Original Article

Left Ventricular End Diastolic Pressure and Acute Coronary Syndromes

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Abstract

Background: Data is lacking in the literature regarding the prognostic impact of left ventricular-end diastolic pressure (LVEDP) across acute coronary syndromes (ACS).

Objective: To assess LVEDP and its prognostic implications in ACS patients.

Methods: Prospective, longitudinal and continuous study of 1,329 ACS patients from a single center between 2004 and 2006. Diastolic function was determined by LVEDP. Population was divided in two groups: A - LVEDP < 26.5 mmHg (n = 449); group B - LVEDP ≥ 26.5 mmHg (n = 226).

Results: There were no significant differences between groups with respect to risk factors for cardiovascular disease, medical history and medical therapy during admission. In group A, patients with non-ST elevation ACS were more frequent, as well as normal coronary angiograms. In-hospital mortality was similar between groups, but one-year survival was higher in group A patients (96.9 *vs* 91.2%, log rank p = 0.002). On a multivariate Cox regression model, a LVEDP ≥ 26.5 mmHg (HR 2.45, 95%CI 1.05 - 5.74) remained an independent predictor for one-year mortality, when adjusted for age, LV systolic ejection fraction, ST elevation ACS, peak troponin, admission glycemia, and diuretics at 24 hours. Also, a LVEDP ≥ 26.5 mmHg was an independent predictor for a future readmission due to congestive HF (HR 6.65 95%CI 1.74 – 25.5).

Conclusion: In our selected population, LVEDP had a significant prognostic influence. (Arq Bras Cardiol 2011; 97(2) : 100-110)

Keywords: Heart failure; ventricular dysfunction, left; acute coronary syndrome/prognoses.

Introduction

After 10 to 20 seconds of coronary artery occlusion, relaxation time starts to shorten with a simultaneous rise in left ventricular end-diastolic pressure (LVEDP). Wall motion abnormalities occur between 15 and 30 seconds after culprit occlusion, and are followed by a drop in ejection fraction. After this cascade, ischemic symptoms and electrical signs of ischemia may ensue. Nevertheless, this presentation is highly variable, and is dependent on collateral flow, collateral perfusion and ischemic preconditioning[1].

According to the 1998 European Society Cardiology working group report about how to diagnose diastolic HF, three obligatory conditions have to be simultaneously satisfied: 1 - the presence of signs of congestive heart failure (HF); 2 - presence of normal or only mildly abnormal left ventricular (LV) systolic function; 3 - evidence of abnormal LV relaxation, filling, diastolic distensibility or diastolic stiffness[2].

The 2007 revised document challenged the third topic, recognizing the difficulties in the assessment of diastolic LV function, and based on recent data[3], the measurement of diastolic LV function was not required to attain the diagnosis of diastolic HF, also named HF with normal ejection fraction. Nevertheless the authors remarked that invasively acquired evidence of diastolic LV dysfunction remains definite evidence of HF with preserved systolic function[4].

Both documents stated that the presence of a LVEDP > 16 mmHg in the presence of a non-dilated left ventricle is synonymous of LV diastolic distensibility reduction and therefore, a marker of LV diastolic dysfunction[5].

Previous authors demonstrated that an elevated pulmonary capillary wedge pressure (PCWP) and a low cardiac index were independent predictors of outcome in the context of acute myocardial infarction (AMI)[6-8]. Most of the present data in the literature on ACS patients and diastolic function is related to the noninvasive echocardiographic assessment of LV diastolic function. As reported by Oh et al[9] a restrictive filling pattern after an AMI was associated with the occurrence of in-hospital HF. Other echocardiographic indexes were also considered of prognostic value, such as the deceleration time (DT) < 140 ms[10-12], and also the E/E' ratio greater than 15, as reported by Hillis et al[13]. This last group observed than in 250 patients

with AMI the E/E' ratio had a prognostic role with respect to all-cause mortality with an incremental value over age and left ventricular ejection fraction. Nevertheless, there was some conflicting data in the literature regarding diastolic function as a maker of prognosis, such as the study ATTenuation by Adenosine of Cardiac Complications (ATTACC), a randomized controlled trial of the addictive value of adenosine over fibrinolysis in ST elevation AMI, which failed to demonstrate the independent prognostic importance of restrictive filling defined by either a DT < 140 ms, or E/A ratio > 2[14].

Due to the lack of prognostic data related to invasively determined left ventricular filling patterns in current ACS patients, namely with respect to LVEDP, we hypothesized that LVEDP would predict an adverse outcome after an ACS. To test this hypothesis, we evaluated the prognostic value of LVEDP in a non-selected single center ACS population admitted for an invasive strategy during the acute phase.

