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ORIGINAL ARTICLE

Non-invasive pressure-volume loops provide incremental value to age, sex, and infarct size for predicting adverse cardiac remodelling after ST-elevation myocardial infarction

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Abstract

Aims

This study aimed to assess the predictive value of non-invasive pressure–volume (PV) loop variables by cardiovascular magnetic resonance (CMR) for determining development of adverse remodelling 3 months after primary percutaneous coronary intervention (PCI) for ST-elevation myocardial infarction (STEMI).

Methods and results

In total, 181 STEMI patients examined with CMR during the index admission (baseline) after primary PCI and at 3-month follow-up in The Third DANish Study of Optimal Acute Treatment of Patients with STEMI (DANAMI-3) study were retrospectively analysed. A time-varying elastance model for generating PV loops from CMR volumetry and brachial blood pressure was used to calculate contractility, arterial elastance, stroke work, potential energy, efficiency, external power, ventriculoarterial coupling, and energy per ejected volume. Adverse remodelling was seen in 28 patients (15%), defined as a concomitant increase in end-diastolic and end-systolic volume of ≥12% from baseline to follow-up. PV loop variables measured at baseline showed predictive value for adverse remodelling, independent of age, sex, and infarct size (IS) by a logistic regression analysis: contractility [odds ratio (OR) 4.6, 95% confidence interval (CI) 1.8–12.4] and efficiency (OR 1.05, 95% CI 1.00–1.11). Furthermore, females showed a higher increase in contractility between the timepoints (ΔContractility = 0.4 ± 0.4 mmHg/mL vs. 0.1 ± 0.4 mmHg/mL, $P < 0.0001$). A higher energy expenditure was seen at baseline in left arterial descending artery infarctions compared to left circumflex artery and right coronary artery infarctions.

Conclusion

Non-invasive PV loop variables by CMR have incremental predictive value to age, sex, and IS for determining development of adverse cardiac remodelling in STEMI patients treated with primary PCI. Furthermore, the PV loop variables show significant differences in post-infarct cardiovascular adaptation between sexes and culprit vessels.

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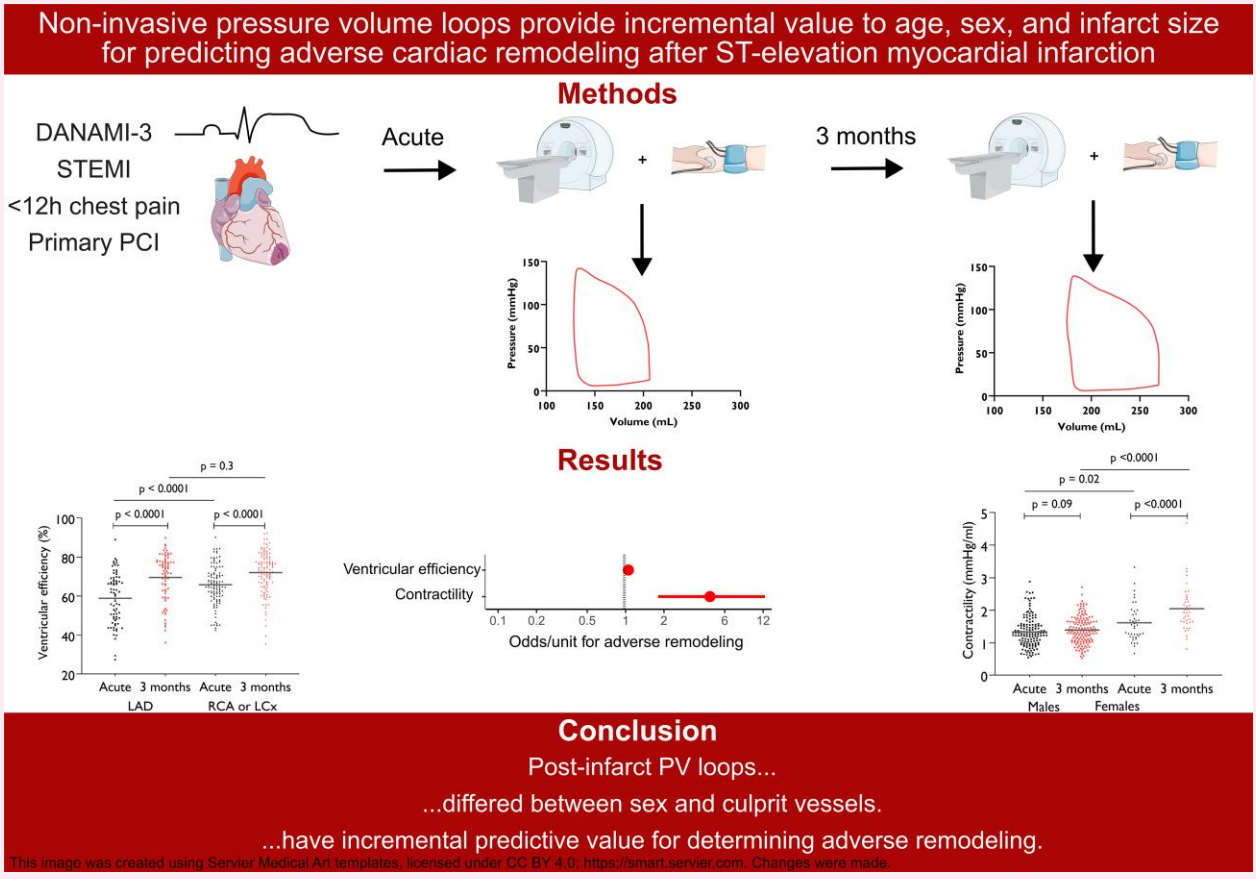
Graphical Abstract



Keywords myocardial infarction • adverse remodelling • gender • sex • contractility • elastance • coupling • stroke work • efficiency

Introduction

Ischaemic heart disease is a major cause of heart failure in the Western world.[1–3] Development of chronic heart failure after myocardial infarction can be foreseen by ventricular dilatation and progressively increased wall stress in a process called adverse remodelling[4–6] associated with poor prognosis.[7]

