ESPVR and the Mechanics of Ventricular Contraction

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Abstract: - This study is written in a way to stress the importance of introducing the active force generated by the myocardium in the formalism describing the pressure-volume relation (PVR) in the left ventricle. Various clinical applications of the end-systolic pressure-volume relation (ESPVR) are also discussed. Attention is given to the calculation of the ejection fraction (EF) and the myocardial longitudinal axis shortening, a subject that is gaining importance in the study of heart disease and heart failure.

Key-Words: - Pressure-volume relation in the left ventricle, end-systolic pressure-volume relation, active force of the myocardium, isovolumic pressure, ejection fraction, myocardial longitudinal axis shortening, cardiac mechanics.

1 Introduction

Extensive studies of the application of the end-systolic pressure-volume relation (ESPVR) and its application to assess the performance of the left ventricle have been published in the literature over the past years [1-10], one can find a review in the work of Burkhoff et al [2]. Various aspects of those studies include the way to relate the contractility of the myocardium to the maximum slope E_{max} of the ESPVR [3], the influence of preload or afterload on ESPVR [4-6], how to express the ventriculo-arterial coupling by using the ratio E_{max}/e_{am} (max. ventricular elastance/max. arterial elastance) and how it affects the ESPVR [7,8], relation between oxygen consumption and the PVA area under ESPVR [9,10], how to express the performance of the left ventricle by using the ratio end-systolic pressure/end-systolic volume [11-13]. One can also mention two books published on the study of the properties of ESPVR [14,15]. Recently there have been attempts to apply the properties of the ESPVR to explain the problem of heart failure with normal ejection fraction (HFnEF) [16-18]. In a series of previous publications I have tried to stress the importance of introducing the active force of the myocardium, called isovolumic pressure P_{iso} by physiologists, in the formalism describing the PVR in the left ventricle [19-23]. This approach has lead to new insight in the way the areas under the ESPVR can be used for clinical applications [24,25], for the study of the relation between the areas under the ESPVR and oxygen consumption [26] and for the study of the non-linear pressure-volume relation in the left ventricle [23]. Extension of these results to the right ventricle was also discussed [27]. These studies were based on a cylindrical model for the left ventricle because of its simplicity; it allows the derivation of the results needed without unnecessary mathematical complications. Once the results are obtained, sophistication by using more elaborate models is possible. Although the approach used in this study can be applied also to the right ventricle [27], we shall restrict our discussion to the left ventricle.

In this study the approach previously described in which P_{iso} is introduced in the formalism describing the PVR is applied to the study of the problem of HFnEF [29], it is known that about half of patients with symptoms of heart failure (HF) have near-normal or normal ejection fraction (EF). We show that new ideas can be introduced by relating EF to ESPVR. The influence of the change in geometry of the left ventricle on EF [30-33] is also discussed along the line of the studies published by Dumesnil et al [34-38].

2 ESPVR

2.1 Active force of the myocardium & PVR

The mathematical formalism is based on a quasi-static approximation of left ventricular contraction, i.e. inertia forces and viscous forces neglected. The left ventricle is represented as a thick-walled cylinder contracting symmetrically (see Fig. 1). The way to introduce the radial active force $D_r(r)$ developed by unit volume of the myocardium in the formalism describing the PVR in the left ventricle has been discussed in previous studies [20-23] by using the theory of large elastic deformation. We shall not repeat the mathematical details of the derivation here, in this study we shall derive in an intuitive way the basic results needed. As shown in Fig.1, the active force/unit volume $D_r(r)$ generated by the myocardium will exert a pressure on the endocardium (inner surface of the myocardium) during an ejecting contraction that is given by

$$\int_a^b D_r(r)dr = \underline{D_r}h \qquad (1)$$

where $\underline{D_r}$ is a value calculated by applying the mean value theorem and $h = b - a$ is the thickness of the myocardium. To follow the usage of physiologist we shall use the notation $\underline{D_r}h = P_{iso}$, the pressure that would have been developed by the myocardium in case of an isovolumic contraction.

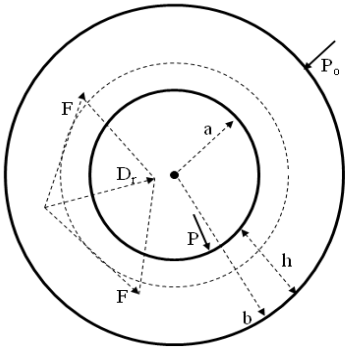

Fig. 1 Cross-section of a thick-walled cylinder representing the left or right ventricle. A helical muscular fibre in the myocardium is projected on the cross-section as a dotted circle. Because of the assumed symmetry of the problem, a radial active force/unit volume of the myocardium D_r is developed. Left ventricular cavity pressure is P, pressure on the epicardium = P_o, inner radius = a, outer radius = b, thickness of the myocardium $h = b - a$.

