Published in: European Journal of Cardio-Thoracic Surgery (2000), vol.17 iss. 3, pp.272-278
Status: Postprint (Author's version)

Increased aortic compliance maintains left ventricular performance at lower energetic cost[1]

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Abstract

Objective: The aim of this study was to investigate left ventricular contractility and energetic cost of cardiac ejection under conditions of acute increase in aortic compliance. **Methods:** In six anaesthetized pigs, ascending aortic compliance was increased by adding a volume chamber in parallel to the ascending aorta. Systemic vascular parameters, including characteristic impedance, peripheral resistance, total vascular compliance, and inertance, were estimated with a four-element windkessel model. Arterial elastance was derived from these parameters. Left ventricular systolic function was assessed by end-systolic pressure-volume relationship (end-systolic elastance), and stroke work. Pressure-volume area was used as a measure of myocardial oxygen consumption. Heart rate remained constant during the experimentation. **Results:** Adding the aortic volume chamber significantly increased vascular compliance from 0.95 ± 0.08 to 1.17 ± 0.06 ml/ mmHg ($P < 0.01$), while inductance, characteristic impedance, peripheral resistance, and arterial elastance remained statistically at basal values, respectively 0.0020 ± 0.0003 mmHg.s^2/ml, 0.105 ± 0.009 mmHg.s/ml, 1.27 ± 0.12 mmHg.s/ml, and 2.43 ± 0.21 mmHg/ml. During the same interval, stroke work and pressure-volume area decreased respectively from 2700 ± 242 to 2256 ± 75 mmHg.ml ($P < 0.01$), and from 3806 ± 427 to 3179 ± 167 mmHg.ml ($P < 0.01$). Stroke work and pressure-volume area decreased at matched end-diastolic volumes. In contrast, end-systolic elastance, ejection fraction, and stroke volume remained statistically unchanged, respectively at 2.29 ± 0.14 mmHg/ ml, 48.1 ± 2.1 %, and 32.4 ± 1.7 ml. **Conclusions:** These data suggest that, when facing an increased aortic compliance, the left ventricle displays unchanged contractility, but the energetic cost of cardiac ejection is significantly decreased. These data may be of clinical importance when choosing an artificial prosthesis for ascending aortic replacement.

Keywords: Aortic compliance; Contractile function; Hemodynamics; End-systolic elastance; Pressure-volume area; Pigs

1. Introduction

Surgery is often requested for thoracic aortic replacement because of aneurysmal disease, acute dissection, or trauma. However, only few data have focused on the consequences of changes in aortic properties on cardiac contractility and on the energetic cost of ventricular ejection.

In physiological conditions, the left ventricle and its after-load are a matched system. It has been demonstrated that optimal ventriculovascular coupling is reached when a maximum energy, or stroke work, is transferred to the vascular tree [1]. In contrast, maximum efficiency occurs when a minimal oxygen consumption is achieved for a given stroke work [1].

Previous publications have evidenced that the efficiency of normal hearts is not altered by ejection into a stiff vascular system [2,3]. However, the energetic cost to the heart for maintaining adequate flow in such conditions is increased. In addition, Burkhoff et al. [4] have also suggested that lowering vascular resistance has positive effects on both contractility and efficiency.

The question remains to be answered, however, as to if an increase in aortic compliance alone, independent of any associated changes in resistance to flow, may influence left ventricular contractility or the energetic cost of cardiac ejection. Indeed, despite the widespread opinion that an increase in aortic compliance may be responsible for significant facilitation of cardiac ejection, evidence with precise in situ measurements of the magnitude of this interaction has not been provided.

The purpose of the present study was to determine in situ whether an acute increase in compliance of the proximal aorta affects positively ventricular contractility, or the energetic cost of cardiac ejection. Chamber

[1] Presented at the 13th Annual Meeting of the European Association for Cardio-thoracic Surgery, Glasgow, Scotland, UK, September 5-8, 1999

