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## Post-myocardial infarction left ventricular remodelling and function in the rat: analysis using the pressure-volume loops\*\*

### Pozawałowa przebudowa i funkcja lewej komory serca u szczura – analiza z zastosowaniem pętli ciśnienie-objętość

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#### Keywords

PV loops, myocardial infarction, left ventricular remodelling

#### Sowa kluczowe

pętla ciśnienie-objętość, zawał mięśnia sercowego, przebudowa lewej komory serca

#### Conflict of interest

##### Konflikt interesów

None

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#### Summary

**Introduction.** Myocardial infarction (MI) triggers left ventricular (LV) remodelling, which is a progressive change of ventricular composition, shape and function. It has been characterised fairly well, though prediction of its outcome still is largely difficult.

**Aim.** To characterise post-MI progression to heart failure using pressure-volume loop technique.

**Material and methods.** Rats were subjected to induction of large non-reperfused MI or sham operation and were followed-up for 3, 7 days or 4 or 8 weeks after the surgery. At each point, they underwent basic echocardiographic assessment and left ventricle pressure-volume (PV) loop recording to obtain multiple parameters characterising LV remodelling, systolic and diastolic performance and preload and afterload.

**Results.** Preload, but not afterload, progressively increased after MI. Transition to heart failure was accompanied by a progressive worsening of systolic performance and active relaxation, while LV compliance did not change much with time. While total cardiac work, represented by total PV area, remained unchanged, efficient haemodynamic stroke work was markedly reduced at the expense of significant increase in inefficient elastic potential energy.

**Conclusions.** Detailed analysis using PV loops provides additional insight into post-MI remodelling and progression to heart failure, indicating that the failing heart becomes “wasteful”, utilising most of its work for haemodynamically inefficient transfer of elastic potential energy rather than for haemodynamically effective stroke work. Improvement in mechanical efficiency of the heart may be a promising strategy for the prevention or treatment of heart failure.

#### Streszczenie

**Wstęp.** Zawał mięśnia sercowego uruchamia zjawisko pozawałowej przebudowy lewej komory serca, co skutkuje zmianą w składzie, kształcie oraz funkcji komory. Choć zawał serca został już dosyć dobrze opisany, w dalszym ciągu trudno jest przewidzieć jego konsekwencje.

**Cel pracy.** Scharakteryzowanie rozwoju pozawałowej niewydolności serca przy użyciu pętli ciśnienie-objętość.

**Materiał i metody.** U szczurów indukowano rozległy, niereperfundowany zawał mięśnia sercowego lub wykonywano operację pozorowaną. Zwierzęta obserwowano przez 3 i 7 dni oraz 4 i 8 tygodni po operacji. W każdym punkcie czasowym wykonywano podstawowe badanie echokardiograficzne oraz cewnikowanie lewej komory serca z rejestracją pętli ciśnienie-objętość w celu pomiaru ciśnienia skurczowego i rozkurczowego oraz pomiaru parametrów charakteryzujących przebudowę lewej komory oraz obciążenie wstępne i następcze.

**Wyniki.** Obciążenie wstępne, ale nie następcze stopniowo rosło po wywołaniu zawału. Rozwojowi niewydolności serca towarzyszyło postępujące pogorszenie sprawności skurczowej oraz aktywnego rozkurczu, natomiast podatność lewej komory nie zmieniła się znacząco w czasie. Całkowita praca serca, reprezentowana przez łączną

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powierzchnię wykreśloną przez pętlę ciśnienie-objętość, pozostała niezmieniona, natomiast praca zewnętrzna zmniejszyła się kosztem znacznego wzrostu nieefektywnej energii potencjalnej.

**Wnioski.** Szczegółowa analiza pętli ciśnienie-objętość pozwala uzyskać dodatkowe informacje o pozawałowej przebudowie lewej komory serca oraz o rozwoju niewydolności serca. Na podstawie analizy pętli można stwierdzić, że niewydolne serce charakteryzuje się swego rodzaju „marnotrawstwem”, gdyż wykorzystuje większość pracy raczej na nieefektywny hemodynamicznie transfer energii potencjalnej niż na hemodynamicznie efektywną pracę zewnętrzną. Poprawa mechanicznej wydajności serca może stanowić obiecującą strategię profilaktyki lub leczenia niewydolności serca.

