Pulse pressure response to the strain of the Valsalva maneuver in humans with preserved systolic function

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Hébert, J. Jean-Louis, Catherine Coirault, Karen Zamani, Guy Fontaine, Yves Lecarpentier, and Denis Chemla. Pulse pressure response to the strain of the Valsalva maneuver in humans with preserved systolic function. J. Appl. Physiol. 85(3): 817–823, 1998.—Arterial pulse pressure response during the strain phase of the Valsalva maneuver has been proposed as a clinical tool for the diagnosis of left heart failure, whereas responses of subjects with preserved systolic function have been poorly documented. We studied the relationship between the aortic pulse amplitude ratio (i.e., minimum/maximum pulse pressure) during the strain phase of the Valsalva maneuver and cardiac hemodynamics at baseline in 20 adults (42 ± 14 yr) undergoing right heart catheterization. They were normal subjects (n = 5) and patients with various forms of cardiac diseases (n = 15), and all had a left ventricular ejection fraction >40%. High-fidelity pressures were recorded in the right atrium and the left ventricle at baseline and at the aortic root throughout the Valsalva maneuver. Aortic pulse amplitude ratio 1) did not correlate with baseline left ventricular end-diastolic pressure, cardiac index (thermodilution), or left ventricular ejection fraction (cineangiography) and 2) was positively related to total arterial compliance (area method) (r = 0.59) and to basal mean right atrial pressure (r = 0.57) (each P < 0.01). Aortic pulse pressure responses to the strain were not related to heart rate responses during the maneuver. In subjects with preserved systolic function, the aortic pulse amplitude ratio during the strain phase of the Valsalva maneuver relates to baseline total arterial compliance and right heart filling pressures but not to left ventricular function.

central venous pressure; arterial compliance; heart period; hemodynamics; baroreceptor reflex; systolic function

THE ARTERIAL PRESSURE CONTOUR during the strain phase of the Valsalva maneuver relates to cardiac status. Arterial pressure decreases during the strain phase of the maneuver in healthy subjects but not in patients with increased pulmonary capillary wedge pressure (2, 10, 23). Given that a wide range of arterial pressure responses is currently observed from typically normal to abnormal responses, the aortic pulse amplitude ratio (i.e., minimum/maximum pulse pressure) has been used to quantify the amount of arterial pressure decrease (2, 23). In patients with various degrees of heart impairment, the pulse amplitude ratio relates to pulmonary capillary wedge pressure (2, 23, 29). Some authors have suggested that the pulse amplitude ratio may improve the assessment of cardiac status (29, 33) and may furnish a noninvasive scale of myocardial dysfunc-

tion (3, 23). Others raised doubts about this, given that an abnormal response is observed in diseases in which the left ventricular (LV) function is preserved (15).

Arterial pressure response during the strain phase of the Valsalva maneuver might reflect either LV function (3, 23), or right-sided pressures (15), or both (2, 10, 29), and it seems of physiological interest to clarify this issue. In this respect, we feel that two points remain poorly documented: 1) until now, the respective roles of LV and right-sided pressures in arterial response during the maneuver have not been studied with use of high-fidelity pressure catheters; and 2) given that arterial compliance is known to influence the aortic pressure-flow relationship (8, 21, 26, 27), compliance may also play a role in aortic pressure response during the maneuver, but no study has so far tested this hypothesis.

The aim of our study was to document simultaneous high-fidelity, left- and right-sided hemodynamics during the Valsalva maneuver in patients with preserved systolic function. We studied the influences of baseline right- and left-sided pressures and arterial compliance on the pulse amplitude ratio during the maneuver. Given that the Valsalva maneuver is usually used to assess autonomic function (6, 7), we also studied the interplay between aortic pressure responses and heart rate responses during the maneuver.

METHODS

Patients

Twenty patients (15 men and 5 women; mean age 42 ± 14 yr) were enrolled in our prospective study, after giving their informed consent. The investigation was approved by the Comité Consultatif de Protection des Personnes dans la Recherche Biomédicale de Bicêtre. For inclusion in the study, 1) patients had to be referred to our laboratory for diagnostic right and left heart catheterization for the investigation of chest pain, heart failure, or other cardiovascular disorders; and 2) their LV ejection fraction (cineangiography) had to be ≥40%. Patients with aortic, mitral, or tricuspid valvular regurgitation were excluded from the study, as were patients with contraindications to the Valsalva maneuver (aortic stenosis, recent myocardial infarction, glaucoma, retinopathy). The final diagnoses were as follows: normal subjects (n = 5), idiopathic dilated cardiomyopathy (n = 3), systemic hypertension (n = 2), atrial septal defect (n = 1), hypertrophic cardiomyopathy (n = 1), coronary artery disease (n = 1), mitral stenosis (n = 1), and arrhythmogenic right ventricular dysplasia (n = 6). Nine patients were not receiving vasoactive drugs. The other patients were taking angiotensin-converting enzyme inhibitors (n =...
3), calcium-channel blockers \(n = 6\), diuretics \(n = 3\), amiodarone \(n = 1\), flecainide \(n = 3\), \(\alpha\)-adrenergic blocking agent \(n = 1\), or nitrates \(n = 1\).