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

2. Material and methods

2.1. Preparation

The investigation conforms to 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 Liège. Experiments were performed on six 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). Anaesthesia was then induced and maintained by a continuous infusion of sufentanil (0.5 µg/kg per h) and sodium pentobarbital (3 mg/kg per h). After endotracheal intubation through a cervical tracheostomy, the pigs were connected to a volume-cycled ventilator (Evita 2, Dräger, Lübeck, Germany) set to deliver a tidal volume of 15 ml/kg at a respiratory rate of 20/min. End-tidal pCO_2 measurements (Capnomac, Datex, Helsinki, Finland) were used to monitor the adequacy of ventilation. Respiratory settings were adjusted to maintain end-tidal pCO_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 per h. 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 midline sternotomy, the pericardium was incised and sutured to the chest wall to form a cradle for the heart, and the root of the ascending aorta was dissected clear of adherent fat and connective tissue. A 7F, 12-electrode (8 mm interelectrode distance) 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) 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) 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) was advanced into the inferior vena cava through a right femoral venotomy. Inflation of this balloon produced a titrable gradual preload reduction. Thrombus formation along the catheters was prevented by administration of 100 U/kg of heparin sodium intravenously just before the insertion.

A 60-cc air chamber was connected to a short canula whose tip was placed in the ascending aorta, perpendicular to the blood flow, and distal to pressure and flow probes. The canula was fixed with two purse string sutures. A representation of so used compliant system, with the instrumentation, is displayed in Fig. 1.

2.2. Experimental protocol

In order to obtain similar states of vascular filling, the animals were infused, when necessary, with a 10% low molecular weight dextran to increase central venous pressure up to 6-7 mmHg over 30 min. Baseline hemodynamic recordings were obtained thereafter from simultaneous measurements of aortic pressure and flow signals necessary to identify parameters of the four-element windkessel model. A first diagram of left ventricular pressure-volume relationship was generated from volume and pressure measurements during gradual decreases in preload by reducing venous return. The caval 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 min. Hemodynamic measurements were then repeated after the aortic compliant air chamber was in operation. For each animal, three measurements were taken at basal state, and three with the compliant chamber in place.

The conductance catheter was connected to a Sigma-5 signal-conditioner processor (Cardiodynamics, Zoetermeer, The Netherlands). 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 system (Codas, DataQ Instruments Inc., Akron, OH), on an IBM-compatible microcomputer at a sampling frequency of 200 Hz and saved on a hard disk for subsequent analysis.

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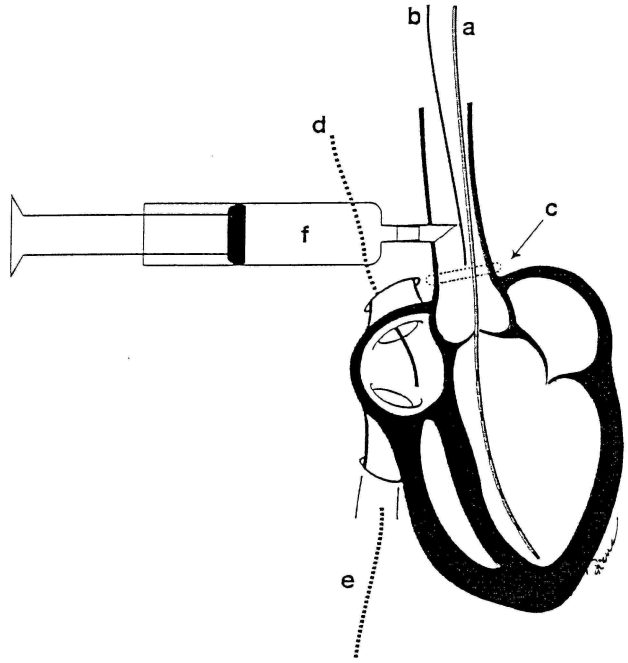
Fig. 1: *Schematic diagram of the surgical compliant preparation, (a) Left ventricular conductance micromanometer-tipped catheter; (b) central aortic micromanometer-tipped catheter; (c) aortic flow probe; (d) right atrial micromanometer-tipped catheter; (e) inferior vena cava Fogarty balloon catheter; (f) compliance chamber.*



2.3. Data analysis

2.3.1. Ventricular systolic function

Left ventricular volumes were inferred using the dual field conductance catheter technique [5,6]. Calibration of the conductance signal to obtain absolute volume was performed by the hypertonic saline method [5]. Therefore, a small volume (1-2 ml) of 10% NaCl solution was injected into the pulmonary artery during continuous data acquisition.

Left ventricular contractile function was assessed by the end-systolic pressure-volume relation, and the stroke work.

