The Pressure Gradient across the Endocardium

Rachad Mounir Shoucri

Royal Military College of Canada, Kingston, Ontario

Abstract

A mathematical formalism for the non-linear end-systolic pressure-volume relation (ESPVR) in the heart ventricles has the interesting feature that the peak active pressure generated by the myocardium (also called peak isovolumic pressure P_{isom} by physiologists) is included in the mathematical formalism describing the ESPVR. In this study we look at the ratio $(P_{isom} – P_m)/P_m$ as an index to segregate between different clinical groups, this ratio can be calculated in a non-invasive way with the mathematical model used. Application to the left ventricle by using clinical data taken from the medical literature is given and discussed. Mathematical relations between the ejection fraction (EF) and the parameters describing the ESPVR are used in a way to get new insight into the problem of heart failure with normal or preserved ejection fraction (HFpEF).

1. Introduction

The end-systolic pressure-volume relation (ESPVR) is the relation between pressure and volume in the left or right ventricle when the myocardium reaches its maximum state of activation during the contraction phase, possible clinical application of this relation has been extensively studied [1-10]. The mathematical model used in this study has been derived in previous publications [8-10], it is based on the theory of large elastic deformation of the myocardium. An interesting feature of this model is the introduction of the peak active force generated by the myocardium in the mathematical formalism describing the non-linear ESPVR. When inertia forces and viscous forces are neglected, the peak active force generated by the myocardium can be equated to the peak isovolumic pressure P_{isom} generated by the myocardium in a non-ejecting contraction. Non-invasive calculation of the ratio $(P_{isom} – P_m)/P_m$ is possible with the mathematical formalism used, and in this study we show how this ratio can be used for the purpose of segregation and classification of different clinical groups. This index can be related to the study of the problem of heart failure (HF) with normal or preserved ejection (HFpEF) as will be indicated, HFpEF is defined as HF with EF > 0.5 [7].

In what follows we first review the mathematical formalism used, then we present some applications to clinical data published in the literature [11-14]. The mathematical formalism applies to the right and left ventricle (LV), we restrict our discussion in what follows to the LV. Previous applications of the mathematical formalism to a wide range of clinical data have shown the consistency of the mathematical formalism used [8-10, and references given therein].

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2. Mathematical formalism

The left ventricle is represented as a thick-walled cylinder contracting symmetrically [8-10] (see Fig. 1). During the contraction phase, the myocardium generates a radial active force per unit volume of the myocardium designated by D_r, which force will develop an active pressure $\int_a^b D_r\, dr \approx P_{iso}$ on the inner surface of the myocardium (endocardium), a = inner radius, b = outer radius, h = b – a = thickness of the myocardium. In a quasi-static approximation (inertia and viscous forces neglected), the equilibrium of forces on the endocardium can be expressed in the form

$$P_{iso} – P = E_2\,(V_{ed} – V) \qquad (1)$$

P is the LV pressure, V the LV volume and it is indicated as V_{ed} at end-diastole (when dV/dt = 0), E_2 is an elastance coefficient that relates the difference of pressures $P_{iso} – P$ to the difference of volumes V_{ed} - V. Near end-systole when the myocardium reaches its maximum state of activation, Eq. (1) can be expressed in the form

$$P_{isom} – P_m = E_{2m}\,(V_{ed} – V_m) \qquad (2)$$

$V_m \approx V_{es}$ (V_{es} the end-systolic volume when dV/dt = 0), P_{isom}, P_m, and V_m are as defined in Eq. (1) but measured at the moment when the myocardium reaches its maximum state of activation. Figure 2 represents a non-linear ESPVR shown as the curve BDC, it is the relation obtained when P_m and V_m are varied and the peak isovolumic pressure P_{isom} is kept constant (as if a balloon is inflated against a constant P_{isom}). From Fig.2, $E_{2m} = \tan\beta_2$ corresponds to the slope of the line CD that

intersects the volume axis at a point indicated as V_{o2}.

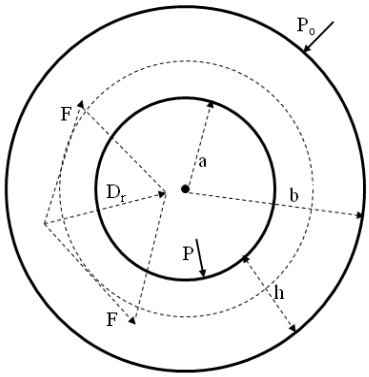

Figure 1: Cross-section of a thick-walled cylinder representing the left ventricle, D_r = active radial force/unit volume of the myocardium, P = left ventricular pressure, P_o = outer pressure (assumed zero) on the myocardium, a = inner radius, b = outer radius, h = b – a = thickness of the myocardium.