Methods

Study population

The present was a continuous, observational, and prospective study of 1,459 consecutive admissions due to ACS, between May 2004 and December 2006, in a single center coronary care unit. We excluded 130 records as they were readmissions. The final population consisted of 1,329 patients. Of these, we selected the ones admitted for an invasive strategy - 786 patients.

AMI was defined according to the Universal Definition of myocardial infarction, as a positive cardiac biomarker (namely troponin I) with symptoms of ischemia or ECG changes indicative of new ischemia (ST and T wave and new bundle branch block)[15].

Regarding ECG data, ST elevation AMI was defined by a new onset of ST elevation > 2 mm in the precordial leads for men and 1.5 mm for women and greater than 1 mm in other leads. Non-ST elevation AMI, in addition to the previous laboratorial and clinical criteria, could be associated or not with ECG ischemic changes (namely ST depression or T wave inversion)[15].

Unstable angina was defined either by new onset angina (at least class III CCS), progressive angina, or angina at rest, with or without ECG ischemic changes, and a negative cardiac biomarker assay[16].

LV systolic function was assessed by echocardiography, according to the Simpson method. The examination considered for this study was performed within 24 hours after the invasive assessment.

LVEDP was determined in the catheterization laboratory using a calibrated fluid filled system before left ventriculography. LVEDP was measured at the Z-point, which was identified on the left ventricular pressure trace as the point at which the slope of the ventricular pressure upstroke changes, approximately 50 ms after the ECG Q wave, and generally coinciding with the ECG R wave[17]. The decision to determine LVEDP was left at the discretion of the hemodynamicist. All the patients were referred to the invasive procedure primarily to diagnose coronary artery disease, and not exclusively for an invasive assessment of LV hemodynamics.

Cardiac biomarkers namely, troponin I and MBCK were assessed daily, and the peak values during hospital stay were used in our analysis.

Population was divided in two groups based on the LVEDP. Group A included 449 patients that had LVEDP < 26.5 mmHg. Group B patients had LVEDP ≥ 26.5 mmHg and comprised 226 individuals. LVEDP was not determined in 111 patients.

This investigation conformed to the principles outlined in the Declaration of Helsinki. The local ethics committee approved the research protocol and informed consent has been obtained from all subjects.

Baseline data and patient follow-up

We analyzed standardized records during admission that included demographic, clinical, electrical, echocardiographic and laboratorial data. Medical therapy, catheterization data, intra-hospital course and discharge medication were also recorded.

We performed a median clinical follow up of 19 months after hospital discharge. The information was collected by phone call, from hospital records or at the outpatient clinic. The primary endpoint was all-cause mortality one year after discharge. Other results were also analyzed, such as the combined result of cardiovascular death, non-fatal infarction, re-admission for unstable angina, and unscheduled percutaneous coronary intervention - MACE, and re-admission for congestive HF one year after the culprit ACS admission.

Statistical analysis

The Kolmogorov-Smirnov test was used to assess if continuous variables were normally or non-normally distributed. Continuous data were presented as mean and standard deviation and compared with the Student t-test. Categorical variables were reported as frequencies and percentages, and the χ^2 test or the exact Fisher tests were used when appropriate.

The cumulative survival curves were constructed with the use of the Kaplan-Meier method and groups were compared with the Log rank test. The observational period started at hospital discharge and lasted for one year.

A multivariate Cox regression analysis was performed for the primary endpoint, and also for HF readmission one year after the ACS. Variables that were significant at the bivariate level (p < 0.05) or that had a clinical relevance, were included in the models.

With the exception of the Kolmogorov-Smirnov all statistical tests were two-tailed and a p value less than 0.05 was deemed significant. The analysis was performed with the SPSS 15 (*Statistical Package for Social Sciences*) from SPSS Inc, Chicago, IL.

Results

LVEDP was available for 675 patients. The mean value for the population was 23.2 mmHg, with a maximum value of 52.0 mmHg, and a minimum of 2.3 mmHg.

The cutoff value of 26.5 mmHg had the highest sensitivity (58%) and specificity (61%) - area under ROC 0.60, for the primary endpoint selected (all-cause mortality).

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The study cohort consisted of 499 male and 176 female individuals with a mean age of 63.5 years. The baseline demographic, clinical characteristics and in-hospital management of both groups of patients are presented in Tables 1 to 4.

A higher LVEDP was associated with STEMI, higher peak values of cardiac biomarkers, a lower left ventricular ejection fraction (LVEF), and a more dilated left ventricle. There was a negative significant correlation between LVEDP and LVEF (r: -0.324, p value < 0.01).

Patients with a lower LVEDP had a lower likelihood of in-hospital HF, were less often prescribed a diuretic at 24 hours (17.4 vs 28.3%, p = 0.001), and had more frequently a normal coronary angiogram.

There were no other significant differences with respect to intrahospital and discharge medical therapy. The in-hospital mortality was similar for both groups (2.4 vs 4.9%, p = 0.095).