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

$$E(t) = P(t)/\left[V(t) - V_{\mathrm{d}}\right] \qquad (1)$$

Where $P(t)$and $V(t)$are, respectively, the instantaneous ventricular pressure and volume, and V_{d} a correction term. V_{d} was calculated by an iterative technique [7]. End-systole (es) was defined as the instant of time in the ejection phase at which $E(t)$reaches its maximum, $E_{\max}$ [8]. It has been demonstrated that $E(t)$and V_{d} are relatively insensitive to preload, at least within physiological ranges [9]. Preload was acutely reduced by inflating the inferior vena cava balloon catheter.

Stroke work (SW) was calculated as the area of each pressure-volume loop and was plotted versus end-diastolic volume (EDV, volume at the lower right corner of the loop) to generate the SW/EDV relation. These relations were highly linear and fit by least-squares regression. Slope and EDV 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/EDV relationship corresponding to that animal in a specific state. EDV was considered to be the independent variable, and SW the dependent variable. To obtain composite SW/EDV plots for the pigs as a group, SW interpolated from the regression equations from individual pigs were averaged at 6-ml intervals of EDV.

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2.3.2. Myocardial energetics

Myocardial energetics was assessed by computation of the 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 [10], and denoted by PVA [11]. It has been demonstrated that PVA is highly correlated with myocardial oxygen consumption [12].

PVA-EDV relationships were obtained by using the same method as described for the composite SW-EDV plots.

2.3.3. Arterial properties

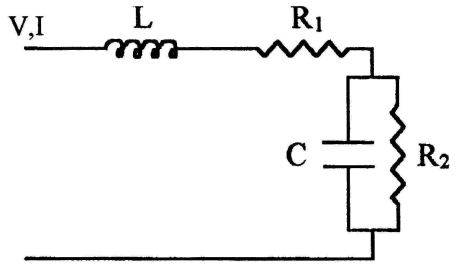
The properties of the arterial system were assessed from pressure and flow measured in the ascending aorta and represented by a four-element windkessel model (WK4) [13]. This lumped model was chosen because of its potential to provide quantitative assessment of the mechanical properties of the systemic vasculature, including aortic compliance, peripheral vascular resistances, characteristic impedance, and inductance. An electric analog of the WK4 is displayed in Fig. 2. 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 is used to reflect characteristic impedance, which depends mainly on the elastic properties of the aorta. Finally, an inductance, L, is introduced to take blood inertia into account. Further, the inductance leads to positive phase angles in the impedance spectrum [14]. The values *of* R_1, R_2, C, and L were estimated by a method previously described [15].

Effective arterial elastance *(*E_a*)* was calculated according to the following equation [9]:

$$E_a = \frac{R_1 + R_2}{T_s + R_2 C\left(1 - e^{-R_2 C/T_d}\right)} \qquad (2)$$

where T_s and T_d are the systolic and diastolic time intervals, respectively. T_s was calculated from the aortic pressure wave, as the time interval between the point just before the abrupt rise and the dicrotic notch. Ventriculo-arterial coupling was quantified by the ratio E_{es}/E_a. It has been demonstrated that maximal SW is achieved when $E_{es}/E_a = 1$ [1].

Fig. 2: *Electric analog of the four-element windkessel model.* R_1 *characteristic impedance;* R_2*, peripheral resistance; C, compliance; L, inductance.*



2.3.4. 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 two-way analysis of variance (fixed effects) with the pig as first effect, and the experimental condition as second effect. When the F ratio of the analysis of variance reached a $P < 0.05$ level, comparisons were made with the Scheffé test [16].

3. Results

The measured and calculated vascular variables during the baseline period and following inclusion of the air chamber in parallel to the ascending aorta are summarized in Table 1. Adding the compliant chamber resulted in slight but statistically significant decreases in systolic pressure, pulse pressure, and mean blood pressure, while heart rate and cardiac output, remained unchanged, as expressed in Table 2.

Fig. 3: displays an example of aortic pressure and flow waveforms and ventricular pressure-volume loops in basal state and with the compliant aortic chamber in place. Aortic flow waveforms are similar in both conditions, but the aortic pressure curve is more rounded, with a decreased systolic peak, when the compliant chamber is in place. In such condition, the pressure-volume loop displays a square shape, with decreased end-systolic pressure and leftward shift.

