment, significant valvular, myocardial, congenital or pericardial heart disease were excluded from the study beside those who are not willing to participate in the study.

Ethical approval was obtained from ethical committee at our institute.

2.3. Procedure

PCI was performed using Philips Allura Expert angiography system. LV catheterization was performed following PCI and after transducer set up using a fluid filled 6Fr pigtail catheter.[9] LVFP greater than 15 mmHg was considered as elevated.[4]

Echocardiography was performed based on the recommendations of the last ASE guidelines for chamber quantification at 2015[10] using GE Healthcare Vivid-E95 echocardiographic machine. PW trans-mitral inflow velocities, tissue Doppler of annular velocities were recorded. Tricuspid regurgitation velocity was measured by continuous-wave Doppler.

Analysis was done off-line using Echo-PAC software (GE Healthcare, Norway). LA volume measurements were calculated using the biplane disk summation method. volumes were measured at 3 points, maximum volume (Vol_{max}) measured just before the opening of the mitral valve, minimal volume (Vol_{min}) measured at the closure of the mitral valve, and the volume just before the atrial contraction, measured at the onset of the P wave on the ECG (Vol_P). The phasic functions of the LA can be derived as:

(1) LA expansion index = $(Vol_{max} - Vol_{min})/Vol_{min}$ X 100
(2) LA passive emptying fraction = $(Vol_{max} - Vol_P)/Vol_{max}$ X 100
(3) LA active emptying fraction= $(Vol_P\text{-}Vol_{min})/Vol_P$.[11]

Peak early (E) and late (A) mitral inflow velocities, E/A ratio and E-wave deceleration time were measured from PW mitral flow. Mitral early (e) and late (a) tissue Doppler velocities was measured and E/e\ ratio was measured.[4]

Speckle-tracking echocardiography (STE) technique is used to generate a strain average curve where LASr and LASct were obtained representing the LA reservoir and contraction functions, respectively. The conduit function was calculated by the difference between these two values.[12]

2.4. Statistical analysis

Statistical analysis were done using SPSS version 28 (IBM, Armonk, New York, United States). Quantitative data were summarized as means and standard deviations or medians and ranges. Categorical data were summarized as numbers and percentages. Quantitative data were compared using independent *t*-test or Mann–Whitney *U* test as appropriate. Correlation analyses were done using Spearman's correlation ROC analyses were done, and based on areas under the curve with 95% confidence intervals, best cutoff point, were identified. All statistical tests were two-sided. *P* values less than 0.05 were considered significant.[13]

3. Results

3.1. General characteristics

The demographic and clinical data of study population are illustrated in (Table 1). NSTE-ACS was the most frequent presentation (61.1%). Two-thirds (59.3%) of patients had intermediate GRACE risk score. The most frequent Killip class was one (88.9%).

Invasive and noninvasive LV parameters are summarized in table (Table 2) and the Left atrial parameters and discology indices are summarized in (Table 3).

3.2. Validity of 2016 ASE/EACVI recommended approach for estimation of left ventricular filling pressure

According to 2016 ASE/EACVI, most patients (83.3%) had nonelevated LA pressure With 26.9% sensitivity, 92.9% specificity, 77.8% PPV, 57.8% NPV,

Table 1. General characteristics of the studied patients.

General characteristics	Value
Age (years)	53 ± 10
Male sex	43 (79.6)
Diabetes mellitus	22 (40.7)
Hypertension	18 (33.3)
Smoking	38 (70.4)
systolic blood pressure (mmHg)	136 ± 25
Diastolic blood pressure (mmHg)	83 ± 10
Heart rate (b/m)	84 ± 14
Weight (kg)	83 ± 13
Height (cm)	167 ± 7
Body mass index	29.8 ± 4.5
Body surface area	1.9 ± 0.2
ECG	
NSTE-ACS	33 (61.1)
STEMI	21 (39.9)
GRACE scoring	
Low risk	6 (11.1)
Intermediate risk	32 (59.3)
High risk	16 (29.6)
KILLIP class	
One	48 (88.9)
Two	6 (11.1)

Data were presented as mean ± SD or number (percentage).

and 61. % overall accuracy. False positive and false negative rates were 7.1% and 73.1%, respectively.

