Heart Failure, End-Systolic Pressure-Volume Relation

Rachad Mounir Shoucri

Royal Military College of Canada, Kingston, Ontario

Abstract

The problem of heart failure with normal or preserved ejection fraction (HFpEF) has been the subject of numerous studies. Mathematical relations between ejection fraction (EF) and the parameters describing linear and non-linear end-systolic pressure-volume relation (ESPVR) have been derived in previous publications. Consequently one can expect a link between observed percentage of heart failure and EF on the one hand, and indexes derived from the ESPVR on the other hand, which is the subject of this study. It is shown that important information can be derived from the ESPVR that can give better insight into the mechanics of ventricular contraction. Applications to clinical data published in the literature show the consistency of the mathematical formalism used.

1. Introduction

Studies of heart failure (HF) with normal or preserved ejection (HFpEF) indicate that about half of patients presenting symptoms of HF have preserved ejection fraction (EF), defined as EF greater than 50% [1-5]. Heart failure is a complex process influenced by several interacting factors, like preload and afterload, inotropic state of the myocardium, coupling of the left ventricle (LV) with its surroundings during filling and ejection. In this study we look at one aspect of a complex problem as explained in what follows.

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. There have been several studies on the way clinical information can be derived from linear or non-linear representations of the ESPVR [6-11]. In this study a mathematical expression describing the non-linear ESPVR derived in previous publications [12-16] from the theory of large elastic deformation of the myocardium is used, the active pressure of the myocardium (also called isovolumic pressure P_{iso} by physiologists) is included in the formalism describing the pressure-volume relation (PVR) and the ESPVR. When ratios of pressures or ratios of areas are calculated, the calculation can be carried out in a non-invasive way. Direct relations between the percentage of HF as reported in [4, 5] and indexes derived from the curvilinear ESPVR that give some insight into the mechanics of ventricular contraction are presented in this study.

In what follows we first review the mathematical formalism used, then we present some new applications to clinical data published in the literature [17, 18] that show the consistency of the mathematical formalism used. The mathematical formalism applies to the left and right ventricle, we restrict our discussion in what follows to the LV.

.

2. Mathematical formalism

The mathematical model used for the left ventricle has been discussed in previous publications [12-16]. Briefly, the left ventricle is represented as a thick-walled cylinder contracting symmetrically (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 of the myocardium, b = outer radius of the myocardium, h = b – a = thickness of the myocardium.

2.1. PVR & ESPVR

In a quasi-static approximation (inertia and viscous forces neglected), the equilibrium of forces on the inner surface of the myocardium is given by

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

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. The right side of Eq. (1) represents the pressure on the endocardium resulting from the change of the ventricular volume from V_{ed} to V. Near end-systole when the myocardium reaches its maximum state of activation, Eq. (1) is written in the form

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

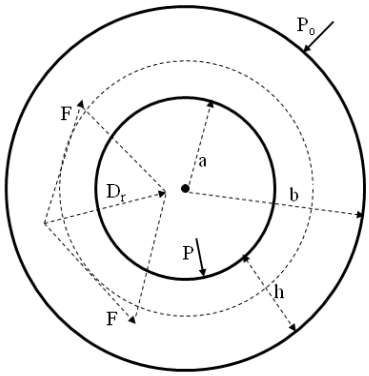

Figure 1: Cross-section of a thick-walled cylinder representing the left ventricle, D_r = active radial force/unit volume of the myocardium, P = left ventricular pressure, P_o = outer pressure (assumed zero) on the myocardium, a = inner radius, b = outer radius, h = b – a = thickness of the myocardium.