From Fig.1 and neglecting the external pressure P_o, the equilibrium of forces on the endocardium is given by

$$P_{iso} - P = E\,(V_{ed} - V) \qquad (2)$$

which simply states in a simplified way that the resultant force acting on the surface of the endocardium is proportional to the change of ventricular volume from end-diastolic value V_{ed} to the value V corresponding to the ventricular pressure P. One should note that $E \equiv E(V)$ is a function of the ventricular volume V, so that Equ. (2) is essentially a non-linear function of the ventricular cavity V. As shown in Fig. 2, near end-systole when the slope E reaches its maximum value E_{max}, equ. (2) is written as

$$P_{isom} - P_m = E_{max}\,(V_{ed} - V_{dm}) \qquad (3)$$

where P_m is the ventricular pressure (assumed for simplicity constant during the ejection phase), the slope E_{max} of the ESPVR corresponds to the maximum state of activation of the cardiac muscle, V_{ed} is the end-diastolic volume (defined when $dV/dt = 0$), V_{dm} is the intercept of the ESPVR with the volume axis, V_m is the value of V when $E = E_{max}$ and is approximately equal to V_{es}, the end-systolic volume (defined when $dV/dt = 0$). It is important to notice that Equs (2) and (3) can be looked at in two ways:
(1) If P_{iso} (or P_{isom}) is kept constant and P and V are varied, one gets the line with slope E (or E_{max}) as if a balloon is inflated against a constant force P_{iso}.
(2) If P_{iso} is allowed to vary with P and V, one gets for the relation between P and V a normal closed loop of an ejecting contraction represented in a simplified way by the rectangle $V_{ed}d_2d_1V_m$ in Fig. 2; in this case the point (P_{iso}, V) will vary near the line d_2d_4 in Fig. 2.

Equs (2) and (3) can be split into two parts:

$$P = E\,(V - V_d) \qquad (4)$$

$$P_{iso} = E\,(V_{ed} - V_d) \qquad (5)$$

and near end-systole

$$P_m = E_{max}\,(V_m - V_{dm}) \qquad (6)$$

$$P_{isom} = E_{max}\,(V_{ed} - V_{dm}) \qquad (7)$$

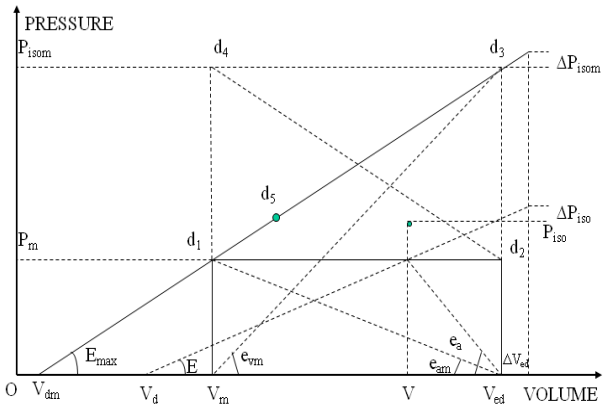

Fig. 2 Simplified drawing of the PVR in the left ventricle, the ESPVR is represented by the line d_3V_{dm} with slope E_{max}; the line with slope E is an intermediate position. During an ejecting contraction $V_{ed}d_2d_1V_m$ represents the pressure-volume loop, the left ventricular pressure is assumed constant with value P_m, the active force of the myocardium P_{iso} will vary near the line d_2d_4 to reach its maximum value P_{iosm} when $E = E_{max}$. Notice the change ΔP_{iso} and ΔP_{isom} corresponding to ΔV_{ed} according to the Frank-Starling mechanism. It is assumed that $V_m \approx V_{es}$ the end-systolic volume.

The variations ΔP_{iso} and ΔP_{isom} corresponding to ΔV_{ed} in Fig. 2 represent a way to express the Frank-Starling

mechanism. Extensive studies have been done in order to apply Equs. (4) and (6) to study of the ESPVR (for a review see [2]). However Equs (2-7) show that there are three different ways to describe the equation of the lines approximating the isochronous pressure-volume relations, and that the active force of myocardium P_{iso} can be included in the equation describing the PVR in an ejecting contraction as in Equs. (2) and (3). The application of these equations to study the PVR in the right ventricle was done in [27] based on experimental data taken from the works of Maughan et al [39] and Brent et al [40]. Application to the left ventricle has also been extensively discussed on the basis of experimental data published in the literature [20-26,28].

