ORIGINAL ARTICLE

Association between high arterial stiffness and left ventricular filling pressures in patients with acute myocardial infarction

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KEY WORDS

heart failure, left ventricular diastolic dysfunction, noninvasive approximation of left ventricular filling pressures, postinfarction myocardial injury, stiffening of arteries

ABSTRACT

INTRODUCTION High arterial stiffness increases the left ventricular (LV) filling pressures in different cardiac disorders. The association between arterial stiffness and LV filling pressures has not been studied so far in patients with acute myocardial infarction (MI).

OBJECTIVES The aim of the study was to assess the association between arterial stiffness and LV filling pressures in patients with acute MI.

PATIENTS AND METHODS Arterial stiffness, measured using the digital volume pulse stiffness index (SI_{DVP}), and LV filling pressures, quantified as the ratio of early transmitral flow velocity to early diastolic septal mitral annulus velocity (E/e'), were evaluated in 263 patients with acute MI (mean age, 63.8 ±11 years; 69 women). The association between high E/e' (>15) and very stiff arteries (SI_{DVP} >18 m/s) was analyzed by logistic regression, with data presented as odds ratios (ORs) and 95% confidence intervals (CIs).

RESULTS A multivariate logistic regression analysis revealed an association between E/e' >15 and SI_{DVP} >18 m/s (OR, 4.7; 95% CI, 1.8–12.3), independently of female sex (OR, 4.3; 95% CI, 1.4–10.2), LV ejection fraction <35% (OR, 3.1; 95% CI, 1.2–8.2), left atrial volume >34 ml/m² (OR, 17.4; 95% CI, 5.8–52.0). There was no significant association between E/e' >15 and previous MI (OR, 2.2; 95% CI, 0.9–5.7).

CONCLUSIONS High arterial stiffness is an independent risk factor for LV diastolic dysfunction in patients with acute MI. A reduction in arterial stiffness may improve LV diastolic function in this patient group.

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INTRODUCTION Various risk factors or cardiovascular diseases (eg, hypertension, diabetes, aging, or ischemic heart disease) predispose towards the development of left ventricular (LV) diastolic dysfunction.[1,2] A community-based study that included apparently healthy individuals reported that approximately 20% of the general population had LV diastolic dysfunction (usually asymptomatic).[3] Arterial stiffness contributes significantly to the development of LV diastolic dysfunction, and both pathologies share similar risk factors.[4] Increased arterial stiffness worsens prognosis in hypertensive patients with high or very high cardiovascular risk.[5]

There are several indices of LV diastolic dysfunction, but the ratio of early transmitral flow velocity (E) to early diastolic septal mitral annulus velocity (e') is the most accurate noninvasive approximation of instantaneous LV filling pressures.[6] An E/e' ratio exceeding 15 (E/e' >15) is considered to indicate abnormally elevated LV filling pressures[7] in various conditions, including acute myocardial infarction (MI).[8]

Although abnormal myocardial contraction is typical for acute MI, LV diastolic dysfunction also worsens at this time.[9] A series of hemodynamic derangements caused by acute MI affects the mechanical and functional properties of arterial walls, including stiffness.[10-12] A decrease in LV stroke volume leads to a reflex increase in vascular resistance and cardiac afterload, which may cause higher systolic and diastolic pressure within the left ventricle.[12]

Higher arterial stiffness is associated with LV aging and diastolic dysfunction in stable coronary artery disease; however, it is unknown whether there is a similar association in patients with acute MI.[13,14] In the present study, we investigated the hypothesis that, regardless of the presence of myocardial injury and contraction abnormalities, there would still be a significant relationship between arterial stiffness and E/e' >15 in acute MI. More precisely, we assumed that there will be a positive association between measures of arterial stiffness and LV diastolic pressures, so patients with high arterial stiffness will present with E/e' >15.