Clinical evaluation of cardiac function after an acute myocardial infarction is mainly based on assessment of blood pressure and left ventricular (LV) volumes to detect adverse remodelling and to guide treatment for prevention of heart failure development.[4] Current guidelines recommend that patients with an ST-elevation myocardial infarction (STEMI) and a reduced LV ejection fraction (LVEF) below 40% before discharge should be re-evaluated after 6–12 weeks with measurement of LVEF.[8] However, measures for predicting adverse remodelling in the acute setting are lacking.[9] Furthermore, current clinical practice has shown limited ability to select patients for volumetric reassessment, resulting in insufficient follow-up and unnoticed adverse remodelling.[10]

Combined measurements of ventricular volume and blood pressure using pressure–volume (PV) loops have been suggested for evaluation of cardiac status in patients with myocardial infarction.[11–14] However, the use of PV loops has so far been limited to small, selected study populations due to the necessity of invasive measurements. Pressure–strain loops by echocardiography have been used and are associated with cardiac remodelling.[15] Recently, a method for non-invasive measurements of PV loops based on cardiovascular magnetic resonance (CMR) that enables investigation of larger patient populations was presented and validated.[16–19] This method has been shown to enable assessment of PV loop variables in patients across heart failure subtypes,[20] early after myocardial infarction,[21] Fontan patients,[22] and in experimental studies of cardioprotection.[23] However, the extent to which non-invasive PV loop variables may predict the development of adverse remodelling remains to be determined.

Therefore, we aimed to assess the predictive value of non-invasive PV loop variables by CMR for determining development of adverse remodelling 3 months post-infarction in patients with STEMI treated with primary percutaneous coronary intervention (PCI).

Methods

The present study is a non-prespecified retrospective cohort sub-study within the randomized prospective Third DANish Study of Optimal Acute Treatment of Patients with ST-segment Elevation Myocardial

Infarction (DANAMI-3) trial, including patients from Rigshospitalet, Copenhagen, Denmark, between 2011 and 2014.[24] All patients provided written informed consent before inclusion. The article was written according to the STROBE Guidelines for observational studies.[25]

Study design

A total of 181 adult patients from the DANAMI-3 cohort with acute chest pain of <12 h duration and STEMI treated with primary PCI were included and analysed.[24] Exclusion criteria were unconsciousness, cardiogenic shock, indication for cardiac bypass surgery, stent thrombosis, coagulopathy, previous reaction to contrast agents, and pregnancy.[24] All patients had diagnostic CMR images acquired at first admission and at 3-month follow-up after primary PCI. Brachial sphygmomanometric blood pressures were acquired during the CMR sub-study. The study outcome was adverse cardiac remodelling, and predictors were PV loop variables, blood pressure, end-diastolic volume (EDV), end-systolic volume (ESV), LVEF, and stroke volume (SV). Patient loss to follow-up was controlled for to discover any selection bias.

CMR imaging

The CMR imaging protocol in the DANAMI-3 trial was previously described.[26,27] In summary, CMR imaging was performed with a 1.5T scanner (Avanto or Espree, Siemens Medical Solutions, Erlangen, Germany). Sequence parameters are demonstrated in Supplementary data online, *Table S1*. Steady-state free precession cine images were acquired in two-, three-, and four-chamber views and in short-axis views (SAX) covering the entire LV before contrast administration. Late gadolinium (Gd) enhancement (LGE) imaging was initiated 10 min after administration of a Gd contrast agent (Gadovist, Bayer, Schering, Berlin, Germany) to assess infarct size (IS). Myocardium at risk (MaR) was assessed from T_2-weighted short tau inversion recovery images acquired before contrast agent administration.

Ventricular volumetric analysis

The software Segment, version 4.0 R11026 and v4.1.0.2 R14368 (http://segment.heiberg.se), was used for the volumetric CMR image analysis.[28] Delineation of the endocardium was performed in all SAX cine slices in end-diastole, end-systole, and diastasis. Papillary muscles were included in the blood pool. The LV volume in all timeframes over one heartbeat was assessed by interpolating the volume of each SAX slice between EDV, ESV, and diastasis in consistency with earlier validations.[16,20,21] Manual corrections were applied in the basal- and apical-most slices when necessary. In cases where a midventricular or apical slice was missing from the SAX stack, an interpolation between the basal and apical slice of the missing slice with visual guidance by the two-, three-, and four-chamber views was performed. SV and LVEF were defined as EDV–ESV and SV/EDV, respectively. Adverse LV remodelling was defined as a concomitant increase in EDV and ESV between baseline and follow-up of ≥12%.[29] Inter- and intra-observer analyses were made in two subsets of 12 patients from the original cohort by a second observer with 14 years of CMR experience.

PV loops

Non-invasive PV loops were generated according to a previously validated method.[16] Time-resolved volumetric CMR data together with brachial sphygmomanometric data were used for calculating the time-varying elastance curve and generating the PV loop. Adjustments of the time-varying constant were performed when necessary to ensure a physiological shape of the PV loop. PV loop variables were calculated according to *Figure 1*. The maximal elastance (E_{max}) or contractility was defined as the slope of the end-systolic PV relationship (ESPVR). Arterial elastance (E_a) was defined as the slope of the curve from the end-systolic point to the end-diastolic point on the *x*-axis. Stroke work (SW) was defined as the area limited by the PV loop, and potential energy (PE) was defined as the area under the ESPVR line, limited by the *x*-axis and the isovolumetric relaxation of the PV loop. Ventriculoarterial coupling (VAC), external power (EP), ventricular efficiency (VE), and energy per ejected volume (EpSV) were calculated from the extracted PV loop variables: $VAC = E_a/E_{max}$, external power = SW × HR, VE = SW/(SW + PE), EpSV = (SW + PE)/SV.