Outcome

With respect to follow up, data was available for 618 (lost-to-follow-up rate of 5.4%) of the discharged patients.

A higher LVEDP was associated with a lower survival status at one, six and twelve months after discharge - Table 5. The cumulative one year survival rate was significantly lower for group B patients (96.9 vs 91.2% log rank p = 0.002) - Figure 1. This difference remained significant for the subgroup with preserved systolic function (LVEF ≥ 40%), but the stratification proposed for LVEDP as a survival marker was not significant for the depressed LV function (LVEF < 40%). The p value for interaction between these last three variables was not significant (0.59).

In the univariate analysis, a LVEDP ≥ 26.5 mmHg was significantly associated with a higher mortality one year after discharge - Table 6, as were age, LVEF, STEMI, diuretics at 24 hours, glycemia at admission, and the peak value of

Table 1 - Baseline characteristics

	All patients	A - LVEDP < 26.5	B - LVEDP ≥ 26.5	p
Number of patients	675	449	226	
Male gender (%)	499/675 (73.9)	337/449(75.1)	162/226 (71.7)	0.35
Age (mean, SD)	63.5 ± 12.4	63.3 ± 11.8	63.8 ± 13.4	0.61
Admission diagnosis (%)				
STEMI	281/654 (43.0)	164/439 (37.3)	117/215 (54.4)	<0.01
NSTEMI	234/654 (35.8)	171/439 (39.0)	63/215 (29.3)	0.01
UA	123/654 (18.8)	94/439 (21.4)	29/215 (13.5)	0.02
Undetermined pattern	16/654 (2.4)	10/439 (2.3)	6/215 (2.8)	0.69
Risk factors cardiovascular disease (%)				
Diabetes	171/671 (25.3)	108/446 (24.2)	63/225 (28.0)	0.29
Dyslipidemia	439/628 (65.0)	283/416 (68.0)	156/212 (73.6)	0.15
Hypertension	440/631 (65.2)	284/418 (67.9)	156/213 (73.2)	0.17
Current smoking habits	153/675 (22.7)	101/449 (22.5)	52/226 (23.0)	0.88
Cardiovascular history (%)				
Previous myocardial infarction	89/616 (13.2)	57/409 (13.9)	32/207 (15.5)	0.61
Previous PCI	67/661 (9.9)	44/439 (10.0)	23/222 (10.4)	0.89
Previous HF	2/310 (0.3)	1/235 (0.4)	1/75 (1.3)	0.39
Previous stroke	36/671 (5.3)	27/446 (6.1)	9/225 (4.0)	0.27
Previous medication (%)				
Aspirin	150/401 (37.4)	106/275 (38.5)	44/126 (34.9)	0.49
Other anti-platelet	51/401 (12.7)	35/275 (12.7)	16/126 (12.7)	0.99
Beta-blocker	86/401 (21.4)	62/275 (22.5)	24/126 (19.0)	0.43
ACE inhibitors	148/401 (36.9)	104/275 (37.8)	44/126 (34.9)	0.58
Statins	133/401 (33.2)	91/275 (33.1)	42/126 (33.3)	0.96
Diuretics	77/401 (19.2)	56/275 (20.4)	21/126 (16.7)	0.38
Nitrates	72/401 (18.0)	52/275 (18.9)	20/126 (15.9)	0.46

STEMI - ST-elevation acute myocardial infarction; NSTEMI - non-ST elevation acute myocardial infarction; UA - unstable angina; PCI - percutaneous coronary intervention; HF - heart failure; ACE - angiotensin-converting enzyme; LVEDP - left ventricular-end diastolic pressure.