PATIENTS AND METHODS From 356 consecutive patients with an acute coronary syndrome who were hospitalized for percutaneous coronary intervention (PCI) from October 2013 to June 2014, 263 patients with confirmed MI (either with ST-segment elevation MI [STEMI] or non-ST segment elevation MI [NSTEMI]) were selected for inclusion in the present single-center study. MI was confirmed on the basis of the Third Universal Definition of Myocardial Infarction.[15] Patients were selected for the study 2 to 4 days after MI and coronary angiography and, if applicable, angioplasty. To be included in the study, patients had to be older than 18 years of age, have a narrowing of the lumen of any coronary artery of at least 50% on angiography, and be in sinus rhythm on resting electrocardiography. Patients were excluded from the study if they had atrial fibrillation, any implanted device, a Killip grade of at least 3 (ie, an unstable hemodynamic condition including pulmonary edema, hypotension with systolic blood pressure of less than 100 mmHg, cardiogenic shock, or current treatment with intravenous catecholamines or intraaortic balloon counterpulsation), active malignancy, chronic kidney disease requiring dialysis, noncardiac disease with a life expectancy of less than 1 year, or did not provide written informed consent to participate in the study (patients who agreed to participate were asked to present for follow-up 12 months after the index discharge from the hospital). All patients were treated according to institutional protocols, which adhered to the current guidelines of the European Society of Cardiology.[16,17] Written informed consent was obtained from all patients before their inclusion in the study. The study was approved by the University Ethics Committee, and the study protocol conformed to the ethical guidelines of the 1975 Declaration of Helsinki.

Clinical examination A detailed medical history, including any pharmacological treatment and results of a physical examination, was obtained from all patients. In addition, body fat was measured by total body impedance (Tanita MC180; Tanita, Tokyo, Japan). All noninvasive tests were performed after patients had been able to walk for at least 1 day after coronary angiography and, if applicable, angioplasty. Tests were performed in a temperature-controlled environment (22–23°C) in the morning. Brachial blood pressure was determined while patients were seated, using the oscillometric method (M-785; Omron Healthcare, Kyoto, Japan) before the measurement of arterial stiffness by the photoplethysmographic method (see below).

Echocardiography Echocardiography was performed while patients were in the supine position with the head elevated (MyLab Class C; Esaote, Genoa, Italy). Digital images were obtained and transferred to a computer workstation (MyLab Desk; Esaote, Genoa, Italy) for further offline analysis. Standard measurements of the cardiac chambers and wall thickness were collected during diastole and systole according to the recommendations of the European Association of Echocardiography and the American Society of Echocardiography.[18] LV ejection fraction (LVEF) was estimated as the mean value from 4- and 2-chamber views according to the modified Simpson's rule.[18] Left atrial (LA) volume was estimated according to the prolate ellipse method using apical 4-chamber and parasternal long-axis views at ventricular end systole (maximum LA size) and the equation $0.523 \times D1 \times D2 \times D3$, where D2 is measured from the mitral annular plane to the back LA wall, D1 is the orthogonal short-axis dimension to D2, and D3 is measured from the blood–tissue interface of the anterior and posterior walls. Finally, the LA volume was normalized to body surface area and presented as ml/m^2.[19] Pulsed-wave Doppler was used to measure the peak velocity of the E wave, whereas tissue Doppler was used to quantify the peak early velocity of the e' wave at the level of the septal mitral annulus; these values were then used to calculate the E/e' ratio.[7]

Digital volume pulse analysis Arterial stiffness was measured photoplethysmographically by a digital volume pulse (DVP) waveform analysis (PulseTrace PCA 2; MicroMedical, Chatham, United Kingdom), as reported previously.[4,20] Briefly, a finger cuff was placed on the middle phalanx of the second or third finger of the nondominant hand, and patients rested in the supine position for 5 minutes to enable cardiovascular adaptation. Arterial stiffness was then measured. Ten consecutive DVPs were recorded and averaged automatically.

The DVP stiffness index (SI_{DVP}) was obtained by dividing a patient's height by the time between the systolic and diastolic peaks of the DVP. The SI_{DVP} is closely correlated with pulse wave velocity (PWV) in large arteries, and is regarded as a "general" measure of large arterial stiffness.[4] The values of SI_{DVP} exceeding 18 m/s (SI_{DVP} >18 m/s) are automatically identified by the PulseTrace device as "very stiff"; in the present study, patients were divided into those with "very stiff" and "not very stiff" arteries.