There have been some attempts to approximate E_{max} by the ratio (ventricular pressure/ventricular volume) as in [12,41]. It is based on the fact that Equs (6) and (7) can be written in the form

$$P_m - P_{dm} = E_{max}\, V_m \tag{8}$$

$$P_{isom} - P_{dm} = E_{max}\, V_{ed} \tag{9}$$

where $P_{dm} = -\, E_{max}\, V_{dm}$ is the pressure-axis intercept of the ESPVR and $V_m \approx V_{es}$. If P_{dm} is small, then it is possible to approximate E_{max} with P_m/V_m. Other ways to estimate P_{isom} and/or E_{max} from single-beat measurement are discussed in the critical review given in [42].

Finally it should be noted that the splitting of the basic equations (2) and (3) as in Equs (4) to (7) is not unique. An alternative way is to write

$$P = e_a\,(V_{ed} - V) \tag{10}$$

$$P_{iso} = e_v\,(V_{ed} - V) \tag{11}$$

and near end-systole

$$P_m = e_{am}\,(V_{ed} - V_m) \tag{12}$$

$$P_{isom} = e_{vm}\,(V_{ed} - V_m) \tag{13}$$

It is easy to show that

$$E_{max} = e_{vm} - e_{am} \tag{14}$$

The elastances e_{vm} and e_{am} are shown in Fig. 2. It is also easy to derive the following relation

$$E_{max}\, V_{dm} = e_{vm}\, V_m - e_{am}\, V_{ed} \tag{15}$$

Given $V_m \approx V_{es}$ the end-systolic volume and V_{ed} the end-diastolic volume, Equs (14) and (15) show that there is an interrelation between the different coefficients describing the *PVR* as shown in Fig. 2, one cannot focus on one coefficient to study the contractility of the cardiac muscle. Notice that $E_{max} = (P_{isom} - P_m)/SV$ and $e_{vm} = P_{isom}/SV$ have the units of pressure/stroke volume. As shown in the review article given in [42], the value of E_{max} estimated by different methods is preload and afterload dependent and is not sensitive to the change in the inotropic state of the cardiac muscle. It is important to stress at this point the importance to give more attention to the active force P_{iso} generated by the myocardium during the systolic phase in the study of the contractility of the cardiac muscle, as well as its inclusion in the study of the PVR as expressed by Equs. (2) and (3). As explained in the next section, the different areas defined under the ESPVR obtained by introducing P_{isom} in Fig. 2 to Fig. 4 have important clinical applications.

2.2 Normal & depressed state of the heart

A first interesting application of the previous results can be derived from Fig. 2 and is shown in Fig. 3. In Fig. 3, d_5 is the middle point of the segment d_3V_{dm} representing the ESPVR. The stroke work *SW*, which is the energy delivered to the systemic circulation, is represented by the area $V_{ed}d_2d_1V_m$. It reaches its maximum value $(SW)_{max}$ when d_1 and d_5 coincide as clearly shown in Fig. 3, in this case $E_{max} = e_{am}$ and the stroke volume $SV = (V_{ed} - V_{dm})/2$.

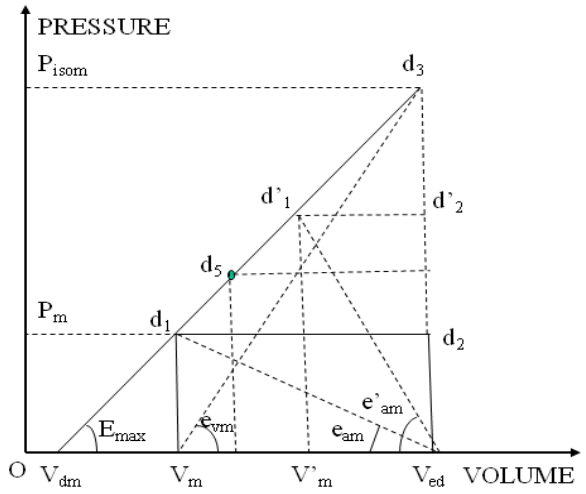

Fig. 3 a) Normal physiological state, d_1 below d_5 and $E_{max}/e_{am} \approx 2$; b) Mildly depressed state of the heart, d_1 and d_5 coincide and $E_{max}/e_{am} \approx 1$; c) Severely depressed state of the heart, d'_1 above d_5 and $E_{max}/e'_{am} < 1$.

