

Value and Limitations of Peak-to-Peak Gradient for Evaluation of Aortic Stenosis

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Background and aim of the study: In patients with aortic stenosis (AS), it has been reported that the transvalvular pressure gradients (ΔP s) may be reduced or even abolished in the presence of concomitant arterial hypertension, but the mechanisms underlying this phenomenon remain unclear. The study aim was to: (i) examine the relationship between systemic arterial hemodynamics and the peak-to-peak (ΔP_{PtoP}), peak ΔP and mean ΔP ; and (ii) propose and validate a new formula for the non-invasive estimation of the ΔP_{PtoP} and of the peak left ventricular systolic pressure (LVSP) using Doppler echocardiography.

Methods: Two fixed stenoses (geometric orifice area 1.0 and 1.35 cm²) and one bioprosthesis (effective orifice area (EOA) 1.2 cm²) were tested in a mock flow circulation model. Systemic vascular resistance (R) was increased from 1,500 to 3,300 dyne·s/cm⁵, and systemic arterial compliance (C) was decreased from 2.9 to 0.9 ml/mmHg, while transvalvular flow was held constant.

Results: Neither C nor R had any significant impact

The transvalvular pressure gradient (ΔP) is one of the major indices used to evaluate the severity of aortic stenosis (AS). The peak and mean ΔP s measured by Doppler echocardiography or by catheterization, and the peak-to-peak ΔP (ΔP_{PtoP}) measured by catheterization, are used routinely for the evaluation of stenosis severity. A major limitation of ΔP is that it is highly dependent on flow conditions. Moreover, it has frequently been reported that ΔP may be reduced in patients with significant AS and concomitant systemic hypertension (1-4). This reduction was generally thought to depend on the simultaneous decrease in

on EOA, peak ΔP and mean ΔP . ΔP_{PtoP} was decreased markedly, however, when C was reduced (bioprosthesis: -15 mmHg (-69%); orifice 1.35 cm²: -24 mmHg (-30%); orifice 1.0 cm²: -15 mmHg (-13%)). Subsequently, an equation was proposed to predict ΔP_{PtoP} from EOA, mean ΔP , and C measured by Doppler echocardiography. LVSP calculated by adding the predicted ΔP_{PtoP} to systolic arterial pressure (SAP) was compared with LVSP measured directly in a dataset of 24 pigs with experimentally induced AS. There was a strong agreement between the estimated and measured LVSP ($r = 0.97$; mean absolute error 5 ± 5 mmHg).

Conclusion: ΔP_{PtoP} should not be used to evaluate AS severity because, as opposed to peak and mean ΔP s, it is highly influenced by C. The new non-invasive method proposed in this study to estimate the LVSP may be useful for obtaining a more accurate estimate of global LV afterload in patients with AS.

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flow that may occur as a result of increased left ventricular (LV) afterload. However, Laskey et al. (2) suggested that ΔP may decrease irrespective of flow as a direct consequence of the increased systemic vascular resistance (R). As opposed to these results, Razzolini et al. (5) found that, for each flow level, ΔP increased linearly with R. In a recent animal study, it was observed that hypertension may cause an important reduction in ΔP s measured by catheterization or by Doppler echocardiography. Multivariate analysis of these results suggested that the impact of hypertension on the peak and mean ΔP s was essentially related to changes in flow rate and valve effective orifice area (EOA), whereas the impact on the ΔP_{PtoP} was also independently determined by the systemic arterial compliance (C). Moreover, the results of the animal study showed that the increase in systemic arterial load (equivalent to severe hypertension in humans) distal

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to the valvular load (equivalent to severe AS in humans) resulted in a dramatic increase in peak LV systolic wall stress, despite a concomitant decrease in ΔP s. The reduction in ΔP s that may occur as a result of systemic hypertension in patients with AS should not be interpreted as reflecting a reduction of the load imposed on the left ventricle. On the contrary, the left ventricle of patients with AS and concomitant systemic hypertension is submitted to two additive loads: a valvular load and an arterial load. Accordingly, it was recently reported that reduced C is a frequent occurrence in patients with AS, and that it contributes independently to the increase in global LV afterload and to the occurrence of LV diastolic and systolic dysfunction in these patients (6).