Table 2 - Hemodynamic, electrical and laboratory data

	All patients	A - LVEDP < 26.5	B - LVEDP ≥ 26.5	p
Hemodynamic data on admission				
Heart rate, bpm (mean, SD)	76.5 ± 15.3	75.2 ± 15.3	78.8 ± 15.4	0.05
Systolic blood pressure, mmHg (mean, SD)	135.0 ± 24.3	136.3 ± 23.2	134.8 ± 26.8	0.46
Diastolic blood pressure, mmHg (mean, SD)	73.9 ± 14.2	73.4 ± 13.7	74.3 ± 15.3	0.48
TIMI risk score ≤ 2 (%)	342/675 (50.7)	236/449 (52.6)	106/226 (46.9)	0.17
TIMI risk score 3 - 4 (%)	276/675 (40.9)	177/449 (39.4)	99/226 (43.8)	0.27
TIMI risk score ≥ 5 (%)	57/675 (8.4)	36/449 (8.0)	21/226 (9.3)	0.57
Body mass index (kg/m²)	27.7 ± 4.8	27.4 ± 4.6	28.3 ± 5.3	0.03
Electrical data on admission (%)				
Sinus Rhythm	613/671 (91.4)	409/446 (91.7)	204/225 (90.7)	0.65
AF	36/671 (5.4)	23/446 (5.2)	13/225 (5.8)	0.74
ST depression	47/671 (7.0)	33/446 (7.4)	14/225 (6.2)	0.57
T wave inversion	96/671 (14.3)	69/446 (15.5)	27/225 (12.0)	0.23
Laboratory (mean, SD)				
Peak Troponin I, U/l	44.5 ± 63.0	33.0 ± 58.2	53.9 ± 69.0	<0.01
Peak MBCK mass, U/l	125.4 ± 177.7	96.9 ± 134.8	171.0 ± 233.2	<0.01
Total cholesterol, mg/dl	194.7 ± 49.6	192.7 ± 48.4	199.0 ± 53.2	0.20
LDL cholesterol, mg/dl	131.2 ± 37.0	130.4 ± 36.1	133.9 ± 39.7	0.34
HDL cholesterol, mg/dl	43.3 ± 10.3	42.4 ± 10.0	44.5 ± 10.5	0.04
Glomerular filtration rate ml/min	71.5 ± 21.5	72.4 ± 20.7	69.4 ± 23.2	0.12
Admission glycemia, mg/dl	149.4± 63.9	155.5 ± 68.4	144.7 ± 59.0	0.06
Admission hemoglobin, g/dl	14.2 ± 1.6	14.2 ± 1.7	14.0 ± 1.6	0.20
Minimum hemoglobin, g/dl	12.4 ± 1.7	12.4 ± 1.7	12.1 ± 1.7	0.06

AF - atrial fibrillation; LVEDP - left ventricular-end diastolic pressure.

Table 3 - In-hospital management

	In the first 24 hours			Medication at discharge		
	A - LVEDP < 26.5	B - LVEDP ≥ 26.5	p	A - LVEDP < 26.5	B - LVEDP ≥ 26.5	p
ASA (%)	436/449 (97.1)	219/226 (96.9)	0.88	388/438 (88.6)	197/215 (87.2)	0.45
Clopidogrel (%)	332/449 (73.9)	179/226 (79.2)	0.13	268/438 (61.2)	138/215 (64.2)	0.46
Beta-Blockers (%)	381/449 (84.9)	184/226 (81.4)	0.25	349/438 (79.7)	169/215 (78.6)	0.75
ACE inhibitors (%)	406/449 (90.4)	206/226 (91.2)	0.76	389/438 (88.8)	187/215 (87.0)	0.49
Statins (%)	444/449 (98.9)	221/226 (97.8)	0.27	417/438 (95.2)	206/215 (95.8)	0.73
Gp IIb/IIIa inhibitors (%)	241/449 (53.7)	136/226 (60.2)	0.11			
LMWH	444/449 (98.9)	221/226 (97.8)	0.27			
Diuretic (%)	78/449 (17.4)	64/226 (28.3)	0.01			
Nitrates (%)	165/449 (36.7)	83/226 (36.7)	0.99			

ASA - acetyl salicylic acid; LMWH - low molecular weight heparin; Gp - glycoprotein; LVEDP - left ventricular-end diastolic pressure.

troponin I. In a composite model that included the previous seven variables, LVEDP as a continuous variable was not an independent predictor of outcome (HR 1.03, 95% CI 0.98 - 1.08, p = 0.17) - Table 6. There were no interactions between LVEDP and LVEF regarding this endpoint, as in a Cox regression model that included only those two variables, they both remained significant (data not shown).

The cumulative freedom from congestive HF in the year after the index hospitalization was significantly higher for the lower LVEDP patients (98.1 *vs* 93.2%, log rank p = 0.004) -

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Table 4 - Echo and cath lab data