Consequently the performance of the left ventricle can be expressed through the ratio E_{max}/e_{am} as follows:
a) We have the normal case with $E_{max}/e_{am} \approx 2$, which corresponds to $P_m/P_{isom} \approx 1/3$ (d_1 below d_5). In this case EF satisfies $SV/V_{ed} > (1 - V_{dm}/V_{ed})/2$. This case corresponds also to maximum efficiency for oxygen consumption in the myocardium [26].

b) Mildly depressed state of the heart with $E_{max}/e_{am} \approx 1$ or $P_m/P_{isom} \approx 1/2$ (d_1 and d_5 coincide), stroke work is $(SW)_{max}$ and EF is given by $SV/V_{ed} = (1 - V_{dm}/V_{ed})/2$).
c) Severely depressed state of the heart corresponding to $E_{max}/e'_{am} < 1$ or $P_m/P_{isom} > 1/2$ (d'_1 above d_5). EF must satisfy $SV/V_{ed} < (1 - V_{dm}/V_{ed})/2$. In this case an increase in P_m causes a decrease in stroke work SW resulting in cardiac insufficiency.

Consequently whether the myocardium is performing work in a normal state, in a mildly depressed state or in a severely depressed state of the myocardium does not depend only on EF, one has to consider also the relation between EF and the volume axis intercept V_{dm} of the ESPVR.

Experimental verification of these results for the left ventricle from experiments on dogs can be found in the work of Burkhoff and Sagawa [43], and from experiments on humans in the work of Asanoi et al [44]. Experiments on dogs confirming these results for the right ventricle can be found in the work of Brimiouille et al [45]. One can see how the addition of the upper area $d_1d_2d_3$ by introducing P_{isom} in Fig. 2 to Fig. 4 has added new understanding of ventricular mechanics.

2.3 Stroke work reserve

Another important application of the areas under the ESPVR can be derived from Fig. 4 by introducing the concept of stroke work reserve SWR; it is the area delimited by the closed contour $d_1d_2d_4d_5$.It is normal to think that in normal conditions, there may be a short term or a long term adaption of the ventricles in a way to maintain a SWR by adjusting the slope of the ESPVR as discussed in [28], the alternative will result in cardiac insufficiency as previously mentioned. We have shown in Fig. 5 the variation of SWR/SW with the difference $SV/V_{ed} - 0.5(1 - V_{dm}/V_{ed})$ based on data taken from Table 1 of Asanoi et al [44] from experiments on human subjects for three clinical groups with ejection fraction SV/V_{ed} >= 60%, between 40%-59%, and < 40%. One should notice that for negative values of SV/V_{ed} - $0.5(1 - V_{dm}/V_{ed})$, SWR is negative in Fig. 5 implying that d_1 is above d_5 in Fig. 3, this corresponds to the case of severely depressed state of the left ventricle. The experimental results shown in Fig. 5 confirm the results summarized in Fig. 3 and Fig. 4, these results show the importance of introducing the active force of the myocardium P_{iso} in the study of the PVR.

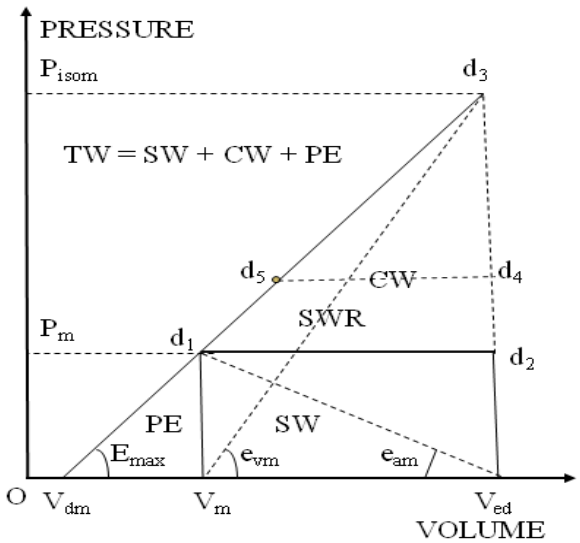

Fig. 4 Stroke work SW = area $V_{ed}d_2d_1V_m$; stroke work reserve SWR = area $d_1d_2d_4d_5$; apparent energy absorbed by the passive medium of the myocardium CW = area $d_1d_2d_3$; apparent energy absorbed by the internal metabolism of the myocardium PE = area $V_{dm}V_md_1$; total area under ESPVR $TW = SW + CW + PE$.

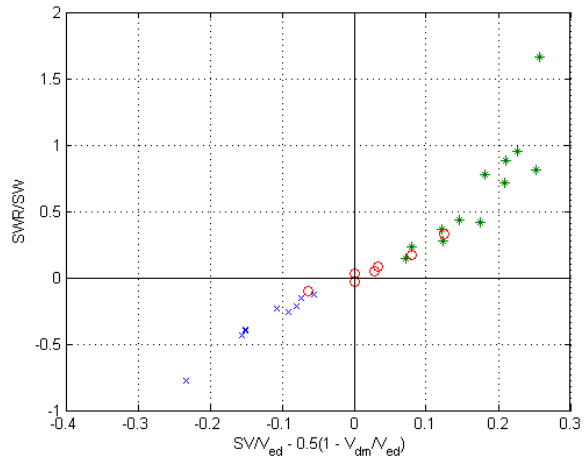

Fig. 5 SWR/SW against $SV/V_{ed} - 0.5(1 - V_{dm}/V_{ed})$ for three clinical cases; 1) EF >= 60% '*'; 2) 40% < EF < 59% 'o'; 3) EF < 40% 'x'. The negative values correspond to d_1 above d_5 in Fig. 3, which is the case of severely depressed state of the heart. Experimental data taken from Asanoi et al [44].