## INTRODUCTION

Myocardial infarction (MI) triggers left ventricular (LV) remodelling, which is a progressive change of ventricular composition, shape and function (1). LV dilation is its most characteristic feature – it is a highly deleterious process and its intensity is significantly related to poor outcome (2). It has been characterised fairly well both in humans and animals, though it is still difficult to predict its eventual outcome, i.e. who develops heart failure and who develops a compensated impairment of ventricular function. Thus, there remains an unmet need to define this process in more detail.

Pfeffer et al. (3) were the first to characterise the remodelling process over 6 months after MI using passive pressure-volume relationships in the rat heart. They demonstrated that only rats with large myocardial infarction (> 40% LV mass) developed progressive LV dilation, while animals with smaller infarcts developed only transient, compensated dilation. However, this method allowed only for indirect assessment of LV dilation and passive diastolic parameters.

Recently, the simultaneous measurement of LV pressure and volume (so-called *beat-by-beat* loops) has become a state-of-the-art approach to assess global cardiac function, both diastolic and systolic, as well as cardiac dimensions directly *in vivo* (4, 5). Thus, the aim of our study was to investigate LV diastolic and systolic function as well as LV volumes in the rat in various points of time after the induction of large MI.

## MATERIAL AND METHODS

This investigation conformed to the National Institutes of Health *Guide for the Care and Use of Laboratory Animals* (NIH Pub. No. 85-23, Revised 1996) and was performed with the approval of the local Ethics Committee for Animal Use.

### Study design

60 male Wistar-Kyoto rats (280-330 g) were used in the study. 44 underwent induction of non-reperfused myocardial infarction, 16 underwent sham operation. Twenty-four hours after the surgery, all animals underwent echocardiography and those with large MI (n = 25) were randomly assigned to one of 4 experimental groups, that were euthanised on day 3 (n = 5), day 7 (n = 6), month 1 (n = 7) and month 2 (n = 7) after MI induction. Sham operated rats were randomly assigned to the corresponding 4 experimental groups, too (each n = 5).

On the day of the euthanasia, each rat underwent echocardiography and pressure-volume loop assessment.

### Induction of myocardial infarction

MI was induced as described previously (6). Briefly, the rats were anaesthetised with ketamine HCl (100 mg/kg body weight, i.p.) and xylazine (5 mg/kg body weight, i.p.), and left thoracotomy was performed. The heart was externalised and a suture (5-0 silk) was placed around the proximal left coronary artery and tightly tied. The heart was internalised, the thorax was closed, and pneumothorax was reduced. The sham operated rats were subjected to the same protocol except that the snare was not tied. Within 24 h, post-MI mortality was 25%.

### Echocardiography

Echocardiography was performed using MyLab25 (Es-aote, Italy) with 13 MHz linear array transducer. Under light anaesthesia (ketamine HCl and xylazine, 75 and 3.5 mg/kg body weight, i.p.) contractility of 12 wall segments visualised in the midpapillary short-axis view and 11 segments visualised in the long-axis view was graded as 1 (normal) or 0 (abnormal) and the total WMI was calculated. As we have previously shown, WMI closely correlated with infarct size and that WMI = 15 corresponded to infarct size ~40%. (6) LV end-diastolic and end-systolic areas were planimetered from the parasternal long-axis view. LV ejection fraction (LVEF) was calculated as (LV diastolic area – LV systolic area)/LV diastolic area.

### Haemodynamic measurements – pressure-volume loops

Rats were anaesthetised with ketamine HCl (100 mg/kg body weight, i.p.) and xylazine (5 mg/kg body weight, i.p.). The animals were put on a heating pad, tracheotomised and put on an animal respirator (respiratory rate 60/min, tidal volume 4 ml). The upper abdominal cavity was opened and through cutting of the diaphragm, the heart was exposed. The left ventricular apex was punctured with a 25G needle and a microtip P-V catheter (SPR-838, Millar Instruments; Houston, TX) was inserted into the LV. Its position was established based on pressure and volume signals. After stabilisation for 5 minutes, the signals were continuously recorded at sampling rate of 1000/s using an ARIA P-V conductance system (Millar Instruments) coupled to a PowerLab/4SP A/D converter (AD Instruments; Mountain

View, CA) and a personal computer. HR, maximal LV systolic pressure (LVSP), LV end-diastolic pressure (LVEDP), maximal slope of systolic pressure increment (+dP/dt) and diastolic pressure decrement (-dP/dt), time constant of LV pressure decay ( $\tau$ ), ejection fraction (EF), end-diastolic volume (LVEDV), end-systolic volume (LVESV), stroke volume (SV), cardiac output (CO), and stroke work (SW) were computed using a cardiac P-V analysis programme (PVAN3.2, Millar Instruments).