The windkessel parameters R_1, R_2, and L were not changed by including the compliant chamber, but compliance C was increased by 23 % ($P < 0.001$). However, despite such an increase, the effective arterial elastance E_a remained statistically unchanged (Table 1).

Table 1: *Vascular consequences of aortic parallel air chamber*[a]

Variable	Basal state	Compliant state
P_{syst} (mmHg)	90 ± 5	85 ± 2*
P_{dia} (mmHg)	58 ± 5	56 ± 2
P_{pulse} (mmHg)	32 ± 5	29 ± 2*
P_{mean} (mmHg)	74 ± 5	70 ± 2*
L (mmHg.s^2/ml)	0.0020 ± 0.0003	0.0026 ± 0.0003
R_1 (mmHg.s/ml)	0.105 ± 0.009	0.113 ± 0.005
R_2 (mmHg.s/ml)	1.27 ± 0.12	1.28 ± 0.07
C (ml/mmHg)	0.95 ± 0.08	1.17 ± 0.06*
E_a (mmHg/ml)	2.43 ± 0.21	2.40 ± 0.13

[a] Data are expressed as mean ± SEM; $n = 6$; P_{syst}, systolic pressure; P_{dia}, diastolic pressure; P_{pulse}, pulse pressure; P_{mean}, mean arterial pressure; L, inductance; R_1 characteristic impedance; R_2, peripheral resistance; C, vascular compliance; E_a, effective arterial elastance. *Significantly ($P < 0.05$) different from measurements with native aorta.

Table 2: *Ventricular and energetic consequences of aortic parallel air chamber*[a]

Variable	Basal state	Compliant state
CO (ml/s)	55 ± 4	51 ± 2
HR (beats/min)	101 ± 4	99 ± 2
SV (ml)	32.4 ± 1.7	30.7 ± 0.8
EF (%)	48.1 ± 2.1	51.6 ± 1.3
EDV (ml)	71 ± 6	64 ± 4
ESP (mmHg)	90.5 ± 6.8	79.5 ± 2.9*
E_{es} (mmHg/ml)	2.29 ± 0.14	2.42 ± 0.12
V_d (ml)	-0.42 ± 0.14	-1.47 ± 0.20
E_{es}/E_a	0.94 ± 0.12	1.0 ± 0.1
SW (ml.mmHg)	2700 ± 242	2256 ± 75*
PVA (mLmmHg)	3806 ± 427	3179 ± 167*

[a] CO, cardiac output; HR, heart rate; SV, stroke volume; EF, ejection fraction; EDV, end-diastolic volume; ESP, end-systolic pressure; E_{es}, end-systolic elastance; V_d, volume intercept; E_a, effective arterial elastance; SW, stroke work; PVA, pressure-volume area. Data are expressed as mean ± SEM; $n = 6$. *Significantly ($P < 0.05$) different from measurements with native aorta.

