The End-Systolic Pressure-Volume Relation and Its Application to the Study of the Contractility of the Cardiac Muscle

RM Shoucri

Royal Military College, Kingston, Ontario, Canada

Abstract

The theory of large elastic deformation is used to develop a model for the contraction of the myocardium in which the active force of the myocardium (active fibre stress) is represented by its components in three perpendicular directions as force per unit volume of the myocardium. New results have been derived in relation to the study of the contractility of the myocardium, the study of the end-systolic pressure-volume relation (espvr) and the areas enclosed under it, as well as the calculation of the active and passive stress in the myocardium. Possibility of non-invasive implementation of some of those results by using for instance M-mode echocardiography is also indicated.

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1. Introduction

In order to model the active force generated by the myocardium, one can use one of the two following approaches. In the first approach, which is the one usually followed, one can start with a complicated study of the orientation of the muscular fibres in the complex structure of the myocardium and then determine a mathematical representation for the active force generated by these muscular fibres. In the second approach, which has been developed in a series of publications by the author [1-8], the active force generated by the myocardium is represented as force/per unit volume of the myocardium with three components along three orthogonal directions (we shall assume symmetric contraction of the myocardium). This second approach has the advantage that it splits the difficulty of the problem in two related but independent problems, one problem is to study the mechanics of cardiac contraction for the purpose of clinical applications based on three perpendicular forces, the other problem is the study of relation between these three perpendicular forces and the complex structure of the myocardium. The evident advantage of the second approach is that one can directly study the mechanics of cardiac contraction without having to worry about the complex structure of the myocardium; it is consequently very useful for clinical applications

In what follows two groups of results are presented. One group is related to the application of the *espvr* to the study of the performance of the cardiac muscle for clinical purposes, the other group is related to the calculation of the total stress induced in the passive medium of the myocardium expressed as the sum a component induced by the intraventricular pressure and a component induced by the active force generated by the myocardium. As shall be seen in what follows, a wide variety of results have been derived by using the mathematical formalism outlined in the next section.

2. Mathematical method

2.1. Pressure-volume relation

The mathematical formalism applies to both the left and the right ventricle [2] and can probably be extended to the four chambers of the heart. In the quasi-static approximation used, the viscous and inertia forces are neglected because they are usually small. The ventricle is represented as a thick-walled cylinder contracting symmetrically. Transverse isotropy with respect to the axis of the cylinder is assumed. As shown in Fig. 1, a helical fibre in the myocardium is projected on the cross-section as a dotted circle and generates a radial active force D expressed per unit volume of the myocardium. The radial active force/unit area acting on the inner surface of the myocardium (radial fibre stress at the endocardium) can be expressed as $\int_a^b D dr = \overline{D}h$, where $\overline{D}$ is an average value calculated by the mean value theorem ($h = b - a$ is the thickness of the myocardium). As shown in Fig. 2, we shall use the subscript m to indicate the value of $\overline{D}h$ as $(\overline{D}h)_m$ when the elastance E reaches its maximum value E_{max} (and similarly for other variables). E_{max} is the slope of the *espvr*.

As can be seen from a simple inspection of Fig. 1, in a quasi-static approximation one can express the equilibrium of forces on the inner surface of the myocardium as:

$$\left(\bar{D}h\right)_m - P_m \approx E_{\max}(V_{ed} - V_m) \quad (1)$$

which can be split into two equations

$$\left(\bar{D}h\right)_m \approx E_{\max}\left(V_{ed} - V_{dm}\right) \quad (2)$$

$$P_m \approx E_{\max}\left(V_m - V_{dm}\right) \quad (3)$$

where V_{ed} is the end-diastolic volume (when $\frac{dV}{dt} = 0$),

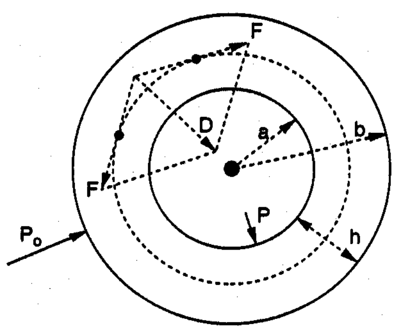

Figure 1: Cross-section of a thick-walled cylinder representing the left or right ventricle. A helical fibre in the myocardium is projected on the cross-section as shown by the dotted circle. a = inner radius, b = outer radius, h = b – a = thickness of the myocardium.