These findings underline the importance of estimating global LV afterload in AS patients. The non-invasive measurement of indices of LV afterload, including LV systolic wall stress (4,7-9), or the valvular-arterial impedance recently proposed by the present authors' group (6), nonetheless requires an estimation to be made of the peak LV systolic pressure (LVSP). This is usually achieved by adding the systolic arterial pressure (SAP) measured by sphygmomanometry to the mean ΔP measured by Doppler echocardiography, because the mean ΔP is generally assumed to be equivalent to $\Delta P_{P_{toP}}$ (10).

The main limitation of previous in-vivo studies has been that it was difficult - or even impossible - independently to control and modify the different hemodynamic parameters (flow rate, C, R, aorta diameter, and valve EOA) involved in the complex interaction between ventricular, valvular and arterial hemodynamics. In an attempt to overcome this limitation, a numerical study and an in-vitro study were performed, using a mock flow circulation model. The study aims were to: (i) examine the relationship between systemic arterial hemodynamics (i.e., C and R) and $\Delta P_{P_{toP}}$, peak ΔP and mean ΔP ; and (ii) propose and validate a formula for accurate estimation of $\Delta P_{P_{toP}}$ and thus of the peak LVSP by Doppler echocardiography.

Materials and methods

Numerical study

A model based on the Windkessel two-element theory was used to describe the theoretical relationship between systemic arterial hemodynamics and ΔP :

$$\frac{dP}{dt} + \frac{P}{R \times C} = \frac{1}{C} Q \quad (1)$$

where P is the instantaneous aortic pressure, C is the systemic arterial compliance, R is the total vascular

resistance, and Q is the transvalvular flow rate.

However, instead of using a constant transvalvular flow during the systolic phase ($Q = cte$), as suggested by the original Windkessel theory, the flow was simulated by the temporal relationship:

$$Q(t) = \begin{cases} Q_0 \sin\left(\frac{\pi t}{T_s}\right) & 0 \leq t \leq T_s \\ 0 & T_s < t \leq T \end{cases} \quad (2)$$

where Q_0 is the maximal flow during systolic phase, T is the cardiac period, and T_s is the systolic duration.

As an initial condition to solve this problem, a condition of recurrence was used:

$$P_0 = P(0) = P(T)$$

It was therefore possible to derive analytically the aortic pressure (see Appendix I), and then to compute the LV pressure by adding ΔP . The instantaneous ΔP across the aortic valve could then be written using the expression introduced by Garcia et al. (11,12):

$$\Delta P(t) = \frac{\rho}{2 ELC_0^2} Q(t)^2 + \frac{2\pi\rho}{\sqrt{ELC_0}} \frac{dQ}{dt} \quad (3)$$

where ELC_0 is the energy loss coefficient of the aortic valve (13,14), which depends on the valve EOA and the aortic cross-sectional area at the level of the sinotubular junction (A_A):

$$ELC_0 = \frac{A_A EOA}{A_A - EOA} \quad (4)$$

The expression of the ventricular pressure during the ejection phase is then:

$$P_v(t) = P(t) + \frac{\rho}{2 ELC_0^2} (Q_0 \sin(\omega t))^2 + \frac{2\pi\rho}{\sqrt{ELC_0}} \omega Q_0 \cos(\omega t) \quad (5)$$

C was varied from 3.0 to 0.5 ml/mmHg and R from 1,332 to 3,330 dyne·s/cm⁵ for three different degrees of AS (EOA = 0.5, 0.75, and 1.0 cm²). For each of these conditions, the ventricular and aortic pressure waveforms were computed using Equations (5) and A1 (see Appendix I), respectively, and the theoretical values of $\Delta P_{P_{toP}}$, peak ΔP and mean ΔP were then determined from these pressure waveforms.

In-vitro study

The pulse duplicator used in this study has been previously described and validated in detail (14-16). It comprises a fluid reservoir, a gear pump, and adjustable systemic arterial resistance and compliance. The pulsatile flow was provided by a computer-controlled direct-current motor coupled to a gear pump (Vi-Corr; Viking Pump, Cedar Falls, IA, USA). The LV

outflow tract and ascending aorta were both circular and rigid. The aortic compliance consisted of a rubber tube enclosed within a hermetic Plexiglas box, filled with water and air, and connected to an air vacuum/compressor.

