Assessment of the viscosity of the pulmonary artery wall

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ABSTRACT: Large artery wall viscosity reduces the efficiency of heart/vessel coupling. The aim of the present study was to assess pulmonary artery wall viscosity through comparison of the static (D_{st}) and dynamic distensibility (D_{dyn}) of the vessel wall.

Right pulmonary artery pressure and diameter was measured in 13 patients and eight healthy volunteers. D_{dyn} was calculated as the relative change in end-diastolic diameter induced by the pressure pulse, and D_{st} as the relative change in mean diameter induced by the change in mean pressure during steady-state exercise.

D_{st} did not differ significantly from D_{dyn} (mean $\pm$ SD 22.8 $\pm$ 19.2 versus 21.0 $\pm$ 18.3 10⁻³ mmHg⁻¹), as tested by paired t-test and analysis of covariance, with age as covariant. End-diastolic diameter increased, whereas D_{st} and D_{dyn} decreased as a function of age ($r=-0.69$ and -0.67 , respectively; $p<0.01$ for both). D_{dyn} did not change from rest to exercise in spite of a 23 $\pm$ 16-beats $\cdot$ min⁻¹ increase in cardiac frequency.

Pulmonary artery wall viscosity was negligible and no increase in wall viscosity occurred during cardioacceleration.

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The arterial wall responds to stress through both elastic and viscous behaviour, the former being related to the elastin and the latter to the collagen and smooth muscle content of the vessel wall [1, 2]. During systole, the elastic behaviour of the arterial wall allows its diameter to increase proportionally to pressure; in the case of a purely elastic arterial wall, the total amount of energy stored would be released during diastole. In reality, however, part of the energy that corresponds to viscous deformation is dissipated within the arterial wall. Wall viscosity reduces the efficiency of heart/vessel coupling, and may place extra load on the ventricle [3].

Wall viscosity is responsible for the difference that exists between the static (D_{st}) and dynamic distensibility (D_{dyn}) of a given vessel [1, 2, 4, 5]. Under static conditions, the change in diameter in response to a given change in distending pressure is determined only by the elastic properties of the vessel wall. Under dynamic conditions, however, when changes in pressure are pulsatile and the time available for distension is limited, wall viscosity impedes distension, resulting in less change in diameter for the same change in pressure [6]. The greater the wall viscosity, the greater the difference between D_{st} and D_{dyn} . D_{st} has been found to be considerably higher than D_{dyn} in systemic arteries, the difference being accounted for by wall viscosity [1, 2, 4, 5].

Information on pulmonary artery wall viscosity is limited and controversial. In the perfused dog lungs, the slope of the static curve relating volume to pressure (*i.e.* lung compliance) was found to be 1.5 times steeper than that of the dynamic curve [7], indicating considerable vessel wall viscosity. In humans, no direct comparison of D_{st} and D_{dyn} of the pulmonary artery has been made, but

the close similarity of pressure and diameter curves recorded from the pulmonary artery has been taken as a sign of low vessel wall viscosity [8]. The age dependence of pulmonary arterial wall distensibility is another controversial issue. Although *in vitro* studies have shown that the pulmonary arterial wall stiffens with age [9, 10], *in vivo* studies have produced equivocal results; a negative correlation between pulmonary compliance and age was reported in one study [11] but no such relation was found in another [12].

In view of the above uncertainties, the relationship between D_{st} and D_{dyn} of the right main pulmonary artery and its age dependence was studied. D_{dyn} was determined from the pressure/diameter relationship during the cardiac cycle, whereas static (or, rather, quasistatic) distensibility was determined using changes in mean pulmonary artery pressure (MPAP) and diameter during physical exercise.

Material and methods

The study population consisted of 21 subjects, 13 patients and eight healthy volunteers, selected from a larger population of 50 subjects. Originally these 50 subjects had volunteered to participate in a study designed to investigate the effect of nitric oxide inhalation on pulmonary arterial pressure. This protocol included the use of Millar catheter for pressure recording. The opportunity to use noninvasive wall-tracking echo equipment after the Millar catheter was introduced but before NO inhalation started was given. Subjects for the present project were selected on the basis that right pulmonary artery diameter and distension could be measured using the

vessel wall-tracking method, as discussed later. Six females and seven males (34–82 yrs) were recruited from among patients undergoing electrophysiological investigation at the Department of Cardiology of the National Korányi Institute of Pulmonology. All of them were free of clinical symptoms of pulmonary hypertension or lung disease. Their cardiac diagnoses were as follows: cardiomyopathy (five patients), aortic stenosis and insufficiency (four), mitral insufficiency (four), tricuspid insufficiency (three) and status after myocardial infarct (four). The mean time interval between myocardial infarction and the present study was six yrs. All patients were in sinus rhythm and breathing spontaneously during the study. Eight healthy volunteers (four females and four males; 21–25 yrs) were also examined using the same protocol. They were recruited from among the staff of the Semmelweis Medical University and medical students. These subjects were free of clinical evidence of pulmonary hypertension or coronary artery, valvular heart or lung diseases. All subjects gave written informed consent to participate in the study, which was approved by the Ethical Committee of the Scientific Health Council, Budapest, Hungary.

