Alteration of left ventriculo-arterial coupling and mechanical efficiency during acute myocardial ischemia

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Aim. **Myocardial revascularisation being frequently performed during acute myocardial ischemia, in a hostile hemodynamic environment, we evaluated left ventriculo-arterial (VA) coupling, left ventricular (LV) mechanical efficiency, and the mechanical properties of the systemic vasculature during acute myocardial ischemia.**

Methods. **In 6 pigs, vascular properties [characteristic impedance (R_1), peripheral resistance (R_2), compliance (C), inductance (L), arterial elastance (E_a)] were estimated with a windkessel model. LV function was assessed by the slope (Ees) of end-systolic pressure-volume relationship (ESPVR), and stroke work (SW) – end-diastolic volume (EDV) relation. Pressure-volume area (PVA) was referred to as myocardial oxygen consumption. VA coupling was defined as E_{es}/E_a, and mechanical efficiency as SW/PVA. After baseline recordings, the left anterior descending coronary artery was ligated and hemodynamic measures obtained every 30 minutes for 3 hours. Data are expressed as mean (SEM).**

Results. **Coronary occlusion induced an ESPVR rightward shift, and decreased Ees from 3.67 (0.33) to 1.92 (0.20) mmHg/ml and the slope of the SW – EDV relationship from 72.3 (3.4) to 40.4 (4.5) mmHg ($p<0.001$), while E_a increased from 3.33 (0.56) to 4.65 (0.29) mmHg/ml ($p<0.005$). This was responsible for a dramatic alteration of VA coupling from 1.22 (0.11) to 0.44 (0.07), ($p<0.001$). While R_2 increased from 1.72 (0.30) to 2.38 (0.16) mmHg.s.ml^{-1} ($p<0.05$) and C decreased from 0.78 (0.16) to 0.46 (0.08) ml/mmHg ($p<0.05$), R_1 and L were unchanged. Coronary occlusion decreased SW from 4 056 (223) to 2 580 (122) mmHg.ml ($p<0.001$), while PVA and SW/PVA decreased from 5 575 (514) to 4 813 (317) mmHg.ml (NS), and from 0.76 (0.04) to 0.57 (0.03) ($p<0.001$), respectively.**

Conclusion. **Acute myocardial ischemia severely altered left ventriculo-arterial coupling and LV mechanical efficiency. Impaired left VA coupling was due to a combination of augmented arterial elastance, secondary to early vasoconstriction later associated with decreased arterial compliance, and decreased LV contractility.**

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The matching concept between the ventricle and the arterial system, or ventriculo-arterial coupling, has been expressed using a quantitative framework based on the principles of energy transfer. According to this framework, the ventricle acts as generator of hydraulic energy, transferring the mechanical energy of the contraction to the blood. Theoretically, it can be assumed that under physiological conditions the left ventricle (LV) and its afterload constitute a matched system. Or, in other words, that maximal energy is transferred from the cardiac contraction to the download arterial circuit.

Indeed, previous experimental studies have shown that the heart and vascular system are considered matched when either optimal external work or maximal mechanical efficiency is provided by the contraction.[1-6]

In a failing heart operating at the limit of the preload reserve, the LV can maximize neither of them.[7] In this situation, the failing LV faces increased peripheral resistances and decreased vascular compliance, secondary to adrenergic adaptations. This results in ventricular-load mismatch. Such a situation could prevail during acute myocardial ischemia.

Therefore, the purpose of this study was to precisely quantify the evolution of left ventriculo-arterial coupling, in conditions of acute myocardial ischemia. Specifically, we planned to evaluate the contribution of peripheral vascular mechanics to the decrease in LV performance during a controlled ischemic procedure.

Chamber properties and energetics were analyzed with the pressure-volume relationship, and ventricular afterload was assessed using the 4-element windkessel model.