IS and MaR analysis

Assessment of IS and MaR in the DANAMI-3 trial has previously been described.[26] In short, this analysis was performed using the software CVI42

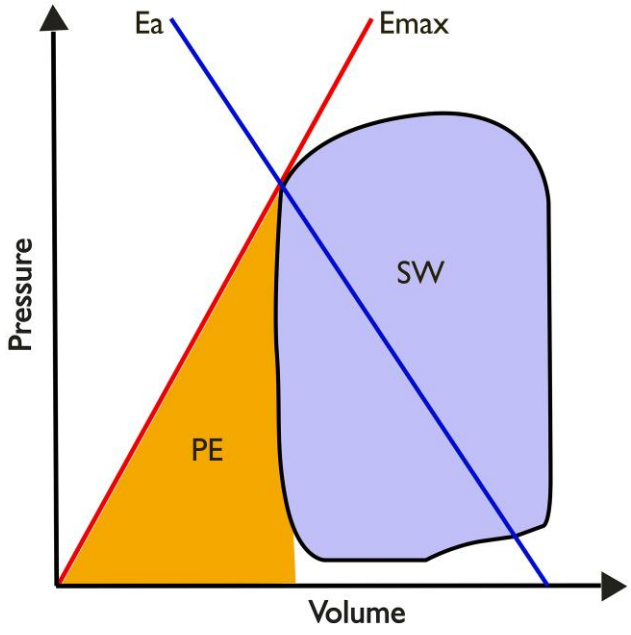


Figure 1 Schematic image of a PV loop in a pressure-volume diagram and PV loop variables. Contractility was defined as the maximal elastance (E_{max}) by the slope of the red line stretching from the origin to the end-systolic pressure-volume point (ESPVR). Arterial elastance (E_a) was defined as the slope of the blue line intersecting the ESPVR and the *x*-axis at the point of end-diastole. Stroke work (SW) was defined as the PV loop area. Potential energy (PE) was defined as the area under the red line, limited by the *x*-axis and the PV loop.

Table 1 Population characteristics

	Total ($n = 181$)	Females ($n = 40$)	Missing (n)	Males ($n = 141$)	Missing (n)	P
Age (years)	58 ± 11	59 ± 12	0	58 ± 11	0	0.8
Symptom duration (min)	175 [128–264]	198 [144–266]	5	172 [125–264]	7	0.2
Peak troponin T (ng/L)	3220 [1109–6140]	1935 [979–3503]	0	3730 [1350–6810]	0	0.003
Infarct size acute (%)	18 ± 11	14 ± 10	3	20 ± 11	9	0.005
Infarct size at 3 months (%)	15 ± 10	12 ± 9	1	16 ± 10	0	0.01
Myocardium at risk (%)	34 ± 11	31 ± 12	4	34 ± 11	9	0.1
LVM acute (g)	129 ± 31	101 ± 19	0	137 ± 28	4	<0.0001
Ejection fraction acute (%)	50 ± 10	53 ± 11	0	49 ± 10	0	0.04
SBP (mmHg)	136 ± 27	131 ± 24	0	138 ± 27	0	0.1
DBP (mmHg)	86 ± 21	84 ± 19	0	87 ± 21	0	0.4
Risk factors						
Diabetes	16 (9%)	3 (8%)	0	13 (9%)	0	1
Active smoker	101 (56%)	24 (60%)	0	77 (55%)	0	0.6
Past smoker	46 (25%)	10 (25%)	0	36 (26%)	0	1
Hypertension	62 (34%)	15 (38%)	1	47 (33%)	0	0.6
Hyperlipidaemia	63 (35%)	18 (45%)	0	45 (32%)	0	0.1
Previous AMI	9 (5%)	3 (8%)	0	6 (4%)	0	0.4
Previous stroke	5 (3%)	0 (0%)	0	5 (4%)	0	0.6
Chronic heart failure	30 (17%)	5 (13%)	0	25 (18%)	0	0.6
Renal insufficiency	1 (<1%)	0 (0%)	6	1 (<1%)	20	1
Treatment						
Beta-blocker	169 (93%)	36 (90%)	0	133 (94%)	0	0.3
ACE-inhibitor	63 (35%)	10 (25%)	0	53 (37%)	0	0.2
ARB	10 (6%)	2 (5%)	0	8 (6%)	0	1
Calcium channel blocker	12 (7%)	2 (5%)	0	10 (7%)	0	1
Spironolactone	2 (1%)	1 (3%)	0	1 (<1%)	0	0.4
Statin	181 (100%)	40 (100%)	0	141 (100%)	0	
Angiography						
TIMI 0–1	116 (64%)	22 (55%)	0	94 (67%)	0	0.2
TIMI 2–3	65 (36%)	18 (45%)	0	47 (33%)	0	0.2
LAD culprit	73 (40%)	17 (43%)	0	56 (40%)	0	0.9
RCA culprit	76 (42%)	18 (45%)	0	58 (41%)	0	0.7
LCx culprit	16 (9%)	1 (3%)	0	15 (11%)	0	0.2
Other	16 (9%)	4 (10%)	0	12 (9%)	0	0.8
Outcome						
Acute myocardial infarct	17 (9%)	7 (18%)	0	10 (7%)	0	0.06
Heart failure	5 (3%)	2 (5%)	0	3 (2%)	0	0.3
All-cause mortality	12 (6%)	2 (5%)	0	10 (7%)	0	1

Population characteristics shown as mean ± SD, median [IQR], or percentage of population. Note that females demonstrated a smaller infarct size compared to males.
LVM, left ventricular mass; SBP, systolic blood pressure; DBP, diastolic blood pressure; ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; LAD, left anterior descending artery; RCA, right coronary artery; LCx, left circumflex artery.

(Circle Cardiovascular Imaging, Calgary, Alberta, Canada) with semi-automatic delineation of the endo- and epicardial borders with papillary muscles included in the myocardial cavity. Hyperintense areas of >2 SD and >5 SD from remote myocardium in the T_2-weighted and LGE images were defined as MaR and IS, respectively.

Statistical analysis

Continuous data were presented as mean ± standard deviation or median (interquartile range) and categorical data as a percentage of the population. Missing data are addressed in *Table 1*. Normal distributions of samples and homoscedasticity were evaluated by QQ plots and residuals vs. fitted graphs, respectively. Logistic regression analyses were applied with adverse cardiac remodelling as outcome variable and each PV loop variable as predictor. One model with age and sex, and another model with age, sex, and IS at baseline were applied and adjusted for. The Hosmer–Lemeshow test was used to validate each model. Depending on distribution, independent *t*-tests, Mann–Whitney *U* test, or Fisher's exact test was used to evaluate group differences in continuous and numeric variables. Paired *t*-tests were used to evaluate differences in PV loop variables between baseline and follow-up. Sex and culprit vessel differences were assessed by mixed models. Adjustments were made for age, IS at follow-up, and culprit vessel in the former comparison and for age, IS at follow-up, and sex in the latter comparison. Simple linear regression