Right heart catheterization and pulmonary artery pressure measurement

All subjects underwent right heart catheterization without premedication in the supine position. A catheter tip micromanometer (Millar SPC-340; size 4 F, Houston, TX, USA) was introduced into the right main branch of the pulmonary artery under fluoroscopic guidance, using standard procedures. Measurements were referred to as zero level at 5 cm below the sternal angle. All catheterization was carried out by the same operator, and no complications were observed during the procedure.

Ultrasonographic measurements

Pulmonary artery diameter and distensions were measured by means of ultrasonography. Measurement of pulmonary artery dimensions was made ≥ 15 min after catheterization. The ultrasound device consisted of a vessel wall-tracking system (WTS) combined with a conventional ultrasound scanner (Scanner 200; Pie Medical, Maastricht, the Netherlands), which has previously been described in detail [13, 14]. In brief, the pulmonary artery was visualized, at first in two-dimensional mode, and then the ultrasound system was switched to M mode and ultrasound was emitted and received along a selected M line visible on the echo-screen. The WTS is a data acquisition system capable of capturing the received and amplified radio frequency (RF) signals. After completion of data acquisition, the data were transferred to a personal computer. The first line acquired was then presented graphically on a display, allowing manual identification of the anterior and posterior boundaries by placing two markers that represent the sample windows for data processing. In order to extract the change in position of either the anterior or the posterior wall, the approach based on the cross-correlation model for corresponding segments of subsequent RF lines was applied. In order to ensure that the signals returned by the same structure

were always considered, the position of the sample windows was adjusted according to the observed displacements (tracking window). The difference between the displacements of signals of the anterior and posterior walls yielded the change in diameter as a function of time, *i.e.* the distension waveform. The minimum distance between the wall signals was defined as the diastolic diameter. Imaging of the right main branch of the pulmonary artery was performed from the suprasternal notch, using a 3.5-MHz mechanical sector transducer, with the subjects in the supine position. A standard limb lead electrocardiogram (ECG) was recorded to obtain R-waves that served as a trigger for activation of the WTS algorithm. Respiration was monitored using inductive plethysmography (Respirace; Ambulatory Monitoring, Inc, Ardsley, NY, USA).

Construction of pressure/diameter loops was carried out using computer software that plots the diameter signal against the pressure signal during the cardiac cycle. Prior to plotting, the two signals need to be synchronized because the hysteresis loop area varies depending on the phase lag between the diameter and pressure signals. Synchronization was performed by aligning the upshoot of the diameter and pressure pulses according to their steepest slopes. In most cases, not much alignment was necessary because pressure and diameter was measured at almost the same site along the right pulmonary artery.

Reproducibility of measurements of dimensions

At least 10–15 successful recordings were obtained during each recording session; repeated measurements were used to assess intrasession intraobserver variability. Two complete series of recordings were obtained in eight subjects by two different observers in order to assess interobserver variability. Measurements were repeated in the same eight subjects within 2 weeks by the same observers, to assess intersession variability. In order to assess the reproducibility of measurements, the coefficient of variation was calculated. The intrasession, interobserver and intersession reproducibility of the measurements of diameter and distension are given in table 1. By comparison, KOOL *et al.* [15] measured pulsatile distension of the common carotid artery, using the WTS with a 7.5-MHz transducer, and reported 7.9 ± 1.6 , 9.2 ± 0.9 and $11.3 \pm 2.6\%$ (mean $\pm$ SEM) for intraobserver intrasession,

Table 1. – Coefficient of variation (reproducibility) of dimension measurements

	Intrasession intraobserver	Intrasession interobserver	Intersession intraobserver
Control			
Subjects n	16	8	8
d	4.3 ± 1.9	4.8 ± 1.6	6.4 ± 3.1
Δd	9.6 ± 3.9	8.5 ± 3.8	15.0 ± 4.3
Exercise			
Subjects n	19	8	8
d	4.8 ± 2.1	6.2 ± 2.3	7.0 ± 2.7
Δd	13.8 ± 4.8	14.7 ± 4.6	17.7 ± 5.4

Data are presented as mean $\pm$ SD. d: end-diastolic diameter of right main pulmonary artery; Δd : change in diameter of right main pulmonary artery from end diastole to peak systole.

intraobserver intersession and interobserver intrasession variabilities.