When the left ventricular pressure $P_m \rightarrow 0$, we have $V_m \rightarrow V_{om}$ in Eq. (2), and we get

$$P_{isom} = E_m (V_{ed} - V_{om}) \qquad (3)$$

$E_m = \tan\alpha$ is the slope of the line CB in Fig. 2, and V_{om} corresponds to the intercept with the volume axis at point B of the curve BDC. The tangent (with slope $\tan\gamma$) at point D to the curve BDC intersects the volume axis at a point corresponding to V_{ot}. The line BD has slope $\tan\beta_1$ as shown in Fig. 2. From trigonometric relations between the triangles one can derive (see also [8])

$$\tan\gamma/e_{am} = SV/(V_m - V_{ot}) = (P_t - P_m)/P_m \qquad (4a)$$

$$\tan\beta_2/e_{am} = SV/(V_m - V_{o2}) = (P_{isom} - P_m)/P_m \qquad (4b)$$

$$\tan\beta_1/e_{am} = SV/(V_m - V_{om}) = (P_s - P_m)/P_m \qquad (4c)$$

P_s is not shown in Fig. 2, and $e_{am} = P_m / SV$ is the arterial elastance. From Eqs (4) the stroke volume $SV \approx V_{ed} - V_m$ (and consequently $EF = SV/V_{ed}$) are related to the slopes describing the curve BDC, and to the intercepts V_{ot}, V_{o2}, and V_{om} shown in Fig. 2 and in Eqs. (4).

3. Criteria of LV performance

For simplicity we assume that P_m is constant during the contraction phase. When the point D on the ESPVR moves on the curve BDC, the stroke work $SW \approx P_m SV$ reaches its maximum value SW_x when the derivative $d(SW)/dV_m$ is zero. Simple calculation as in [8] gives

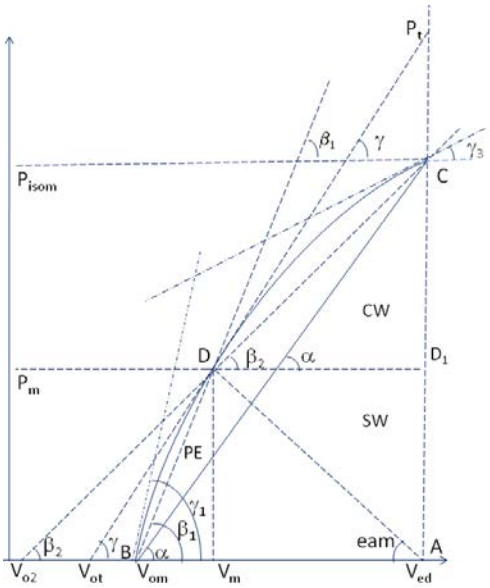

Figure 2: ESPVR represented by the curve BDC, intercept with the horizontal volume axis is B (corresponding to V_{om}). Stroke work SW ≈ area AD_1DV_m, PE = area determined by arc(BD)V_mB, CW = area determined by arc(DC)D_1D. TW = CW + SW + PE is total area under the ESPVR. Ventricular pressure P_m, P_{isom} is the peak isovolumic pressure. V_{ot} corresponds to the intercept with the volume axis of the tangent (with slope $\tan\gamma$) at point D, V_{o2} corresponds to the intercept of the line CD (with slope $\tan\beta_2$) with the volume axis; $e_{am} = P_m/SV$ is the arterial elastance.

$$\tan\gamma = e_{am} \quad \text{and} \quad SV = V_m - V_{ot} \qquad (5)$$

or equivalently $V_m = (V_{ed} + V_{ot})/2$. The stroke work reserve SWR is defined as

$$SWR = SW_x - SW \qquad (6)$$

SWR can be considered as a measure of the amount by which the energy SW delivered to the systemic load can increase. Consequently one can distinguish the following criteria of performance for the left ventricle:

a) $SW < SW_x$ and $SV > (V_m - V_{ot})$, with $\tan\gamma > e_{am}$. In this case an increase in the afterload P_m results in an increase in SW as expected, a normal state of the left ventricle.

b) $SW = SW_x$ and $SV = (V_m - V_{ot})$, with $\tan\gamma = e_{am}$ and SWR =0. In this case an increase in afterload P_m results in a mild decrease in SW causing cardiac insufficiency.

c) $SW < SW_x$ and $SV < (V_m - V_{ot})$, with $\tan\gamma < e_{am}$. In this case an increase in afterload P_m results in a severe decrease in SW causing severe cardiac insufficiency.