	A - LVEDP < 26.5	B - LVEDP ≥ 26.5	p
Echocardiographic data			
Left atrium, mm °	41.4 ± 6.6	41.4 ± 6.5	0.97
LV end systolic diameter, mm °	38.9 ± 6.9	41.7 ± 7.8	<0.01
LV end diastolic diameter, mm °	56.2 ± 6.6	58.4 ± 6.6	<0.01
LVEF, % °	54.6 ± 9.05	48.8 ± 11.2	<0.01
LVEF < 40% *	58/447 (13.0)	64/226 (28.3)	<0.01
LV shortening fraction, % °	31.5 ± 5.5	29.8 ± 6.2	0.01
LV motility wall abnormality *	233/332 (70.2)	146/175 (83.4)	0.01
Mitral regurgitation *	202/359 (56.3)	115/191 (60.2)	0.73
Pulmonary artery systolic pressure, mmHg °	32.4 ± 10.4	31.9 ± 11.0	0.81
Cath lab data			
Time to balloon (primary angioplasty), hours	2.0 ± 1.9	1.5 ± 1.5	0.06
Coronary angiogram ≤ 48 hours *+	79/224 (35.3)	30/70 (42.9)	0.25
Coronary angiogram > 48 hours * +	145/224 (64.7)	40/70 (57.1)	0.25
Normal coronary angiogram *	68/418 (16.3)	19/211 (9.0)	0.01
1 vessel coronary disease *	172/418 (41.1)	91/211 (43.1)	0.64
2 vessel coronary disease *	96/418 (23.0)	52/211 (24.6)	0.64
3 vessel coronary disease *	77/418 (18.4)	49/211 (23.2)	0.16
Fully revascularized*	172/350 (49.1)	94/192 (49.0)	0.96
Partially revascularized*	89/350 (26.0)	50/192 (26.0)	0.88
Not revascularized*	89/350 (25.4)	48/192 (25.0)	0.91
Stent*	258/418 (61.7)	133/211 (63.0)	0.75
Drug eluting stents*	181/258 (70.2)	91/132 (68.9)	0.81
Surgical revascularization*	16/418 (3.8)	6/211 (2.8)	0.53

*° - mean ± SD; * - %; + for non-ST elevation ACS; LVEF - left ventricular ejection fraction, LVEDP - left ventricular-end diastolic pressure.*

Table 5 - Outcomes in the hospital and 1 year after discharge

	A - LVEDP < 26.5	B - LVEDP ≥ 26.5	OR (95% CI)	p
Length of stay (days)	5.2 ± 2.5	5.9 ± 3.7		<0.01
In-hospital mortality (%)	11/449 (2.4)	11/226 (4.9)	1.99 (0.88 – 4.51)	0.01
In-hospital diagnosis of heart failure (%)	128/446 (28.7)	84/225 (37.3)	1.48 (1.05 – 2.08)	0.02
Overall mortality 30 days (%)	1/414 (0.2)	4/204 (2.0)	8.12 (0.91 – 72.2)	0.03
Overall mortality 6 months (%)	9/414 (2.2)	14/204 (6.9)	3.16 (1.39 – 7.17)	<0.01
Overall mortality 1 year (%)	13/414 (3.1)	18/204 (8.8)	2.81 (1.41 – 5.62)	0.01
Cumulative mortality 30 days (%)	12/449 (2.7)	15/226 (6.6)	2.48 (1.18 – 5.22)	<0.01
Cumulative mortality 6 months (%)	20/449 (4.5)	25/226 (11.1)	2.48 (1.41 – 4.37)	<0.01
Cumulative mortality 1 year (%)	24/449 (5.3)	29/226 (12.8)	2.40 (1.43 – 4.03)	<0.01
MACE 1 year (%)	46/414 (11.1)	33/204 (16.2)	1.45 (0.96 – 2.19)	0.08
HF 1 year (%)	8/414 (1.9)	14/204 (6.9)	3.59 (1.51 – 8.33)	0.01