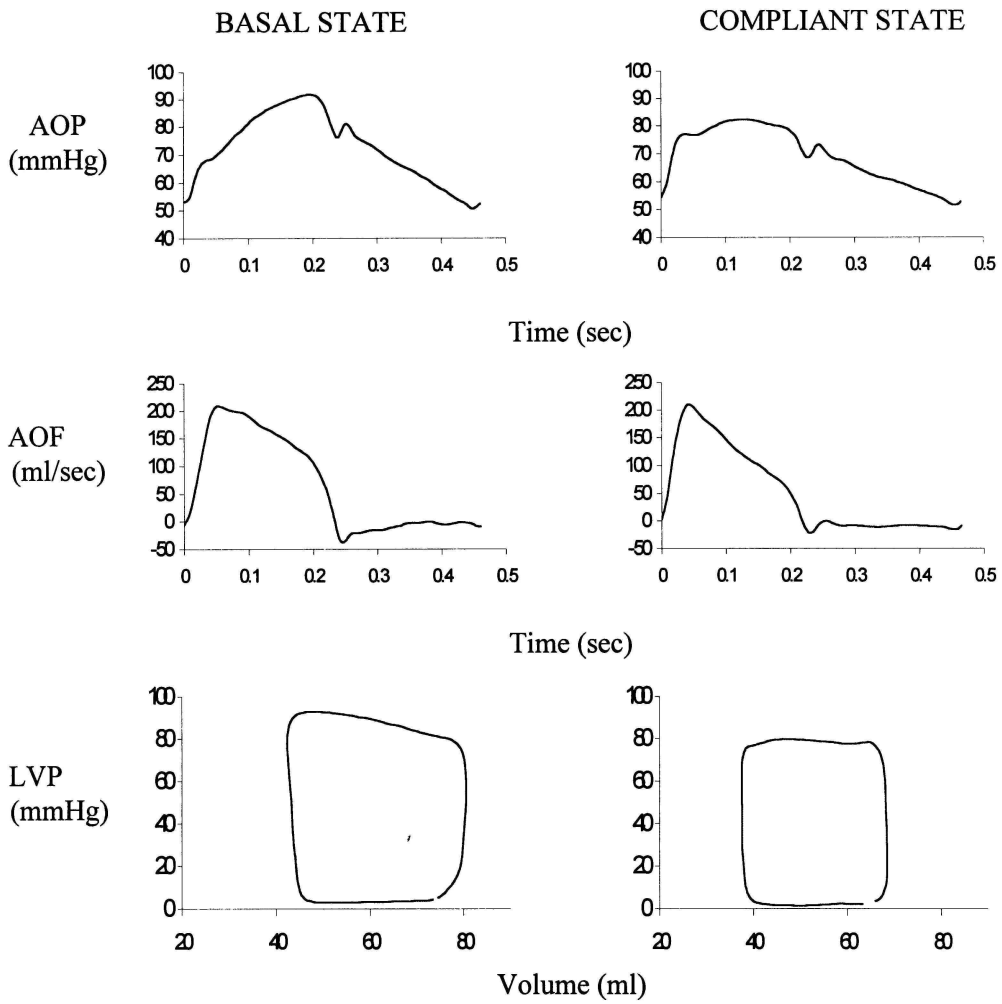
Fig. 4 shows an example of ventricular pressure-volume loops generated by graded reduction of venous return in basal and in compliant states. Adding a compliant chamber did not lead to significant changes neither in left ventricular contractility, appreciated through E_{es}, nor in ejection fraction (EF) (Table 2). The decrease in end-diastolic volume (EDV) was not statistically significant. The coupling between the left heart and the systemic vasculature (E_{es}/E_a) remained at the same level. But the energetic cost of left ventricular ejection, evaluated by PVA, was dramatically reduced by 27 % with the compliant chamber in place, mainly because of a significant decrease in SW (Fig. 5). At a same EDV, SW and PVA were significantly lowered by adding the compliant chamber (Fig. 6).

4. Discussion

This study investigated, on anaesthetized pigs, the effects of an acute increase in proximal aortic compliance on left ventricular contractility and on the energetic cost of cardiac ejection. Aortic pressure and flow waves analysis with the four-element windkessel model evidenced that including a compliant chamber in parallel to the ascending aorta resulted in increased vascular compliance, while characteristic impedance, peripheral resistance,

inertance, and effective arterial elastance remained at baseline values. Facing this particularly compliant environment, the left ventricle displayed unchanged contractility. Cardiac output remained at the same level as during the control period but, interestingly, the energetic cost of pump working, measured by PVA, was drastically reduced. The significant decreases in SW and in PVA with the compliant chamber in place were observed at matched EDV, suggesting that this was not solely a Starling effect.

Fig. 3: *Typical examples of aortic pressure (AOP) waveforms (top panels), aortic flow (AOF) waveforms (middle panels), and left ventricular pressure (LVP)-volume loops (bottom panels) in basal and compliant conditions.*



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 [11]. It is accepted that PVA is directly correlated with myocardial oxygen consumption [12].

The decrease in PVA that we observed was mostly due to decrease in SW. According to Sagawa et al. [9], SW can be calculated using the following equation:

$$\mathrm{SW} = E_a\left[(\mathrm{EDV} - V_d)/(1 + E_a/E_{es})\right]^2 \qquad (3)$$

Applying measured values for E_a, EDV, V_d, and E_{es} (Table 2) to Eq. (3), calculated values for SW are 2750 mmHg.ml at basal state, and 2590 mmHg.ml with the compliant chamber in place. Correlation with measured values is excellent at baseline, but not in compliant state (Table 2). That means that the slight, not statistically significant, decrease in EDV observed from basal to compliant state is not sufficient to explain such a decrease in SW. This is further demonstrated by Fig. 6: for the same EDV, both SW and PVA are decreased in the

compliant state. Such a decrease in SW at constant EDV, without changes neither in contractility nor in effective arterial elastance, can be explained by the change in the ejection pattern (Fig. 3) with the compliant chamber in place.