Materials and methods

Preparation

The investigation conforms with the *Guide for the Care and Use of Laboratory Animals* published by the US National Institutes of Health (NIH Publication No.85-23, revised 1996). All experimental procedures and protocols used in this investigation were reviewed and approved by the ethical committee of the Medical Faculty of the University of Liege. Experiments were performed on 6 healthy pure pietran pigs of either sex weighing from 20 to 26 kg. The animals were premedicated with intramuscular administration of ketamine (20 mg/kg) and diazepam (1 mg/kg). Anesthesia was then induced and maintained by continuous infusion of sufentanil (0.5 $\mu g.kg^{-1}.h^{-1}$) and sodium pentobarbital (3 $mg.kg^{-1}.h^{-1}$). Spontaneous movements were prevented by pancuronium bromide (0.1 mg/kg). After endotracheal intubation through a cervical tracheostomy, the pigs were connected to a volume-cycled ventilator (Evita 2, Drager, Liibeck, Germany) set to deliver a tidal volume of 15 ml/kg at a respiratory rate of 20/min. End-tidal CO_2 measurements (Capnomac, Datex, Helsinki, Finland) were used to monitor the adequacy of ventilation. Respiratory settings were adjusted to maintain end-tidal CO_2 between 30 and 35 mmHg. Arterial oxygen saturation was monitored closely and maintained above 95% by adjusting the FiO_2 as necessary. Any metabolic acidosis was corrected by slow intravenous administration of sodium bicarbonate. Throughout the experiment, normal saline was infused at a rate of 10 $ml.kg^{-1}.h^{-1}$. Temperature was maintained at 37°C by means of a heating blanket. A standard lead electrocardiogram was used for the monitoring of heart rate (HR). The chest was opened with a mid-sternotomy, the pericardium was incised and sutured to the chest wall to form a cradle for the heart, and the root of the aorta was dissected clear of adherent fat and connective tissue. A conductance micromanometer-tipped catheter (Cardiodynamics, Zoetermeer, The Netherlands) was inserted through the right carotid artery and advanced into the left ventricle. A micromanometer-tipped catheter (Sentron pressure measuring catheter, Cordis, Miami, FL, USA) was inserted through the right femoral artery and advanced into the ascending aorta. A 14-mm diameter perivascular flow probe (Transonic Systems Inc., Ithaca, NY, USA) was closely adjusted around the aorta 2 cm downstream to the aortic valve. The micromanometer-tipped catheter was manipulated so that the pressure sensor was positioned just distal to the flow probe. Right atrial pressure was measured with a micromanometer-tipped catheter inserted into the cavity through the superior vena cava. A 6F Fogarty balloon catheter (Baxter Healthcare Corp., Oakland, CA, USA) was advanced into the inferior vena cava through a right femoral venotomy. Inflation of this balloon produced a titrable leftward shift in pressure-volume loops by reducing venous return. Thrombus formation along the catheters was prevented by administration of 100 U/kg of heparin sodium intravenously just before the insertion.

Experimental protocol

To provide similar states of vascular filling, the animals were continuously infused with Ringer lactate (5 $ml.kg^{-1}.h^{-1}$), and, when necessary, with hydroxyethylstarch 6% to increase central venous pressure up to 6-7 mmHg over 30 minutes. Baseline hemodynamic recording was obtained thereafter from simultaneous measurements of aortic pressure and flow waves necessary to identify the 4-element windkessel model parameters. A 1st diagram of left ventricular pressure-volume relationship was generated from volume and pressure measurements at baseline and after stepwise decreases in preload by reducing venous return. The occlusion was limited to a few seconds in duration in order to avoid reflex responses. All measurements were taken immediately after the animal was briefly disconnected from the ventilator to sustain end-expiration. After deflation of the inferior vena cava balloon, the animals were allowed to rest for an additional 30 minutes. The left anterior descending (LAD) coronary artery was then ligated, immediately distal to the origin of the 1st diagonal artery. After 15 minutes, hemodynamic measurements were taken and repeated every 15 minutes for a total period of 180 minutes.

Percent risk area to the LV caused by LAD occlusion was estimated as follows. After cardiac arrest was induced by KC1, hearts were removed and monastral blue was injected proximal to the LAD occlusion site. Hearts were then fixed in 10% Formalin and sliced into 5 short-axis sections ~ 1 cm

thick. Each section was further divided into 16 equally spaced radial segments. The segments were classified as risk areas if they appeared stained. The overall extent of percent risk area was calculated as the total mass of all dye-stained segments divided by the total LV mass. The risk area was 30±4% in this study.

Volume measurements

Left ventricular volumes were inferred using the dual field conductance catheter technique.[8, 9] To convert measured segmental conductances G(i), to absolute segmental volumes V(i), the following formula was used:

$V(i) = (1/\alpha)\ (\Lambda^2/\sigma_b)\ [G(i) - G_p(i)]$

where Λ is the interelectrode distance of the catheter and σ_b the specific conductivity of blood. $G_p(i)$ is the so-called parallel conductance of segment (i) and is introduced to correct the spreading of electric field in the structures surrounding the ventricular cavity. The slope factor α takes into account the non-homogeneity of the electric field in the cavity.[8]

Blood conductivity was determined frequently throughout the study. Parallel conductances $G_p(i)$ were determined at the end of each acquisition by the saline method.[8] In order to transiently change the specific conductivity of blood in the left ventricle, a small volume (1-2 ml) of 10% NaCl solution was injected into the pulmonary artery during continuous data acquisition. For each beat, end-systolic conductance was then plotted against end-diastolic conductance. A linear regression was performed and the obtained relation was extrapolated to the point where end-systolic conductance equals end-diastolic conductance. At this point, the ventricular cavity has no contribution to the conductance, which is then only due to surroundings structures. The slope factor α was computed by identifying cardiac output with mean aortic flow, as measured by the flow probe.