The fluid used in the model was a mixture of water and glycerol (67/33, v/v), of viscosity 3.5 cp. The flow rate was measured using an electromagnetic flowmeter (Cliniflow II; Carolina Medical Electronics, King, NC, USA), and pressure measurements were performed using Millar catheters under a sampling frequency of 300 Hz. The LV pressure was measured 20 mm upstream of the valve, and the aortic pressure 100 mm downstream of the valve, in order to determine peak (ΔP_{peak}), mean (ΔP_{mean}), and peak-to-peak (ΔP_{ptoP}) transvalvular pressure gradients. The valve EOA was calculated using the following formula (16):

$$\text{EOA} = \left(\frac{1}{A_A} + \sqrt{\frac{2 \Delta P_{\text{mean}}}{\rho Q^2}} \right)^{-1} \quad (6)$$

Systemic compliance was calculated using the two-area method introduced by Liu et al. (17). Systemic resistance was calculated using the ratio of mean aortic pressure to mean transvalvular flow rate.

Experimental conditions

Two fixed stenoses (plates with circular orifices with a geometric area of 1.0 and 1.35 cm²) and a Medtronic Mosaic 21-mm valve (EOA 1.2 cm²) were tested in the model. To simulate the different situations that might occur in hypertensive patients, R was increased from 1,500 to 3,300 dyne-s/cm⁵ (four levels), while for each level of R the C was varied between 0.9 and 2.9 ml/mmHg (four levels). All experiments were performed at a heart rate of 60 bpm, with a LV ejection time of 300 ms and stroke volume of 83 ± 17 ml. The shape of the flow waveform was maintained constant ($Q^2 = \text{Cte}$), as this may affect the ΔP -values, regardless of mean flow rate.

The ΔP_{ptoP} is difficult to determine using a simple

mathematical expression, but was estimated using a non-linear regression analysis of the in-vitro results. The peak LVSP was then computed by summation of the SAP and ΔP_{ptoP} predicted from the regression equation.

Animal study

In order to validate the new mathematical expression proposed for the estimation of peak LVSP, a dataset obtained in 24 pigs with experimentally induced AS was used. Details of this animal study have been described previously (4). Briefly, a severe supravalvular AS was created in 24 pigs using an umbilical tape tightened around the aorta approximately 2 cm downstream of the aortic valve annulus. Systemic hypertension was induced either by banding of the distal thoracic aorta or by infusion of phenylephrine. The ΔP across the stenosis was measured with Doppler echocardiography and by catheterization, first at normal systemic arterial pressure, and subsequently during hypertension. Six of the 24 animals had two hypertension stages; hence, the protocol resulted in 54 data points. Some of these data were used in a previous publication (4).

Other investigators have also proposed estimating LVSP by adding peak ΔP or mean ΔP to the SAP (10,18). Thus, three formulae were tested that could be used for non-invasive estimation of peak LVSP: (SAP + ΔP_{peak}); (SAP + ΔP_{mean}); and (SAP + ΔP_{ptoP} predicted from Eq. (7)). The LVSP estimated by these formulae was compared with that measured directly by catheterization. In order to provide a more clinical perspective to these results, the valve EOA, peak ΔP , mean ΔP and C measured by Doppler echocardiography and sphygmomanometry were used in these formulae (Table I).

Statistical analysis

Data were expressed as mean ± SD, and compared using a *t*-test. Statistical analysis of the association of variables was performed using the Pearson correlation

Table I: Measurement methods of hemodynamic parameters required for non-invasive estimation of peak left ventricular systolic pressure.

Parameter	Method	Equation
SAP	Sphygmomanometry	
EOA	Doppler echocardiography	Continuity equation
ΔP_{mean}	Doppler echocardiography	Simplified Bernoulli equation
C	Doppler echocardiography (SV) and sphygmomanometry (PP)	$C = \text{SV}/\text{PP}$

ΔP_{mean} : Mean transvalvular pressure gradient; C: Systemic arterial compliance; EOA: Effective orifice area; PP: Arterial pulse pressure; SAP: Systolic arterial pressure; SV: Stroke volume.