The arterial system acts as an hydraulic filter to minimize the work load of the heart by damping the fluctuations in pressure and flow arising from intermittent output [17,18], and by uncoupling the left ventricle from high-resistance terminal arterioles [17,19,20].

In an earlier study reported by Kelly et al. [2], markedly decreased aortic compliance owing to diversion of blood flow through a graft conduit was associated with an inevitable increase in characteristic impedance. In these conditions, neither indexes of chamber systolic function nor efficiency were altered, but systolic arterial pressure and the cardiac energetic cost of delivering a given stroke volume were significantly augmented.

Fig. 4: *Typical examples of pressure-volume relations in basal and compliant conditions. LVP, left ventricular pressure.*

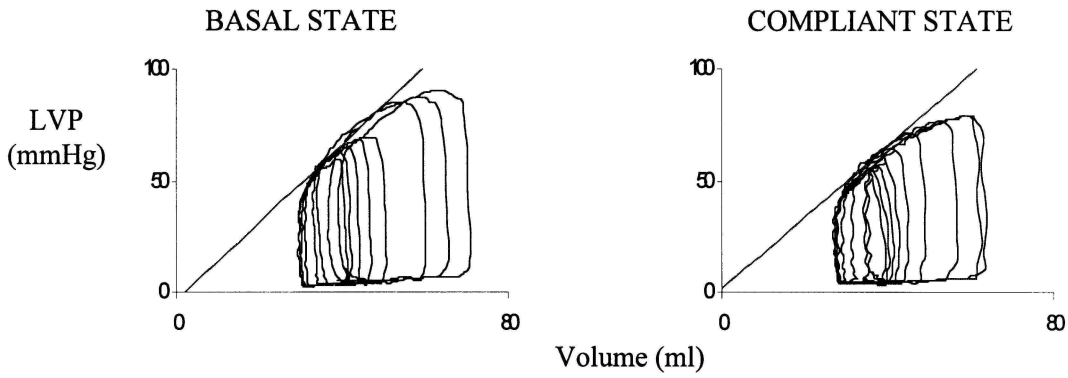


Fig. 5: *Typical examples of stroke work (SW) and pressure-volume area (PVA) in basal and compliant conditions. LVP, left ventricular pressure.*

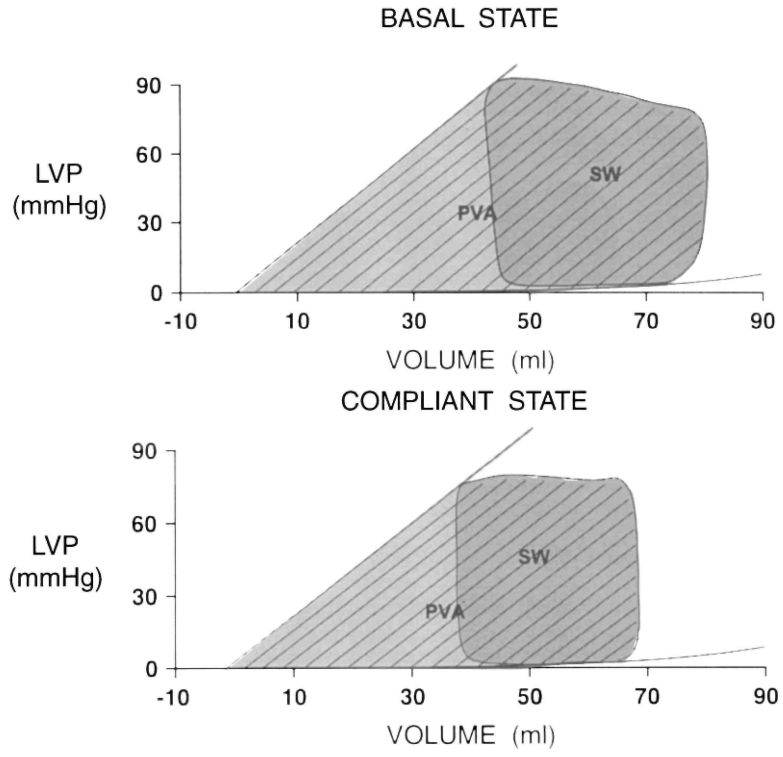
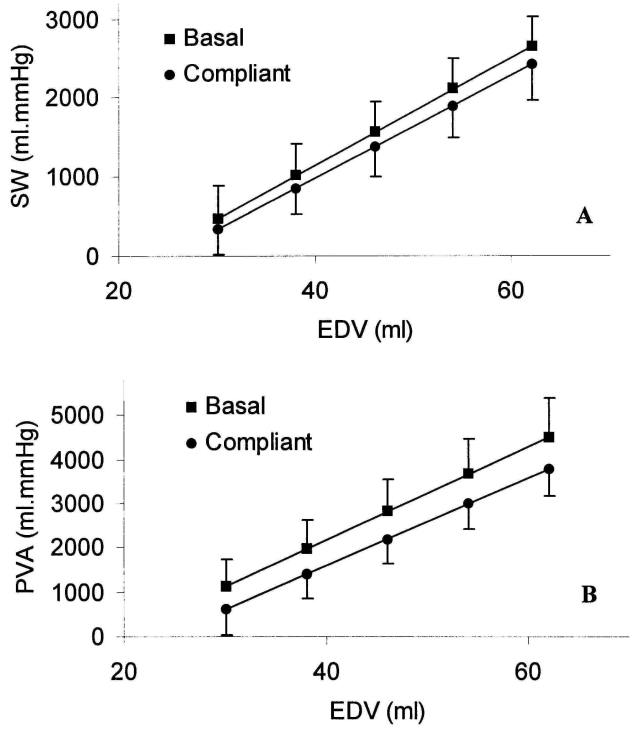