TABLE 1 Clinical characteristics of the study patients

Continuous data		
parameter	mean ± SD	median (IQR)
age, y	64 ±11	63 (57–71.8)
BMI, kg/m^2	28.0 ±4.5	27.6 (25.2–31)
total body fat, %	26.6 ±7.9	25.7 (21.4–31.7)
heart rate, bpm	70.6 ±12.2	69.2 (61.9–76.9)
systolic blood pressure, mmHg	116 ±18	113.4 (103.9–126.6)
diastolic blood pressure, mmHg	69 ±11	69.3 (61.9–75.7)
pulse pressure, mmHg	45.9 ±13.3	43.5 (38–52.6)
creatinine, mg/dl	0.9 ±0.3	0.9 (0.8–1.1)
eGFR, ml/min/1.73 m^2	89.1 ±27.0	88.0 (72.5–101.8)
maximum cardiac troponin T, ng/l	1478 ±2284	626.5 (123–1703)
E/e'	10.7 ±5.1	9.3 (7.8–11.6)
LVEF, %	49.8 ±11.4	52 (43–58.8)
LA volume, ml	44.2 ±15.8	40.9 (33–51.9)
LV end-diastolic volume, ml	94.6 ±34.5	88.8 (74.5–107)
LV end-systolic volume, ml	49.5 ±28.4	42 (33–56.7)
LV mass index, g/m^2	122 ±36	114.8 (96.7–140)
TAPSE, mm	21.8 ±4.1	22 (19–25)
dichotomized data		
parameter	n	%
female sex	69	26.2
primary PCI	213	81.0
previous MI	67	25.5
NSTEMI	117	44.5
hypertension	204	77.6
diabetes	77	29.3
smoker	101	38.4
ex-smoker	94	35.7
aspirin	260	98.9
clopidogrel	260	98.9
ACEI	249	94.7
β-blocker	237	90.1
statin	259	98.5
aldosterone antagonist	75	28.5
calcium antagonist	45	17.1
diuretic	58	22.1
digoxin	2	0.8
nitrate	26	9.9
angiotensin AT2 receptor blocker	5	1.9
E/e' >15	37	14.1
LVEF <35%	54	20.5
LA volume >34 ml/m^2	28	10.6
SI_{DVP} >18 m/s	70	26.6

Abbreviations: ACEI, angiotensin-converting enzyme inhibitor; BMI, body mass index; E/e', early transmitral flow velocity to early diastolic septal mitral annulus velocity ratio; eGFR, estimated glomerular filtration rate (according to the Modification of Diet in Renal Disease); IQR, interquartile range; LA, left atrial; LV, left ventricular; LVEF, left ventricular ejection fraction; MI, myocardial infarction; NSTEMI, non-ST-segment elevation myocardial infarction; PCI, percutaneous coronary intervention; SI_{DVP}, digital volume pulse stiffness index; SD, standard deviation; TAPSE, tricuspid annular plane systolic excursion

Statistical analysis The Shapiro–Wilk test revealed that only some of the continuous variables were normally distributed. Thus, continuous data were presented as the mean ± standard deviation and as the median with the interquartile range in parentheses. When comparing patients with an E/e' ratio of 15 or lower and those with the ratio exceeding 15, the Mann–Whitney test was used for continuous data, whereas the binomial test was used for proportions of dichotomized data.

The association between E/e' >15 and SI_{DVP} >18 m/s was analyzed by univariate and multivariate logistic regression. Because E/e' differs between men and women, sex was added to the regression models.[21] Similarly, because previous MI may contribute to increased E/e', it was also added to the models. LV filling pressures can also be affected by LV systolic function, so LVEF was included in the logistic regression models. Finally, because increased LA volume is the consequence of earlier diastolic dysfunction and not the result of a sudden adaptation to acute MI, LA exceeding 34 ml/m^2 was also included in the logistic regression analysis. Thus, model selection was guided by clinical and physiological knowledge rather than being the result of an automatic (eg, stepwise) procedure.[7,18] Five covariates were used, so the model could have been overfitted. Consequently, as a quality control for the logistic regression models, we used the drop-one-out method, removing one of the covariates from the 5-covariate model, as well as determining areas under the curve (AUCs), the Akaike Information Criterion (AIC), and residual deviance.[22] In this way, we investigated whether a simpler model would be more appropriate for the data.

Statistical analyses were performed using the MedCalc Statistical Software version 12.7.7 (MedCalc Software bvba, Ostend, Belgium; http://www.medcalc.org) and R package version 2.13.1 (The R Foundation for Statistical Computing, United States; http://www.r-project.org). All tests were 2-sided and a *P* value of less than 0.05 was considered significant.

RESULTS The clinical characteristics of patients included in the study are listed in TABLE 1. The study cohort consisted of 69 women and 194 men, with a mean age of approximately 64 years. On average, patients were overweight with approximately 25% of total body weight accounted for by fat. Systolic and diastolic blood pressures and creatinine concentrations were normal, whereas estimated glomerular filtration rate, LVEF, and tricuspid annular plane systolic excursion (TAPSE) were nearly normal. The distribution of cardiac troponin T was skewed, with the median less than half of its mean (TABLE 1); both values suggest at least a medium MI.