MACE - major adverse cardiovascular endpoint; HF - heart failure; LVEDP - left ventricular-end diastolic pressure.
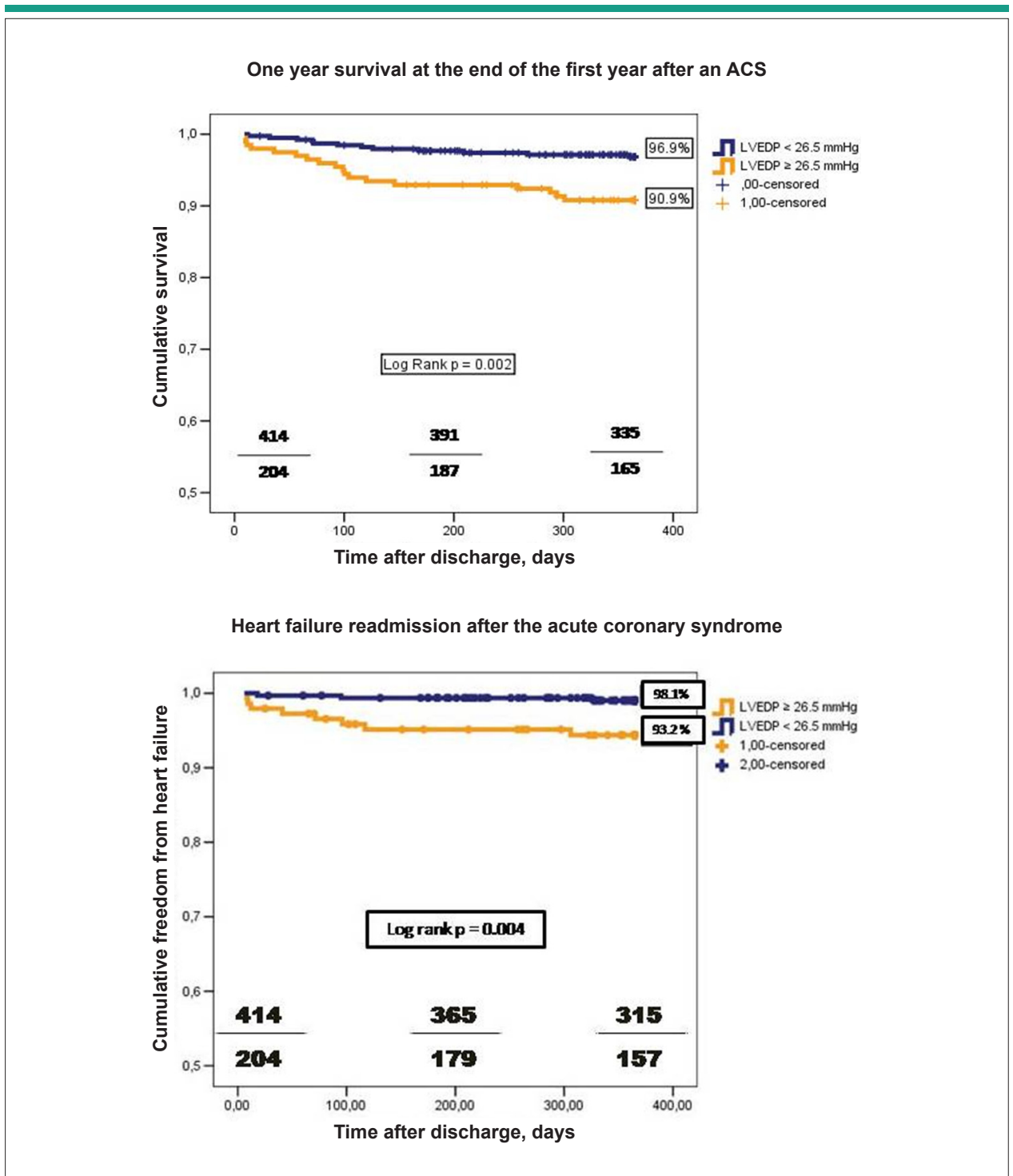
Figures 1. e 2 - *Outcomes with respect to overall survival and HF readmission one year after the ACS.*

Figure 2. The proposed stratification of the LVEDP also had a significant impact in the subpopulation with LVEF ≥ 40%, but not in the ones with LVEF < than 40%. The p value for the interaction of LVEDP, LVEF, and HF in the follow-up was not significant (0.37). LVEDP as a continuous variable remained an independent predictor of HF readmission, in a composite model that included LVEDP (as a continuous variable), age,

LVEF, peak troponin I, STEMI, TIMI risk score, diuretics at 24 hours and atrial fibrillation - Table 7.

Discussion

Our data confirmed LVEDP as a risk stratification variable during an ACS. As a continuous variable and after adjustment,

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	Survivors	Deceased	OR (95% CI)	p
Number	587	31		
Female gender*	150/587 (25.6)	7/31 (22.6)	0.85 (0.36 – 2.01)	0.71
STEMI*	238/570 (41.8)	19/29 (65.5)	2.65 (1.21 – 5.80)	0.01
Diabetes*	142/587 (24.2)	11/31 (35.5)	1.72 (0.81 – 3.68)	0.16
Hypertension*	386/553 (69.8)	22/27 (81.5)	1.90 (0.71 – 5.11)	0.19
Atrial fibrillation *	29/587 (4.9)	1/31 (3.2)	0.64 (0.08 – 4.87)	0.67
ECG ST depression *	41/587 (7.0)	1/31 (3.2)	0.44 (0.06 – 3.34)	0.42
Normal coronary angiogram*	85/587 (14.5)	1/31 (3.2)	0.20 (0.03 – 1.46)	0.08
Three vessel disease*	114/587 (19.4)	10/31 (32.3)	1.98 (0.91 – 4.31)	0.08
Complete percutaneous revascularization*	248/502 (49.4)	11/30 (36.7)	0.59 (0.28 – 1.27)	0.18
Diuretics 24 hours *	102/587 (17.4)	15/31 (48.4)	4.46 (2.13 – 9.31)	<0.01
Peak troponin I higher (U/l) °	33.7 ± 51.4	92.9 ± 102.0		<0.01
Glycemia admission (mg/dl) °	144.1 ± 60.3	184.9 ± 66.0		<0.01
Age (years) °	62.9 ± 12.1	71.3 ± 109		<0.01
LVEDP (mmHg) *	23.0 ± 8.1	27.3 ± 11.7		<0.01
LVEF (%) °	53.2 ± 9.9	45.1 ± 11.4		<0.01
BMI (kg/m²) °	27.7 ± 4.8	27.0 ± 3.5		0.41
Glomerular filtration rate (ml/min) °	72.4 ± 20.4	71.6 ± 26.0		0.82