Experimental verification of these results can be found for the LV in [4,5], and for the right ventricle in [6].

4. Applications to clinical data

Figure 3 shows some clinical results verifying the results of the preceding discussion. It is calculated by using clinical data taken from from Azancot el al [11].

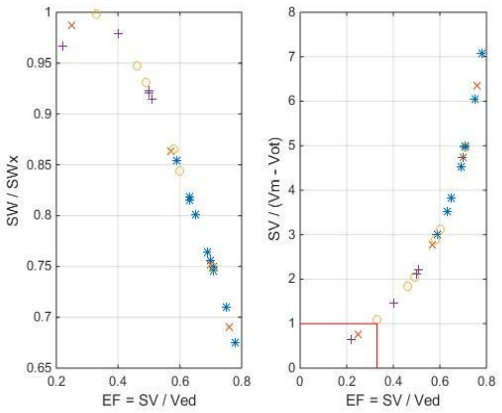

Figure 3: (right) Relation shows that for $SV/(V_m - V_{ot}) \approx 1$ we have $EF \approx 0.33$; (left) Relation shows that for $EF \approx 0.33$ we have $SW/SWx \approx 1$; normal *, hypertrophy x, dilated MC +, volume overload o. Data taken from Azancot et al [11].

The right side of Fig. 3 shows that for the critical value of $SV/(V_m - V_{ot}) \approx 1$ we have a value for EF ≈ 0.33, which corresponds to $SW/SWx \approx 1$ as seen on the left side. From Fig. 4 we see that for $SW/SWx \approx 1$ we have

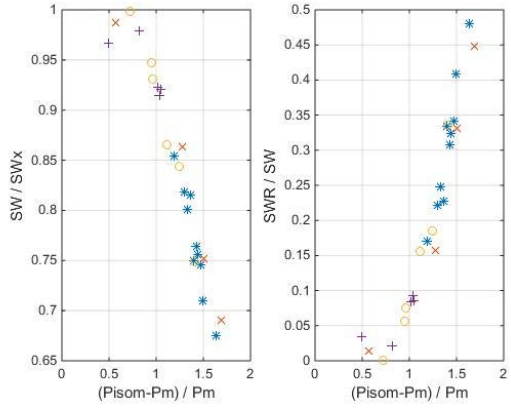

Figure 4: (left) Relation shows $(P_{isom} - P_m)/P_m \approx 0.6$ for $SW/SW_x \approx 1$; (right) Relation shows that for $(P_{isom} - P_m)/P_m \approx 0.6$ we have $SWR/SW \approx 0$; normal *, hypertrophy x, dilated MC +, volume overload o. Data taken from Azancot et al [11].

$SWR/SW \approx 0$ and $(P_{isom} - P_m)/P_m \approx 0.6$.

We have used another group of clinical data obtained from echocardiography measurements on five groups of patients taken from [12]. The relation between percentage of HF and EF was taken from [13] and it is reproduced in Fig. 5 (left side). The least square fit curve shown on the left side of Fig. 5 was calculated and used to derive the relation between percentage of HF and EF for data taken from [12] as shown on the right side of Fig. 5. Note in Fig. 5 (right side) that the normal group (*) appears around the minimum of the curve, with EF ≈ 0.67.

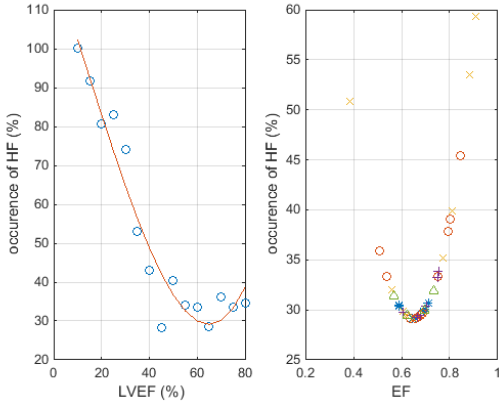

Figure 5: (left) Relation between percentage of HF and percentage of left ventricular EF, least square fit is used to calculate the right side, data from [13]; (right) Relation between percentage of HF and EF for five clinical groups; normal *, aortic stenosis o, aortic valvular regurgitation +, mitral regurgitation ^, miscellaneous cardiomyopathies x. Data from Dumesnil et al [12].