Systolic wall tension was calculated as (mean left ventricular systolic pressure)  $\times$  LV radius; while radius was calculated as  $\sqrt[3]{(3 \times \text{LV} / 4 \pi)} + \text{wall thickness}$ , while diastolic wall tension was calculated using LVEDP instead of mean left ventricular systolic pressure.

### Statistical analysis

All results are given as means  $\pm$  SEM. Differences for parameters obtained at each time point were evaluated

using two-way ANOVA, followed by a Dunnett test in case of significance (Statistica software). Differences were considered significant at the level of  $P < 0.05$ .

### RESULTS

Table 1 demonstrates that infarct size measured by echocardiography did not differ between animals followed-up 3, 7 days and 1 and 2 months after the induction of MI.

Figure 1 shows representative tracings of LV pressure and LV volume and derived PV loops from the sham operated rat and rat with a large MI after 8 weeks of follow-up.

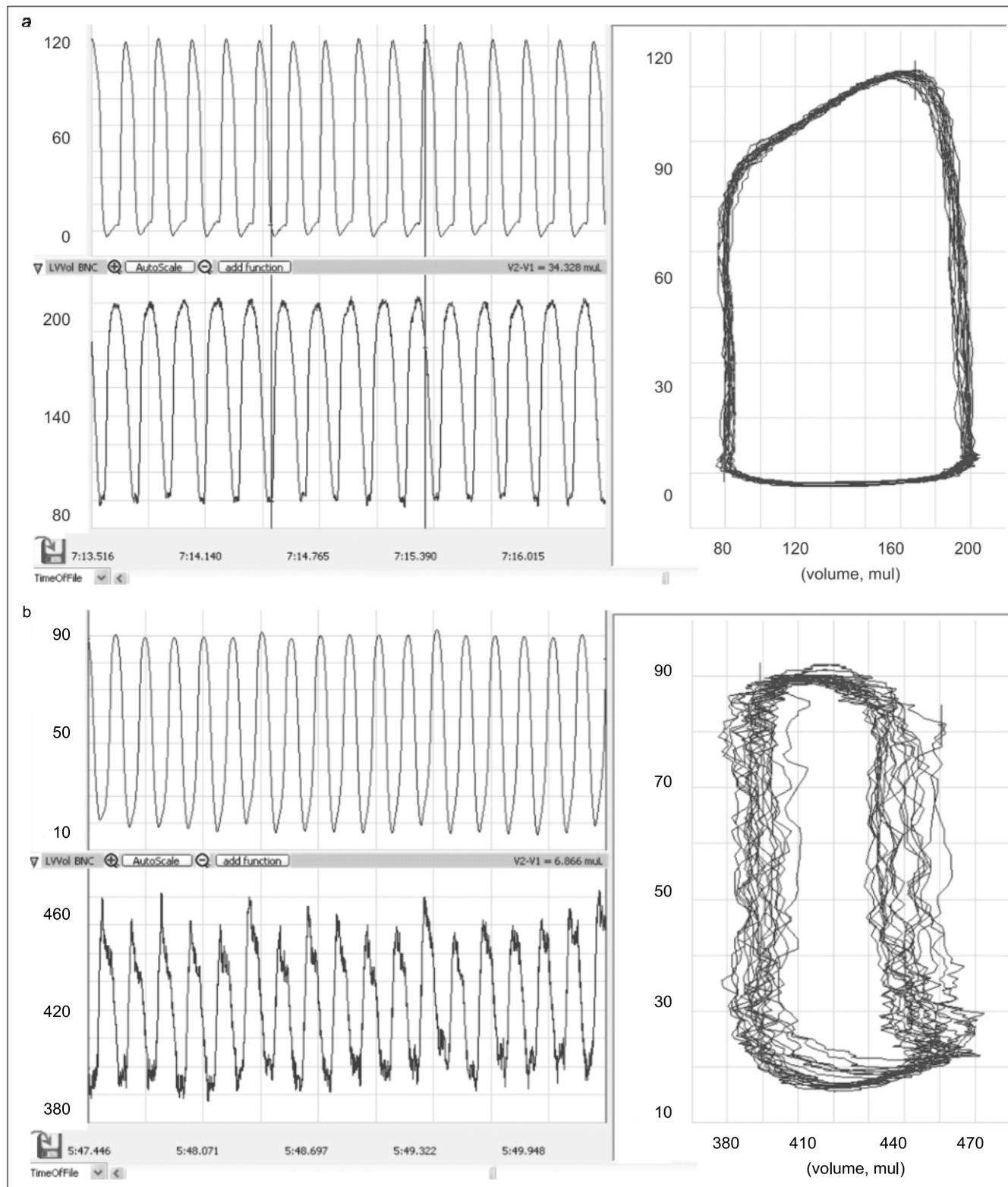
Figure 2 shows representative PV loops from a sham operated rat and rats with a large MI after 3 and 7 days and 4 and 8 weeks of follow-up. There is a clear progressive LV dilatation, demonstrated by rightward displacement of the PV loop, as a function of time after MI. It is accompanied by the reduction in stroke volume (SV), LV systolic pressure and elevation of LVEDP.