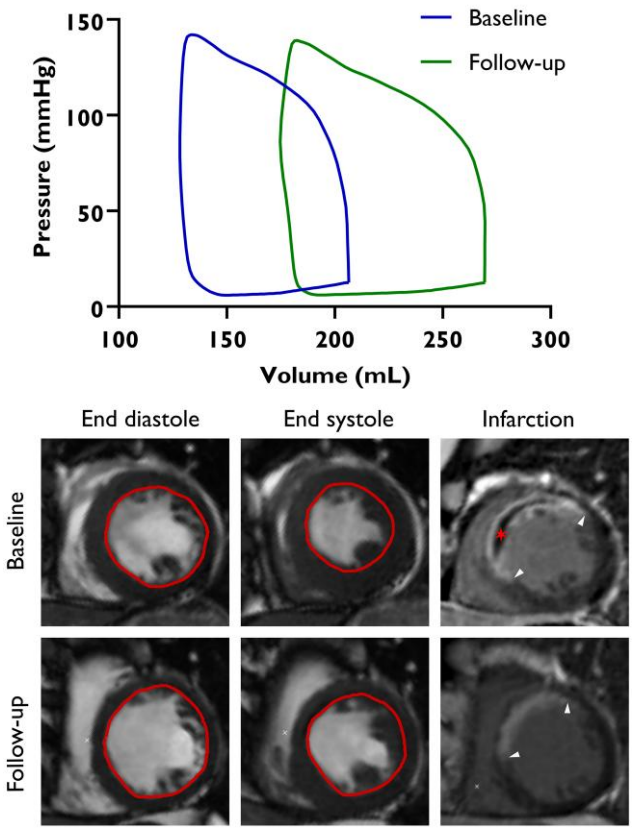


Figure 2 Example of volumetric measurements in CMR images and corresponding PV loops. The upper diagram shows two pressure-volume (PV) loops at baseline (blue, leftward PV loop) and at follow-up (green, rightward PV loop) in the same patient after myocardial infarction (40% infarct size). The lower diagram shows the left ventricular (LV) cardiovascular magnetic resonance (CMR) images in the corresponding patient at baseline (top row) and follow-up (bottom row). CINE images in end-diastole (ED), end-systole (ES), and late gadolinium enhancement (LGE) images are demonstrated in the left, middle, and right columns, respectively. The red line, the white arrows, and the red star demarcate the LV endocardium, infarct borders, and microvascular obstruction, respectively. Note the rightward shift of the PV loop at follow-up showing the dilation of the LV in ED and ES shown in the CINE images.

analyses were performed for ratio of EDV and ESV at follow-up over baseline against each respective PV loop variable and conventional measurement. Intra- and inter-observer variability were assessed by Bland–Altman. A *P*-value below 0.05 was considered statistically significant. All statistics and graphs were performed using R V4.2.2 and GraphPad Prism V10.0.3 for Windows (GraphPad Software, Boston, MA, USA, www.graphpad.com).[30]

Ethics approval

The study was approved by the regional ethics committee and the institutional ethics committee in Denmark.

Results

Of the 1620 patients included in the DANAMI-3 trial at Rigshospitalet, 181 patients undergoing cardiac MR at baseline and 3-month follow-up, with full LV coverage, were included in the study. A flow diagram of the study inclusion is demonstrated in Supplementary data online, *Figure S2*.[26] The included patients were compared to the non-included DANAMI patients at the same centre, showing no significant differences except for lower age in the included patients (see Supplementary data online, *Table S3*).

Population characteristics

Patient characteristics are demonstrated in *Table 1*. Examples of volumetric assessment in CMR images and corresponding PV loops are demonstrated in *Figure 2*. Infarct size was significantly lower in females compared to males ($14 \pm 10\%$ vs. $20 \pm 11\%$, $P = 0.005$), despite having similar symptom duration [198 (144–266) min vs. 172 (125–264) min, $P = 0.2$] and MaR ($31 \pm 12\%$ vs. $34 \pm 11\%$, $P = 0.1$). Also, LVEF was higher in females compared to males (53 ± 11 and 49 ± 10, $P = 0.04$). Risk factors, medical treatment, and clinical outcome did not differ between the sexes.

PV loop variables at baseline and follow-up

PV loop variable values at baseline and follow-up are shown in *Figure 3*. Contractility increased, whereas arterial elastance (E_a) and ventriculoarterial coupling (VAC) decreased between baseline and follow-up, indicating ventriculoarterial recoupling in the chronic infarct state. External power (EP) and stroke work (SW) increased, whereas potential energy (PE) decreased, causing an increase in ventricular efficiency (VE) and decrease in energy per ejected volume (EpSV) between the timepoints. Notably, major overlap between baseline and follow-up was seen for all variables. Intra- and inter-observer variability of the PV loop variables are presented in Supplementary data online, *Table S4*.