The symbols have the same meaning as in Eq. (1), $V_m \approx V_{es}$ the end-systolic pressure (when dV/dt = 0). Figure 2 represents a non-linear ESPVR shown as the curve BDC, with peak isovolumic pressure P_{isom}, $E_{2m} = \tan\beta_2$ corresponds to the slope of the line CD that intersects the volume axis at a point indicated as V_{o2}. The relation between P_m and V_m in Eq. (2) when P_{isom} is kept constant gives the ESPVR (as if a balloon is inflated against a constant P_{isom}). When the left ventricular pressure $P_m \rightarrow 0$, we have $V_m \rightarrow V_{om}$ in Eq. (2), and we get

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

$E_m = \tan\alpha$ 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 trigonometry relations between the triangles one can derive (see also [15])

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

$$\tan\beta_2 / e_{am} = SV / (V_m - V_{o2}) \quad (4b)$$

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

where $e_{am} = P_m / SV$ is the arterial elastance. It is clear that the stroke volume $SV \approx V_{ed} - V_m$ (and $EF = SV/V_{ed}$) are related to the slope parameters describing the ESPVR, and the intercepts V_{ot}, V_{o2}, and V_{om} shown in Eqs. (4).

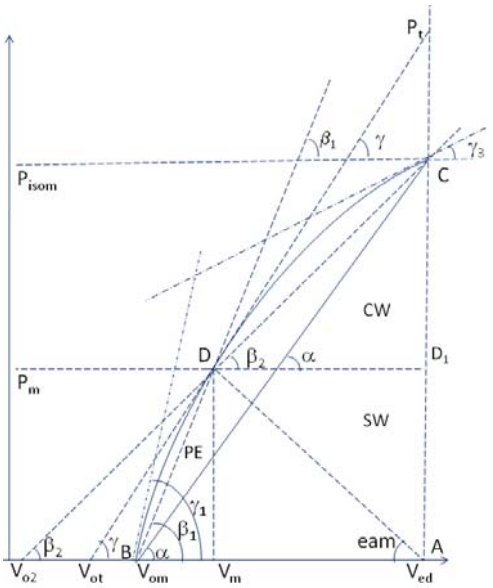

Figure 2: ESPVR represented by the curve BDC, intercept with the horizontal volume axis is B (corresponding to V_{om}). Stroke work SW ≈ area AD_1DV_m, PE = area determined by arc(BD)V_mB, CW = area determined by arc(DC)D_1D. TW = CW + SW + PE is total area under the ESPVR. Ventricular pressure P_m is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

2.2. Criteria of performance for LV

For simplicity we assume that P_m is constant during the contraction phase. When the point D 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 [15] gives in this case

$$\tan\gamma = e_{am} \quad (5a)$$

$$SV = V_m - V_{ot} \quad (5b)$$

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

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

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, which corresponds to a normal state of the heart.

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, which corresponds to a mildly depressed state of the heart.

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, which corresponds to a severely depressed state of the heart.

Experimental verification of these results can be found for the LV in [8, 9], and for the right ventricle in [10].

3. Applications to clinical data

Clinical data obtained from echocardiography measurements on five groups of patients were taken from [17, 18]. The relation between percentage of HF and EF was taken from [4] and it is reproduced in Fig. 3 (left side). The least square fit curve shown on the left side of Fig. 3 was calculated and used to derive the relation between percentage of HF and EF taken from [17, 18] as shown on the right side of Fig. 3. Note in Fig. 3 (right side) that the normal group (*) appears around the bottom of the curve, and corresponds to an optimal EF ≈ 0.67.

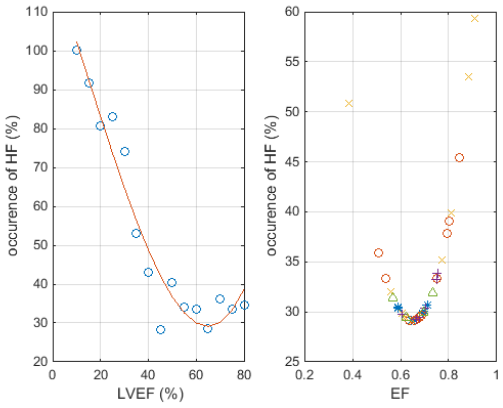

Figure 3: (left) Relation between percentage of HF and percentage of left ventricular EF, data from [4]; (right) Relation between percentage of HF and EF calculated by using the least square fit shown on the left side, data for five clinical groups from [17,18]; normal *, aortic stenosis o, aortic valvular regurgitation +, mitral regurgitation ^, miscellaneous cardiomyopathies x.