3.3. Relation of LA parameters and invasively measured LV filling pressure

Table 4 compares Left atrial indices in patient with normal (<15 mmhg) verses elevated LVFP. Table 5 shows the Correlation between LV pre-A pressure and left atrial indices regardless of the LV ejection fraction. Table 6 shows the Correlation between LV pre-A pressure and left atrial indices according to EF (higher or $\leq$ 50%) (Fig. 1).

3.4. ROC analysis of expansion index (EI) in distinguishing those with elevated LV filling pressure

ROC analysis identified (EI) of 107.4% as the best cutoff point, sensitivity and specificity were 84.6% and 85.7%, respectively, Significant AUC of 0.871, with a 95% CI ranging from 0.775 to 0.967 ($P < 0.001$) (Fig. 2).

Table 2. Left ventricular parameters.

LV parameters	
Invasive measures	
LV pre-A pressure	15 (2–29)
Elevated LV pre-A pressure	26 (48.1)
Noninvasive measure	
Ejection fraction (%)	47.7 ± 12.9
EF > 50%	27 (50.0)
LV GLS	−14 ± 4.1
Impaired GLS	48 (88.9)

Data were presented as mean ± SD or median (min–max).

3.5. ROC analysis of aLASr in distinguishing those with elevated LV filling pressure

ROC analysis identified aLASr less than or equal to 28 as the best cutoff point, sensitivity and specificity were 73.1% and 96.4%, respectively, AUC of 0.910, with a 95% CI ranging from 0.834 to 0.986 ($P < 0.001$) (Fig. 3).

3.6. Prediction of elevated LV filling pressure

Multivariate logistic regression analysis was done to predict elevated LV filling pressure, controlling for five variants. All predictors are shown in (Table 7).

4. Discussion

ACS is one of the main causes of morbidity and mortality worldwide Sanchis-Gomar and colleagues.[14] The rise of LVFP is a significant prognostic marker that changes early during acute ischemia, however, invasive LVFP measurement is

Table 3. Left atrial parameters.

Left atrial parameters	
Volumetric indices	
Maximal volume (cm^3)	53 (21–102)
minimal volume (cm^3)	23 (8–74)
pre-A volume (cm^3)	36.4 (15–89)
Total LAEF (%)	49.8 ± 12.5
Expansion-index (%)	109.8 (21.7–300)
Active emptying fraction (%)	31.6 (9.8–56.3)
Passive emptying fraction (%)	25.5 (5.4–53.8)
Speckle tracking indices	
LASr (%)	32 (7–57)
LAScd (%)	−15 (−34 to −1)
LASct (%)	−17 (−30 to −2)
Pw Trans-mitral inflow parameters	
Peak E wave velocity (cm/s)	66 ± 21
E wave DT (seconds)	152 (63–325)
Peak A wave velocity (cm/s)	71.5 (1.04–155)
E:A ratio	0.9 (0.3–2.9)
Tissue Doppler of the mitral annulus	
Peak e prime Velocity (cm/s)	6 (2–17)
E:e ratio	9.4 (3.9–23.7)
TR Vmax	
<2.8 M/S	42 (77.8)
>2.8 M/S	12 (22.2)

Data were presented as mean ± SD or median (min–max).
DT, deceleration time; LAScd, left atrial strain of the conduit function; LASct, left atrial strain of the conduit function; LASr, left atrial strain of the reservoir function; TR Vmax, maximal velocity of tricuspid regurgitation.

