Editorial

Clinical applications of the areas under ESPVR

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Indexes of cardiac performance

It has long been observed that the use of the ejection fraction (EF) to assess the condition of the heart offers serious limitations (1). It is estimated that half of the patients presenting with symptoms of cardiomyopathies and heart failure (HF) have preserved EF defined as EF >50%. It was shown in (2) that the areas under the end-systolic pressure-volume relation (ESPVR) in the heart ventricles are sensitive indexes to reflect the state of the myocardium, a review of some clinical applications of indexes derived from the ESPVR can be found in (3). An objective of the study by Doyle *et al*. (4) is precisely to show that areas under the ESPVR, or bivariate combination of areas with another index, can be used as a prognostically useful tool for studying cases of women with suspected myocardial ischemia.

The ESPVR is the relation between pressure and volume in the left or right ventricle when the myocardium reaches its maximum state of activation near end-systole (2,3). There have been several studies on the ESPVR (3,5-7), most of these studies have focused on the use of the maximum slope E_{max} and the volume axis intercept V_{om} of the ESPVR in order to assess the state of the myocardium. Because of the difficulty to calculate V_{om}, some researchers have tried to neglect V_{om} and to approximate $E_{max} \approx$ (end-systolic pressure/end-systolic volume) (4). Such an approximation can only be justified if it is proven that the results obtained contain useful reliable clinical information. In what follows we introduce some relations that reflect the way the energetic of cardiac contraction is related to the areas under the ESPVR, and how the EF is also influenced by these areas. It may provide some background for the study published in (4).

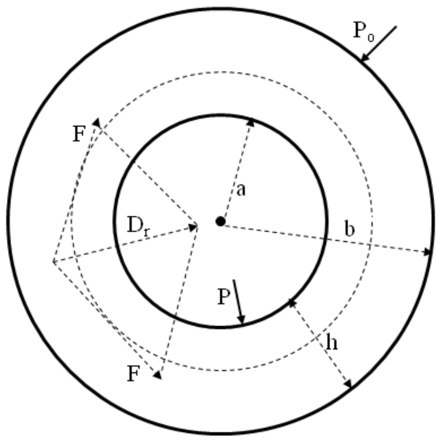

Figure 1 Left ventricle represented by the cross-section of a thick-walled cylinder. D_r, active radial force/unit volume of the myocardium; P, left ventricular pressure; P_o, outer pressure (assumed zero) on the myocardium; a, inner radius; b, outer radius; h = b - a = thickness of the myocardium

Mathematical formalism

PVR

As in previous publications (8-11), the left ventricle is represented as a thick-walled cylinder contracting symmetrically (*Figure 1*). A radial active force D_r (force per unit volume of the myocardium) is developed by the myocardium during the contraction phase. The active pressure on the inner surface of the myocardium (endocardium) is given by $\int_a^b D_r\, dr = P_{iso}$, where a = inner radius of the myocardium, b = outer radius of the myocardium. We neglect inertia and viscous forces since they are relatively small. The equilibrium of forces on the

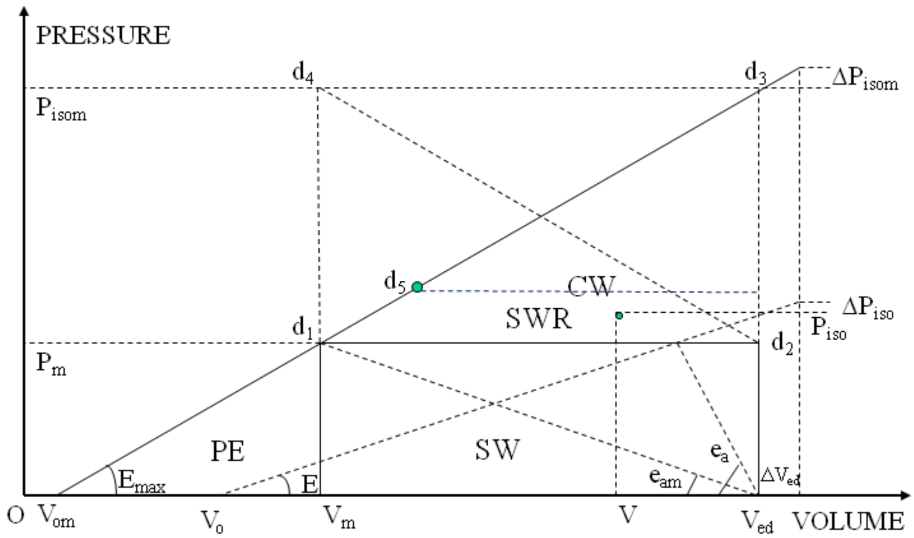

Figure 2 Simplified PVR in the left ventricle, $V_{ed}d_2d_1V_m$ represents the pressure-volume loop in a normal ejecting contraction (area SW). The ESPVR is represented by the line d_3V_{om} with midpoint d_5 and slope E_{max}, the line with slope E is an intermediate position. The left ventricular pressure P_m is assumed constant during the ejection phase. The changes ΔP_{iso} and ΔP_{isom} correspond to ΔV_{ed} according to the Frank-Starling mechanism

endocardium can then be expressed in the form:

$$P_{iso}-P = E\,(V_{ed}-V) \quad [1]$$

P is the left ventricular pressure, V is the corresponding left ventricular volume, V_{ed} is the end-diastolic volume (the largest volume when dV/dt =0). The right-hand side of Equation [1] is the pressure on the endocardium resulting from the elastic deformation of the myocardium. When the elastance E reaches its maximum value E_{max} near end-systole (maximum state of activation of the myocardium), we can write Equation [1] as follows:

$$P_{isom}-P_m = E_{max}\,(V_{ed}-V_m) \quad [2]$$

We take $V_m \approx V_{es}$ the end-systolic volume when dV/dt = 0.