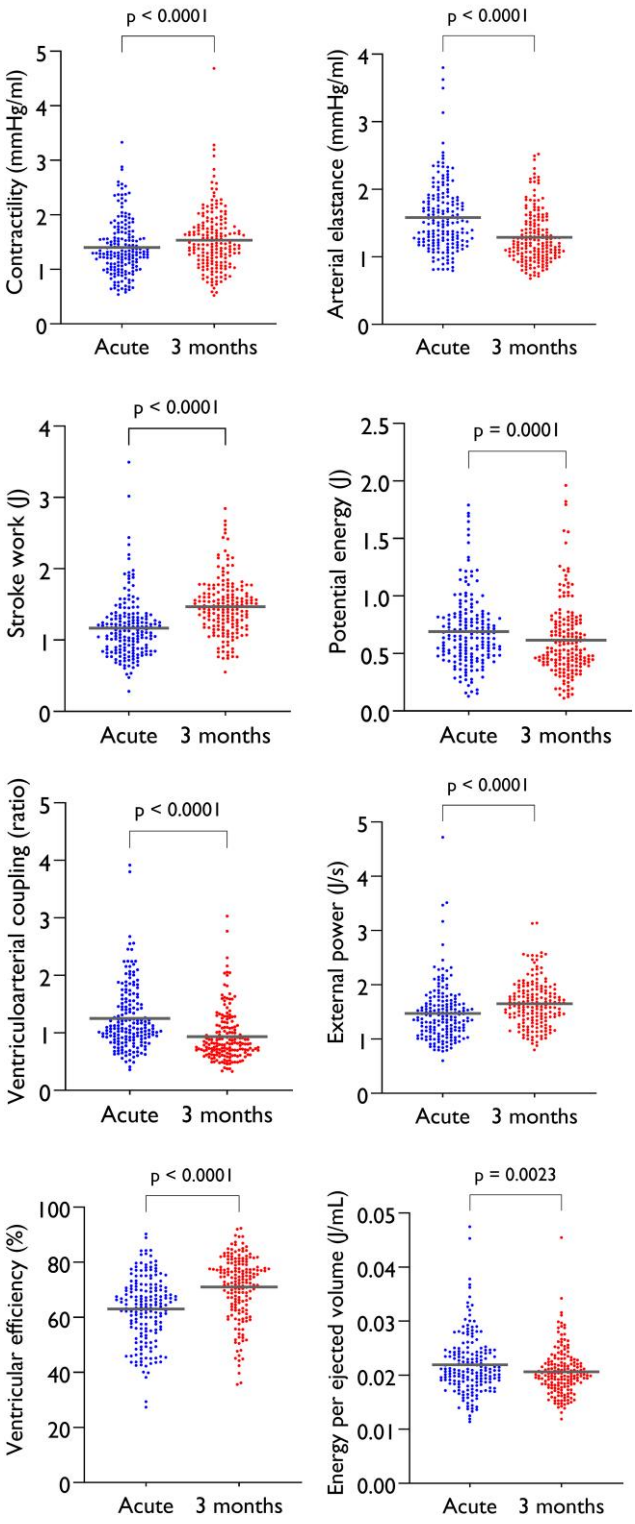


Figure 3 PV loop variables acute and at 3 months after myocardial infarction. Mean is shown by the grey horizontal line.

PV loop variables and cardiac remodelling

In total, 28 patients (15%) developed adverse cardiac remodelling at follow-up. In the first logistic regression model (*Table 2*, Model 1), E_a, SV, and EDV at baseline were predictive of adverse cardiac remodelling despite adjustments for age and sex (E_a estimate: 2.9, $P = 0.01$; SV estimate: 0.97, $P = 0.01$; and EDV estimate: 0.99, $P = 0.03$). However, contractility (estimate: 4.6, $P = 0.002$), VE (estimate: 1.05, $P = 0.048$), LVEF (estimate: 1.06, $P = 0.04$), EDV (estimate: 0.98, $P = 0.002$), and ESV

Table 2 Associations between acutely measured PV loop variables and adverse cardiac remodelling

Variable	Model 1 ($n = 181$)		Model 2 ($n = 169$)	
	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value
Contractility (mmHg/mL)	2.0 (0.9–4.4)	0.08	**4.6 (1.8–12.4)**	**0.002**
Arterial elastance (mmHg/mL)	**2.6 (1.2–5.5)**	**0.01**	2.1 (0.9–4.9)	0.09
Stroke work (J)	0.5 (0.2–1.6)	0.3	0.9 (0.2–3.0)	0.9
External power (J/s)	1.2 (0.5–2.5)	0.7	1.5 (0.6–3.6)	0.4
Potential energy (J)	1.1 (0.3–4.2)	0.8	0.3 (0.1–1.6)	0.2
Ventriculoarterial coupling	1.3 (0.6–2.5)	0.5	0.5 (0.2–1.4)	0.2
Ventricular efficiency (%)	1.00 (0.96–1.03)	0.9	**1.05 (1.00–1.11)**	**0.048**
Energy per ejected volume (mJ/mL)	1.07 (0.997–1.15)	0.05	1.03 (0.96–1.12)	0.4
Ejection fraction (%)	1.00 (0.96–1.04)	0.9	[a]	[a]
Stroke volume (mL)	**0.97 (0.94–0.99)**	**0.01**	0.98 (0.95–1.00)	0.1
Systolic blood pressure (mmHg)	1.01 (0.99–1.02)	0.2	1.01 (0.99–1.03)	0.2
EDV	**0.99 (0.97–0.998)**	**0.03**	**0.98 (0.96–0.99)**	**0.002**
ESV	0.99 (0.98–1.01)	0.3	**0.97 (0.95–0.99)**	**0.005**

Multivariate models with adjustments for age and sex (Model 1) or age, sex, and IS at baseline (Model 2). $P < 0.05$ are noted in bold.
OR, odds ratio.
[a]Poor goodness of fit due to significant Hosmer–Lemeshow test.

(estimate: 0.97, $P = 0.005$) were predictive of adverse cardiac remodelling when adjusting for IS at baseline (*Table 2*, Model 2). Non-adjusted comparisons of PV loop variables, blood pressure, and volumetric measurements concerning cardiac volumetric remodelling measured by ratio of ESV and EDV between baseline and follow-up are shown in *Figure 4* and Supplementary data online, *Figure S5*, respectively.

PV loop differences due to sex and culprit vessel

Differences in PV loop variables between baseline and follow-up for males and females are shown in *Figure 5* and *Table 3*. A significantly higher contractility and E_a with no effect on VAC were seen in females compared to males at baseline and follow-up in the former and at follow-up in the latter. Also, contractility increased between baseline and follow-up in females but remained unchanged in males. E_a decreased more in males than females between baseline and follow-up. PV loop-derived cardiac energetics showed a similar EpSV, and VE in females compared to males at baseline, despite a significantly lower PE, SV, and SW. The result of SW remained significant after heart rate adjustment as EP remained significantly lower in females at baseline. The same result was seen for PE, SV, and SW during follow-up. EpSV decreased in males but increased in females between baseline and follow-up. Differences in PV loop variables between left arterial descending artery (LAD), and left circumflex artery (LCx) and right coronary artery (RCA) infarctions are shown in *Table 4*. Larger increases in LVEF, SV, and VE and larger decreases in E_a, EpSV, PE, and VAC were seen in LAD infarctions compared to LCx and RCA infarctions between baseline and follow-up. LAD infarctions showed larger MaR but similar IS to LCx and RCA infarctions (36% vs. 32%, $P = 0.04$ and 20% vs. 18%, $P = 0.3$).

Discussion

This study demonstrates the incremental predictive value of non-invasive PV loop variables, beyond traditional risk factors like age, sex, and IS, in determining development of adverse remodelling in STEMI patients undergoing primary PCI. To the best of our knowledge, this is the first study to investigate PV loop variables at baseline and follow-up in myocardial infarct patients. All variables improved on a group level with significant differences between females and males and differences between culprit vessels. Our findings highlight the potential of these variables to identify patients at higher risk for adverse remodelling.