In Fig. 4 (left side) the relation between percentage of HF and the ratio SW/TW (stroke work/total area under ESPVR) is shown, one can notice a minimum in the curve around SW/TW ≈ 0.5. One can assume that the total area TW (see Fig. 2) reflects the total energy needed by the LV to perform its function. It appears that under optimal conditions the LV will normally function in an apparent state of matching between the source and the load, where one half of the total energy generated is given to the systemic load. In Fig. 4 (right side), the relation between percentage of HF and SW_x/TW (critical ratio when SWR = 0) is shown, it has a minimum around SW_x/TW ≈ 0.63.

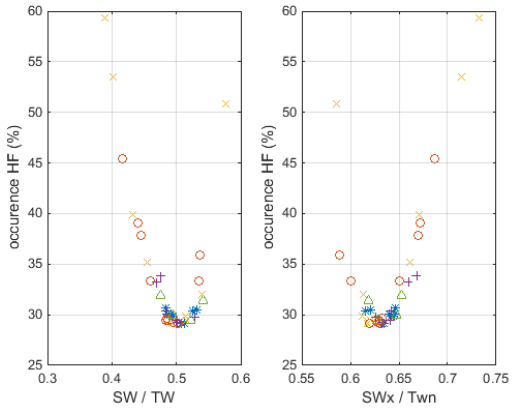

Figure 4: (left) Relation between percentage of HF and the ratio of areas SW/TW; (right) Relation between percentage of HF and the ratio of areas SW_x/TW; normal *, aortic stenosis o, aortic valvular regurgitation +, mitral regurgitation ^, miscellaneous cardiomyopathies x.

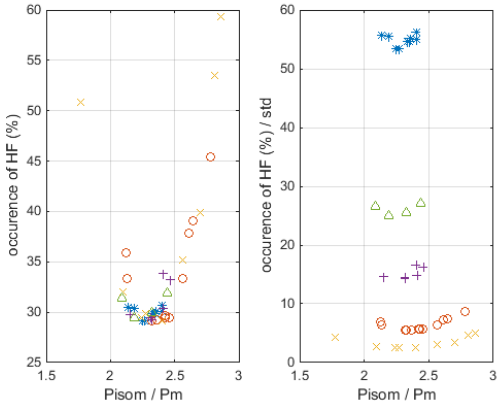

Figure 5: (left) Relation between percentage of HF and the ratio P_{isom}/P_m ; (right) same relation with the ordinates divided by the standard deviation for each group; normal *, aortic stenosis o, aortic valvular regurgitation +, mitral regurgitation ^, miscellaneous cardiomyopathies x.

In Fig. 5 (left side) the relation between the percentage of HF and the ratio P_{isom}/P_m (peak isovolumic pressure /ventricular pressure) is shown, with a minimum in the curve around P_{isom}/P_m ≈ 2.3. In Fig. 5 (right side) we have divided the ordinates by the respective standard deviation of each group in a way to separate the graphical display of each group, the group with the smallest standard deviation (normal *) appears at the top. Note that the minima of the curves in Fig. 5 (right side) are practically vertically aligned. Note also in Figs. 3 to 5 (left) that the

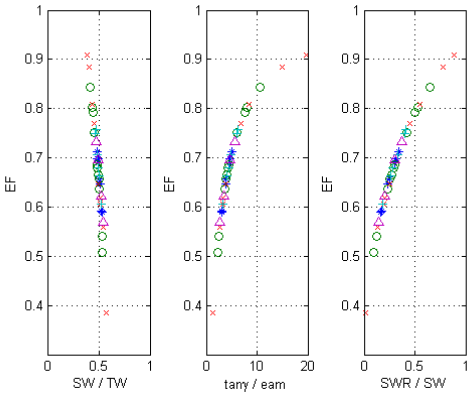

Figure 6: Relations between EF and some indexes derived from the ESPVR.

normal group appears around the minimum of the curves.

Figure 6 shows the relation between EF and some indexes derived from ESPVR. Note that for EF ≈ 0.67 (minimal occurrence of HF as shown in Fig. 3), we have SW/TW ≈ 0.5, $\tan\gamma/e_{am}$ ≈ 4 (and $\tan\alpha/e_{am}$ ≈ 2), and SWR/SW ≈ 1/3. Note also that for EF → 0.33 we have SW/TW → 0.63, and $\tan\gamma/e_{am}$ → 1 (corresponding to SWR = 0).