**Tab. 1.** Hemodynamic parameters in sham operated and post-myocardial infarction rats at various time points after induction of myocardial infarction

	Sham operated (n=16)	3 days (n=5)	7 days (n=5)	4 weeks (n=6)	8 weeks (n=5)
General parameters					
Body weight, g	343 $\pm$ 21	325 $\pm$ 18	333 $\pm$ 23	342 $\pm$ 24	352 $\pm$ 26
Infarct size, % left ventricle	0	43 $\pm$ 4*	45 $\pm$ 3*	43 $\pm$ 4*	41 $\pm$ 5*
Heart rate, beats/min	395 $\pm$ 29	395 $\pm$ 23	393 $\pm$ 19	390 $\pm$ 28	382 $\pm$ 23
Integrated performance					
LVEF, %	59 $\pm$ 3	44 $\pm$ 4*	39 $\pm$ 3*	22 $\pm$ 3*	11 $\pm$ 3*
SV, $\mu$ l	126 $\pm$ 12	108 $\pm$ 12	105 $\pm$ 12	84 $\pm$ 9*	51 $\pm$ 9*
SW, mmHg * ml	12.2 1.0	9.6 $\pm$ 0.9*	8.0 $\pm$ 0.9*	5.7 $\pm$ 0.8*	2.9 $\pm$ 0.6*
CO, ml/min	49.8 $\pm$ 3.7	42.7 $\pm$ 3.5	41.3 $\pm$ 3.9	32.9 $\pm$ 3.3*	20.4 $\pm$ 2.6*
CI, ml*min <sup>-1</sup> /kg	145 $\pm$ 11	131 $\pm$ 10	124 $\pm$ 12	96 $\pm$ 9*	57 $\pm$ 6*
Ea/Ees	0.69 0.07	1.28 $\pm$ 0.10*	1.57 $\pm$ 0.08*	3.58 $\pm$ 0.45*	7.94 $\pm$ 1.01*
PE, mmHg * ml	5.3 0.3	7.8 $\pm$ 0.8*	8.4 $\pm$ 0.5*	13.9 $\pm$ 1.0*	15.8 $\pm$ 1.3*
PVA, mmHg * ml	17.5 1.5	17.3 $\pm$ 1.6	16.4 $\pm$ 1.6	19.5 $\pm$ 2.0	18.7 $\pm$ 1.8
SW/PVA, %	69.7 $\pm$ 6.0	55.2 $\pm$ 4.1*	49.1 $\pm$ 4.3*	29.2 $\pm$ 3.5*	15.5 $\pm$ 0.9*
Afterload					
LV systolic wall tension, mmHg * mm	0.35 $\pm$ 0.11	0.36 $\pm$ 0.11	0.35 $\pm$ 0.08	0.37 $\pm$ 0.10	0.37 $\pm$ 0.12
LVESP, mmHg	122 $\pm$ 12	117 $\pm$ 10	108 $\pm$ 9	99 $\pm$ 8*	89 $\pm$ 9*
Ea, mmHg/ $\mu$ l	0.96 $\pm$ 0.12	1.08 $\pm$ 0.14	1.02 $\pm$ 0.10	1.18 $\pm$ 0.12	1.70 $\pm$ 0.15*
Preload					
LVEDP, mmHg	5 1	9 $\pm$ 5	13 $\pm$ 3*	15 $\pm$ 3*	19 $\pm$ 4*
LVEDV, $\mu$ l	212 $\pm$ 16	246 $\pm$ 22	273 $\pm$ 21*	383 $\pm$ 35*	458 $\pm$ 30*
LV diastolic wall tension, mmHg * mm	0.017 $\pm$ 0.002	0.033 $\pm$ 0.002	0.050 $\pm$ 0.003	0.067 $\pm$ 0.004	0.091 $\pm$ 0.008
Systolic performance					
dP/dt <sub>max</sub> , mmHg/s	8023 $\pm$ 1454	6032 $\pm$ 1023	5234 $\pm$ 935*	4356 $\pm$ 798*	3872 $\pm$ 583*
Ees, mmHg/ $\mu$ l	1.40 $\pm$ 0.21	0.84 0.14*	0.65 $\pm$ 0.11*	0.35 $\pm$ 0.08*	0.24 $\pm$ 0.06*
LVDP, mmHg	117 $\pm$ 10	108 $\pm$ 10	95 $\pm$ 10*	84 $\pm$ 10*	71 $\pm$ 6*
Diastolic performance					
dP/dt <sub>min</sub> , mmHg/s	5234 1102	4203 $\pm$ 889	3604 $\pm$ 556*	3002 $\pm$ 455*	2834 $\pm$ 344*
Tau-Glantz, ms	11.9 $\pm$ 1.2	13.1 $\pm$ 1.1	13.6 $\pm$ 1.5	16.5 $\pm$ 2.2*	18.3 $\pm$ 3.3*
EDPVR, mmHg/ $\mu$ l	0.042 0.006	0.052 $\pm$ 0.005	0.056 $\pm$ 0.006	0.053 $\pm$ 0.006	0.048 $\pm$ 0.006