Data collection

All measurements were performed at end expiration. The conductance catheter was connected to a Sigma-5 signal-conditioner processor (Cardiodynamics, Zoetermeer, The Netherlands). The electromagnetic flow-probe was connected to a flow-meter (HT 207, Transonic Systems Inc., Ithaca, NY, USA), and each micromanometer-tipped catheter to the appropriate monitor (Sentron pressure monitoring, Cordis, Miami, FL, USA).

All analog signals and the ventricular pressure-volume loops were displayed on screen for continuous monitoring. The analog signals were continuously converted to digital form with an appropriate software (Codas, DataQ Instruments Inc., Akron, OH, USA) at a sampling frequency of 200 Hz.

Data analysis

Ventricular systolic function

Left ventricular contractile function was assessed by the end-systolic pressure-volume relation (ESPVR), and the preload recruitable stroke work (PRSW).

The instantaneous pressure-volume relationship was considered in terms of a time-varying elastance E(t), defined by the following relationship:

$$E(t) = P(t)/ [V(t) - V_0]$$

where P(t) and V(t) are respectively the instantaneous ventricular pressure and volume, and V_0 a correction term. End-systole (es) was defined as the instant of time in the ejection phase at which E(t) reaches its maximum, E_{max}.[10] It is generally accepted that E(t) and V_0 are insensitive to preload, at least within physiological ranges. This implies that the time to E_{max}, or T_{max}, is not affected by preload changes and that the end-systolic points (P_{es}, V_{es}) satisfy the linear equation $P_{es} = E_{es}$ (V_{es}-V_0), and hence are aligned. Preload was acutely reduced by inflating the inferior vena cava balloon catheter. As V_0 cannot be measured directly, it was determined for each run by an iterative approach. It was first assigned the value 0 and the initial end-systolic points for each preload-changing heart cycle were determined at maximal P(t)/V(t). Linear regression of these end-systolic pressure and volume points was performed and from the resulting equation a new V_0 was calculated. End-systolic pressure and volume points were determined again and linear regression was repeated. This process was repeated until the difference between 2 successive values of V_0 was smaller than a preset error value of 0.1 ml. The

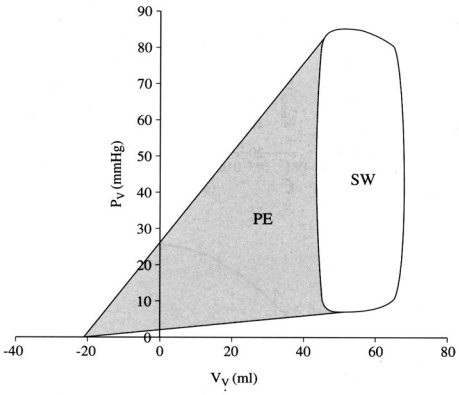

Fig. 1.—Pressure-volume area (PVA). P_v: ventricular pressure; V_v: ventricular volume; SW: stroke work; PE: potential energy. PVA=SW+PE.

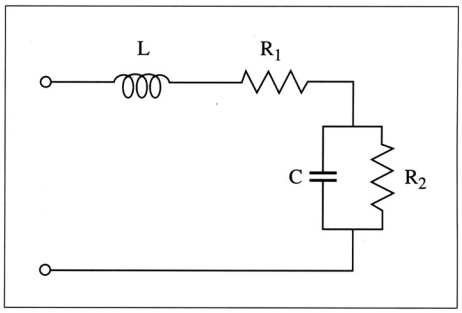

Fig. 2.—Electrical analog of the 4-element windkessel (WK4) model. R_1: characteristic impedance; R_2: peripheral resistance; L: inductance; C: compliance.

resulting slope was termed E_{es} and used for subsequent analysis.

Stroke work (SW) was the integrated area of each pressure-volume loop and was plotted against end-diastolic volume (V_{ed}; volume at the lower right corner of the loop) to generate the SW-V_{ed} relation (preload recruitable stroke work). These relations were highly linear and fit by least-squares regression. Slope and V_{ed} intercept were determined several times for each state and each animal. By averaging all the slopes and intercepts corresponding to a given state in a given animal, we obtained the mean SW/V_{ed} relationship corresponding to that animal in a specific state. V_{ed} was considered to be the independent variable, and SW the dependent variable. To obtain composite SW/V_{ed} plots for the pigs as a group, SW interpolated from the regression equations from individual pigs were average at 6 ml intervals of V_{ed}.