4. Conclusion

This study has presented results that suggest new lines of research to study HF in terms of parameters and indexes derived from ESPVR that can be measured or calculated in a non-invasive way when ratios of pressures and areas are calculated as explained in [12-16]. Overlap between results of five clinical groups in Figs. 3 to 6 shows the difficulty to segregate between different clinical groups. We have shown in Fig. 5 (right side) that dividing data by the respective standard deviation of each clinical group can segregate between those clinical groups. This procedure introduces a problem of classification, given new data how to choose the proper standard deviation in order to classify them, a problem that is under study. Bivariate (or multivariate) analysis of data seems to be superior to univariate analysis for classifying clinical groups.

References

[1] Chatterjee K, Massie B. Systolic and diastolic heart failure: differences and similarities. J Cardiac Fail 2007; 13:569-76.
[2] Najjar S. Heart failure with preserved ejection fraction. J. Am Coll Cardiol 2009; 54: 419-21.
[3] Kerkhof PLM, Kresh JY, Li JK-J, Heyndrickx GR. Left ventricular volume regulation in heart failure with preserved ejection fraction. Physiol Rep 2013; 1(2): 1-10
[4] Da Mota JPGF, Intelligent modeling to predict ejection fraction from echocardiographic reports. MSc thesis in Mech Eng, IST Técnico Lisboa, Portugal, Nov 2013.
[5] Curtis JP, Sokol SI, Wang Y, Rathore SS, Ko DT, et al. The association of left ventricular ejection fraction, mortality, and cause of death in stable outpatients with heart failure. J Am Coll Cardiol 2003; 42 (3): 736-42.
[6] Blaudszun G, Morel DR. Relevance of the volume-axis intercept, V_o, compared with the slope of the end-systolic pressure-volume relationship in response to large variations in inotropy and afterload in rats. Exp Physiol 2011, 96: 1179-95
[7] Burkhoff D, Mirsky I, Suga H. Assessment of systolic and diastolic ventricular properties via pressure-volume analysis; a guide for clinical, translational, and basic researchers. Am J Physiol Hear Circ 2005; 289: H501-12
[8] Asanoi H, Sasayama S, Kameyama T. Ventriculoarterial coupling in normal and failing heart in humans.Circ Res 1989, 65: 91-8.
[9] Burkhoff D, Sagawa K. Ventricular efficiency predicted by an analytical model. Am J Physiol 1989; 250: R1021-27
[10] Brimioulle S, Waulthy P, Ewalenko P, Rondelet B, Vermeulen F, Kerbaul F, Naeije R. Single-beat estimation of the right ventricular end-sytolic pressure-volume relationship. Am J Physiol Heart Circ 2003, 284: H1625-30
[11] Sunagawa K, Maugham WL, Sagawa K. Optimal arterial resistance for the maximal stroke work studied in isolated canine left ventricle. Circ Res 1985; 56: 586-95.
[12] Shoucri RM. Theoretical study of the pressure-volume relation in left ventricle. Am J Physiol Heart Circ 1991; 260: H282-91
[13] Shoucri RM. The end-systolic pressure-volume relation and its application to the study of the contractility of the cardiac muscle. Computers in Cardiology 2006; 33: 297-300.
[14] Shoucri RM. ESPVR, ejection fraction and heart failure. Cardiovasc Eng. 2010; 10: 207-12.
[15] Shoucri RM. Ejection fraction and ESPVR: A study from a theoretical perspective. Int Heart J 2013; 54: 318-27.
[16] Shoucri RM. Non-invasive calculation of non-linear ESPVR: theoretical study and clinical applications. In: 2nd IEEE-BHI International Conference on Biomedical and Health Informatics; Valencia, Spain, June 1-4, 2014: 468-71.
[17] Dumesnil JG, Shoucri RM, Laurenceau JL, Turcot J. A mathematical model of the dynamic geometry of the intact left ventricle and its application to clinical data. Circulation 1979; 59: 1024-34.
[18] Dumesnil JG, Shoucri RM. Effect of the geometry of the left ventricle on the calculation of ejection fraction. Circulation 1982; 65: 91-8.

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