Table 4. *Left atrial parameters according to LV filling pressure.*

	Elevated LV filling pressure		P-value
	Yes ($n = 26$)	No ($n = 28$)	
Volumetric indices			
Maximal volume (cm^3)	54 (102–22)	53 (84–21)	0.965
minimal volume (cm^3)	29 (74–11)	22 (39–8)	0.016[a]
pre-A volume (cm^3)	42.5 (89–15)	33.5 (49–17)	0.085
Total LAEF (%)	41.8 ± 11.4	57.1 ± 8.3	<0.001[a]
Expansion index (%)	73.2 (146.2–21.7)	134.8 (300–59.1)	<0.001[a]
Active emptying fraction (%)	29.7 (53.6–9.8)	38.7 (56.3–17)	0.022[a]
Passive emptying fraction (%)	13.3 (45.2–5.4)	30.4 (53.8–7.7)	<0.001[a]
Speckle tracking indices			
LASr (%)	24 (40–7)	38 (57–24)	<0001[a]
LAScd (%)	−9 (−2 to −19)	−21 (−1 to −34)	<0.001[a]
LASct (%)	−15 (−2 to −24)	−19 (−6 to −30)	0.002[a]
Doppler indices			
Peak E wave velocity	70 ± 24	63 ± 19	0.257
E wave DT	142 (325–7)	172 (242–63)	0.057
Peak A wave velocity	72.5 (155–1.04)	71 (122–2)	0.782
E:A ratio	0.8 (2.9–0.4)	0.9 (1.7–0.3)	0.319
Peak e prime Velocity	6 (10–4)	8 (17–2)	0.001[a]
E:e ratio	11.5 (23.7–5.2)	8.3 (20.9–3.9)	0.021[a]

DT, deceleration time; LA, left atrium; LAScd, left atrial strain of the conduit function; LASct, left atrial strain of the conduit function; LASr, left atrial strain of the reservoir function.
[a] Significant; Data were presented as mean ± SD or median (min–max).

still difficult particularly in ACS patients Durmaz and colleagues.[1] The recommended algorithm to estimated LVFP Nagueh and colleagues[4] have not been validated in patients with ACS Durmaz and colleagues.[1]

The most important finding of our study was that the diagnostic algorithm for evaluation of LVFP recommended by ASE/EACVI Nagueh and colleagues[4] has limited value in patients with ACS. Most patients (83.3%) had non-elevated LA pressure and false negative rates of 73.1%. The assessment of left atrium parameters especially the reservoir

Table 5. *Correlation between LV pre-A pressure and left atrial parameters regardless of the LV ejection fraction.*

	LV pre-A pressure	
	R	P
Maximal volume	0.13	0.349
minimal volume	0.392	0.003[a]
pre-A volume	0.271	0.047[a]
Total LA ejection fraction	−0.567	<0.001[a]
Expansion index	−0.567	<0.001[a]
Active emptying fraction	−0.360	0.008[a]
Passive emptying fraction	−0.286	0.036[a]
LASr	−0.590	<0.001[a]
LAScd	−0.393	0.003[a]
LASct	−0.475	<0.001[a]
Peak E Wave velocity	0.074	0.594
E wave DT	−0.2	0.147
Peak A wave velocity	0.163	0.239
E:A ratio	−0.044	0.754
Peak e prime Velocity	−0.021	0.882
E:e ratio	−0.322	0.019[a]
Maximal volume	0.283	0.04[a]

DT, deceleration time; LA, left atrium; LAScd, left atrial strain of the conduit function; LASct, left atrial strain of the conduit function; LASr, left atrial strain of the reservoir function; r, Correlation coefficient.
[a] Significant.

Table 6. *Correlation between LV pre-A pressure and left atrial parameters according to EF.*

	LV pre-A pressure (EF < 50)		LV pre A pressure (EF>50%)	
	r	P	R	P
Maximal volume	0.141	0.483	−0.014	0.943
minimal volume	0.440[a]	0.021	0.202	0.312
pre-A volume	0.214	0.283	0.103	0.608
Total LA ejection fraction	−0.466[a]	0.014	−0.563	0.002
Expansion index	−0.466[a]	0.014	−0.563	0.002
Active emptying fraction	−0.312	0.113	−0.373	0.056
Passive emptying fraction	−0.058	0.772	−0.133	0.509
LASr	−0.447[a]	0.019	−0.450[a]	0.018
LAScd	−0.159	0.429	−0.332	0.09
LASct	−0.489[a]	0.01	−0.33	0.093
Peak E Wave velocity	0.214	0.283	−0.017	0.932
E wave DT	−0.229	0.251	0.051	0.801
Peak A wave velocity	−0.122	0.545	0.166	0.409
E:A ratio	0.331	0.092	−0.302	0.125
Peak e prime Velocity	−0.052	0.799	−0.326	0.097
E:e ratio	0.054	0.795	0.246	0.216

r: Correlation coefficient.
DT, deceleration time; LA, left atrium; LAScd, left atrial strain of the conduit function; LASct, left atrial strain of the conduit function; LASr, left atrial strain of the reservoir function.
[a] Significant.