Myocardial energetics

Myocardial energetics was assessed by computation of pressure-volume area (PVA). In the time-varying elastance model of the ventricle, the total energy generated by each contraction is represented by the total area under the end-systolic pressure-volume relation line and the systolic segment of the pressure-volume trajectory, and above the end-diastolic pressure volume relation curve,[11] and denoted by PVA (Figure 1).[12] PVA is the sum of SW, or the energy that the ventricle delivers to the blood at ejection, and potential energy (PE), necessary to overcome the viscoelastic properties of the myocardium itself. It has been demonstrated that PVA was highly correlated with myocardial oxygen consumption.[13] Mechanical efficiency was defined as the SW/PVA ratio

Arterial properties

Arterial properties were assessed from ascending aortic pressure and flow measurements and represented with a 4-element windkessel model.[14] An electrical analog of the WK4 is displayed in Figure 2. In this model, the resistor R_2 represents the resistive properties of the systemic bed, which are considered to reside primarily in the arteriolar system. The capacitor C, placed in parallel with R_2, represents the compliant properties of the systemic vessels. The resistor R_1 represents the characteristic impedance, which level depends prominently on the elastic properties of the aorta. Finally, an inductance L is introduced to take blood inertia into account. Further, the inductance restores positive phase angles at high frequencies of the impedance spectrum.[15]

The values of R_1, R_2, C, and L were estimated by a method previously described.[16]

Effective arterial elastance (E_a) was calculated according to the following equation:[17]

$$E_a=\frac{R_1+R_2}{T_s+R_2C(1-e^{-R_2C/T_d})}$$

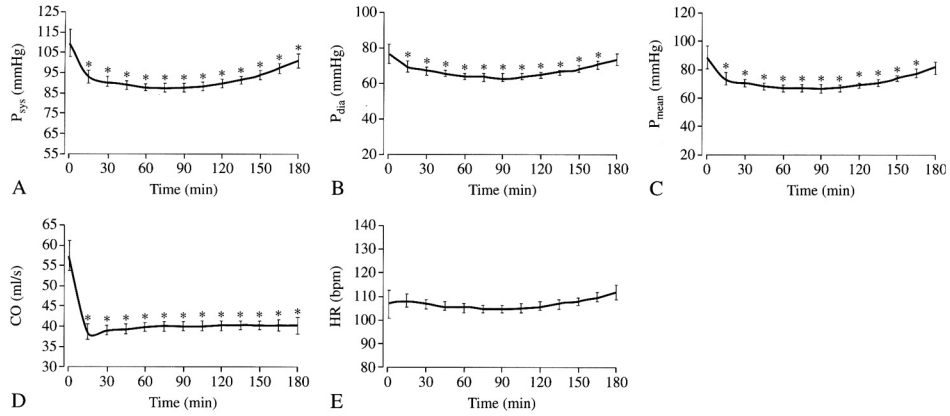

Fig. 3.—Evolution of aortic pressures, aortic flow, and heart rate during myocardial ischemia, induced by ligation of the LAD coronary artery. The ligation was placed immediately after baseline recordings (T0). A) P_{sys}: systolic aortic pressure; B) P_{dia}: diastolic aortic pressure; C) P_{mean}: mean aortic pressure; D) CO: cardiac output; E) HR: heart rate. *p<0.05 *vs* T0.

where T_s and T_d are the systolic and diastolic time intervals, respectively. T_s was calculated, in the aortic pressure wave, as the time interval between the point just before the abrupt rise and the dicrotic notch.

Ventriculo-arterial coupling was appreciated through the ratio E_{es}/E_a.

Statistical analysis

Data are expressed as mean±standard error of the mean (SEM). Changes in ventricular and arterial parameters, and offsets for various relationships, were evaluated by a 2-way analysis of variance (fixed effects) with the pig as 1st effect, and the experimental condition as 2nd effect.

When the Snedecor F was significant, multiple comparisons were made with the Scheffé test.[18] Results of statistical tests were considered significant for a level of uncertainty of 5% (p<0.05). Statistical tests were performed using the software Statistica (Statsoft Inc., OK, USA).

Results

Ligation of the LAD coronary artery induced a significant (p<0.005) decrease in systolic and mean aortic pressures, and, to a lesser extent (p<0.05), in diastolic aortic pressure (Figure 3). This decrease was the most prominent after 15 minutes of ischemia (T15), while aortic pressures began to rise after T90 although without reaching statistical significance. While heart rate remained stable, aortic flow severely decreased from 57.3±3.7 ml/min at baseline, to 39.0±1.9 ml/min at T15 (p<0.001). Thereafter, cardiac output remained stable throughout the experiment (Figure 3).