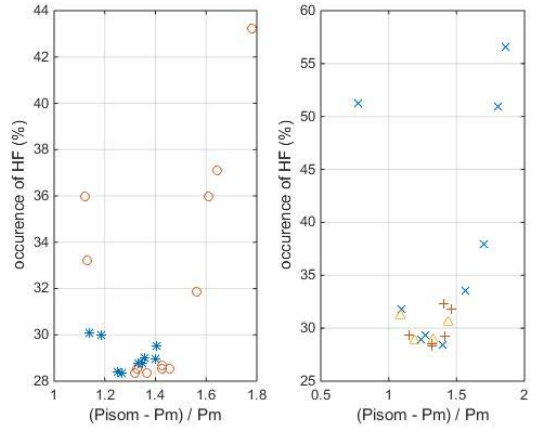

Figure 6: Relation between $(P_{isom} - P_m)/P_m$ and percentage of HF, normal * and aortic stenosis o, on the left side; on the right side aortic valvular regurgitation +, mitral regurgitation ^, miscellaneous cardiomyopathies x,. Data from Dumesnil et al.

From Eq (4b) and the least square fit shown in Fig 5 (left), the relation between $(P_{isom} - P_m)/P_m$ and the percentage of HF is calculated in Fig. 6. We have shown separately on the left side the normal group (*), and the aortic stenosis group (o) for the purpose of clarity. Note the minimum observed for $(P_{isom} - P_m)/P_m \approx 1.33$ in Fig. 6. Note also in Fig. 6 (left) that only part of the group of aortic stenosis overlaps with the normal group, a similar observation applies to the right side of Fig. 6.

Figure 7 compares results for aortic stenosis (o) with the normal group (*). One can observe three apparent groupings of the data of aortic stenosis:

a) a grouping with low $(P_{isom} - P_m)/P_m$ corresponding to low EF but high SW/TW, indicating low values of TW

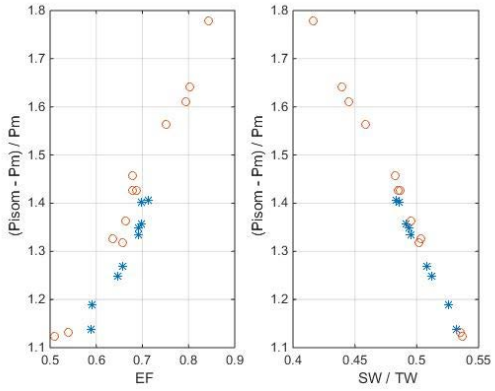

Figure 7: (left) Relation between $(P_{isom} - P_m)/P_m$ and EF; (right) Relation between $(P_{isom} - P_m)/P_m$ and SW/TW; normal group *, aortic stenosis o. Note the three groupings for cases of aortic stenosis.

and P_{isom}, and possible depressed state of the myocardium. One can assume that the total area TW under the ESPVR reflects the total energy needed by the LV (including the myocardium) to perform its function.

b) A grouping around the normal group, with $(P_{isom} - P_m)/P_m \approx 1.33$ corresponding to EF ≈ 0.67 and SW/TW ≈ 0.5 (SW/TW = stroke work/total area under ESPVR).

c) A grouping with high $(P_{isom} - P_m)/P_m$ corresponding to high EF but low SW/TW, indicating high values for TW and P_{isom}, corresponding to a possible case of hypertension (and possibly high resistance to aortic flow).

5. Discussion

A Numerical calculation of the values of V_{om}, V_{ot}, and V_{o2} (see Fig. 2) allows the calculation of several parameters of the curve BDC representing the ESPVR, from which important indexes can be derived like in Eqs. (4). In this study we have given special attention to the non-invasive calculation of $(P_{isom} - P_m)/P_m$ by using Eq. (4b), results of application of this index to clinical data have been presented in Figs 3 to 7 that show that bivariate (and possibly multivariate) analysis of data is superior to univariate analysis of data (like by using only EF). Figures 5 to 7 show that cases of HFpEF appear with values of EF > (EF for normal group (*)). Further assessment of these results requires an invasive measurement of the ventricular pressure P_m.

6. Conclusion

The curve showing the percentage variation of HF can be implemented for routine clinical work in a non-invasive way with several indexes derived from the ESPVR, when ratios of pressures and areas are calculated. EF appears as one index of several indexes that can be applied for non-invasive routine clinical work.

References

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Address for correspondence.

Rachad Mounir Shoucri
Department of Mathematics and Computer Science
Royal Military College of Canada, Kingston, Ontario, K7K 7B4
shoucri-r@rmc.ca