Protocol

Subjects were instrumented (electrodes mounted, catheter introduced), rested for 15 min in the supine position and then a 5-min recording of pulmonary artery diameter and pressure, together with ECG and respiration, made. The subjects then performed exercise in the supine position. They had their legs elevated and feet positioned on a bicycle ergometer (Jaeger ER-900L, Würzburg, Germany). The load was increased until exercise induced an increase in MPAP of 5–15 mmHg, depending upon age and pulmonary distensibility. The applied load ranged 75–200 W, and resulted in an increase in MPAP of 8 ± 5 mmHg and in cardiac frequency of 23 ± 16 beats·min⁻¹ (mean $\pm$ SD). Steady state was verified by stable cardiac frequency and pulmonary arterial pressure. The load was maintained at the steady-state level for 5 min, during which time the above variables were continuously recorded. The ultrasound transducer was kept in the same position throughout the recording period.

Data analysis

The D_{dyn} of the pulmonary artery was calculated as $2\Delta d/\Delta P$, where d is end-diastolic diameter, Δd change in diameter from end diastole to peak systole and ΔP pulse pressure. d , Δd and ΔP were measured and D_{dyn} calculated on a beat-by-beat basis and averaged. D_{st} was defined as $2\Delta d/(\bar{d} \Delta \text{MPAP})$, where $\bar{d}$ mean diameter averaged for the pulse, and Δd is change. In each subject, 10–15 end-expiratory cardiac cycles were used for analysis both at rest and during steady exercise.

Statistical analysis

Data are presented as mean $\pm$ SD. Differences between D_{st} and D_{dyn} were tested by paired t-test and analysis of covariance, using age as covariant. Relationships between distensibility parameters and other variables (age, MPAP and cardiac frequency) were evaluated by simple and multiple linear regression analyses. Statistical analyses were performed using the StatSoft (Tulsa, OK, USA), STATISTICA for Windows, Release 5.0, package.

Results

Representative pressure and diameter curves for one cardiac cycle recorded from the right main branch of the pulmonary artery in a young healthy subject are presented in figure 1. Figure 1c shows the pressure/diameter hysteresis loop for this cycle. The pressure/diameter relationship appears to be linear in the diastolic/systolic pressure range. The hysteresis loop is narrow, with a small area, indicating low wall viscosity. Diastolic/systolic pulmonary arterial pressure/diameter relations for a younger and an older subject are compared in figure 2. In the younger subject, end-diastolic diameter was smaller at

Fig. 1. – Representative a) pressure; and b) diameter recordings from the right main branch of the pulmonary artery in a young healthy subject. c) Pressure/diameter hysteresis loop (constructed from a and b). PAP: pulmonary artery pressure.

rest and dilated more in response to a smaller pulse pressure than in the older subject. In response to the rise in pressure induced by exercise, the pressure/diameter relations shifted to the right, approximately along the axes of the control relations. The slope of the diastolic/systolic pressure/diameter relation reflects D_{dyn} , whereas the slopes of the lines connecting mean pressure and diameter indicate D_{st} . D_{dyn} and D_{st} did not seem to differ considerably in either subject. In systemic arteries, the pressure/diameter relation was found to shift markedly upwards during pressure responses, indicating significantly higher D_{st} than D_{dyn} [1, 2, 5]. The clinical characteristics of all the subjects are given in table 2.

In all the present subjects, physical exercise produced a significant increase in MPAP (8 ± 5 mmHg), but did not lead to an upward shift of the pressure/diameter relation, *i.e.* D_{st} did not differ significantly from D_{dyn} (22.8 ± 19.2 versus 21.0 ± 18.3 10^{-3} mmHg⁻¹). Also, D_{dyn} did not change significantly between rest and exercise (21.0 ± 18.3 versus

Fig. 2. – Representative diastolic/systolic pulmonary artery pressure (PAP) and diameter data for a 21-yr-old (square symbols) and a 44-yr-old (round symbols) subject. (●, ■ : rest; ○, □ : exercise; - - - : connecting mean pressure and diameter). Data are presented as mean $\pm$ SD (n=15).

17.7 $\pm$ 11.9 10^{-3} mmHg $^{-1}$). The difference between D_{st} and D_{dyn} did not exhibit any trend when plotted against mean distensibility, and the limit of agreement calculated according to the method of Bland and Altman [16] amounted to 1.9 $\pm$ 11.6 10^{-3} mmHg $^{-1}$ (mean difference $\pm$ 2SD). D_{st} was proportional to D_{dyn} across subjects, as shown by linear regression analysis ($r=0.95$, $p<0.001$) (fig. 3), with the regression line falling almost on the line of identity.

The end-diastolic diameter of the right pulmonary artery increased ($r=0.77$, $p<0.005$), whereas distension with the pressure pulse tended to decrease, with age ($r=-0.4$, NS), resulting in a significant reduction in D_{dyn} with increasing age ($r=-0.67$, $p<0.01$). D_{st} exhibited similar reduction with age ($r=-0.69$, $p<0.01$), and the age relations of D_{st} and D_{dyn} did not differ significantly when tested by analysis of covariance, using age as covariant (fig. 4).