Applying the 4-element windkessel model to the aortic pressure and flow waveforms, we observed that peripheral resistance R_2 significantly (p<0.01) increased from 1.72±0.30 to 2.38±0.16 mmHg.s.ml^{-1}, between baseline and T15, measurement after which it remained stable (Figure 4). Characteristic impedance R_1 and inductance L did not significantly changed. Compliance C increased during the 1st hour of myocardial ischemia (from 0.78±0.16 to 1.06±0.05 ml/mmHg; p=0.027), than subsequently decreased to values statistically lower than at baseline (0.46±0.08 ml/mmHg at T180; p=0.017 *vs* baseline).

As a consequence, effective arterial elastance E_a changed from 3.33±0.56 to 4.65±0.29 mmHg/ml, between baseline and T15 (p<0.005). This augmentation was maintained during the entire period of myocardial ischemia (Figure 4).

As represented in Figure 5, coronary occlusion induced an early decrease in end-systolic volume

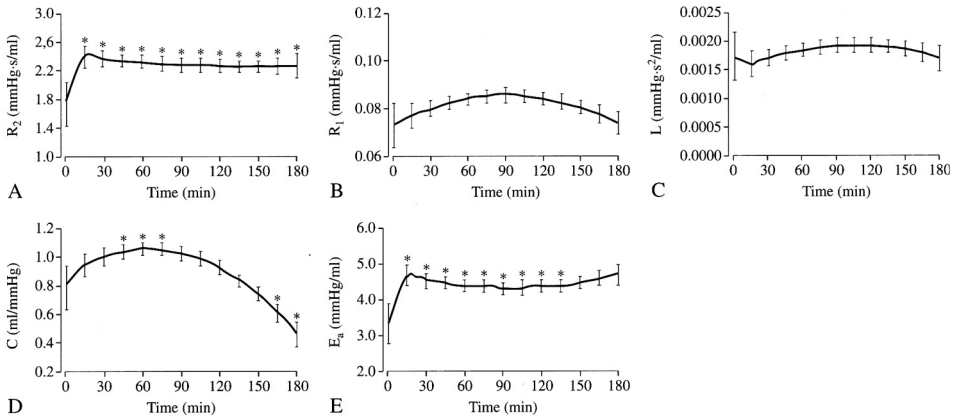

Fig. 4.—Evolution of 4-element windkessel model parameters and effective arterial elastance during myocardial ischemia, induced by ligation of the LAD coronary artery. The ligation was placed immediately after baseline recordings (T0). A) R_2: peripheral resistance; B) R_1: characteristic impedance; C) L: inductance; D) C: compliance; E) E_a: effective arterial elastance. *p<0.05 *vs* T0.

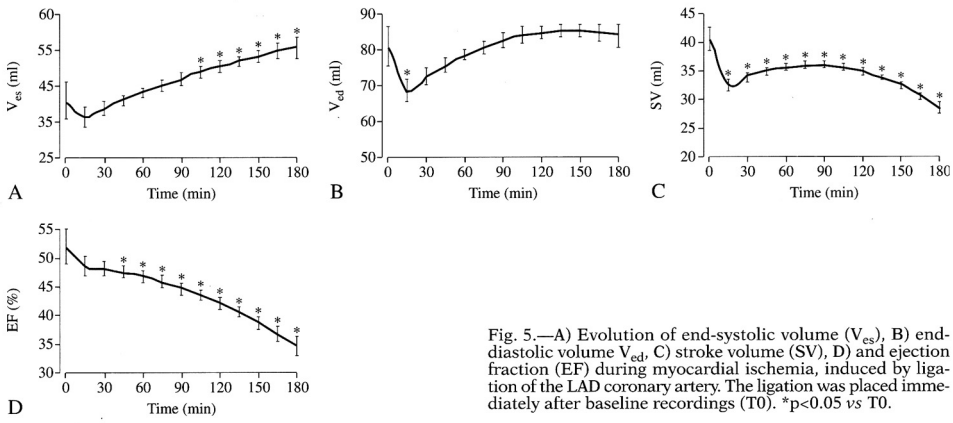

Fig. 5.—A) Evolution of end-systolic volume (V_{es}), B) end-diastolic volume V_{ed}, C) stroke volume (SV), D) and ejection fraction (EF) during myocardial ischemia, induced by ligation of the LAD coronary artery. The ligation was placed immediately after baseline recordings (T0). *p<0.05 *vs* T0.