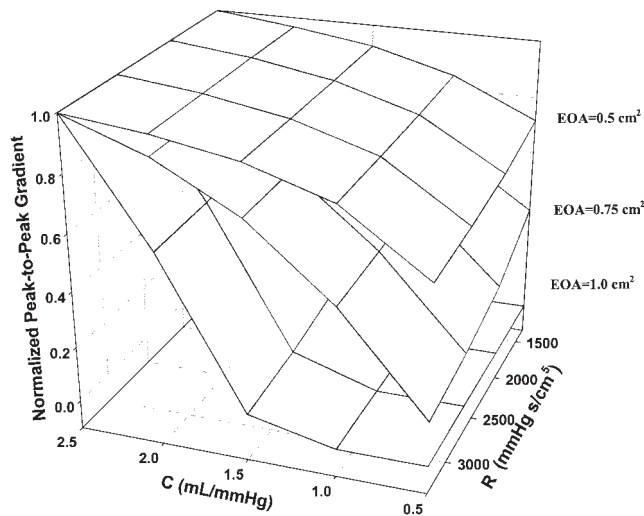


Figure 1: Theoretical variation in normalized peak-to-peak transvalvular pressure gradient with respect to systemic arterial compliance (C) and systemic vascular resistance (R) for three different degrees of aortic stenosis severity (valve effective orifice area (EOA) = 0.5, 0.75, and 1.0 cm²).

coefficient, and graphs were constructed using the corresponding regression equation. A p-value <0.05 was considered to be statistically significant.

Results

Numerical study

The numerical simulations performed using the theoretical model described in Eqs. (1), (2), (3) and (5) suggest that R and C have no direct effect on peak and mean ΔP_s . These simulations also suggested that $\Delta P_{P_{top}}$ was independently influenced by C, but not by R (Fig. 1). Figure 1 shows the normalized $\Delta P_{P_{top}}$ (i.e., normalized with respect to the $\Delta P_{P_{top}}$ value at the lowest level of C) as a function of C and R for three different degrees of AS (EOA = 0.5, 0.75, and 1.0 cm²). The $\Delta P_{P_{top}}$ was markedly reduced when C decreased, and the reduction appeared to be relatively more important for less severe stenosis. For the 1.0-cm² stenosis, the $\Delta P_{P_{top}}$ was almost completely abolished, falling from 21 to 7 mmHg, during which time C fell from 3.0 to 0.5 ml/mmHg.