Variations of SW/TW, PE/TW, CW/TW and SWR/SW with E_{max}/e_{am} have been discussed in [24,25]. We show here some results based on the experimental data taken from Asanoi et al [44]. In Fig. 6 we show the variation of SWR/SW with EF = SV/V_{ed}, notice the results surrounded by a black rectangle indicating preserved EF (EF ≈ 0.55) but mildly depressed state of the heart ($SWR/SW \approx 0$). In Fig. 7 we show the relation between SWR/SW and E_{max}/e_{am}, notice that SWR/SW is negative for $E_{max}/e_{am} < 1$. In Fig. 8 we show the relation between CW/TW and Emax/eam, that $CW/TW = 0.25$ for $E_{max}/e_{am} = 1$ (d_1 and d_5 coincide in Fig.3). Fig. 9 show the relation between CW/TW and SWR/SW, notice that $SWR/SW = 0$ for $CW/TW = 0.25$. These relations give a clear picture of the importance of the interrelation between the different areas under ESPVR in studying the mechanics of cardiac contraction.

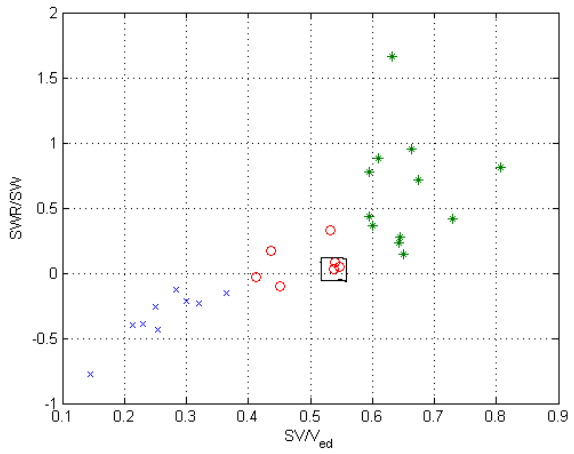

Fig. 6 Relation between *SWR/SW* and the ejection fraction SV/V_{ed}; notice the results in a black rectangle showing preserved $EF \approx 0.55$, but mildly depressed state of the heart ($SWR/SW \approx 0$). Data correspond to three clinical cases; 1) $EF >= 60\%$ '*'; 2) $40\% < EF < 59\%$ 'o'; 3) $EF < 40\%$ 'x'. Experimental data are taken from Asanoi et al [44].

Also these relations give a good indication of the consistency of the mathematical formalism used Evidently a crucial problem for the clinical application of these results is the measurement or calculation of E_{max} or V_{dm} in a non-invasive way that is important for the routine clinical implementation of these results (for an interesting review of different experimental approaches concerning the measurement of E_{max} or V_{dm} one can refer for instance to [42]).

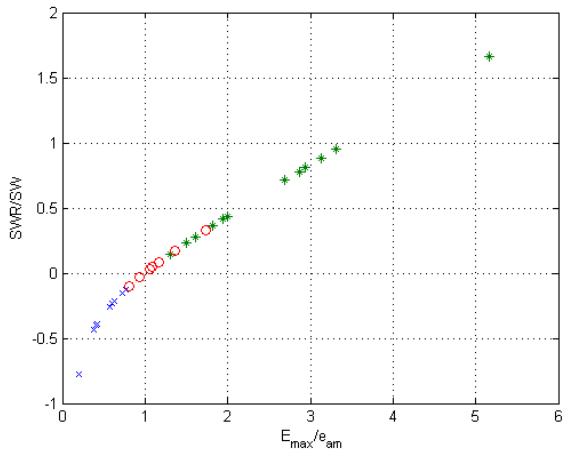

Fig. 7 Relation between *SWR/SW* and E_{max}/e_{am} for three clinical cases; 1) $EF >= 60\%$ '*'; 2) $40\% < EF < 59\%$ 'o'; 3) $EF < 40\%$ 'x'. Notice that $SWR/SW = 0$ for $E_{max}/e_{am} = 1$. Experimental data are taken from Asanoi et al [44].