Resting MPAP ranged 11–42 mmHg, and was >20 mmHg in six subjects (table 2). It is of note that none of these subjects had any complaints or symptoms that were related to lung function or pulmonary circulation prior to the study. In accordance with earlier findings [17, 18], pulmonary artery distensibility was lower in hypertensive subjects as compared to the remaining subjects with normal pulmonary pressure (8.5 $\pm$ 5.5 versus 28.5 $\pm$ 19.8 10^{-3} mmHg $^{-1}$ for D_{st} and 7.4 $\pm$ 3.5 versus 26.5 $\pm$ 19.1 10^{-3} mmHg $^{-1}$ for D_{dyn}). When pulmonary artery distensibility was related using forward stepwise multiple regression to both age and MPAP, the contribution of MPAP approached significance (table 3). Conversely neither D_{st} , nor D_{dyn} was related to resting cardiac frequency.

Discussion

The present study is the first in which the issue of pulmonary artery wall viscosity has been directly addressed. It was found that D_{st} and D_{dyn} did not differ to any significant extent in humans, regardless of age. This finding implies that pulmonary artery wall viscosity, determined mainly by collagen and smooth muscle content, is relatively unimportant and that elastic elements in the vessel wall are predominantly responsible for its

physical behaviour. The elastic pulmonary arterial tree stores the potential energy generated by the heart during systole and restores it during diastole, maintaining adequately high driving pressure at the periphery [6]. The difference between the stored and restored quantities of energy is dissipated, mainly due to wall viscosity, and arterial wall viscosity is considered the main source of pressure-wave attenuation along the arterial tree [19]. The very low wall viscosity of proximal pulmonary arteries, suggested by the present data, results in efficient heart/vessel coupling both at rest and during cardioacceleration.

Measurement of pulmonary artery dimensions with the ultrasound wall-tracking system

In earlier studies, this ultrasound technique was used to investigate superficial arteries [13, 14]. The short distance between ultrasound source and target object allowed the use of high-frequency transducers (7.5–10 MHz), yielding high spatial resolution (5–200 μ m). Since the right pulmonary artery is situated 5–8 cm below the supra-sternal notch, a 3.5-MHz transducer with a spatial resolution of $\sim$ 0.5 mm had to be used in the present study. In this way, the pulmonary artery diameter was determined to within $\sim$ 1 mm. The conditions for measuring distension with the WTS, however, are far more favourable. Once the vessel wall has been identified, and a sample window positioned within the RF signal, the WTS algorithm tracks wall displacements with great accuracy. HOEKS *et al.* [13] demonstrated *in vitro* that, with a 7.5-MHz transducer, this technique can resolve diameter changes of <1 μ m. In the present study, a 3.5-MHz transducer was used *in vivo*. KAWASAKI *et al.* [20] and LANGE *et al.* [21], using wall-tracking echo systems *in vivo* with 3.5-MHz transducers, reported 5 and 8 μ m as the smallest detectable movement.

Because the present study is the first in which the WTS has been used on the pulmonary artery, the technique needs validation in this new setting. PAZ *et al.* [22] used magnetic resonance imaging to study right pulmonary artery wall distensibility in nine healthy volunteers with a mean age of 42.9 yrs (range 28–49 yrs), and reported a mean $\pm$ SD pulsatile change in cross-sectional area of 21.5 $\pm$ 11.2%. In a subgroup of nine of the present subjects of similar age (mean 42.1 yrs; range 23–44 yrs), the corresponding value was 20.0 $\pm$ 9.8%. BOGREN *et al.* [17] studied the main pulmonary artery using MRI and reported a pulsatile change in cross-sectional area of 23% (range 17–30%). In earlier work on the aortic arch, in which the wall-tracking technique was used with a 3.5-MHz transducer, the recorded data were in agreement with data in the literature obtained by various techniques (angiography, mechanical and ultrasonic calliper, and magnetic resonance imaging) [23].

The WTS technique has been used previously to measure aortic arch diameter and distension, failing in only 10% of the subjects studied [23]. In the present study, the success rate for measuring pulmonary artery dimensions was much lower (<50%). Two types of difficulty were encountered. In some cases, mainly in older subjects, the quality of the M-mode image was simply not satisfactory for WTS analysis. In other cases, movement of the lower wall of the right pulmonary artery produced

Table 2. – Clinical characteristics of subjects at rest (control) and during exercise