\*p < 0.05 vs. sham operated rats.

CO, cardiac output; CI, cardiac index; Ea, Effective arterial elastance; EDPVR, end diastolic pressure-volume ratio; Ees, LV end-systolic elastance ratio; Ea/Ees, Effective arterial elastance to LV end-systolic elastance ratio; LV, left ventricle; LVDP, left ventricular developed pressure; LVEDP, left ventricular end diastolic pressure; LVEDV, left ventricular end diastolic volume; LVESV, left ventricular end systolic pressure; LVEF, left ventricular ejection fraction; PE, elastic potential energy; PVA, pressure-volume area; SW, stroke work; SW/PVA, stroke work to pressure-volume area: mechanical efficiency of the heart; SV, stroke volume.

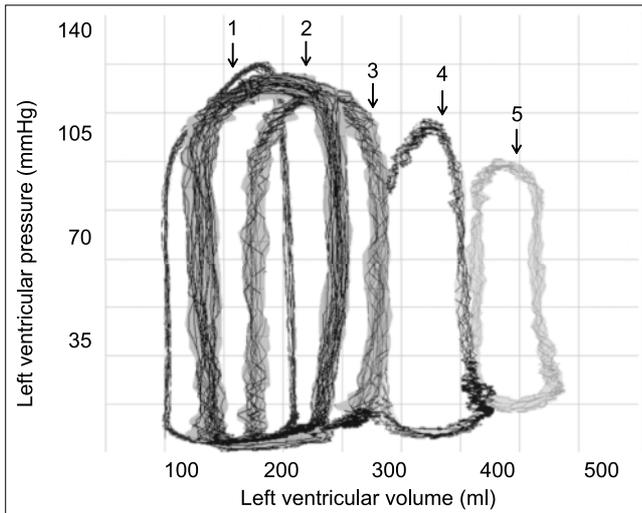


**Fig. 1.** Representative tracings of left ventricular (LV) pressure and LV volume and derived pressure-volume (PV) loops from the sham operated rat (A) and rat with a large myocardial infarction after 8 weeks of follow-up (B). Upper left panel presents LV pressure (in mmHg), lower left panel presents LV volume (in  $\mu\text{l}$ ), while right panel presents derived PV loops (vertical axis: LV pressure in mmHg). Quality of PV loops is poorer in post-MI rat, due to worse quality of volume recording, probably related to a large scar.