Catheterization Technique

Patients were studied according to our routine protocol (4, 5, 13). They were unsedated and were investigated at least 12 h after the previous intake of usual treatment. Right and left heart catheterizations were performed by using the Seldinger technique from the femoral vein and artery, as previously described (4, 13). The 5-Fr right heart and 6-Fr left heart pressure-measuring catheters were equipped with two high-fidelity transducers, one at the tip and the other 10 cm from the tip (Cordis/Sentron, Roden, The Netherlands) (14). Catheters were advanced so as to obtain simultaneous right atrial and ventricular and LV and aortic root pressure recordings. This enabled us to record right atrial and LV pressures immediately before the Valsalva maneuver. In three patients with peripheral arterial disease of the lower limbs, we used the percutaneous brachial artery approach (22). Pressure data were recorded on a personal computer with customized software (sampling rate 500 Hz). Mean pressure in the right atrium was calculated by dividing the area under the curve by the heart period.

Protocol and Calculations

Valsalva maneuver. Pressure data were obtained at baseline after a 10-min equilibration period. Thereafter, the calibrated Valsalva maneuver was performed at a pressure of 40 mmHg for 15 s (13). In healthy subjects, four phases are classically observed (12, 16). In phase I (onset of strain), there is a transient rise in aortic pressure. In phase II (continuous straining), a biphasic response is generally observed, consisting of a reduction in systolic aortic pressure (phase IIa), followed by a secondary rise in systolic aortic pressure, after \(\sim 5\) s, to resting values (phase IIb). In phase III (release of the strain), aortic pressure suddenly drops. In phase IV (pressure overshoot), systolic and pulse aortic pressures overshoot above resting values, thus leading to heart period increases via baroreceptor reflex stimulation.

A typical abnormal response is generally observed in patients with congestive heart failure and increased pulmonary capillary wedge pressure (10). In these patients the pulse pressure remains virtually unchanged, whereas both systolic and diastolic aortic pressure levels are shifted upward. On the release of the maneuver, the aortic blood pressure immediately returns toward normal (12, 15, 33). Overall, this leads to the typical “square-wave” blood pressure response (3).

Aortic pulse amplitude ratio. In clinical practice a wide range of arterial pressure responses are observed, from a typically normal response to a square-wave response, and the aortic pulse amplitude ratio has been used to quantify arterial pressure decrease (2). We therefore calculated the aortic pulse amplitude ratio, i.e., the ratio of the lowest aortic pulse pressure during active straining (phase II) to the greatest aortic pulse pressure at onset of the strain (phase I; Ref. 2; Fig. 1). Pulse pressure was calculated as systolic pressure minus diastolic pressure.

Heart period responses and Valsalva ratio. The beat-to-beat heart period was calculated throughout the maneuver. It is generally agreed that sympathetic stimulation during the strain is reflected by reflex tachycardia (phases IIa and IIb) and vasoconstriction, as reflected by diastolic aortic pressure increases during phase IIb (16). Baroreceptor reflex stimulation of the parasympathetic drive during phase IV was quantified by calculating the so-called Valsalva ratio, as previously recommended (7). The Valsalva ratio is defined (6) as the largest R-R interval during the poststrain phase IV divided by the shortest R-R interval during the strain (phase II). According to Ewing et al. (7) a Valsalva ratio \(>1.21\) is considered normal. Heart period responses and the Valsalva ratio were studied in 17 patients. In three patients, heart period responses and the Valsalva ratio could not be studied because of ventricular premature beats during phase IV \((n = 2)\) or ventricular pacing \((n = 1)\).