ESPVR

Equations [1] and [2] are represented graphically in a simplified way in *Figure 2*. The ESPVR is a relation between P_m and V_m when the peak isovolumic pressure P_{isom} is kept constant, it is represented by the line d_3V_{om} with slope E_{max}.

During a normal ejecting contraction the PVR is represented by the rectangle $V_{ed}d_2d_1V_m$. Equation [2] can be split into the following form:

$$P_m = E_{max}\,(V_m-V_{om}) \quad [3]$$

$$P_{isom} = E_{max}\,(V_{ed}-V_{om}) \quad [4]$$

We can distinguish the following cases described by the ratio E_{max}/e_{am} (maximum ventricular elastance/maximum arterial elastance) and the stroke volume SV ≈ $V_{ed}-V_m$ (see *Figure 2*).

(I) Normal physiological state of the heart, with d_1 below d_5 on the line d_3V_{om}. In this case we have SV > $(V_{ed}-V_{om})/2$, with $E_{max}/e_{am} \approx 2$ and $P_{isom}/P_m \approx 3$. This case corresponds to maximum efficiency for O_2 consumption by the myocardium.

(II) Mildly depressed state of the heart, with d_1 and d_5 coinciding. In this case we have SV ≈ $(V_{ed}-V_{om})/2$, with $E_{max}/e_{am} \approx 1$ and $P_{isom}/P_m \approx 2$. The stroke work SW reaches its maximum value SW_{max}.

(III) Severely depressed state of the heart, with d_1 above d_5 on the line d_3V_{om}. In this case we have SV < $(V_{ed}-V_{om})/2$, with E_{max}/e_{am} <1 and P_{isom}/P_m <2.

Notice from *Figure 2* that in cases (II) and (III) an increase in pressure P_m causes a decrease of the stroke work SW, resulting in cardiac insufficiency.

Experimental verification of these results can be found in (5) (left ventricle) and in (6) (right ventricle) for experiments on dogs, and in (7) for results obtained from patients.

We have the following areas under the ESPVR:

(I) SW = P_m (SV), energy delivered to the systemic circulation;

(II) PE = $P_m(V_m-V_{om})/2$, potential energy apparently

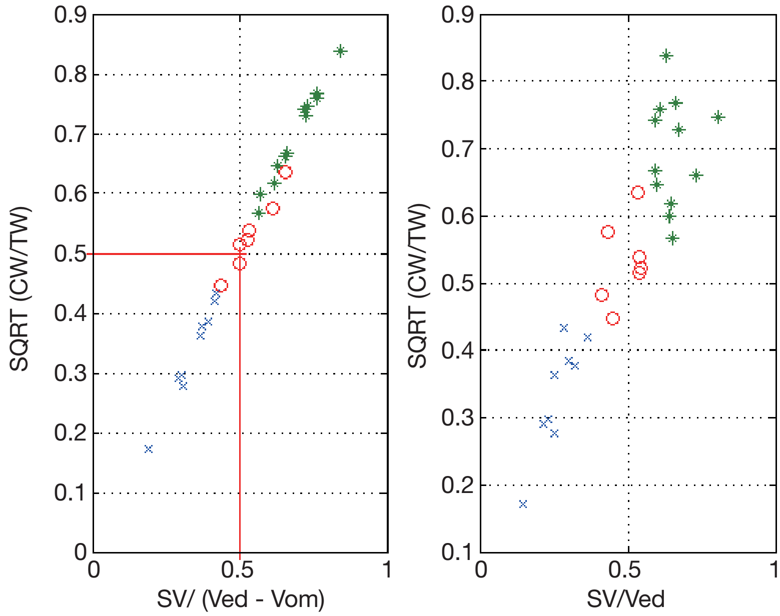

Figure 3 Graphical verification of [5] (left side), and similar relation with the EF = SV/V_{ed} (right side). Experimental data taken from Asanoi *et al*. (7). Data correspond to three clinical groups: (I) EF≥60% '*'; (II) 40% < EF <59% 'o'; (III) EF <40% 'x'

related to the internal metabolism of the myocardium;

(III) CW = (P_{isom}–P_m) SV/2, energy apparently absorbed by the passive medium of the myocardium;

(IV) SWR = SW_{max}–SW, stroke work reserve. It is the reserve energy that can be delivered to the systemic circulation when afterload represented by P_m is increased.

We have SW + PE + CW = TW the total area under ESPVR. One can derive the following relation for the stroke volume:

$$SV = (CW/TW)^{1/2} (V_{ed} - V_{om}) \quad [5]$$

Which shows how SV (and EF = SV/V_{ed}) is determined by the areas under the ESPVR. When CW/TW = 1/4 (d_1 and d_5 coincide in *Figure 2*), we get from Equation [5] SV = (V_{ed}-V_{om})/2. Experimental verification is shown in *Figure 3*. We also have:

$$E_{max}/e_{am} = 2 \times CW/SW \quad [6]$$

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