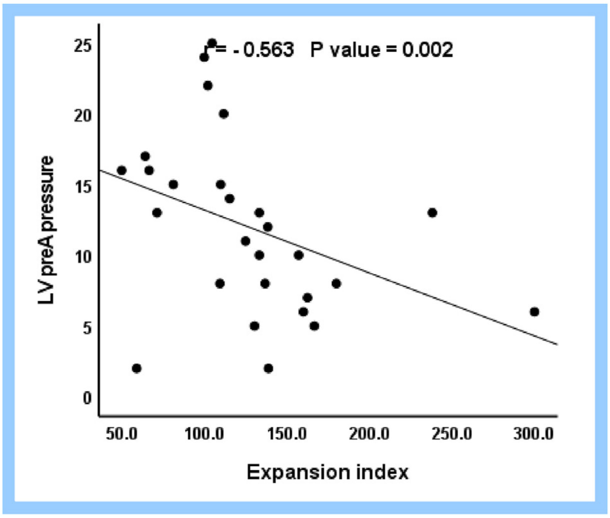

Fig. 1. Correlation between LV pre-A pressure and EI in those with EF > 50%.

function has a significant correlation with invasively measured LVFP.

Our findings are concordant with the study of Durmaz and colleagues[1] which included 180 patients with STEMI, they demonstrated a poor correlation between invasively measured LVFP and ASE/EACVI recommended algorithm.

Our results demonstrated a variable degree of significant correlations between invasive LV pre-a pressure measurement and left atrium functions assessed by two-dimensional echocardiography, speckle tracking and Doppler techniques. LVFP showed intermediate degree of correlation with LA reservoir function either measured by volumetric method 'expansion index 'or two dimensional-speckle tracking 'LASr' and also, total LA ejection fraction. LVFP showed less degree of correlation with minimal LA volume, active emptying fraction, and left atrium strain of the conduit phase 'LAScd', and contraction phase 'LASct'. LVFP showed weak correlation with E/e and pre-A volume and no correlation with E/A ratio.

LA reservoir function parameters either measured with two-dimensional speckle tracking technique or volumetric technique correlate better with LVFP in patient with EF greater than 50%. The best cutoff point for expansion index regardless of the EF was less than or equal to 107.4%, at which sensitivity and specificity were 84.6% and 85.7%, respectively, and the best cutoff point for LASr was less than or equal to 28%, at which sensitivity and specificity were 73.1% and 96.4%, respectively.

Our findings are concordant with the study of Hsiao and colleagues[15] which included 521 patient with ACS. They demonstrated a significant correlation between invasively measured LVFP and LA reservoir function assessed by volumetric method 'expansion index'. In a recent study done by Khan and colleagues,[16] left atrial reservoir function assessed by two dimensional speckle tracking technique has been shown to have a significant correlation with invasively measured LVFP in

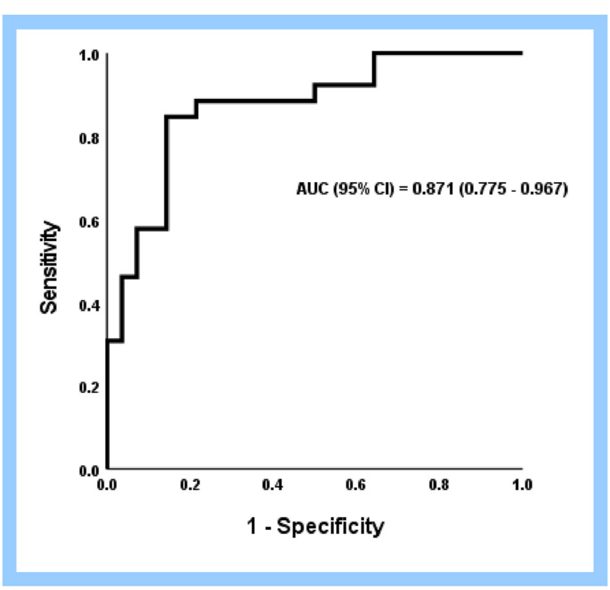

Fig. 2. ROC analysis (EI) in distinguishing those with elevated LV filling pressure.