As indicated in TABLE 1, less than half of the patients had NSTEMI, 25% had a previous MI, most were being treated with antihypertensive medication, nearly 40% were current smokers, 36% were

ex-smokers, and 30% had diabetes. Primary PCI was performed in more than 80% of the patients, with the remaining patients undergoing coronary artery bypass grafting or conservative treatment. Nearly all patients were receiving dual antiplatelet treatment, angiotensin-converting enzyme inhibitors (ACEIs), or angiotensin receptor blockers (ARBs; together, 96.6%), and 90% were on β-blockers; 22% of the patients were on diuretics and less than 30% were on aldosterone antagonists. E/e' >15 was found in 14% of the patients; 27% were identified as having "very stiff" arteries (SI_{DVP} >18 m/s); LVEF was reduced (ie, <35%) in 20% of the patients; and 10.6% of the patients had a dilated left atrium (>34 ml/m^2).

Comparison of patients with E/e' ≤15 versus those with E/e' >15 The clinical characteristics of patients with an E/e' ratio of 15 or lower (n = 226) and those with an E/e' ratio exceeding 15 (n = 37) are given in TABLE 2.

Patients with E/e' >15 were significantly older, had slightly lower diastolic blood pressure, had lower maximal cardiac troponin T, LVEF, and TAPSE, and had increased LA, LV systolic and LV diastolic volumes, and an increased LV mass index in comparison with patients with E/e' ≤15. A higher proportion of patients with E/e' >15 were female, had a previous MI, and had diabetes. Furthermore, 50% of the patients with E/e' >15 had SI_{DVP} >18 m/s, and nearly half of the patients presented with at least moderately compromised LV systolic function and LVEF <35%, and LA volume >34 ml/m^2. Patients with E/e' >15 were also more likely to be treated with diuretics and aldosterone antagonists.

Association of E/e' >15 with high arterial stiffness and other clinical covariates The results of univariate and multivariate logistic regression analyses with E/e' >15 as the dependent variable and SI_{DVP} >18 m/s, female sex, previous MI, LVEF <35%, or LA volume >34 ml/m^2 as independent variables are presented in TABLE 3.

Univariate logistic regression revealed that SI_{DVP} >18 m/s was significantly associated with an increased risk of E/e' >15. All other parameters were significantly associated with a higher risk of E/e' >15, with previous MI having the weakest association and LA volume >34 ml/m^2—the strongest. The effects of female sex and LVEF <35% on the risk of E/e' >15 were comparable to those of SI_{DVP} >18 m/s.

Because there were only 37 patients with E/e' >15, the multivariate logistic regression with 5 covariates should be treated as an exploratory analysis only. However, to get to the 5-covariate model and to assess its reliability and quality, we first tested 3 separate models with 4 covariate combinations that always included SI_{DVP} >18 m/s (the drop-one-out method). Finally, we tested the 5-covariate model with SI_{DVP} >18 m/s and all other predetermined covariates. Across all analyses, the 5-covariate model showed the best results, as evidenced by the highest AUC (0.873; 95% confidence interval [CI], 0.827–0.911), the lowest AIC (148.1), and the lowest residual deviance (136.1), compared with all 4-covariate models tested. The closest 4-covariate model with excluded previous MI presented an AIC of 148.7 and residual deviance of 138.7, while the worst model with excluded LA volume >34 ml/m^2 showed an AIC of 174.53 and residual deviance of 164.5. Even though the 5-covariate model is more complex, it explains the dependence of E/e' >15 on the other variables much better, particularly on SI_{DVP} >18 m/s. In addition, the trade-off between the fit of the model to the data and the penalty for the number of covariates was the best for this model, as evidenced by the AIC.

In the 5-covariate multivariate logistic regression model, SI_{DVP} >18 m/s was significantly associated with E/e' >15. In this model, previous MI made the weakest contribution, which was clinically but not statistically significant (P = 0.075). Patients with LA volume >34 ml/m^2 had the highest risk of E/e' >15 (with an almost 15-fold increase in OR), followed by female sex (~6-fold increase in OR) and SI_{DVP} >18 m/s (~4-fold increase in OR). The effect of SI_{DVP} >18 m/s on E/e' >15 was independent of the other parameters in this model.