° mean ± SD; * %

Multivariate Cox regression analysis for overall mortality one year after the ACS			
Variables	HR	p value	95% C I
Peak troponin I	1.01	<0.01	1.00 – 1.01
Age	1.05	0.02	1.01 – 1.09
Glycemia admission	1.01	0.02	1.00 – 1.01
Diuretics 24 hours	2.35	0.048	1.01 – 5.48
LVEDP	1.03	0.17	0.98 – 1.08
STEMI	1.13	0.80	0.44 – 2.90
LVEF	0.99	0.45	0.96 – 1.02

Number of events - 27; Population - 490 patients; Chi square - 47.3; p < 0.01. LVEF - left ventricular ejection fraction; LVEDP - left ventricular end diastolic pressure; ECG - Eletrocardiogram; BMI - body mass index.

LVEDP had a prognostic impact regarding HF readmission after an ACS - for each 1 mmHg increase, the relative risk increased 1.10 times (1.04 to 1.16). On the contrary, LVEDP was not an independent predictor with respect to in-hospital mortality, one-year mortality and one-year ischemic complications (MACE rate). The cutoff of 16 mmHg used to identify LV diastolic dysfunction[4], was not an univariate predictor of follow-up mortality. It was associated with a higher rate of readmission for HF (data not shown), but with lower sensitivity and specificity.

Prognosis

As previously reported, a higher PCWP - a maker of LV diastolic distensibility, in the context of acute MI was associated with larger infarcts[18] and with a worse LV systolic function[19].

In our population, a higher LVEDP was more frequently related with STEMI, and with higher peak values of troponin I. That was in agreement with the work of Bronzear et al[20], as ischemic myocardium was associated with higher LV filling pressures and reduced left ventricular distensibility during pace-induced ischemia.

Our work also corroborated the previous clinical data reported by Killip and Kimball in 1967, as a higher LV filling pressure was synonymous of an in-hospital diagnosis of HF[21].

Similarly to recently published data on the Forrester invasive classification, PCWP was not an independent predictor of in-hospital outcome[8], as LVEDP was not in our study. This lack of prognostic influence could have the following explanations: first, although the present cohort represented a consecutive group of patients, not all patients submitted to a coronary angiogram were submitted to an invasive assessment of LV diastolic function. The in-hospital mortality for the 111 patients submitted to a coronary angiogram and whose diastolic function was not assessed was 9%, and therefore an exclusion of the highest risk patients might have occurred. Second,

Table 7 - Univariate predictors of readmission for congestive heart failure one year after the ACS

	No event	Event	OR (95% CI)	p
Number	596	22		
Female gender*	151/596 (25.3)	6/22 (27.3)	1.11 (0.43 – 2.88)	0.84
STEMI*	243/578 (42.0)	14/21 (66.7)	2.76 (1.10 – 6.93)	0.03
Diabetes*	146/596 (24.5)	7/22 (31.8)	1.10 (0.83 – 1.48)	0.44
Hypertension*	392/560 (70.0)	16/20 (80.0)	1.71 (0.57 – 5.20)	0.34
TIMI risk score ≤ 2*	311/596 (52.2)	3/22 (13.6)	0.15 (0.04 – 0.49)	<0.01
LVEDP ≥ 26.5mmHg *	190/596 (31.9)	14/22 (63.6)	3.74 (1.54 – 9.07)	0.02
Atrial fibrillation *	27/596 (4.5)	3/22 (13.6)	3.33 (0.93 – 11.94)	0.05
Normal coronary angiogram*	85/596 (14.3)	1/22 (4.5)	0.29 (0.04 – 2.16)	0.20
Incomplete percutaneous revascularization*	259/511 (50.7)	14/22 (66.7)	1.95 (0.77 – 4.90)	0.15
Diuretics 24 hours *	107/596 (18.0)	10/22 (45.5)	3.81 (1.60 – 9.04)	0.01
LVEDP (mmHg) º	22.8 ± 8.2	30.8 ± 8.6		<0.01
Peak troponin I (U/l) º	35.0 ± 53.3	88.5 ± 104.6		<0.01
Age (years) º	62.9 ± 12.1	74.2 ± 7.1		<0.01
LVEF (%) º	53.2 ± 9.9	41.1 ± 10.0		<0.01
BMI (kg/m²)º	27.7 ± 4.8	28.0 ± 3.0		0.77