Cardiac output and total arterial compliance. After pressure recordings had been completed, thermodilution cardiac output was measured in triplicate, and two consecutive monoplane LV cineangiographies and coronary angiograms were performed. Baseline total arterial compliance was estimated by using the area method (21), with compliance estimated as follows:

\[
\text{Total arterial compliance (ml/mmHg)} = \frac{\text{stroke volume}}{K} \cdot (\text{end-systolic aortic pressure} - \text{end-diastolic aortic pressure})
\]

where \(K\) is an area coefficient calculated as the area under the pressure curve throughout the cardiac cycle divided by the area under the pressure curve throughout the diastolic period. Total arterial compliance indirectly reflects the viscoelastic properties of large arteries (21).

Statistics

Results are expressed as means \(\pm SD\). Pressure data at baseline were averaged out over 10 consecutive cycles. Correlations were tested by using the least squares method. Throughout phases I, IIa, and IIb, both the heart period and pressure data were compared by using Student’s paired \(t\)-test, after analysis of variance. The P values take into account the Bonferroni correction. Comparisons among patients with
LV end-diastolic pressure $<12$ mmHg ($n = 10$) and LV end-diastolic pressure $>12$ mmHg ($n = 10$) were performed by using the unpaired Student's t-test. A P value $<0.05$ was considered statistically significant.

### RESULTS

Standard hemodynamics at baseline are presented in Table 1.

#### Aortic Pulse Pressure and Pulse Amplitude Ratio

During the Valsalva maneuver, maximum (phase I) aortic pulse pressure ranged from 20 to 112 mmHg (mean $\pm$ SD $= 58 \pm 24$ mmHg), and minimum (phase II) aortic pulse pressure ranged from 12 to 31 mmHg ($22 \pm 5$ mmHg). This resulted in an aortic pulse amplitude ratio (minimum/maximum aortic pulse pressure) ranging from 0.19 to 0.85 (0.45 $\pm$ 0.19).

There was a negative relationship between maximum (phase I) aortic pulse pressure at the onset of strain and total arterial compliance ($r = -0.76$, $P < 0.01$). Conversely, the maximum aortic pulse pressure did not correlate with LV end-diastolic pressure or with mean right atrial pressure. There was no relationship between minimum (phase II) aortic pulse pressure during strain and LV end-diastolic pressure, mean right atrial pressure, or total arterial compliance.

There was no relationship between the aortic pulse amplitude ratio and the baseline value of LV end-diastolic pressure ($r = -0.33$; Fig. 2A), cardiac index ($r = -0.05$), and LV ejection fraction ($r = -0.31$). The pulse amplitude ratio was similar in patients with baseline LV end-diastolic pressure $\leq 12$ mmHg ($n = 10$) and in patients with LV end-diastolic pressure $>12$ mmHg ($n = 10$) (0.48 $\pm$ 0.019 and 0.42 $\pm$ 0.19, respectively; $P$ = not significant; Fig. 3A). There was a positive linear relationship between the aortic pulse amplitude ratio and mean right atrial pressure ($r = 0.58$, $P < 0.01$; Fig. 2B). The pulse amplitude ratio was higher in patients with baseline mean right atrial pressure $>6$ mmHg ($n = 10$) than in patients with mean right atrial pressure $\leq 6$ mmHg ($n = 10$) (0.54 $\pm$ 0.15 and 0.35 $\pm$ 0.19, respectively; $P < 0.05$; Fig. 3B).

There was a positive linear relationship between the aortic pulse amplitude ratio and total arterial compliance ($r = 0.59$, $P < 0.01$; Fig. 4). The pulse amplitude ratio was higher in patients with baseline compliance $>1.67$ ml/mmHg ($n = 10$) than in patients with compliance $<1.67$ ml/mmHg ($n = 10$) (0.62 $\pm$ 0.22 and 0.40 $\pm$ 0.18, respectively; $P < 0.05$). When the influence of arterial compliance was taken into account, the aortic pulse amplitude ratio and mean right atrial pressure were still related (partial correlation coefficient $= 0.51$, $P < 0.01$).

#### Heart Period Responses and Valsalva Ratio

We also tested the potential link between aortic pressure responses and heart period responses. There was a biphasic change in aortic pressures during the strain (Fig. 5A). As expected, systolic and diastolic pressures fell significantly from phase I to phase IIa (each $P < 0.01$), whereas systolic and diastolic pressures increased significantly during phase IIb (each $P < 0.01$). Figure 5A shows that pulse pressure significantly decreased from phase I to phase IIa ($P < 0.01$), whereas it remained unchanged during phase IIb. The heart period decreased throughout the strain of the Valsalva maneuver ($P < 0.001$; Fig. 5B).