V_{es}, and in end-diastolic volume V_{ed}, respectively from 40.7±5.0 to 36.5±2.8 ml (NS), and from 81.3±5.5 to 69.0±3.3 ml (p<0.05), between baseline and T15. Subsequently, V_{es} linearly increased, reaching 55.5±2.9 ml at T180 (p<0.001 *vs* baseline), while V_{ed} increased more slowly to stabilize at 85.5±1.7 ml at T150 (NS *vs* baseline). This resulted in a severe decrease in stroke volume SV and in ejection fraction EF, which decreased throughout the experimentation, from 52.0±3.0% at baseline to 34.7±1.8% at T180 (p<0.001).

Ligation of the LAD coronary artery was responsible for a significant (p<0.001) decrease of left ventricular contractility, as appreciated by end-systolic elastance E_{es} which also decreased, from 3.67±0.33 mmHg/ml at baseline to 1.92±0.20 mmHg/ml at T15 (Figure 6). Subsequently, E_{es} remained unchanged until T90, then slowly

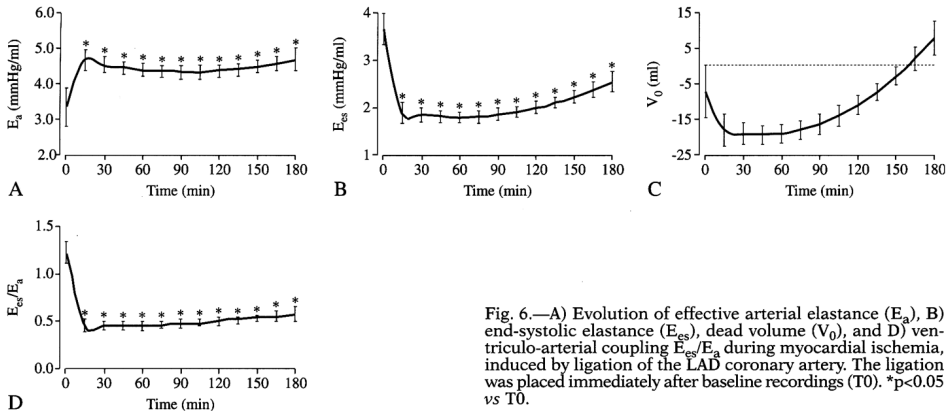

Fig. 6.—A) Evolution of effective arterial elastance (E_a), B) end-systolic elastance (E_{es}), dead volume (V_0), and D) ventriculo-arterial coupling E_{es}/E_a during myocardial ischemia, induced by ligation of the LAD coronary artery. The ligation was placed immediately after baseline recordings (T0). *p<0.05 *vs* T0.

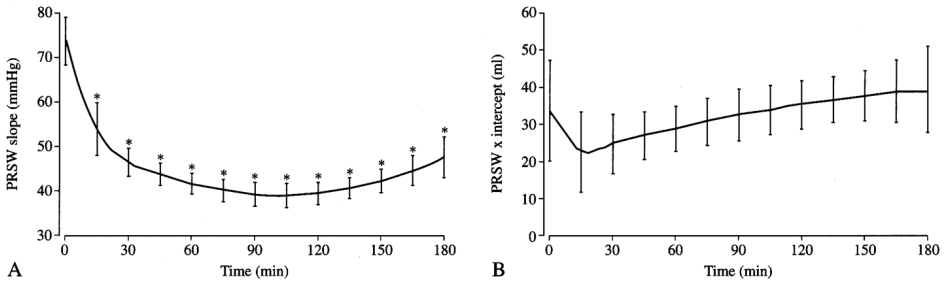

Fig. 7.—Evolution of the stroke work (SW) - end-diastolic volume (V_{ed}) relation (preload recruitable stroke work, PRSW) during myocardial ischemia, induced by ligation of the LAD coronary artery. The ligation was placed immediately after baseline recordings (T0). A) PRSW slope, slope of the SW-V_{ed} relation; B) PRSW x intercept, intercept of the SW-V_{ed} relation with the x axis. *p<0.05 *vs* T0.

increased to reach 2.55±0.22 mmHg/ml at T180 (NS *vs* T90). The insignificant changes in V_0 are illustrated in Figure 6.

The decrease of LV contractility was also appreciated by the significant (p<0.001) narrowing of the slope of the SW-V_{ed} relation (Figure 7). In addition, end-systolic pressure P_{es} and the dP/dt_{max} index showed a parallel evolution, with a significant (p<0.001) drop between baseline and T15 (Figure 8).

Systemic ventriculo-arterial coupling E_{es}/E_a was severely altered, decreasing from 1.22±0.11 to 0.44±0.07 between baseline and T15 (p<0.001). The coupling between the LV and the systemic vasculature remained seriously altered during the 180 minutes of ischemia (Figure 6).