### INTEGRATED PERFORMANCE

As table 1 indicates, there was a progressive reduction in ejection fraction (EF) and SV as well as cardiac output (CO) and cardiac index (CI) during the follow-up after MI. Ratio of arterial elastance ( $E_a$ ) to LV end-systolic

elastance ( $E_{es}$ ) was highly elevated, which was accompanied by progressive reduction in stroke work (SW) at the expense of elastic potential energy (PE), while the total cardiac work, represented by the total pressure-volume area (PVA) remained essentially unchanged.



**Fig. 2.** Representative pressure-volume (PV) loops obtained in sham operated hearts (curves no. 1), and hearts followed-up after MI for 3 days (no. 2), 7 days (no. 3), 4 weeks (no. 4) and 8 weeks (no. 5).

### PRELOAD AND AFTERLOAD

Preload, expressed as either LVEDP, LVEDV or wall tension, highly increased with time (tab. 1).

On the other hand, afterload, expressed as LV systolic wall tension (integrated LV pressure x LV radius), did not change at all during the follow-up after MI: LV dilation was completely compensated by the reduction in LV systolic pressure (tab. 1).

### SYSTOLIC AND DIASTOLIC PERFORMANCE

All indices of LV systolic performance, contractility, expressed as maximum rate of increase of LV pressure during systole ( $dP/dt_{max}$ ) or LV end-systolic elastance ( $E_{es}$ ), a load-independent parameter of LV contractility – slope of end-systolic pressure-volume relation (ESPVR, see fig. 3), and LV developed pressure, indicated progressive worsening of LV systolic performance with time (tab. 1).

Diastole can be divided into two phases: an active, energy-consuming LV relaxation and passive LV stretching by the inflowing blood. Both parameters of the first phase of the LV diastole, maximum rate of decrease of LV pressure during systole ( $dP/dt_{min}$ ) and time constant of relaxation ( $\tau$ -Glantz) indicated progressive reduction in the rate of relaxation, resulting in prolongation of the active phase of LV relaxation. On the other hand, end-diastolic pressure-volume relation, a parameter analysing passive compliance (or stiffness), did not change significantly (tab. 1).

### DISCUSSION

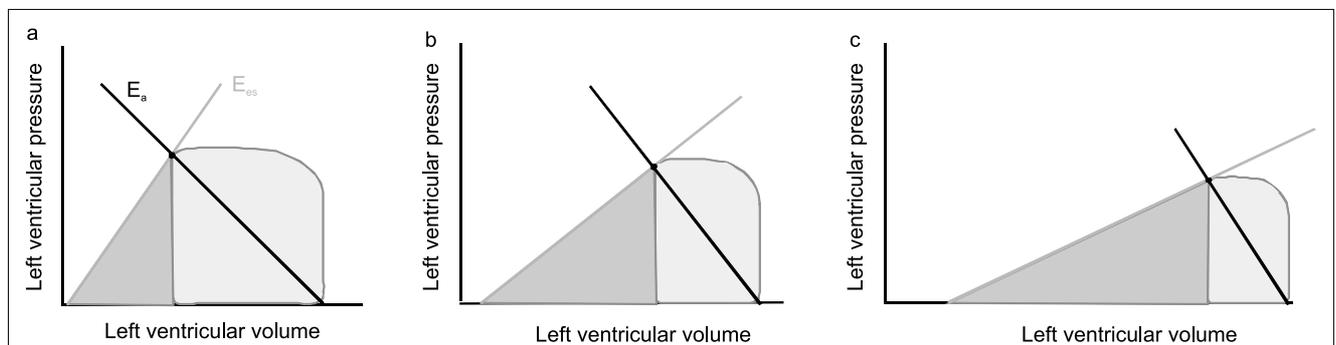
For the first time, we have performed a detailed analysis of left ventricular performance and remodelling at various time points after a large myocardial infarction in the rat, to investigate the phenomena underlying progression to heart failure.