The Valsalva ratio ranged from 1.09 to 2.33 (1.56 $\pm$ 0.34). The Valsalva ratio was deemed normal (i.e., $>1.21$) in 76% of the subjects. There was no relationship between the Valsalva ratio and the pulse amplitude ratio (Fig. 6).
DISCUSSION

To the best of our knowledge, our study is the first to have been performed with the use of simultaneous left- and right-sided high-fidelity pressure catheters in humans during the Valsalva maneuver. We studied normal subjects and patients with various forms of cardiac diseases, all of whom had preserved LV systolic function. The aortic pressure response to the strain of the Valsalva maneuver was related to right ventricular filling pressure and total arterial compliance but not to LV end-diastolic pressure. Thus, in populations similar to ours, the pressure responses during the Valsalva maneuver would not help to detect increased LV end-diastolic pressure. From a physiological point of view, our results are consistent with a major role of arterial compliance and central venous pressure in the pressure responses to this respiratory maneuver.

The pulse amplitude ratio (i.e., minimum/maximum pulse pressure) furnishes a precise scale quantifying the amount of arterial pressure decrease during the strain phase of the Valsalva maneuver (2, 23). The aortic pulse amplitude ratio did not correlate with baseline LV ejection fraction or cardiac index, and this is consistent with previous studies (2, 29). Given that LV filling pressure is an important indicator of cardiac function, its indirect determination (i.e., without LV catheterization) is of major interest to clinicians. It has been suggested that the pulse amplitude ratio may relate to LV filling pressure in cardiac patients (2, 23, 29) and furnish a scale of myocardial dysfunction (3, 23). In our study, this did not hold true in subjects with LV ejection fraction ≥40% and LV end-diastolic pressure <25 mmHg. In this population, graded aortic pulse pressure responses to the strain during the Valsalva maneuver were observed, without the square-wave phenomenon. Other researchers have reported that unchanged pulse amplitude during the strain of the Valsalva maneuver results primarily from elevation of right ventricular filling pressures (15), and our results are consistent with this hypothesis. In studies of patients with mitral stenosis, Judson et al. (15) have reported that the square-wave response does not directly correlate with the severity of the obstruction at the valvular orifice but rather with the degree of failure of the right ventricle. In normal subjects, a square-wave response is induced when large volumes of blood are rapidly infused; aortic pressure response normalizes after either sustained venous pooling or venesection (15).

Our results are also fairly consistent with the curves of vascular function, as defined by Guyton et al. (11). Systemic venous return is driven by the pressure difference between mean systemic filling pressure and mean right atrial pressure. Venous return is affected by peripheral factors (blood volume in the large and compliant venous reservoir, skeletal muscle contraction) and central factors (intrathoracic pressures, right ventricular function, right atrial mean pressure) (11, 19, 28, 31). In normal subjects, the venous reservoir is slightly repleted, and mean right atrial pressure is low. Large intrathoracic veins tend to collapse during normal inspiration, and venous return is impeded during the end-inspiratory phase. During the strain of the Valsalva maneuver, this phenomenon is enhanced and sustained, thus leading to venous blockage, responsible for the physiological decrease of aortic pulse pressure (25). Driving pressure in the venous vessels is reduced either in cases where there is a significant repletion of the venous system or as a consequence of any factor leading to an elevation of the filling pressures of the right heart. Large systemic veins at their intrathoracic entry point remain fully open during the strain (1, 9), leading to a merely preserved flow through the pulmo-
ary system, the left ventricle (17, 20), and the aorta. With the exception of patients with significant intracardiac shuntages, the role of the pulmonary blood volume as a reservoir remains moderate (11).

No correlation was found between the pulse amplitude ratio and mean right atrial pressure in a previous study (2). This could be due to the use of fluid-filled catheters coupled to classic transducers, because mean right atrial pressure obtained from this recording system is somewhat imprecise. Although Schmidt and Shah (29) have found that patients with abnormal arterial response have a significantly higher mean right atrial pressure than do patients with normal response, they conclude that increased LV filling pressure plays a primary role in arterial response (determined by using cuff sphygmanometer and auscultation). Similarly, McIntyre et al. (23) stated that the pulse amplitude ratio (digital photoplethysmography) mainly relates to pulmonary capillary wedge pressure, although patients they observed presented a positive relationship between mean right atrial pressure and the aortic pulse amplitude ratio. From a physiological point of view, however, these results (23, 29) must be considered with caution given the following: 1) from aorta to peripheral arteries, there is a well-known pulse wave amplification, the magnitude of which varies from subject to subject; 2) digital photoplethysmography leads to an unpredictable pressure bias relative to aortic root pressure (18); and 3) all invasive pressures were fluid-filled recorded.