DISCUSSION In the present study, we showed that the presence of very stiff arteries, defined as SI_{DVP} >18 m/s, is associated with increased LV filling pressures, as estimated by E/e' >15, in acute MI. Although a similar association between arterial stiffness and LV aging and diastolic dysfunction has been described in other diseases,[4,14,23-28] we have shown for the first time that this association exists in patients with acute MI and that high arterial stiffness is associated with increased LV filling pressures independent of sex, at least moderately reduced LVEF, previous MI, and dilated LA.

The association between increased arterial stiffness and impaired LV diastolic function has been described before in patients with stable coronary artery disease, but not in those with acute MI. For example, a positive correlation has been reported between central pulse-wave velocity (PVW, a measure of arterial stiffness) and LV filling pressures in patients undergoing cardiac catheterization for suspected or known coronary artery disease.[13] Similarly, a positive association has been found between arterial compliance and LV end-diastolic pressure or E/e' in patients undergoing elective cardiac catheterization.[28] Giannatassio et al[23] found a link between aortic or carotid artery distensibility and measures of LV diastolic function in patients with heart failure; specifically, better arterial distensibility was correlated with a higher ratio of early (E wave) to late (A wave) mitral flow velocities and a shorter deceleration time of early mitral flow velocity. The association between LV diastolic dysfunction and higher arterial stiffness has also been investigated in healthy people

TABLE 2 Clinical characteristics of the patients depending on the E/e' ratio

Continous data					
parameter	E/e' ≤15		E/e' >15		*P* value
	mean ± SD	median (IQR)	mean ± SD	median (IQR)	
age, y	62.8 ±10.9	63.0 (56.0–70.0)	69.5 ±10.2	70.0 (59.8–79.3)	0.001
BMI, kg/m^2	28.1 ±4.4	27.8 (25.3–31.1)	27.4 ±5.0	26.9 (23.8–30.1)	0.25
total body fat, %	26.4 ±7.7	25.7 (21.5–31.1)	27.4 ±8.9	28.3 (20.6–34.6)	0.55
heart rate, bpm	70.6 ±12.0	69.4 (61.9–76.7)	70.6 ±13.3	66.4 (59.4–79.2)	0.78
systolic blood pressure, mmHg	116 ±18	113.4 (104.5–125.2)	115 ±18	112.6 (100.2–128.5)	0.77
diastolic blood pressure, mmHg	70.0 ±10.9	69.9 (62.5–76.1)	65.4 ±11.4	66.8 (59.2–71.8)	0.029
pulse pressure, mmHg	45.4 ±13.2	43.1 (37.4–51.7)	49.2 ±13.2	49.0 (39.4–57.9)	0.09
creatinine, mg/dl	0.9 ±0.3	0.9 (0.8–1.0)	0.9 ±0.3	0.9 (0.8–1.1)	0.91
eGFR, ml/min/1.73 m^2	89.0 ±25.4	89.3 (73.2–101.9)	89.9 ±35.8	83.6 (65.9–101.6)	0.65
maximum cardiac troponin T, ng/l	1607 ±2411	718.5 (135.0–1812.0)	680 ±903	338.0 (61.0–968.0)	0.02
E/e'	9.0 ±2.3	8.8 (7.4–10.4)	20.8 ±5.7	19.0 (16.2–23.9)	<0.0001
LVEF, %	51.3 ±10.3	53.0 (45.0–59.0)	40.6 ±13.9	41.0 (32.5–50.8)	<0.0001
LA volume, ml	41.7 ±13.7	39.0 (32.0–49.4)	59.5 ±18.8	62.2 (43.8–72.3)	<0.0001
LV end-diastolic volume, ml	92.0 ±31.6	87.9 (73.9–103.9)	111 ±46	105.1 (78.1–142.3)	0.01
LV end-systolic volume, ml	46.0 ±23.8	40.2 (32.4–52.2)	70.8 ±42.0	57.5 (40.9–91.0)	0.0001
LV mass index, g/m^2	119 ±33	113.1 (96.0–137.0)	140 ±50	132.1 (105.7–171.6)	0.004
TAPSE, mm	22.2 ±3.9	22.0 (20.0–25.0)	19.8 ±4.6	19.0 (16.0–23.3)	0.002
dichotomized data					
parameter	E/e' ≤15 (n = 226)		E/e' >15 (n = 37)		*P* value
	n	%	n	%	
female sex	49	21.7	20	54.1	<0.0001
primary PCI	185	81.9	28	75.7	0.51
previous MI	50	22.1	17	45.9	0.004
NSTEMI	103	45.6	14	37.8	0.48
hypertension	173	76.5	31	83.8	0.44
diabetes	59	26.1	18	48.6	0.009
smoker	88	38.9	13	35.1	0.80
ex-smoker	80	35.4	14	37.8	0.92
aspirin	223	98.7	37	100	0.88
clopidogrel	224	99.1	36	97.3	0.90
ACEI	214	94.7	35	94.6	0.71
β-blocker	207	91.6	30	81.1	0.09
statin	223	98.7	36	97.3	0.94
aldosterone antagonist	56	24.8	19	51.4	0.002
calcium antagonist	40	17.7	5	13.5	0.69
diuretic	41	18.1	17	45.9	0.0004
digoxin	1	0.4	1	2.7	0.63
nitrate	22	9.73	4	10.8	0.92.
angiotensin AT2 receptor blocker	4	1.8	1	2.7	0.78
LVEF <35%	37	16.4	17	45.9	<0.0001
LA volume >34 ml/m^2	10	4.4	18	48.6	<0.0001
SI_{DVP} >18 m/s	49	21.7	21	56.8	<0.0001