As Pfeffer et al. (3) demonstrated in their pivotal work, induction of a large MI results in progressive LV remodelling, involving progressive LV dilatation and reduction in LV contractility. However, PV loops allow for a much more comprehensive analysis of LV performance. In our discussion, we would like to focus on (1) preload and afterload, (2) interactions between arterial system and the left ventricle and (3) cardiac work.

### PRELOAD AND AFTERLOAD

There is a commonly held suspicion that both preload and afterload are increased in heart failure (7) though due to difficulties in their calculation, precise measurements are lacking. Furthermore, their changes in the process of development of heart failure have never been systematically studied.

All three indices of preload, LVEDV, LVEDP and diastolic wall tension (a product of LVEDP and LV radius) progressively rose during the follow-up after MI, and the latter was more than five-fold its baseline value.



**Fig. 3.** Schematic representation of pressure-volume loops in sham operated rats (a), animals followed-up for 7 days (b) and 8 weeks (c) after induction of myocardial infarction (MI).  $E_a$  denotes effective arterial elastance, a marker of impedance of arterial tree, while  $E_{es}$  denotes left ventricular (LV) end-systolic elastance, a marker of LV contractility.  $E_a/E_{es}$  ratio corresponds to ventricular-arterial coupling. The bright and dark coloured figure denotes pressure volume area (PVA), a marker of total cardiac work. Bright segment of the PV loop corresponds to haemodynamically effective stroke work (SW), while dark one – to elastic potential energy. SW/PVA ratio denotes mechanical efficiency of the heart. (a):  $E_a/E_{es} \sim 0.7$  ensures normal LV ejection fraction (LVEF, approximately 60%), high stroke work and mechanical efficiency of the heart. (b) Seven days after MI progressive reduction in LV contractility ( $\downarrow E_{es}$ ) in combination with mild increase in  $E_a$  result in  $E_a/E_{es} \sim 1.3$  that results in reduction of LVEF, worsening of mechanical efficiency of the heart (SW/PVA ratio), though stroke volume is essentially preserved. (c) Eight weeks after MI, further reduction in LV contractility ( $\downarrow\downarrow E_{es}$ ) in combination with mild increase of  $E_a$  result in  $E_a/E_{es} \sim 8$ , making preservation of LVEF and SV impossible due to marked reduction of mechanical efficiency of the heart.

Surprisingly, afterload did not change significantly in post-MI hearts. This was probably due to the fact that it is a product of arterial (mirrored by LV) systolic pressure and LV radius. Although LVEDV increased by more than 2-fold, LV radius increased by only 40% 8 weeks after MI, and this was offset by reciprocal reduction in LV systolic pressure.

### EFFECTIVE ARTERIAL ELASTANCE AND VENTRICULAR-ARTERIAL COUPLING

Left ventricular performance is coupled with arterial environment. These both factors determine end-systolic part of the PV loop (fig. 3). When several pressure-volume loops are obtained from the same subject during acute preload or afterload alterations with unchanged contractility, the left upper corners of the pressure-volume loop (end-systolic pressure-volume points) describe the end-systolic pressure-volume relation (ESPVR). This LV end-systolic elastance ( $E_{es}$ ), defined as the slope of the ESPVR, is linear (fig. 3).  $E_{es}$  is a load-independent index of left ventricular contractility, superior to other generally utilised parameters, including LV ejection fraction, which is afterload dependent.