Age yrs	Control						Exercise						
	f_R beats·min ⁻¹	MPAP mmHg	ΔP mmHg	d cm	Δd cm	D_{dyn} 10 ⁻³ mmHg ⁻¹	f_R beats·min ⁻¹	MPAP mmHg	ΔP mmHg	d cm	Δd cm	D_{dyn} 10 ⁻³ mmHg ⁻¹	D_{st} 10 ⁻³ mmHg ⁻¹
21	60	11±1.0	10±0.9	0.80±0.04	0.17±0.021	44.3±4.3	65	15±1.0	11±1.0	0.88±0.03	0.15±0.023	33.8±4.5	40.7±4.3
21	75	20±1.3	7±1.0	0.91±0.04	0.12±0.013	38.6±5.2	99	28±1.3	10±1.2	1.04±0.05	0.21±0.024	41.7±4.4	42.1±4.6
21	65	13±0.6	5±0.5	1.06±0.04	0.06±0.008	27.9±3.3	75	15±0.5	5±0.4	1.09±0.05	0.06±0.007	23.0±2.4	27.8±3.5
21	58	18±0.6	6±0.6	1.00±0.06	0.05±0.008	19.6±2.4	62	22±0.6	9±0.9	1.01±0.04	0.08±0.008	20.3±3.1	14.9±1.5
23	80	17±1.0	5±0.8	0.78±0.04	0.13±0.012	66.7±6.2	100	28±1.2	10±1.0	1.05±0.06	0.19±0.011	36.3±2.6	64.0±8.1
23	70	16±0.5	13±0.6	0.98±0.04	0.15±0.016	23.6±3.4	85	20±1.2	13±1.1	1.04±0.05	0.16±0.023	23.7±1.4	29.1±3.1
24	80	18±1.1	8±1.0	0.88±0.04	0.08±0.009	25.1±1.4	92	24±0.6	8±0.7	0.96±0.01	0.13±0.016	36.6±4.0	37.0±4.0
25	85	18±1.1	8±1.0	0.80±0.03	0.19±0.014	62.5±5.8	112	27±1.3	11±1.1	1.09±0.04	0.13±0.015	32.2±3.7	69.8±8.4
34	80	39±1.2	26±1.1	1.03±0.05	0.04±0.004	3.2±0.4	110	50±2.6	27±1.5	1.11±0.02	0.04±0.007	2.3±0.2	13.9±1.6
44	64	15±1.0	17±1.1	1.28±0.04	0.11±0.008	10.2±2.1	78	20±1.0	23±1.0	1.34±0.05	0.10±0.014	6.3±0.3	15.2±1.4
45	105	28±1.3	12±0.9	0.99±0.01	0.06±0.008	10.3±2.6	128	37±1.3	16±1.0	1.02±0.06	0.13±0.016	16.5±2.5	11.0±1.9
45	70	36±1.3	9±0.8	1.30±0.04	0.07±0.005	11.9±2.0	96	48±1.5	10±1.1	1.35±0.06	0.08±0.012	11.9±4.4	7.6±1.1
46	60	16±0.9	7±0.9	1.18±0.03	0.07±0.014	18.0±1.7	68	18±1.0	8±1.0	1.20±0.04	0.09±0.010	20.4±5.4	25.0±2.8
47	75	42±2.2	35±1.9	1.43±0.05	0.19±0.013	7.6±1.1	118	58±2.3	56±2.3	1.44±0.07	0.22±0.021	5.6±0.3	1.7±0.2
52	75	19±1.1	6±0.6	1.56±0.08	0.11±0.009	25.3±3.2	90	24±0.9	8±0.9	1.65±0.08	0.14±0.019	20.6±2.7	25.0±3.1
54	70	14±1.0	12±1.0	1.35±0.04	0.09±0.010	11.5±1.2	81	17±1.0	10±0.9	1.38±0.06	0.10±0.015	6.6±0.7	14.5±1.9
56	70	19±1.0	7±0.8	1.27±0.03	0.06±0.008	14.2±1.3	104	40±2.5	8±0.7	1.54±0.08	0.06±0.008	10.3±1.1	19.9±2.1
69	63	42±2.5	22±1.7	1.43±0.06	0.12±0.013	7.6±0.8	88	53±2.9	21±2.8	1.46±0.05	0.10±0.011	6.9±0.9	2.5±0.3
73	78	27±1.3	22±1.5	1.38±0.04	0.05±0.006	3.5±0.4	89	36±1.4	25±1.2	1.46±0.07	0.09±0.014	4.6±2.8	14.3±1.5
79	80	17±1.0	7±0.6	1.57±0.07	0.02±0.004	4.9±0.5	96	26±1.1	7±0.5	1.58±0.09	0.04±0.007	7.6±0.6	1.4±0.3
82	55	18±1.1	16±1.0	1.14±0.06	0.04±0.003	4.9±0.7	68	29±0.9	20±1.0	1.14±0.04	0.06±0.007	5.6±0.5	1.6±0.2

Data are presented as mean±SD. f_R : cardiac frequency; MPAP: mean pulmonary artery pressure; ΔP : pulmonary pulse pressure; d: end-diastolic diameter of the right main pulmonary artery; Δd : change in diameter from end diastole to peak systole; D_{dyn} : dynamic distensibility; D_{st} : static distensibility. (1 mmHg=0.133 kPa.)