Fig. 6: *(A) Composite stroke work (SW)-end-diastolic volume (EDV) plots (n = 6) in basal state (slope = 68.3 mmHg; intercept = 23 ml) and in compliant state (slope = 65.2 mmHg; intercept = 25 ml). (B) Composite pressure-volume area (PVA)-end-diastolic volume (EDV) plots (n = 6) in basal state (slope = 105.6 mmHg; intercept =19 ml) and in compliant state (slope = 99.6 mmHg; intercept = 24 ml).*



To our knowledge, there has been no in vivo study that has attempted to evaluate the effects of a known *increase* in aortic compliance on left ventricular contractility or on the energetic cost of cardiac ejection. The design of our study allowed reliable measurements of vascular compliance. It should be emphasized, however, that all existing methods of estimating arterial compliance are based on windkessel models. It is therefore impossible to validate these model-derived estimates using alternative, in vivo approaches, which are unable to provide absolute values for compliance.

The attachment of an air chamber to the ascending aorta increased, as expected, the total arterial compliance, and provided results that mirrored the data obtained by Kelly et al. [2]. Furthermore, our results evidenced that augmentation of aortic compliance reduced the systolic load through a mechanism of buffering the elevation of blood pressure during ejection.

With the compliant chamber in place, aortic pressure rose more slowly, as compared to basal conditions. This implies that, for the same stroke volume, the systolic time interval increased and that, at constant heart rate, the diastolic time interval decreased. This explains how E_a remained unchanged, despite significant change in aortic compliance.

Finally, peripheral resistance remained unchanged. This suggests that introducing the compliant chamber does not induce changes in blood pressure of enough significance to trigger baroreflex intervention. This is consistent with the observed insignificant effects on heart rate.

In conclusions, the present study shows that in normal hearts, the effects of solely increased aortic compliance on contractile function are minimal, but the energetic cost of pump working is significantly reduced under such conditions. The interested topic of clinical importance would be the application of the experimental model to test different aortic prostheses regarding their impact on aortic compliance. Thus the contribution of aortic grafts to an increased work load and oxygen demand could be analyzed, with clinical relevance in patients with reduced coronary reserve who need aortic replacement surgery. In these patients, our results suggest that a soft, more compliant prosthesis would be beneficial. However, further investigations are needed to address more specifically the interactions between aortic compliance and diseased hearts, with reduced coronary reserve.

Acknowledgements

This work was supported by grants from the ARC 94/99-177 of the Communauté Française de Belgique, from the Caisse de Prévoyance des Médecins, and from the Leon Fredericq Foundation, University of Liège.

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