Abbreviations: see **TABLE 1**

and patients with hypertension, diabetes mellitus, or other cardiovascular risk factors. For example, a positive association has been reported between E/e' and brachial–ankle PWV in an apparently healthy population.[24] In another study, a positive relationship was described between indices of arterial stiffness (aortic and brachial pulse pressure, carotid–femoral PWV) and measures of diastolic function quantified as LA volume in individuals aged 65 years or older and with at least 2 additional risk factors for atrial fibrillation.[25] Russo et al[21] observed a significant

TABLE 3 Results of univariate and multivariate logistic regression analyses

Parameter	Univariate model	*P* value	Multivariate model	*P* value
SI_{DVP} >18 m/s	4.74 (2.30–9.77)	<0.0001	4.67 (1.77–12.33)	0.002
female sex	4.25 (2.07–8.73)	0.0001	3.83 (1.44–10.23)	0.007
LVEF <35%	4.34 (2.08–9.07)	0.0001	3.07 (1.15–8.22)	0.026
previous MI	2.99 (1.46–6.14)	0.003	2.21 (0.85–5.71)	0.105
LA volume >34 ml/m^2	20.46 (8.28–50.54)	<0.0001	17.37 (5.8–51.98)	<0.0001

Data are presented as odds ratios with 95% confidence intervals in parentheses.

Abbreviations: see TABLE 1

association between indices of arterial stiffness (ratio of central pulse pressure to LV stroke volume index and total arterial compliance) with LV diastolic function (E/A and E/e'), and Moltram et al[26] reported an association between arterial compliance and LV diastolic function in patients with hypertension and no clinical evidence of coronary artery disease. In patients with diabetes mellitus, a significant correlation was reported between diastolic dysfunction and carotid–femoral PWV.[27] Most of these studies (performed in either healthy people or various patient groups) showed that the association between arterial stiffness and LV diastolic function, including E/e', is independent of covariates such as age, sex, body mass index, or cardiovascular risk factors.[13,14,24-27]

To date, the relationship between E/e' >15 and SI_{DVP} >18 m/s has not been investigated in the setting of acute MI. In the present study, we evaluated this relationship in consecutive acute MI patients (STEMI or NSTEMI) who were treated according to current guidelines.[16] Primary PCI was performed in 80% of the patients, although all underwent coronary angiography with the intention to treat with angioplasty. Nearly all the patients dual antiplatelet, statin, ACEI, or ARB treatment, and most were on β-blockers. The mean age, number of men, and other risk factors (eg, overweight/obesity, hypertension, diabetes, or previous MI) in the present study cohort were comparable to those in other clinical studies on patients with acute MI.[16] Although the median maximum cardiac troponin T level suggested at least medium MI, the hemodynamic condition of the patients in the present study was quite good: mean heart rate and blood pressure were normal, and LVEF and TAPSE were nearly normal.