Fig. 3. – Relationship between the static (D_{st}) and dynamic distensibility (D_{dyn}) of the pulmonary artery across subjects. $D_{st}=0.99 D_{dyn}+1.82$, $r=0.95$, $p<0.001$.

bizarre patterns. The authors suspect that the proximity of contracting cardiac chambers might have caused pulmonary artery wall movements not related to intravascular pressure. Owing to this high failure rate, the WTS method cannot be recommended for routine clinical use for the measurement of pulmonary artery distension and elastic variables.

Pulmonary artery pressure and diameter have previously been measured in one study [8]. These measurements were performed, however, during open chest surgery with the pulmonary artery exposed. It is known that surgical manipulations alter the distensibility of exposed arteries [24], and it is an open question as to what extent wall viscosity is affected during surgical procedures.

Static and dynamic distensibility of the pulmonary artery

The present data suggest that D_{st} and D_{dyn} of the pulmonary artery are not significantly different. This finding is at variance with animal data reported by LINEHAM *et al.* [7], who found the slope of the static pressure/volume curve of the perfused lung to be 1.5 times greater than that of the dynamic curve. The reason for this

Fig. 4. – Linear regression of static (D_{st} ; $\circ$; - - -) and dynamic distensibility (D_{dyn} ; $\bullet$; —) of the pulmonary artery against age. $D_{st}=-0.64 \text{ age}+50.72$, $r=0.69$, $p<0.01$; $D_{dyn}=-0.60 \text{ age}+46.00$, $r=0.67$, $p<0.01$.

Table 3. – Forward stepwise regression of factors influencing pulmonary artery distensibility

Dependent variable	Independent variable	B	ΔR^2	F	p-value*
D_{dyn}	Age yrs	-0.59	0.44	15.45	0.003
	MPAP mmHg	-0.28	0.07	2.79	0.11
D_{st}	Age yrs	-0.56	0.47	17.03	0.005
	MPAP mmHg	-0.35	0.08	3.55	0.07

*: for obtaining an F value greater than the given F; F to entry=1. B: standardized regression coefficient; ΔR^2 : amount of additional variability explained by the given variable; F: F-statistic for testing $R=0$; Fall: F-statistic for testing all $R=0$; D_{dyn} : dynamic distensibility; D_{st} : static distensibility; MPAP: mean pulmonary artery pressure. D_{dyn} : $R^2=0.52$, $F_{all}=9.85$, $p<0.001$; D_{st} : $R^2=0.59$, $F_{all}=8.17$, $p<0.001$.

discrepancy is not clear, but methodological differences might be responsible. In the study of LINEHAM *et al.* [7], the pulmonary veins were occluded at constant arterial inflow rate and the dynamic and static elastic behaviour of the whole pulmonary circulatory system was derived from analysis of arterial and venous pressure response curves. It is not clear which segments of the pulmonary vasculature, and to what extent, were responsible for the observed changes. In the present study, physiological forcings were used and the elastic behaviour of an identified segment of the right pulmonary artery determined. The present results are in line with data obtained from patients undergoing open-heart surgery, in whom the pressure and diameter of the main pulmonary artery was measured locally by invasive means [8]. The shape of the pressure and diameter curves were strikingly similar, indicating no phase differences between the two signals, *i.e.* no significant effect of vessel wall viscosity. In the ascending aorta, the similarity between the contours of pressure and diameter curves obtained using the same technique was considerably less [25]. The relationship between instantaneous distending pressure and the diameter of the pulmonary artery was also studied in the thoracotomized dog [26]. The pressure/diameter hysteresis loop was found to be narrow, and its area remained small after noradrenalin administration, indicating negligible viscous resistance of the vessel wall, even after smooth muscle activation.

Effect of cardiac frequency

The distensibility of systemic arteries is a frequency-dependent phenomenon due to viscoelasticity of the arterial wall [1, 2, 6]. Pulmonary artery elastic parameters were shown to be independent of pulsatile frequency, *i.e.* of cardiac frequency in *in vivo* studies or of the frequency of applied pressure forcings in *in vitro* experiments [18, 27]. The present results corroborate these earlier findings. The cardiac frequency of the present subjects during exercise increased by ~25%, but this increase in cardiac frequency was not accompanied by a significant reduction in D_{dyn} . In addition, cardiac frequency did not appear to be a significant predictor of either D_{dyn} or D_{st} of the pulmonary artery when studied in a multiple regression design. The independence of distensibility of the rate of distension indicates low wall viscosity.