Stroke work SW and pressure-volume area PVA respectively decreased from 4053±223 to 2580±122 mmHg.ml (p<0.001), and from 5575±514 to 4813±314 mmHg.ml (NS), between baseline and T15. As a consequence, mechanical efficiency (SW/PVA) became lower from 0.76±0.04 to 0.57±0.03, a 25% decrease between baseline and T15 (p<0.001). Subsequently, SW, PVA, and SW/PVA did not significantly changed (Figure 9).

Discussion

This study, conducted in anesthetized pigs, investigated the effects of regional myocardial ischemia

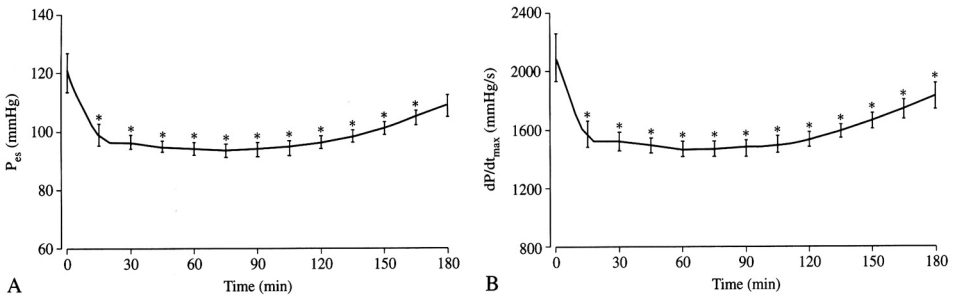

Fig. 8.—A) Evolution of end-systolic pressure (P_{es}), and B) dP/dt_{max} during myocardial ischemia, induced by ligation of the LAD coronary artery. The ligation was placed immediately after baseline recordings (T0). $p<0.05$ *vs* T0.

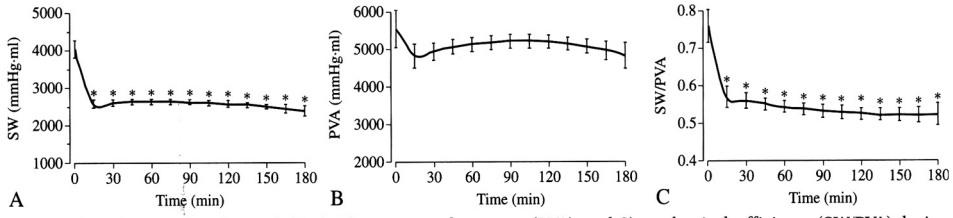

Fig. 9.—A) Evolution of stroke work (SW), B) pressure-volume area (PVA), and C) mechanical efficiency (SW/PVA) during myocardial ischemia, induced by ligation of the LAD coronary artery. The ligation was placed immediately after baseline recordings (T0). *$p<0.05$ *vs* T0.

on global LV function and on the coupling between the LV and the systemic vasculature.

Analysis of ventricular pressure-volume relations showed that ligation of the LAD coronary artery induced a decrease in end-systolic elastance, associated with a progressive rightward shift of the pressure-volume loops. The decrease in stroke work without significant change in pressure-volume area was responsible for a severe alteration in mechanical efficiency.

The augmentation of effective arterial elastance, associated with the decrease of end-systolic elastance induced a spectacular ventriculo-arterial mismatch. Analysis of aortic pressure and flow waveforms by the 4-element windkessel model suggested that the augmentation of E_a was due to an early increase in peripheral resistances, later combined with a decrease in arterial compliance. Inductance and characteristic impedance did not significantly change in the same interval.

Left ventricular function

Kass *et al.*[19] showed that coronary occlusion, during percutaneous coronary angioplasty in humans, significantly altered systolic and diastolic chamber function. Systolic dysfunction was characterized by a rightward shift of the end-systolic pressure-volume relation, particularly marked for proximal LAD occlusions. In addition, they showed that coronary occlusion also narrowed chamber systolic function indices, such as the end-systolic pressure-volume relation slope and preload recruitable stoke work.[19]

Other studies in isolated canine ventricles [20] and in closed-chest [21] and open-chest dogs [22] have reported rightward shifts of the ESPVR with acute regional ischemia. The magnitude of this shift varied directly with the extent of ischemic myocardium.

Earlier studies with coronary occlusion in isolated [20] and *in vivo* [21] canine hearts have shown little changes in ESPVR slope. However, in a more

recent *in vivo* canine study, Kass *et al.*[22] found that end-systolic elastance was frequently reduced, with a strong correlation between the amount of reduction and the baseline elastance value. The higher the baseline value, the larger the reduction of elastance during ischemia.