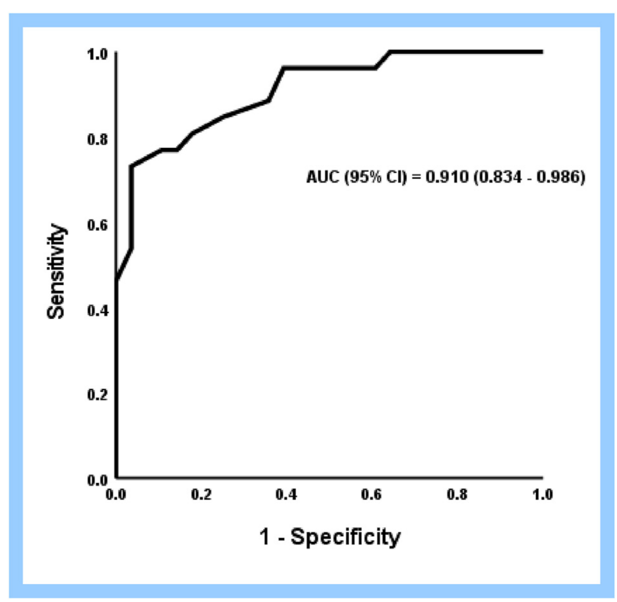

Fig. 3. ROC analysis of LASr in distinguishing those with elevated LV filling pressure.

Table 7. Multivariate logistic regression analysis to predict elevated LV filling pressure.

	OR (95% CI)[b]	*P*-value
V min	1.078 (1.010–1.151)	0.024[a]
Total LAEF	0.824 (0.735–0.923)	<0.001[a]
Expansion index	0.951 (0.924–0.980)	<0.001[a]
Active emptying fraction	0.939 (0.884–0.998)	0.042[a]
Passive emptying fraction	0.877 (0.813–0.947)	<0.001[a]
aLASr	0.638 (0.478–0.852)	0.002[a]
aLAScd	0.815 (0.725–0.916)	<0.001[a]
aLASct	0.822 (0.717–0.941)	0.005[a]
Peak E prime V	0.527 (0.333–0.835)	0.006[a]
E:e ratio	1.296 (1.083–1.551)	0.005[a]

95% CI, 95% confidence interval; DM, HTN, and smoking; OR, Odds ratio.
[a] Significant.
[b] Adjusted for age, gender.

patient suspected to have HF. The new article, published recently by the ESC in June 2022, added the left atrial reservoir function measured by 2D speckle tracking technique in the diagnostic work up in the noninvasive assessment of LVFP in case of inability to record TR velocity. It recommended a cutoff point less than 18% to consider impaired LASr, this cutoff point is lower than our results which seems to be due to the chronicity of the cardiovascular diseases of the population that included in the study Opescu and colleagues.[17]

Acute systolic and diastolic dysfunction in ACS patients causes a quick increase in left ventricular pressure without structural remodeling of the heart chambers, which in turn has an impact on the LA. These patients' subset differs from chronic patients Secundo Junior and colleagues.[18]

In our study we have observed no correlation between E/A ratio, TR Vmax and LAVI and invasively measured LVFP. We have found poor correlation between increased LVEDP and mitral E wave deceleration time, and also the preload dependency of mitral deceleration time might limit its clinical utility in ACS settings.

TDI of the mitral annulus is not a global diastolic parameter so it is not suitable for assessing LVFP in patients with AMI, also we have demonstrated a slight correlation between E/e′ ratio and invasively measured LVFP.

5. Conclusion

LA reservoir function parameters identify the early increases in LV filling pressures in patients with ACS, especially with EF greater than 50%. Assessment of left atrium reservoir function by two-dimensional speckle technique is more accurate than the volumetric technique.

Limitations

Our study has some limitations. First, the small number of patients included in the study limits its statistical power, and thus, further large-scale studies are needed to validate the findings of this study. Second: we couldn't study the patients with hemodynamic instability and patients requiring inotropic Support (16 patients) because of patient's criticality.

Conflict of Interest

None declared.

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