PV loop variables at 3-month follow-up

PV loop variables showed recoupling and favourable cardiac energetics at follow-up compared to baseline. The improvement in all variables could partly be explained by recovery of stunned myocardium at follow-up compared to the acute setting. This is consistent with an earlier study demonstrating a prolonged reduced regional mechanical function in the acute setting after primary PCI, albeit with the potential of recovery.[31] However, stunning could not explain the change in PV loop variables for all patients.

PV loop variables and adverse cardiac remodelling

Contractility, efficiency, EDV, ESV, and LVEF were predictive of the development of adverse cardiac remodelling independent of age, sex, and IS. Patients with higher contractility, efficiency, or LVEF and lower EDV or ESV at baseline after STEMI were more prone to develop adverse cardiac remodelling. This may reflect that patients with LV volumes closer to normal range are more prone to an increase in EDV and ESV than patients with already established cardiac disease and deranged LV morphology. Furthermore, patients with low contractility at baseline due to myocardial stunning are likely to regain function at follow-up, partly explaining why lower contractility at baseline showed lower odds per unit for developing adverse remodelling. Alternatively, the correlation between high contractility at baseline and development of adverse remodelling could indicate a reduced contractile reserve and therefore higher likelihood of developing adverse remodelling. However, further studies are needed to investigate the mechanisms

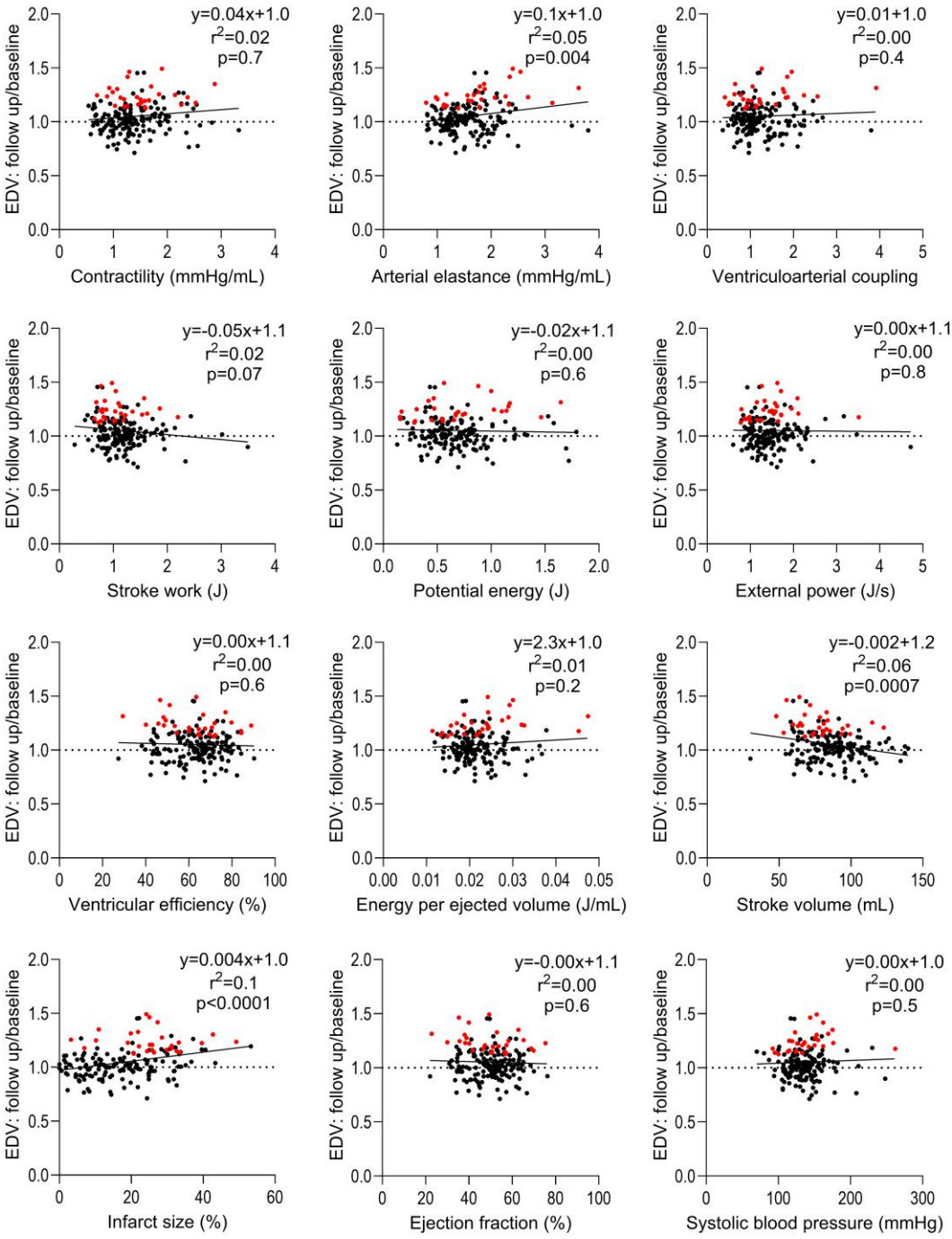


Figure 4 Cardiac volumetric remodelling against PV loop variables, blood pressure, and volumetric measurements. $EDV_{FOLLOW\text{-}UP}/EDV_{BASELINE}$ against pressure-volume loop variables, blood pressure, and volumetric measurements measured acutely after myocardial infarction. Red data points show patients developing adverse cardiac remodelling. EDV, end-diastolic volume.

by which contractility and adverse remodelling are related as well as its long-term prognostic value. Automatic segmentation using artificial intelligence may increase the speed of analysing non-invasive PV loops and thereby enable larger populations to be studied. Future studies validating automatic segmented PV loops against manual PV loops are needed.