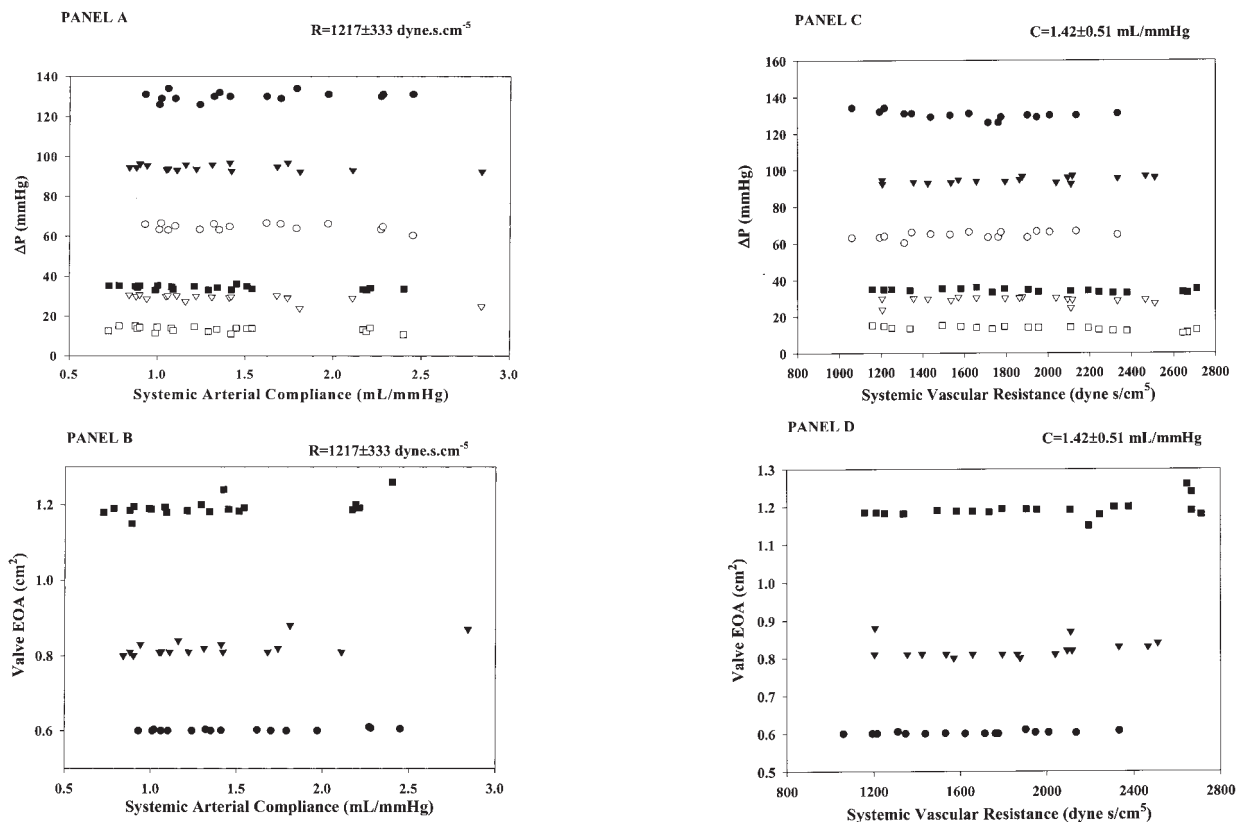


Figure 2: Effect of systemic arterial compliance (C) and systemic vascular resistance (R) on peak and mean transvalvular pressure gradients (ΔP_s) (panels A and C) and effective orifice area (EOA) (panels B and D). Panels A, B: Systemic vascular resistance (R) was maintained constant at $1,217 \pm 333$ dyne·s/cm⁵, and C was varied from 0.9 to 2.9 ml/mmHg. Panels C, D: Compliance (C) was maintained constant at 1.42 ± 0.51 ml/mmHg, and R was varied from 1,500 and 3,300 dyne·s/cm⁵. ●, circular orifice 1.0 cm²; ▼, circular orifice 1.35 cm²; ■, Medtronic Mosaic 21-mm valve. Closed symbols indicate peak ΔP ; open symbols indicate mean ΔP .

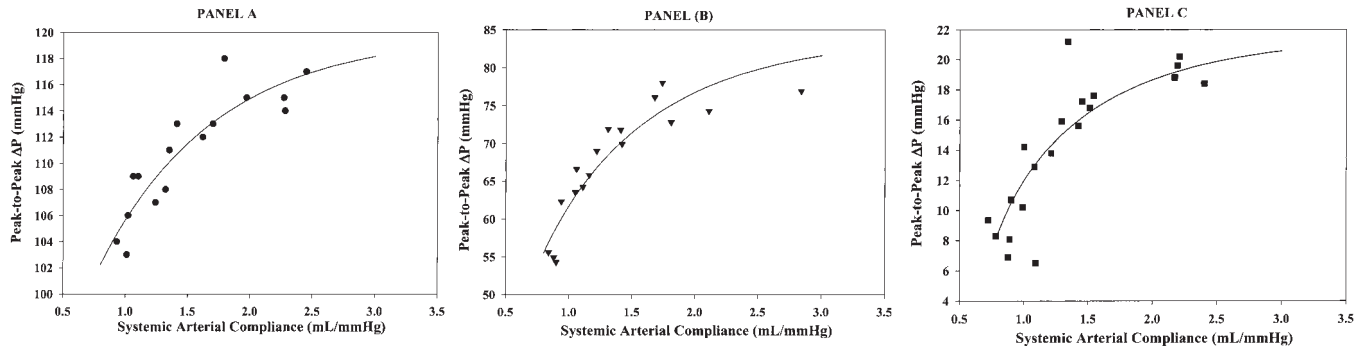


Figure 3: Effect of systemic arterial compliance on peak-to-peak transvalvular pressure gradient. Panel A: Circular orifice 1.0 cm²; Panel B: circular orifice 1.35 cm²; Panel C: Medtronic Mosaic 21-mm valve.