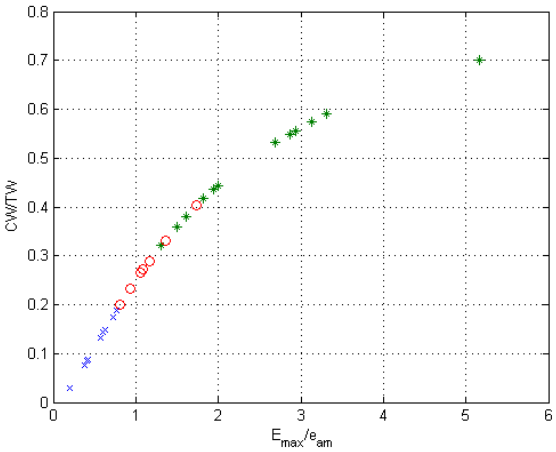

Fig. 8 Relation between *CW/TW* and E_{max}/e_{am} for three clinical cases; 1) $EF >= 60\%$ '*'; 2) $40\% < EF < 59\%$ 'o'; 3) $EF < 40\%$ 'x'. Notice that $CW/TW = 0.25$ for $E_{max}/e_{am} = 1$. Experimental data are taken from Asanoi et al [44].

Figs. (7) and (8) reflect the influence of the ventriculo-arterial coupling expressed by the ratio E_{max}/e_{am} on the energetic balance of the cardiac contraction as expressed by the different areas under ESPVR. The study of the interrelationship between the three areas *PE*, *SW* and *CW* under the ESPVR and its application to the study of the ventriculo-arterial coupling, and how to use it to differentiate between different cardiomyopathies is a field that has not been fully investigated [24,25].

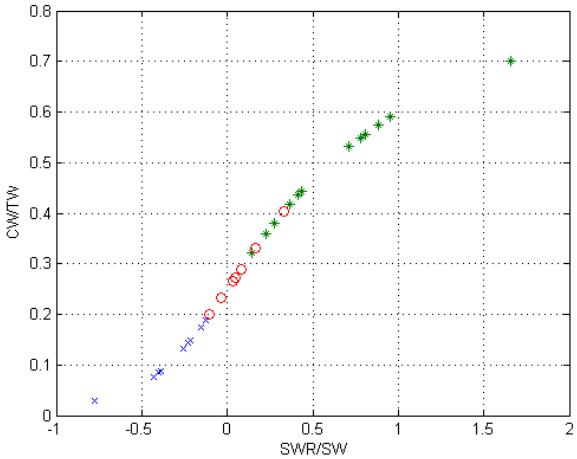

Fig. 9 Relation between *SWR/SW* and *CW/TW* for three clinical cases; 1) $EF >= 60\%$ '*'; 2) $40\% < EF < 59\%$ 'o'; 3) $EF < 40\%$ 'x'. Notice that $SWR/SW = 0$ for $CW/TW = 0.25$. Experimental data are taken from Asanoi et al [44].

Although the variation of *SWR/SW* as a function of the ejection fraction SV/V_{ed} as shown in Fig. 6 do not reveal a clear mathematical relation, the respective variation of *SWR/SW* and *CW/TW* with respect to

$SV/(V_{ed} - V_{dm})$ as shown in Fig. 10 and Fig. 11indicates a more predictable relationship. The difficulty in the implementation again is in the way to measure or to calculate V_{dm}.

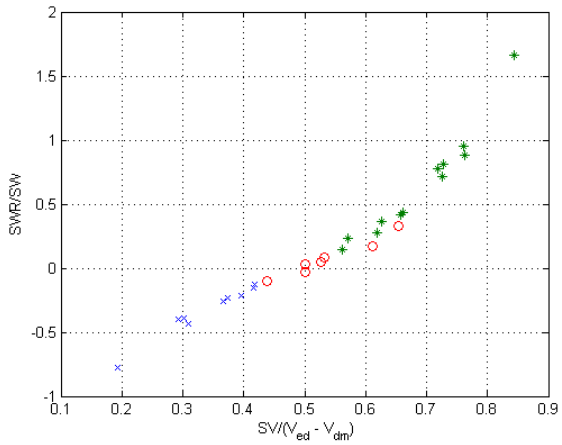

Fig 10 Relation between *SWR/SW* and $SV/(V_{ed} - V_{dm})$ for three clinical cases; 1) *EF* >= 60% '*'; 2) 40% < *EF* < 59% 'o'; 3) *EF* < 40% 'x'. Notice that *SWR/SW* = 0 for $SV/(V_{ed} - V_{dm})$ = 0.5. Experimental data are taken from Asanoi et al [44].