Effect of exercise

Smooth muscle tone in the pulmonary artery is likely to be affected by exercise, which might result in altered wall elasticity and viscosity. Exercise is associated with sympathoadrenergic activation and increased plasma catecholamine levels. Catecholamines evoke smooth muscle contraction in the pulmonary arterial wall *in vitro*, and affect wall elasticity [28]. During exercise, however, when blood pressure is elevated, the change in diameter reflects the net effect of passive dilatatory forces and active smooth muscle contraction. How the balance is set in the pulmonary artery during exercise is not known. Data available from humans for the also elastic-type carotid artery suggest the dominance of passive dilatatory forces during pressor responses induced by vasoactive drugs [14] or physical exercise [29]. Similarly, it has been concluded that carotid artery diameter is determined predominantly by passive mechanisms, since no differences were observed in pressure/diameter relations during pressor responses produced by different vasoconstrictor drugs in the rat [1]. Were smooth muscle activation during pressor responses to tend to reduce D_{st} , then it would also reduce the difference between D_{st} and D_{dyn} , *i.e.* wall viscosity. Recently, however, it was shown that sustained changes in smooth muscle tone did not influence aortic wall viscosity [30].

Influence of age

Systemic arteries are known to become stiffer with increasing age [31]. A similar age-related decline in pulmonary artery distensibility was demonstrated in the present study. The predictive power of the age relation may appear to be low ($r^2=0.5$), due to the great variation in distensibility at younger ages. However, $r^2=0.5$ means that 50% of the difference in distensibility was accounted for by age. The present data are in line with a number of earlier observations, obtained both *in vitro* and *in vivo* [9, 10]. PASIERSKI *et al.* [12], however, employing the conventional ultrasound M-mode technique for measuring vessel diameter, found that the elastic modulus (the ratio of pulmonary arterial pressure to vessel wall strain) was independent of age, and was related only to pulmonary arterial pressure. It is a common finding that pulmonary artery distensibility is reduced in patients with pulmonary hypertension [17, 18]. In the study of PASIERSKI *et al.* [12] MPAP ranged 15–56 mmHg, with most of the patients being hypertensive, suggesting that the effect of age on pulmonary artery stiffness was overwhelmed by the dominating influence of pulmonary artery pressure.

Effect of cardiac pathology

All of the present patients had cardiac conditions, and none suffered from pulmonary hypertension or lung disease. Nevertheless, in cardiac patients with myocardial infarction or cardiac failure, the plasma catecholamine level is elevated and the renin/angiotensin system activated. *In vitro* studies show that catecholamines evoke smooth muscle contraction in the pulmonary arterial wall

[28] and angiotensin II induces hypertrophy of pulmonary artery myocytes [32]. It has been suggested that active contraction of vascular smooth muscle may change the viscosity as well as the elasticity of the arterial wall [33]. More recently, however, BAUER *et al.* [28] reported that, in contrast with the static modulus, the dynamic elastic modulus and the coefficient of wall viscosity were virtually uninfluenced by smooth muscle tone, when various arterial segments were studied *in vitro* under the condition of activation induced by noradrenalin and relaxation induced by papaverine. BOUTOUYRIE *et al.* [30] confirmed *in vivo* that wall viscosity was not influenced by smooth muscle tone. The above observations were made on systemic arteries, and it remains to be established whether pulmonary arteries behave in a similar fashion. The present data suggest that this may be the case, since dynamic and static distensibilities were similar in different subjects, irrespective of their clinical diagnosis, *i.e.* of possible differences in plasma catecholamine and angiotensin II level.

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References

1. Glaser E, Lacolley P, Boutouyrie P, *et al.* Dynamic versus static compliance of the carotid artery in living Wistar-Kyoto rats. *J Vasc Res* 1995; 32: 254–265.
2. Lichtenstein O, Safar ME, Mathieu E, Poitevin P, Levy BI. Static and dynamic mechanical properties of the carotid artery from normotensive and hypertensive rats. *Hypertension* 1998; 32: 346–350.
3. Nichols WW, O'Rourke M. MacDonald's blood flow in arteries. London, Edward Arnold, 1990; pp. 398–419.
4. Boutouyrie P, Bézine I, Lacolley P, *et al.* *In vivo/in vitro* comparison of rat abdominal aorta wall viscosity. *Arterioscler Thromb Vasc Biol* 1997; 17: 1346–1355.
5. Lénárd Zs, Fülöp D, Visontai Zs, Jokkel G, Reneman R, Kollai M. Static versus dynamic distensibility of the carotid artery in humans. *J Vasc Res* 2000; 37: 103–111.
6. Bergel DW. The dynamic elastic properties of the arterial wall. *J Physiol* 1961; 158: 458–469.
7. Linehan JH, Dawson CA, Rickaby DA, Bronikowski TA. Pulmonary vascular compliance and viscoelasticity. *J Appl Physiol* 1986; 61: 1802–1814.
8. Greenfield JC, Griggs DM. Relation between pressure and diameter in main pulmonary artery of man. *J Appl Physiol* 1963; 18: 557–559.
9. Learyod BM, Taylor MG. Alterations with age in the viscoelastic properties of human arterial walls. *Circ Res* 1966; 18: 278–292.
10. Hosoda Y, Kawano K, Yamasawa F, Ishii T, Shibata T, Inayama S. Age-dependent changes of collagen and elastin content in human aorta and pulmonary artery. *Angiology* 1984; 10: 615–621.
11. Gozna ER, Marble AE, Shaw A, Holland JG. Age-related changes in the mechanics of the aorta and pulmonary artery of man. *J Appl Physiol* 1974; 36: 407–411.
12. Pasierski TJ, Starling RC, Binkley PF, Pearson AC. Echocardiographic evaluation of pulmonary artery distensibility. *Chest* 1993; 103: 1080–1083.