º mean ± SD; * %

Multivariate Cox regression analysis for readmission due to congestive heart failure one year after the ACS			
Variables	HR	p value	95% C I
LVEDP	1.10	<0.01	1.04 – 1.16
Age	1.10	0.01	1.02 – 1.16
Peak troponin I	1.01	0.03	1.00 – 1.01
Diuretics 24 hours	1.44	0.49	0.52 – 3.94
LVEF	0.98	0.31	0.95 – 1.02
Atrial fibrillation	0.94	0.95	0.12 – 7.38
STEMI	0.73	0.63	0.21 – 2.57
TIMI risk score ≤ 2	0.27	0.09	0.06 – 1.27

Number of events - 17; Population - 489; Chi square - 52.1 ; p < 0.01. LVEF - left ventricular ejection fraction; LVEDP - left ventricular-end diastolic pressure.

medical treatment with nitrates, diuretics and vasodilators influenced the loading conditions of the LV, and consequently LVEDP, and lastly, time evolution of the ACS might have had an impact on myocardial ischemia, development of fibrosis and changes in LV geometry, which also influenced filling pressures and LV distensibility[22].

As previously described, early myocardial stunning may transiently increase LVEDP with subsequent normalization of filling pressures over the long term[23]. That associated with the exclusion of the 111 patients could also in our opinion explain the lower sensitivity and specificity of the proposed cutoff for LVEDP for the primary outcome of our analysis.

The importance of diastolic function as a marker of prognosis was in agreement with previous authors that analyzed the role of various echocardiographic markers, such as E/A ratio, the DT of the E wave, and the E/E' ratio[9-13].

The E/E' is the most reliable method of diastolic function assessment as correlation with LV filling pressures, and contrary to other indexes, it is present even in patients with preserved systolic function. When the E/E' ratio exceedes 15, LV filling pressures are elevated and when the ratio is lower than 8, LV filling pressures are low[24]. An E/E' ratio ranging from 8 to 15 is considered suggestive, but not diagnostic, of diastolic LV dysfunction and other non-invasive investigations need to be performed to confirm the diagnosis of diastolic dysfunction[4]. Other disadvantages of the E/E´ ratio are due to the fact that tissue Doppler cannot separate active contraction from passive tethering, annular velocities vary depending on the location of the sample, and are influenced by "local" acute myocardial infarction and the presence of mitral annulus calcification[12]. Analyzing data from the work of Hill et al[13], an E/E' ratio greater than 15 had a prognostic significance, but the mean E/E' ratio for the selected 250 patients post-AMI was 13.8 ± 6.8, which was precisely in the "grey" zone area of the diastolic function assessment[13]. Nevertheless, the E/E' ratio > 15 was an independent predictor of survival in the follow up. In our population, LVEDP also remained an independent predictor of

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survival as a categorical variable (with a cutoff of 26.5 mmHg, data not shown), but lost that capacity as a continuous one.

From diastolic to congestive HF

The higher prognostic value of invasive hemodynamic versus clinical signs of elevated filling pressures had already been described by Shell et al[25]. In our population we observed that the assessment of diastolic function had a higher predictive value for congestive HF readmission than clinical variables such as the Killip-Kimball class, and even the percutaneous revascularization grade.

The natural history of HF from an ischemic etiology is based on the development of diastolic dysfunction, followed by diastolic HF, and finally by the onset of systolic HF[26]. Pressure overload of the LV will cause myocyte stretching, increased wall stress, poorer subendocardial perfusion, and reduced energy production, which in turn will lead to neurohormonal activation and ventricular remodeling. These compensatory mechanisms are deleterious, and therefore will lead in the future to loss of LV systolic function and impaired survival.

Our data strongly support this paradigm, as diastolic function was a determinant of congestive HF future admission, and therefore of LV remodeling namely in the group of patients with preserved systolic function. In the population with LVEF under 40% during the index ACS, diastolic function was not powerful enough to determine prognosis - systolic dysfunction overcame diastolic dysfunction.

This subset of ACS patients with preserved ejection fraction and higher LVEDP should therefore not be stereotyped as low-risk, and neurohormonal blocking, vasodilators and probably diuretics could have a crucial importance.

Study limitations

Although the present cohort represented a consecutive group of patients, not all patients submitted to a coronary angiogram had an invasive assessment of LV diastolic function as this was performed at the discretion of the invasive cardiologist. Moreover, only 60% of the 1,329 patients admitted to our coronary care unit were submitted to an invasive strategy. Therefore an exclusion of the highest risk patients might have occurred. We also regret our lost-to-follow-up rate of 5.4%.

Either systolic or diastolic indexes reflected instantaneous measurements, and could vary across the ACS period. Therefore a single measurement might not reflect the best prognostic index. Furthermore, there were no reports on the diastolic function previous to the index ACS admission, nor there was a noninvasive echocardiographic assessment of the mitral inflow.

Conclusions

In our ACS population, LVEDP was an independent predictor of a future HF readmission.

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 post-graduation program.

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