In our experimental study, we found that, in addition to a rightward ESPVR shift, occlusion of mid-LAD resulted in a significant decrease in ESPVR slope (end-systolic elastance). This change was mirrored by reductions in other accepted index of myocardial contractility,[23] such as the preload recruitable stroke work, and the relation between dP/dt_{max} and end-diastolic volume.

In contrast to the often qualitative assessment of abnormal wall motion and regional function, typically using echocardiography, we used quantitative methods to assess global function. Regional measurements have been shown effective, however, it should be kept in mind that wall thickening is clearly load-dependent and may improve substantially when afterload is reduced. In contrast, the systolic pressure-volume relations used in this study have been shown to be relatively load-independent and therefore, despite the fact that the original simple concept is disputed,[24, 25] can be considered to reflect mainly myocardial properties.[23, 26-28]

Myocardial energetics

Pressure-volume area (PVA) represents the amount of energy generated by the left ventricle and is defined as the sum of external mechanical work, or stroke work, and of potential energy necessary to overcome the viscoelastic properties of the myocardium itself.[12] It is accepted that PVA is directly correlated with myocardial oxygen consumption.[12, 13] In our study, coronary occlusion induced a significant diminution of stroke work. Because pressure-volume area did not significantly change, potential energy increased. This resulted in a severe alteration of mechanical efficiency.

Ventriculo-arterial coupling

Using the conductance catheter technique, Seki *et al.*[29] assessed, in anesthetized open-chest dogs, the evolution of left ventriculo-arterial coupling during acute myocardial ischemia. They found that, during regional ischemia, ESPVR shifted to the right while E_{es}/E_a and work efficiency (SW/PVA) decreased. In their study, the decrease of E_{es}/E_a was mainly due to an augmentation of E_a. However, because E_a was calculated as the ratio of stroke volume to end-systolic pressure, they were unable to differentiate the effects of vasoactive peripheral adaptations, of from those on arterial compliance or characteristic impedance. Indeed, E_a incorporates the principal elements of vascular load, including peripheral resistances, arterial compliance and characteristic impedance. Theoretically, a given augmentation of E_a can result from either peripheral vasoconstriction or decrease in arterial compliance or a combination of both. It is interesting to note that the consequences of such specific changes may affect cardiac pumping function differently.[3, 30]

In our study, we found changes in ESPVR and work efficiency that were similar to the results reported by Seki *et al.*[29] However, in our study, the important decrease of the E_{es}/E_a ratio was due to an augmentation of E_a combined with a decrease of E_{es}. In this regard, our results differed from those reported by Seki *et al.*,[29] where end-systolic elastance remained unaltered.

In addition, in order to further study the underlying mechanisms explaining the augmentation of E_a, we applied the 4-element windkessel model which provides a detailed analysis of mechanical aortic properties. Such an application enabled us to suggest that the augmentation of E_a was due to an increase in peripheral resistance. This variation occurred early and was later combined with a decrease in arterial compliance. During the same interval, inductance and characteristic impedance remained unchanged.

Clinical implications

Because the augmentation of arterial elastance is due to a combination of vasoconstriction and decrease in vascular compliance, the management of ventriculo-arterial mismatch accompanying acute myocardial ischemia should include not only vasodilators, but also drugs that have been shown to improve vascular compliance, such as dobutamine.[29] Furthermore, in addition to its vascular properties, dobutamine improves LV contractility, but at a cost of significantly increased myocardial oxygen consumption.

Another therapeutic approach for restoring ventriculo-arterial coupling during acute myocardial ischemia is intra-aortic balloon contrepulsation. Such treatment not only increases myocardial contractility through coronary blood flow augmentation, but also decreases LV afterload through a mechanism of increased vascular compliance and vasodilatation.[31] In addition, the augmentation of cardiac performance occurs without increased myocardial oxygen consumption.

Conclusions

Acute coronary occlusion induced a decrease of end-systolic elastance, associated with a progressive rightward shift of pressure-volume loops. The decrease in stroke work, without significant variations in pressure-volume area severely altered mechanical efficiency.

The augmentation of effective arterial elastance associated with a decrease of end-systolic elastance was responsible for a severe alteration of left ventriculo-arterial coupling. Analysis of aortic pressure and flow waveforms using the 4-element windkessel model showed that the augmentation of E_a was due to an early augmentation of peripheral resistances, later combined with a decrease of arterial compliance. Other arterial properties, such as characteristic impedance and inductance, did not significantly change.

Treatment of acute myocardial ischemia should therefore not only be directed to the use of drugs known to increase LV contractility, but also aimed at reducing arterial elastance.

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