In-vitro study

The effects of C and R on peak and mean ΔPs and valve EOA obtained in in-vitro experiments are illustrated in Figure 2 (panels A and B, respectively). As predicted by the theoretical model, C and R had no significant effect on peak and mean ΔPs, or on valve EOA. In contrast, changes in C had a major influence on ΔP_{PtoP} (Fig. 3); when C was reduced from 2.9 to 0.9 ml/mmHg, the ΔP_{PtoP} fell by 15 mmHg (-69%) in the Mosaic 21-mm bioprosthetic valve, by 24 mmHg (-30%) in the circular rigid orifice 1.35 cm², and by 15 mmHg (-13%) in the circular rigid orifice 1.0 cm². As predicted by the theoretical results, the effect of C on ΔP_{PtoP} was more pronounced in mild/moderate AS than in severe AS. ΔP_{PtoP} was estimated using a non-linear regression analysis of the in-vitro results:

$$\Delta P_{PtoP} = \frac{\Delta P_{mean}}{1 + (7.88 \text{ EOA} - 1) e^{-\sqrt{C}}} \quad (7)$$

It should be emphasized that all the parameters included in this equation can easily be measured using non-invasive methods (Table I). EOA and mean ΔP can indeed be measured by Doppler echocardiography,

while C can be calculated as the ratio of stroke volume (measured by Doppler echocardiography) to pulse pressure (measured by sphygmomanometry) (6,19). This equation indicated that, for a fixed stenosis severity (i.e., fixed EOA), ΔP_{PtoP} decreased with respect to C and became much lower than mean ΔP at low C levels.

Animal study

The animal data were used to test the three formulae described above. When compared to peak LVSP measured by catheterization, the mean absolute errors were 27 ± 16 mmHg for the formula (SAP + ΔP_{peak}), 13 ± 9 mmHg for the formula (SAP + ΔP_{mean}), and 5 ± 5 mmHg for the formula (SAP + ΔP_{PtoP} predicted from Eq. (7)) (Table II; Fig. 4). The first formula (SAP + ΔP_{peak}) overestimated peak LVSP in all situations, but the overestimation was much more important at low levels of C (Table II; Fig. 4, panel A). The second formula (SAP + ΔP_{mean}) overestimated peak LVSP in the presence of low C (Table II; Fig. 4, panel B). In contrast, the third formula (SAP + ΔP_{PtoP} predicted from Eq. (7)) provided an accurate estimation of LVSP, regardless of the level of C (Table II; Fig. 4, panel C).

Table II: Mean absolute errors for different formulae used for non-invasive estimation of peak left ventricular systolic pressure (LVSP).

Formula to estimate peak LVSP	Absolute error (mmHg)			
	All data (n = 54)	C < 0.6 (ml/mmHg) (n = 7)	0.6 < C < 1.3 (ml/mmHg) (n = 35)	C > 1.3 (ml/mmHg) (n = 12)
SAP + ΔP _{peak}	27 ± 16*	33 ± 11*	30 ± 15*	16 ± 17*
SAP + ΔP _{mean}	13 ± 9*	17 ± 6*	15 ± 9*	5 ± 4*
SAP + predicted ΔP _{PtoP}	5 ± 5	5 ± 3*	6 ± 5	4 ± 4

*Significant difference versus peak LVSP measured by catheterization.

ΔP: Transvalvular pressure gradient; ΔP_{mean}: Mean ΔP; ΔP_{peak}: Peak ΔP; ΔP_{PtoP}: Peak-to-peak ΔP; C: Systemic arterial compliance; SAP: Systolic arterial pressure.