Sex and culprit vessel differences post-infarction

Females had smaller IS despite similar MaR, age, and symptom duration compared to males, indicating that females may benefit from a protective effect on infarct evolution as previously hypothesized.[32]

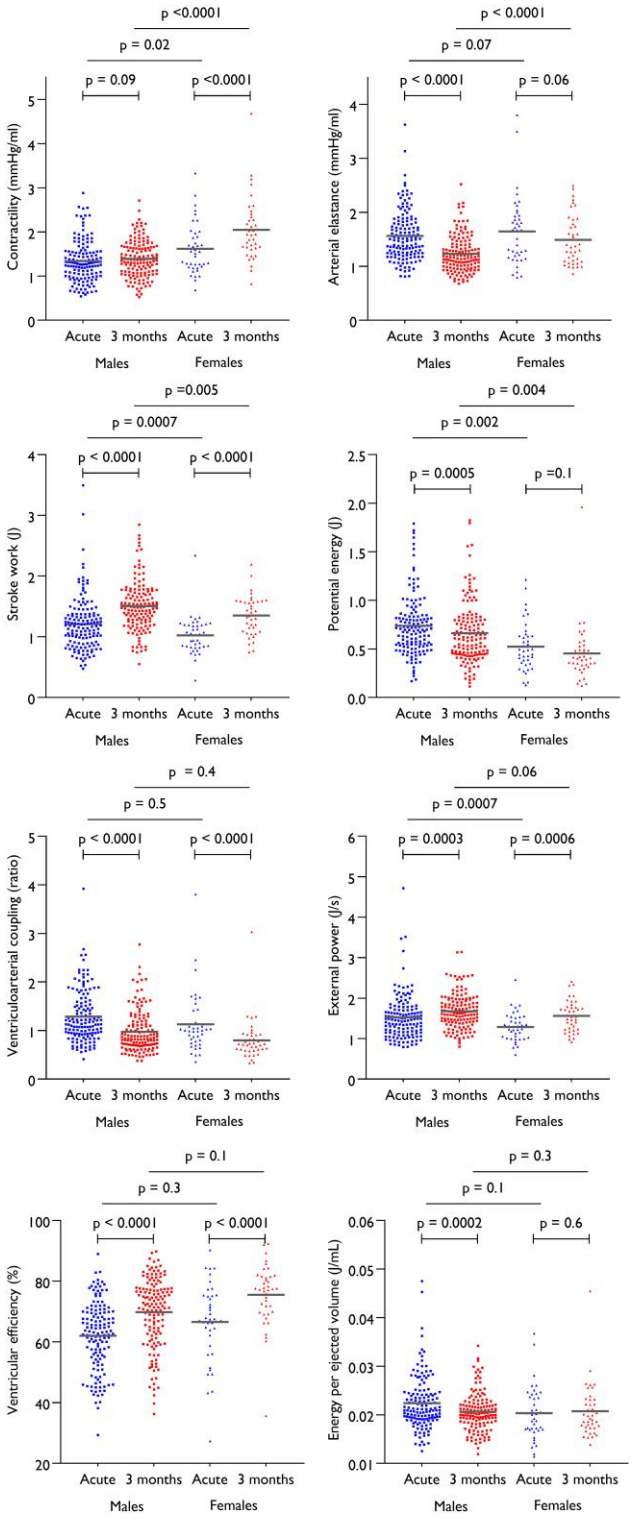


Figure 5 PV loop variables acute and at 3 months after myocardial infarction separated by sex. Mean is shown by the grey horizontal line. Adjustments were made for age, infarct size (IS) measured at follow-up, and culprit vessel. One patient was not included due to missing IS. Note the increase in contractility from baseline to follow-up in females.

Table 3 Adjusted mixed model comparing males and females at baseline and follow-up after myocardial infarction

PV loop variable	Baseline ($n = 180$)			Follow-up ($n = 180$)			Follow-up—baseline ($n = 180$)		
	Males	Females	*P*	Males	Females	*P*	Males	Females	*P*
E_{max} (mmHg/mL)	1.3 ± 0.5	1.6 ± 0.6	0.02	1.4 ± 0.4	2.0 ± 0.7	<0.0001	0.1 ± 0.4	0.4 ± 0.4	<0.0001
E_a (mmHg/mL)	1.6 ± 0.5	1.7 ± 0.7	0.07	1.2 ± 0.3	1.5 ± 0.5	<0.0001	−0.3 ± 0.5	−0.2 ± 0.6	0.046
Stroke work (J)	1.2 ± 0.4	1.0 ± 0.3	0.0007	1.5 ± 0.4	1.4 ± 0.3	0.005	0.3 ± 0.4	0.3 ± 0.3	0.6
Potential energy (J)	0.7 ± 0.3	0.5 ± 0.3	0.002	0.7 ± 0.3	0.5 ± 0.3	0.004	−0.1 ± 0.2	−0.1 ± 0.3	0.8
VAC	1.3 ± 0.5	1.1 ± 0.6	0.5	1.0 ± 0.4	0.8 ± 0.4	0.4	−0.3 ± 0.4	−0.3 ± 0.5	0.8
External power (J/s)	1.5 ± 0.6	1.3 ± 0.4	0.0007	1.7 ± 0.4	1.6 ± 0.4	0.06	0.2 ± 0.5	0.3 ± 0.4	0.2
Ventricular efficiency (%)	62 ± 11	66 ± 13	0.3	70 ± 12	75 ± 10	0.1	8 ± 9	9 ± 11	0.5
EpSV (J/mL)	0.022 ± 0.006	0.020 ± 0.006	0.1	0.021 ± 0.004	0.021 ± 0.005	0.3	−0.002 ± 0.005	0.001 ± 0.007	0.03
Systolic BP (mmHg)	138 ± 27	131 ± 24	0.08	140 ± 19	150 ± 26	0.03	2 ± 28	19 ± 34	0.002
Diastolic BP (mmHg)	87 ± 21	84 ± 19	0.4	79 ± 12	83 ± 16	0.2	−7 ± 22	−1 ± 19	0.1
Ejection fraction (%)	49 ± 10	53 ± 11	0.3	56 ± 10	61 ± 9	0.1	7 ± 7	8 ± 9	0.6
Stroke volume (mL)	88 ± 19	79 ± 18	0.0005	107 ± 20	89 ± 16	<0.0001	18 ± 17	10 ± 13	0.006

Groups presented as mean ± standard deviation. $P < 0.05$ was defined as significant. Each analysis was adjusted for age, culprit vessel, and final IS. Note the larger difference in E_{max} (contractility) between baseline and follow-up in females compared to males.
BP, blood pressure; E_a, arterial elastance; EpSV, energy per ejected volume; VAC, ventriculoarterial coupling.