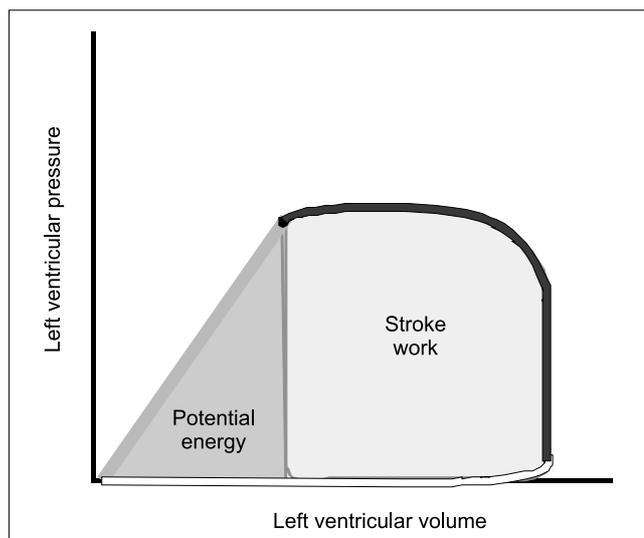
Systolic arterial pressure changes essentially linearly with stroke volume, rising proportionally to the rise of stroke volume. This suggests that slope of the curve relating arterial pressure to stroke volume is constant. And this is indeed the case: this parameter is termed effective arterial elastance ( $E_a$ ) and is a good marker of resistance that the arterial tree offers to the inflowing blood (8).

Thus the ventricular-arterial coupling can be assessed utilising pressure-volume loops, using the ratio of  $E_a$  to  $E_{es}$  (fig. 3). Studies indicate that this  $E_a/E_{es}$  ratio ranges from 0.62 to 0.82 in healthy humans (9). De Tombe et al. (10) demonstrated in isolated blood-perfused canine hearts that stroke work was maximised at  $E_a/E_{es}$  0.80, while energetic efficiency at  $E_a/E_{es}$  ~0.70, however both parameters remained >90% of their optimal values provided  $E_a/E_{es}$  did not rise above 1.3.

We show that 3 days after MI there was a significant reduction in EF and  $E_a/E_{es}$ , almost doubled, though it was still below this 1.3 threshold (tab. 1). And indeed, stroke volume and cardiac output were remarkably preserved. Four and eight weeks after MI induction,  $E_a/E_{es}$  reached 3.6 and almost 8, which was accompanied by severe haemodynamic compromise. What is interesting, arterial elastance changed little and majority of this change was caused by a significant reduction in contractility. This concept is provided on figure 3.

### CARDIAC WORK AND EFFICIENCY

Figure 4 shows that the pressure volume area (PVA) is an area circumscribed by 1) the end-diastolic pressure-volume relation curve (EDPVR, yellow), 2) the systolic part of the pressure-volume curve (purple) and 3) systolic pressure-volume relation curve (ESPVR, green). Theoretical considerations and experimental studies suggest that PVA is closely correlated with total cardiac work and energy expenditure during



**Fig. 4.** Schematic representation of pressure-volume loop. The bright and dark coloured figure denotes pressure volume area (PVA), a marker of total cardiac work. Bright segment of the PV loop corresponds to haemodynamically effective stroke work (SW), while dark one – to elastic potential energy. SW/PVA ratio denotes mechanical efficiency of the heart. See text for further details.

a single cardiac cycle. Many studies demonstrated that PVA is a good marker of myocardial oxygen consumption (11, 12). Figure 4 indicates that PVA can be subdivided into two areas: PV proper, circumscribed by the actual pressure-volume changes during the cardiac cycle (blue area in fig. 4) that corresponds to stroke work or external cardiac work, i.e. haemodynamically efficient work; and a red triangular area that corresponds to potential energy transferred to LV wall during the cardiac cycle. This latter part is responsible for haemodynamically inefficient, “wasted” part of cardiac work. Thus, the ratio of SW to PVA represents an index of mechanical efficiency of the heart.

PVA did not change during the follow-up after MI: although the LV volumes significantly increased, this was offset by reduction of LV systolic pressure (See fig. 3 for schematic presentation). However, there were dramatic changes in the stroke work, potential energy and mechanical efficiency of the heart: stroke work progressively decreased, while potential energy progressively increased with time after MI, which was responsible for the reduction in mechanical efficiency of the heart from almost 70% to little more than 15%.

### CONCLUSIONS

In conclusion, our data demonstrate that the process of post-MI progression to heart failure is accompanied by reduction in LV systolic performance and the impairment of active LV relaxation. But the most striking is progressive reduction of stroke work and mechanical efficiency of the heart and these factors may be responsible for overall failure of cardiac performance. Improvement in mechanical efficiency of the heart may be a promising strategy for the prevention or treatment of heart failure.

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