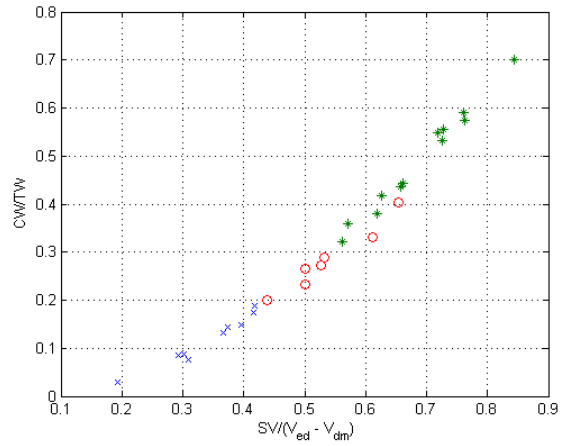

Fig. 11 Relation between *CW/TW* and $SV/(V_{ed} - V_{dm})$ for three clinical cases; 1) *EF* >= 60% '*'; 2) 40% < *EF* < 59% 'o'; 3) *EF* < 40% 'x'. Notice that *CW/TW* = 0.25 for $SV/(V_{ed} - V_{dm})$ = 0.5. Experimental data are taken from Asanoi et al [44].

Fig. 12 shows the relation between V_{dm} as given in the work of Asanoi et al [44] and the same values as calculated from Equ. (15). Again in spite of the simplicity of the linear model for the ESPVR used in this study, the results shown in Fig. 12 give further confirmation of the consistency of the mathematical formalism used. A study of a non-linear model of the *ESPVR* can be found in [23] and references given therein. We feel however that a good understanding of the linear model of the *ESPVR* is a necessary prelude to the study of a non-linear model.

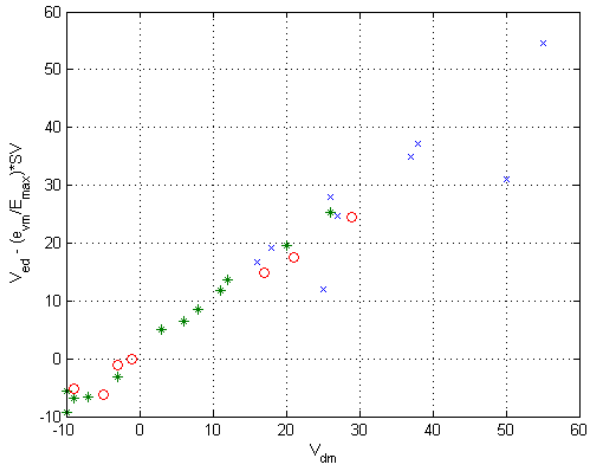

Fig. 12 Relation between values of V_{dm} taken from Asanoi et al [44], and the same values as calculated from Equ. (15) for three clinical cases; 1) *EF* >= 60% '*'; 2) 40% < *EF* < 59% 'o'; 3) *EF* < 40% 'x'.

Other applications resulting from introducing the active force P_{isom} in the mathematical formalism describing the PVR and not discussed in this study include the study of the non-linearity of the preload recruitable stroke work PRSW [46,47], and the application of the cylindrical model to study the stress induced in the myocardium by introducing the active force P_{iso} in the formalism describing stress-strain relations [48-50]. This approach has been developed by using both large elastic deformation and linear elasticity.

2.4 Mid-wall shortening and wall thickening

We have seen how the value of the ejection fraction EF is related to the *ESPVR*, in this section we consider briefly how the *EF* is influenced by the geometry of the ventricles. In a model in which the left or right ventricle is represented as a thick-walled cylinder contracting symmetrically (see Fig. 1), the cavity volume V is given by

$$V = \pi a^2 L \tag{16}$$

where a is the inner radius of the myocardium and L the length of the myocardium. The inner radius a can be expressed as

$$a = R - h/2 \tag{17}$$

that reflects the effect of mid-wall shortening expressed by mid-wall radius $R = (a + b)/2$, and wall thickening expressed by $h = b - a$; b is the outer radius of the myocardium. The volume of the myocardium V_ω is assumed to be incompressible and is given by

$$V_\omega = 2\pi RhL \tag{18}$$

It is easy to show that

$$V/V_\omega = 0.5\,(R/h - ½)^2/(R/h) \tag{19}$$

and

$$\Delta V/V = (1 + \Delta a/a)^2\,(1 + \Delta L/L) - 1 \tag{20}$$

The variations ΔV, Δa and ΔL are usually measured between end-diastole and end-systole. Verification of these relations is discussed in the work by Dumesnil et al [34-36]. Equs (16) to (20) explain the important fact that the ejection fraction $EF = \Delta V/V_{ed}$ can be expressed as a complex function of mid-wall shortening $\Delta R/R$, longitudinal shortening $\Delta L/L$ and wall thickening $\Delta h/h$ during the contraction phase, and it is influenced by the geometry of the ventricle expressed by the ratio R/h. From Equ. (18) one can derive the following relation