13. Hoeks APG, Brands PJ, Smeets FAM, Reneman RS. Assessment of the distensibility of superficial arteries. *Ultrasound Med Biol* 1990; 16: 121–128.
14. Bonyhay I, Jokkel G, Karlocai K, Reneman R, Kollai M. Effect of vasoactive drugs on carotid diameter in humans. *Am J Physiol* 1997; 273: H1629–H1636.
15. Kool MJF, van Merode T, Reneman RS, Hoeks APG, Struyker Boudier HAJ, Van Bortel LMAB. Evaluation of reproducibility of a vessel wall movement detector system for assessment of large artery properties. *Cardiovasc Res* 1994; 28: 610–614.
16. Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. *Lancet* 1986; 8: 307–310.
17. Bogren HG, Klipstein RH, Mohiaddin RH, *et al.* Pulmonary artery distensibility and blood flow patterns: a magnetic resonance study of normal subjects and of patients with pulmonary arterial hypertension. *Am Heart J* 1989; 118: 990–999.
18. Zuckerman BD, Orton EC, Stenmark KR, *et al.* Alteration of the pulsatile load in the high-altitude calf model of pulmonary hypertension. *J Appl Physiol* 1991; 70: 859–868.
19. Bertram CD. Energy dissipation and pulse wave attenuation in the canine carotid artery. *J Biomech* 1980; 13: 1061–1073.
20. Kawasaki T, Sasayama S, Yagi S, Asakawa T, Hirai T. Non-invasive assessment of the age related changes in stiffness of major branches of the human arteries. *Cardiovasc Res* 1987; 21: 678–687.
21. Lanne T, Stale H, Bengtsson H, *et al.* Noninvasive measurement of diameter changes in the distal abdominal aorta in man. *Ultrasound Med Biol* 1992; 18: 451–457.
22. Paz R, Mohiaddin H, Longmore DB. Magnetic resonance assessment of the pulmonary arterial trunk anatomy, flow, pulsatility and distensibility. *Eur Heart J* 1993; 14: 1524–1530.
23. Studinger P, Lénárd Zs, Reneman R, Kollai M. Measurement of aortic arch distension wave with echo-track technique. *Ultrasound Med Biol* 2001; (in press).
24. Angell-James JE, Lumley JSP. The effects of carotid endarterectomy on the mechanical properties of the carotid sinus and carotid sinus nerve activity in atherosclerotic patients. *Br J Surg* 1974; 61: 805–810.
25. Greenfield JC Jr, Patel DJ. Relation between pressure and diameter in the ascending aorta of man. *Circ Res* 1962; 10: 778–781.
26. Patel DJ, Schilder DP, Mallos AJ. Mechanical properties and dimensions of the major pulmonary arteries. *J Appl Physiol* 1960; 15: 92–96.
27. Slife DM, Latham RD, Sipkema P, Westerhof N. Pulmonary arterial compliance at rest and exercise in normal humans. *Am J Physiol* 1990; 258: H1823–H1828.
28. Bauer RD, Busse R, Schabert A. Mechanical properties of arteries. *Biorheology* 1982; 19: 409–424.
29. Fülöp D, Lénárd Zs, Studinger P, Jokkel G, Kollai M. Pressure-diameter relation in the carotid artery during and after dynamic exercise. *J Physiol* 2000; 526: 146.
30. Boutouyrie P, Boumaza S, Challande P, Lacolley P, Laurent S. Smooth muscle tone and arterial wall viscosity an *in vivo/in vitro* study. *Hypertension* 1998; 32: 360–364.
31. Reneman RS, Van Merode T, Hick PJJ, Muyltjens AMM, Hoeks APG. Age related changes in carotid artery wall properties in men. *Ultrasound Med Biol* 1986; 12: 465–471.
32. Morrell NW, Upton PD, Kotecha S, *et al.* Angiotensin II activates MAPK and stimulates growth of human pulmonary artery smooth muscle *via* AT1 receptors. *Am J Physiol* 1999; 277: L440–L448.
33. Gow BS. The influence of vascular smooth muscle on the viscoelastic behaviour of blood vessels. In: Bergel DH, ed. *Cardiovascular Fluid Dynamics*. London, Academic Press, 1972; pp. 65–110.