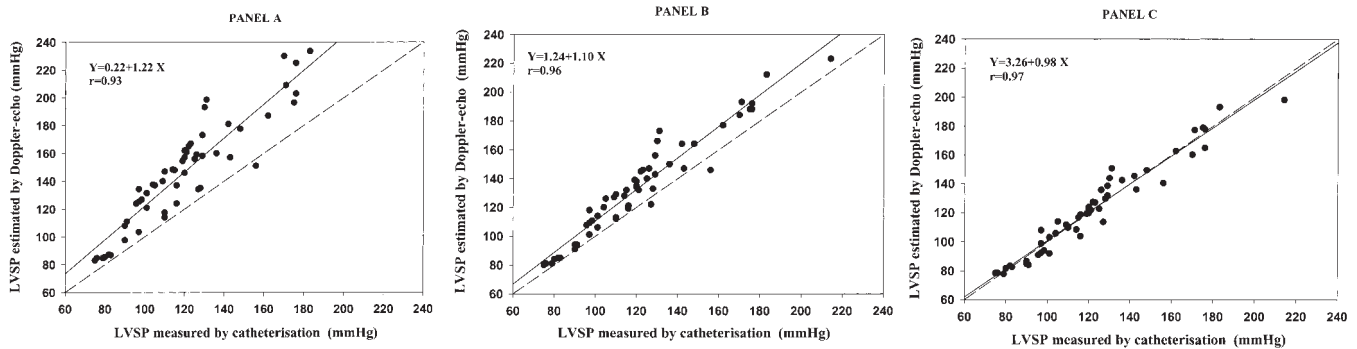


Figure 4: Correlation between peak left ventricular systolic pressure (LVSP) measured by catheterization in 24 pigs with AS, and LVSP estimated by Doppler echocardiography using the following formulae: Panel A: [systolic arterial pressure (SAP) + peak transaortic pressure gradient (ΔP)]; Panel B: [SAP + mean ΔP]; Panel C: [SAP + peak-to-peak ΔP predicted by Eq. (7)].

Discussion

In contrast to previous in-vivo studies, it was possible in the present study independently to control and modify the various parameters involved in valvular and vascular hemodynamics. The major findings of the study were that:

Changes in C and/or R had no direct effect on peak ΔP , mean ΔP , and valve EOA. Hence, these findings confirm that the significant reductions in peak and mean ΔP s observed in AS patients with hypertension are likely due to a concomitant variation in flow rate and/or EOA.

A decrease in C is associated with a marked reduction in $\Delta P_{P_{toP}}$, which is independent of other hemodynamic parameters. Hence, $\Delta P_{P_{toP}}$ cannot be used to assess AS severity because it is also highly influenced by systemic arterial hemodynamics.

It is possible to estimate $\Delta P_{P_{toP}}$ and thereby peak LVSP by Doppler echocardiography and sphygmomanometry. The non-invasive estimation of LVSP may be useful to assess LV afterload in AS patients.

The major implication of the present study was that a reduction in C may indeed cause a marked decrease in $\Delta P_{P_{toP}}$ and thus lead to a major underestimation of stenosis severity. In this context, it should be emphasized that up to 40% of adult patients with AS have an abnormally low C (6), and that $\Delta P_{P_{toP}}$ is still often used to evaluate AS severity in adults (20-22) as well as in children (23,24). Hence, $\Delta P_{P_{toP}}$ should not be used to evaluate AS severity and in particular, the recording of a low $\Delta P_{P_{toP}}$ should not be used to exclude the presence of a severe stenosis. To this effect, Christensen et al. (22) reported the clinical outcome in a subset of 12 patients in whom a conservative strategy was adopted on the basis of low invasive peak-to-peak pressure. All of these patients had a preserved LV function at baseline, and were not offered aortic valve replacement despite markedly reduced aortic valve EOA values

(<1.0 cm² in 10 patients, and 1.0-1.3 cm² in two) and the presence of symptoms. At 2.5 years' follow up, six patients had died, three had experienced further symptom progression and underwent aortic valve replacement, and three had a major worsening of their symptomatic status despite optimal medical treatment.

In patients with AS, LV afterload may be increased not only as result of the stenosis (i.e., valvular load) but also as a result of reduced C and/or increased R (i.e., vascular load). To this effect, it should be pointed out that the prevalence of hypertension has been reported as 30-40% in patients with AS (6,25-27). When AS coexists with hypertension, the left ventricle faces a double pressure overload, and this may adversely affect LV function and patient outcome (6,26). As emphasized in previous studies (4,6,26), the assessment of LV afterload should thus become an integral part of the routine Doppler echocardiographic examination of patients with AS, as it may have direct and important implications with regard to LV function and patient prognosis. Nonetheless, the non-invasive measurement of indices of LV afterload requires the estimation of peak LVSP. In the Doppler echocardiography laboratory, this parameter is generally estimated by adding SAP and mean ΔP as a substitute for $\Delta P_{P_{toP}}$. However, as shown in Table II, this approach overestimates the peak LVSP and thus LV afterload in patients with reduced C. A more accurate estimation of LVSP can be obtained by adding SAP to $\Delta P_{P_{toP}}$ predicted by Eq. (7). Hence, by correcting mean ΔP for the influence of C, the new method proposed in the present study provides a more accurate assessment of LVSP. Interestingly, the new method is easily applicable to the clinical setting, as the three parameters included in Eq. (7) – that is, valve EOA, mean ΔP and C – are easily measurable in the context of routine Doppler echocardiography (6). The calculation of C simply requires the measurement of stroke volume and pulse pressure (Table I).