$$(1 + \Delta R/R)(1 + \Delta h/h)(1 + \Delta L/L) = 1 \tag{21}$$

It shows that the variation of the long axis $\Delta L/L$ can be calculated in a non-invasive way by measurement of the variations $\Delta R/R$ and $\Delta h/h$ in the transverse direction for instance by M-mode echocardiography. Equ. (21) shows also that in cases of aortic stenosis a decrease in longitudinal axis shortening $\Delta L/L$ can be a compensated by an increase in $\Delta R/R$ and $\Delta h/h$ in a way to maintain a constant ejection fraction EF as is evident from Table 1 in [34], and further discussed in [35,36].

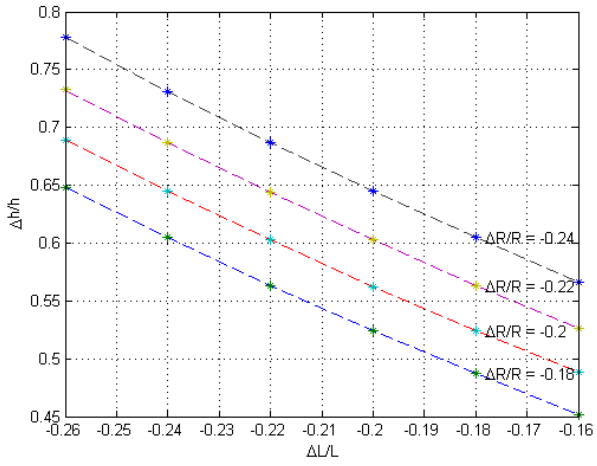

Fig. 13 Relation between $\Delta L/L$, $\Delta h/h$ for given $\Delta R/R$ during the contraction phase of the ventricles as calculated from Equ. (21).

Similarly Table 1 in [34] indicates that $\Delta V/V_\omega$ can be calculated in a non-invasive way by using Equ. (19) and is superior to $\Delta V/V_{ed}$ in discriminating between cases of aortic stenosis and normal cases.

It is now well recognized that cases of heart disease or heart failure can have normal ejection fraction. A preserved ejection fraction can be the result of change in mid-wall shortening $\Delta R/R$ and change in wall-thickening $\Delta h/h$ in a way to compensate for reduced longitudinal shortening $\Delta L/L$ as expressed by Equ. (21) and shown in Fig. 13, but it does not imply that the systolic function of the muscular pump is necessarily normal. Fig. 13 show simulated results that show the influence of longitudinal variation $\Delta L/L$ on wall thickening $\Delta h/h$ for specific values of mid-wall radius shortening $\Delta R/R$ as calculated from Equ. (21). Moreover the study of the change in left ventricular chamber size during systole should take into consideration the contribution the effect of the geometry of the chamber as expressed by the ratio R/h in Equ. (19). Extensive studies of myocardial fibre structure and its influence on the mechanism of systolic wall thickening can be found in the work of several authors, some of them are given in [51-58]. In [58] the importance of the study of the asynchrony between longitudinal, radial and wall thickening during the early systolic phase of contraction has been stressed, which points to the need of studying first derivative with respect to time (velocity) and second derivative (acceleration) of these variables. Finally the model discussed in this study can be incorporated into more sophisticated models for heart contraction [59].

3 Conclusion

The subject of heart failure with preserved ejection fraction (*HFpEF*) has been recently the object of intensive research. It is known that hypertension appears to play an important role in heart failure associated with a preserved ejection fraction ($EF > 0.5$), and that about three quarter of patients with heart failure has a history of hypertension. Moreover about half the patient with symptoms of heart failure have normal or near-normal ejection fraction.

This study has discussed two models to calculate the ejection fraction. The first model is based on the ESPVR and the way the ejection fraction is influenced by the forces acting on the myocardium (expressed through the ratio E_{max}/e_{am}, (see Equs. (3) to (13)). The second model takes into account the geometry of the left ventricle as expressed by Equs. (20) and (21). Still more work is needed to make the link between these two models. These two models have been discussed in this study in an attempt to shed some light on the problem of HFpEF. The difficulty with the implementation of these two approaches, especially the first one, is the difficulty of non-invasive measurement of all the parameters needed.

Some results have also been presented that point to the importance of the different areas under ESPVR for problems of clinical diagnosis. The areas under the *ESPVR* are sensitive indices of the state of the myocardium. Finally future possible development should include the study of the dynamics of ventricular contraction with the acceleration included in the mathematical formalism describing the ventricular contraction. It is the early acceleration of the contracting myocardium that gives to the blood the momentum that projects into the aorta.

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