In the present study, patients with E/e' >15 were likely to be older, more often female, with previous MI, diabetes, more common adverse remodeling of the LV and LA, and with greater impairment of LV and right ventricular systolic function. These patients were also more likely to be on diuretics. Together, the data show that patients with acute MI and an increased E/e' ratio have a more severe form of heart failure. However, multivariate logistic regression revealed that even in these patients the risk of an increased E/e' ratio is still significantly related to high arterial stiffness. Another important finding of the present study is that the association between E/e' >15 and SI_{DVP} >18 m/s is independent of sex, at least moderate systolic LV dysfunction, previous MI, and LA dilation. This finding is of great importance since there are sex differences in the course and outcomes of acute MI.[29]

Increased LV filling pressures are responsible for LA dilation.[7,17] E/e' >15 reflects instantaneous LV diastolic function and increased LV filling pressures.[7,17] However, the process of adverse remodeling and enlargement of the LA is long-lasting and reflects the presence of increased LV filling pressures over time, providing evidence of chronic impairment of diastolic function existing prior to the current MI.[7,17,30] A rapid increase in LV filling pressures during an acute MI is probably not sufficient to cause dilation of the LA exceeding 34 ml/m^2. Thus, in the present study, we assumed that patients with an LA volume exceeding 34 ml/m^2 at the time of acute MI had existing LV diastolic dysfunction. It is possible that increased LV filling pressures and LA dilation may have been caused by previous MI in some patients. In the present study, individuals with a history of MI were more likely to have E/e' >15 and LA volume >34 ml/m^2 (data not shown).

Because of the relatively small number of patients with E/e' >15, we had to restrain the number of covariates added to the regression model in addition to SI_{DVP} >18 m/s. We chose sex as one of the covariates because it is one of the strongest determinants of both LV diastolic dysfunction and arterial stiffness. As the remaining covariates, we chose factors that could influence E/e', specifically: 1) LVEF <35%, to account for the effect of MI on contractility; 2) previous MI and LA volume >34 ml/m^2, to take into account the possibility of preexisting LV diastolic dysfunction; and 3) an already increased E/e' ratio before the current MI. For the exploratory reasons, we also tested 2 additional logistic regression models (data not shown). First, adding information about the type of MI, either STEMI or NSTEMI had no significant association with the presence of E/e' >15 (P = 0.494) and did not influence the effects of SI_{DVP} >18 m/s. Second, we analyzed the potential influence of the interaction between LVEF <35% and previous MI on the presence of E/e' >15. However, this interaction had no significant association with E/e' >15 (P = 0.45), and did not influence the effects of SI_{DVP} >18 m/s.

Adding so many covariates to the final and exploratory models in addition to SI_{DVP} >18 m/s enabled us to show that the relationship between diastolic function and arterial stiffness remained significant, independent of other covariates that could potentially affect E/e'.

A potential explanation for our findings is as follows. LV diastolic dysfunction is usually aggravated by coexisting myocardial systolic dysfunction.[9] Postinfarction impairment of myocardial contractility leads to a reduction in cardiac output, with a reflex increase in vascular resistance.[12] The high arterial stiffness changes the propagation of the pulse waveform throughout the aorta and arteries by increasing PWV and accelerating the return of reflected pressure waves from the periphery to the ascending aorta.[31] In the case of very stiff arteries, the returning waves come back to the aortic root at late systole, when blood ejection from the left ventricle is incomplete. An immediate consequence of this is increased afterload, whereas long-term consequences include LV remodeling with hypertrophy, a reduction in compliance, and the development of diastolic dysfunction.[32] In this way, higher arterial stiffness may translate into increased E/e' over the longer term. In the present study, we demonstrated that, in acute MI, high arterial stiffness contributes to LV diastolic dysfunction, regardless of existing compromised LV contractility, previous MI, and LA dilation (probably caused by earlier diastolic dysfunction). If so, then it is likely that treatment aimed at reducing arterial stiffness during acute MI may decrease E/e' and improve LV diastolic function. In a recent study, Imbalzano et al[33] showed that, in patients with higher arterial stiffness, LVEF recovers less effectively in a 3- and 6-month follow-up.[33] Prospective studies are needed to investigate whether a decrease in arterial stiffness in acute phase of MI will improve diastolic and systolic function recovery in further observation. If this was confirmed, then the assessment of SI_{DVP} could become a simple and widely available tool for identifying patients with acute MI and higher risk of heart failure for proper treatment.[34]

The present study has several limitations. First, we focused on patients who were in a stable hemodynamic condition, that is, without pulmonary edema, cardiogenic shock, or requiring intravenous catecholamines. We are aware that data from such patients might influence our findings. However, we believe that the inclusion and exclusion criteria that we applied helped us collect individuals representative of the majority of contemporarily treated postinfarction patients. Second, we constructed a multivariate logistic regression model to analyze the association between general arterial stiffness and diastolic dysfunction focusing on SI_{DVP} >18 and other contributing factors. However, because of the smaller number of patients with E/e' >15 than anticipated, our regression model should only be considered as an exploratory model. Another limitation is the use of indirect measures of diastolic dysfunction and arterial stiffness, namely, E/e' >15 and SI_{DVP} >18 m/s, respectively. Both parameters can be easily measured using noninvasive techniques and have been used in numerous basic and clinical studies thus far; indeed, it has even been stated that E/e' >15 is the best single indirect predictor of elevated LV filling pressure and LV diastolic dysfunction.[7,20] The lack of adjustment of our findings to mean arterial pressure, age, and heart rate as well as diabetes or used medications might be considered as the third potential limitation. However, as we have seen, the 5-covariate model is the largest model possible in this study in view of the sample size. For this reasons, we have not adjusted our findings to other, already known factors that influence arterial stiffness.