In concordance with having smaller IS, females were also shown to improve their contractility whereas males were unchanged between baseline and follow-up. Infarctions within the LAD territory showed a higher energy expenditure, ventriculoarterial decoupling, and a lower efficiency at baseline compared non-LAD infarctions. This difference was not seen at follow-up. The improvement of PV loop variables in LAD infarctions could potentially be explained by more stunning and thus greater recovery of function in this group.[32]

Clinical implications

Mean IS (18%), mean LVEF at follow-up (57%), and median duration between pain onset and primary PCI (175 min) in the present study are comparable to previous CMR outcome studies after STEMI,[33–35] showing consistency with the well-developed organization for treating STEMI patients in Denmark.[36–38] The findings from this study may offer a new clinical approach for early identification of patients prone to develop adverse cardiac remodelling after acute infarction. While current clinical practice is relying on follow-up examinations for detecting the development of adverse cardiac remodelling, non-invasive PV loop variables could potentially offer predictive value to guide treatment strategy in the acute infarct setting independent of IS. Patients at higher risk for adverse remodelling could benefit from a closer follow-up strategy to detect and possibly prohibit the adverse remodelling process.

Limitations

The findings in the present study should be interpreted in the light of some limitations. Since the study was retrospective, no power calculation was performed for this sub-study of the DANAMI-3 trial. A methodological limitation to the study is that the evaluation of MaR and IS was performed by the 2 and 5 SD from remote, respectively, which previously has been shown to have a limited agreement to reference.[39] In a single-centre study, however, the bias is reasonably similar for all included patients since all the examinations were performed on the same MR scanner. Furthermore, T_1 and T_2 mapping, which could provide additional characterization of the myocardial injury, was not performed in the current study. Also, the use of feature tracking to determine adverse cardiac remodelling was beyond the scope of this study. The conclusions from the study should be interpreted in the light of the single-centre design with a relatively small study population, which may predispose to selection bias as not all included patients underwent CMR, and only patients with baseline and follow-up examinations were included in the study.

Conclusion

Non-invasive PV loop variables by CMR have incremental predictive value to age, sex, and IS for determining development of adverse cardiac remodelling in STEMI patients treated with primary PCI. Furthermore, the PV loop variables show significant differences in post-infarct cardiovascular adaptation between sexes and culprit vessels.

Supplementary data

Supplementary data are available at *European Heart Journal - Imaging Methods and Practice* online.

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Consent

All participants provided written informed consent.

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Table 4 Adjusted mixed model comparing different culprit vessels at baseline and follow-up after myocardial infarction

PV loop variable	Baseline ($n = 180$)			Follow-up ($n = 180$)			Follow-up—baseline ($n = 180$)		
	LAD	RCA or LCx	*P*	LAD	RCA or LCx	*P*	LAD (*P*)	RCA or LCx (*P*)	*P*
E_{max} (mmHg/mL)	1.3 ± 0.5	1.4 ± 0.5	0.3	1.5 ± 0.5	1.6 ± 0.6	0.2	0.1 ± 0.4 (0.009)	0.1 ± 0.4 (0.0004)	0.8
E_a (mmHg/mL)	1.8 ± 0.6	1.5 ± 0.4	<0.0001	1.3 ± 0.3	1.3 ± 0.4	0.8	−0.5 ± 0.5 (<0.0001)	−0.2 ± 0.5 (0.0002)	0.0002
Stroke work (J)	1.1 ± 0.4	1.2 ± 0.4	0.02	1.4 ± 0.4	1.5 ± 0.4	0.1	0.3 ± 0.3 (<0.0001)	0.3 ± 0.4 (<0.0001)	0.5
Potential energy (J)	0.7 ± 0.3	0.7 ± 0.3	0.049	0.6 ± 0.3	0.6 ± 0.3	0.98	−0.1 ± 0.3 (<0.0001)	−0.04 ± 0.2 (0.1)	0.02
VAC	1.5 ± 0.7	1.1 ± 0.4	<0.0001	1.0 ± 0.5	0.9 ± 0.4	0.4	−0.5 ± 0.5 (<0.0001)	−0.2 ± 0.3 (<0.0001)	<0.0001
External power (J/s)	1.4 ± 0.4	1.5 ± 0.6	0.2	1.6 ± 0.4	1.7 ± 0.4	0.05	0.2 ± 0.4 (0.008)	0.2 ± 0.5 (<0.0001)	0.6
Ventricular efficiency (%)	59 ± 13	66 ± 10	<0.0001	70 ± 12	72 ± 11	0.3	11 ± 10 (<0.0001)	6 ± 8 (<0.0001)	0.0009
EpSV (J/mL)	0.023 ± 0.006	0.021 ± 0.005	0.003	0.021 ± 0.004	0.021 ± 0.004	0.5	−0.003 ± 0.005 (<0.0001)	−0.000 ± 0.006 (0.7)	0.002
Systolic BP (mmHg)	138 ± 25	135 ± 28	0.4	139 ± 20	144 ± 21	0.2	1 ± 26 (0.7)	9 ± 33 (0.003)	0.1
Diastolic BP (mmHg)	88 ± 19	85 ± 22	0.3	79 ± 14	81 ± 12	0.5	−9 ± 19 (0.0007)	−4 ± 23 (0.05)	0.2
Ejection fraction (%)	47 ± 11	52 ± 9	0.0001	56 ± 11	58 ± 10	0.4	9 ± 8 (<0.0001)	6 ± 7 (<0.0001)	0.001
Stroke volume (mL)	80 ± 17	90 ± 19	0.0005	100 ± 18	104 ± 22	0.3	20 ± 15 (<0.0001)	14 ± 17 (<0.0001)	0.01

Groups presented as mean ± standard deviation. $P < 0.05$ was defined as significant. Each analysis was adjusted for age, sex, and final IS. Note the higher VAC and EpSV between LAD infarctions compared to LCx and RCA infarctions at baseline. Also note the non-differences seen at follow-up.
BP, blood pressure; E_a, arterial elastance.

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Data availability

The data underlying this article will be shared on reasonable request.

Lead author biography

This study was a collaboration between Lund University and Copenhagen University. Theodor Lav is a PhD student in the Cardiac MR Group at the Department of Clinical Physiology, Lund University and Skåne University Hospital. The thesis aims to investigate microvascular disease in patients with diabetes by different MRI techniques.

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