In a recent study (6), the proposal was made to esti-

mate global LV afterload in AS patients with the "valvulo-arterial impedance" calculated as the ratio of $SAP + \Delta P_{\text{mean}}$ (as an estimate of peak LVSP) and stroke volume index. Valvulo-arterial impedance therefore represents the valvular and arterial factors that oppose ventricular ejection by absorbing the mechanical energy developed by the left ventricle. This new index was found to be the strongest independent predictor of LV diastolic and systolic dysfunction in this series of AS patients. The new method proposed in the present study (see Eq. (7) and Table I) for the estimation of peak LVSP could further improve the accuracy and predictive value of the valvulo-arterial impedance that may be particularly useful when assessing LV afterload in the presence of AS, hypertension, or both. This method could also improve the clinical performance of other indices, such as peak LV systolic wall stress, that require peak LVSP for their calculation.

Study limitations

In the present study, the effect of systemic hypertension on the transvalvular pressure gradients was evaluated using theoretical and in-vitro approaches. As described above, in the in-vitro model the LV outflow tract and ascending aorta were both circular and rigid; hence, this model is characterized by infinite ventricular input impedance. In such circumstances, the LV flow waveform may contain some low-frequency oscillations (28) that are transmitted to the LV pressure and therefore to the instantaneous transvalvular pressure gradient. In the particular case of low transvalvular pressure gradients (TPGs), the peak-to-peak TPG may, therefore, vary as a consequence of LV pressure waveform oscillations, without any variation in the systemic arterial compliance. However, this is not the case in the present study as the TPGs were significantly high and the pump used for the in-vitro study was sufficiently powerful to generate a flow waveform without any low-frequency oscillations (12). Therefore, any variation in peak-to-peak TPG observed in vitro may be related only to a variation in the systemic arterial compliance.

In conclusion, ΔP_{PtoP} should not be used to evaluate AS severity because, in contrast to peak ΔP and mean ΔP , it is heavily influenced by C . In particular, a low ΔP_{PtoP} cannot be used to exclude the presence of a severe AS. The new non-invasive method proposed herein to estimate LVSP may be useful for obtaining a more accurate estimate of global LV afterload in patients with AS.

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Appendix I

The solution of Eq. (1) using the instantaneous flow $Q(t)$ (Eq. (2)) can be written as:

$$P(t) = \begin{cases} \frac{Q_0}{C \times \left(1 + \left(\frac{1}{\tau\omega}\right)^2\right)} \left(\frac{1}{\tau\omega^2} \sin(\omega t) - \frac{1}{\omega} \cos(\omega t) \right) + \left(P_0 + \frac{Q_0}{C \times \omega} \left(\frac{1}{1 + \left(\frac{1}{\tau\omega}\right)^2} \right) \right) e^{-\frac{t}{\tau}} & 0 < t < T_s \\ \left(P_0 + \frac{Q_0}{C \times \omega} \left(\frac{1}{1 + \left(\frac{1}{\tau\omega}\right)^2} \right) \left(1 + e^{\frac{T_s}{\tau}} \right) \right) e^{-\frac{t}{\tau}} & T_s < t < T \end{cases} \quad (A1)$$

where

$$P_0 = \frac{Q_0}{C \times \omega} \left(\frac{1}{1 + \left(\frac{1}{\tau\omega}\right)^2} \right) \left(\frac{e^{\frac{T_s}{\tau}} + 1}{e^{\frac{T_s}{\tau}} - 1} \right)$$

τ is a time constant, i.e., the product of R and C and ω is the pulsation. This equation was used to compute the aortic pressure waveform.