Our results indicate that pulse amplitude ratio also related to baseline total arterial compliance. Total arterial compliance is known to influence the aortic pressure-flow relationship (8, 21, 26, 27). From a theoretical point of view, one could predict a poor relationship between stroke volume and aortic pulse pressure in subjects with high arterial compliance and a stronger relationship between stroke volume and aortic pulse pressure as compliance decreases (26). This may well explain the positive relationship between compliance and the pulse amplitude ratio in our study. Further studies are needed to pinpoint the role of arterial compliance in hemodynamic responses to the Valsalva maneuver in patients with depressed systolic function.

In an attempt to explain the lack of relationship between the pulse amplitude ratio and LV end-diastolic pressure, some distinctive features of our study need to be specified. First, to the best of our knowledge, our study is the first to have been performed with the use of simultaneous left- and right-sided high-fidelity pressure catheters. This is especially valuable, given that significant increases in blood volume and/or venous resistance result in minute increases in right atrial pressure because of the high compliance of the venous system (11). A previous study has used the left high-fidelity pressure catheter, but it focused on aortic wave reflection during the maneuver (24). Second, we focused on subjects with preserved systolic function. Their LV end-diastolic pressure was moderately elevated (<25 mmHg), and this could have revealed the prominent influence of right ventricular filling pressure and total arterial compliance on the pulse amplitude ratio. Third, it is widely agreed that LV end-diastolic pressure strongly depends on the compliance of the ventricular myocardium, and it is therefore a less satisfactory index of LV preload than is LV volume; conversely, given the high compliance of the atrial myocardium, right atrial pressure reflects right ventricular preload. This could explain the relationship between pulse amplitude ratio and right atrial pressure but not LV end-diastolic pressure. Finally, arterial data were obtained at the aortic root level, thus minimizing the influence of pressure wave amplification on the pathophysiological analysis of the maneuver. This is especially valuable if one considers the relationship observed between total arterial compliance and pulse amplitude ratio in our study.
We also studied the potential interplay between aortic pressure responses and heart rate responses during the Valsalva maneuver. The Valsalva maneuver is usually used to assess autonomic function (6, 7). Indeed, this respiratory effort leads to sympathetic stimulation during phase II and parasympathetic stimulation via baroreceptor reflex stimulation during phase IV. The question thus arises as to how autonomic status influences aortic pulse pressure responses in the Valsalva maneuver. During phase II, both the continuous decreases in the heart period and the secondary rise in diastolic pressure (phase IIb) point to acute sympathetic stimulation. Importantly, aortic pulse pressure remained unchanged during phase IIb, and this is consistent with our hypothesis that pulse pressure decrease during the strain is mainly of mechanical origin (i.e., reduced systemic venous return). As far as the release of the strain is concerned (phase IV), there was no relationship between the pulse amplitude ratio and the Valsalva ratio. It is important to note that 76% of the patients had a normal Valsalva ratio (>1.21), meaning that our results do not apply to dysautonomic patients, who must be studied specifically.

The implications of our study need to be discussed. First, it has been suggested that blood pressure responses to the strain of the Valsalva maneuver could help to predict increased LV filling pressure (23). Our study indicates that this does not hold true at the aortic root level in patients with an LV ejection fraction <40% and that the results of the maneuver should be interpreted cautiously in populations similar to ours. Second, our results show the importance of arterial compliance in the interpretation of the hemodynamic effects of the Valsalva maneuver. It remains to be documented whether compliance also has a prominent role in the blood pressure responses during other respiratory maneuvers.

The limitations of our study need to be discussed. The design of the study (simultaneous high-fidelity pressure recordings) prevented the inclusion of a greater number of subjects. However, the fact that we could observe a statistically significant relationship between aortic pulse pressure ratio and both right atrial pressure and total arterial compliance in 20 subjects should be interpreted as a strength of the study. Furthermore, given that both normal subjects and patients (e.g., hypertensive patients) were included, a huge range of baseline aortic pressures was observed (the pulse pressure ranging from 20 to 112 mmHg: 58 ± 24 mmHg), and this tended to reinforce the clinical relevance of our study. Finally, we wish to emphasize the fact that some scattering in the relationships observed suggests that factors other than right atrial pressure and total arterial compliance may be involved in the aortic pressure response to the strain of the Valsalva maneuver, and further studies are needed to confirm this.

In conclusion, aortic pulse pressure response to the strain phase of the calibrated Valsalva maneuver appeared to be related to total arterial compliance and right heart filling pressure in subjects with preserved LV systolic function.

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