Our study has potential practical relevance. Evaluation of the arterial stiffness in postinfarction patients is not a routine clinical management. However, such measurement might be helpful in identifying patients with stiffer arteries who are at a higher risk of various cardiovascular complications,[4,5] and in a better personalization of the postinfarction medical management. The majority, but not all, of the contemporary pharmacological agents applied in survivors of MI have also proven beneficial effects on arterial stiffness, eg, ACEIs, angiotensin receptor blockers, statins, or selected β-blockers with vasodilating properties such as carvedilol and nebivolol.[35] Maybe these drugs should be preferable in postinfarction individuals who present with an increased arterial stiffness; however, this is only a clinical speculation that requires further studies.

In conclusion, high arterial stiffness is associated with increased LV filling pressures in acute MI, and this association is independent of a patient's sex, the presence of at least moderate LV systolic dysfunction, previous MI, and dilated left atrium.

Contribution statement AW, PG, and AM conceived the idea of the study and contributed to the design of the research. All authors were involved in data collection. AM, TK, and AM acquired the data and, together with the remaining authors, analyzed and interpreted the data. PG and JP performed the statistical analysis. AM, AW, JP, and PG prepared the manuscript. All authors edited and approved the final version of the manuscript. AW coordinated funding for the project.

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ARTYKUŁ ORYGINALNY

Wysoka sztywność tętnicza a ciśnienia napełniania lewej komory u pacjentów z ostrym zawałem serca

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nieinwazyjna ocena ciśnień napełniania lewej komory, niewydolność serca, pozawałowe uszkodzenie mięśnia sercowego, rozkurczowa niewydolność lewej komory, sztywnienie tętnic

STRESZCZENIE

WPROWADZENIE Wysoka sztywność tętnicza wpływa na wzrost ciśnień napełniania lewej komory (LK) w różnych chorobach mięśnia sercowego. Do tej pory nie zbadano tej zależności u pacjentów z ostrym zawałem serca.

CELE Celem badania była ocena związku między sztywnością tętniczą a ciśnieniami napełniania LK u pacjentów z ostrym zawałem serca.

PACJENCI I METODY U 263 pacjentów z ostrym zawałem serca (średnia wieku 63,8 ±11 lat; 69 kobiet) oznaczono wskaźnik sztywności tętniczej za pomocą cyfrowej analizy objętości fali tętna (*digital volume pulse stiffness index* – SI_{DVP}) i oceniono ciśnienia napełniania LK, ustalając stosunek wczesnorozkurczowej prędkości napływu mitralnego do wczesnorozkurczowej prędkości pierścienia mitralnego (E/e'). Związek między wysokim E/e' (>15) a bardzo sztywnymi tętnicami (SI_{DVP} >18 m/s) analizowano z wykorzystaniem regresji logistycznej, natomiast wyniki przedstawiono jako iloraz szans (*odds ratio* – OR) z 95% przedziałem ufności (*confidence interval* – CI).

WYNIKI Wieloczynnikowa regresja logistyczna wykazała związek między E/e' >15 a SI_{DVP} >18 m/s (OR 4,7; 95% CI 1,8–12,3) niezależnie od płci żeńskiej (OR 4,3; 95% CI 1,4–10,2), frakcji wyrzutowej LK <35% (OR 3,1; 95% CI 1,2–8,2) oraz objętości lewego przedsionka >34 ml/m^2 (OR 17,4; 95% CI 5,8–52,0). Nie wykazano związku między E/e' >15 i wcześniej przebytym zawałem serca (OR 2,2; 95% CI 0,9–5,7).

WNIOSKI Wysoka sztywność tętnicza jest niezależnym czynnikiem ryzyka rozwoju niewydolności rozkurczowej LK u pacjentów z ostrym zawałem serca. Obniżenie sztywności tętniczej może poprawić czynność rozkurczową LK w tej grupie chorych.

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