$(\bar{D}h)_m$ is the radial active force/unit area acting on the endocardium, P_m is the ventricular pressure and V_m is the ventricular volume when the ventricular elastance *E* reaches its maximum value $E_{\max}$. The intercept of the *espvr* with the volume axis is V_{dm} as shown in Fig. 2. One can usually assume $V_m \approx V_{es}$ the end-systolic volume (when $dV/dt = 0$). The external pressure P_o and the end-diastolic pressure P_{ed} are neglected in our calculations.

The results summarized by Eqs. (1)-(3) have been derived by using the theory of large elastic deformation [1], but can be understood in a simple way by considering the fact that the quasi-static equilibrium of forces in Fig. 1 is proportional to the change in ventricular volume. These results correspond to a two-dimensional model for the left ventricle which is a good approximation for the ventricular contraction near the equatorial region. It is clear that Eqs. (1) to (3) represent three different ways to express the equation of the *espvr* in Fig. 2.

Eq. 1 can be looked at in two ways: 1) if $(\bar{D}h)_m$ is held constant and P_m and V_m are varied as if a balloon is blown up against a constant $(\bar{D}h)_m$, we get the *espvr* represented in a simplified way by the line d_3V_{dm} in Fig. 2; 2) if $\bar{D}h$ is allowed to vary as *P* and *V* vary, we get the *P-V* loop of a cardiac cycle in a normal ejection represented in a simplified way by the rectangle $V_{ed}d_2d_1V_m$ in Fig. 2.

2.2. Stress induced in the myocardium

It can be shown [7-9] by using the theory of linear elasticity that the total stress induced in the passive medium of the myocardium can be expressed as the sum of a stress due to *P* and a stress due to $\bar{D}h$. One gets

$$\sigma_{total} = \left(\sigma_{total}\right)_p + \left(\sigma_{total}\right)_d, \quad (4)$$

with $$\sigma_{total} = \sqrt{\sigma_r^2 + \sigma_c^2 + \sigma_L^2} \quad (5)$$

$$\sigma_r = \left(\sigma_r\right)_p + \left(\sigma_r\right)_d, \quad \sigma_c = \left(\sigma_c\right)_p + \left(\sigma_c\right)_d, \quad \sigma_L = \left(\sigma_L\right)_p + \left(\sigma_L\right)_d \quad (6)$$

The subscripts r, c and L indicate the stress in the radial, circumferential and longitudinal directions respectively. The subscript p indicates the stress induced by *P* and the subscript d indicates the stress induced by $\bar{D}h$. Application of this approach is discussed in what follows.

3. Results

3.1. Contactility of the cardiac muscle

Several contractility indexes of clinical interest like ejection fraction, stroke volume, the rate of rise of the systolic pressure have been used to assess the performance of the ventricles. Some other indexes are directly related to the pressure-volume relation (*pvr*) like the maximum ventricular elastance E_{max} or slope of the *espvr*, the interrelation between different areas under the *espvr* and their relation of oxygen consumption [3], adaptation of the *espvr* to short-term or long term change in systemic load conditions [4,5]. It is shown in what follows how the ratio E_{max}/e_{am} (maximum ventricular elastance/ corresponding arterial elastance, see Fig. 2) can be used to assess the contractility of the cardiac muscle by studying the relative position of the point d_1 with respect to d_5 (see Fig 2). The interrelation between the three areas appearing under the *espvr* in Fig. 2 is very important and can be used to differentiate between different cardiomyopathies [4].

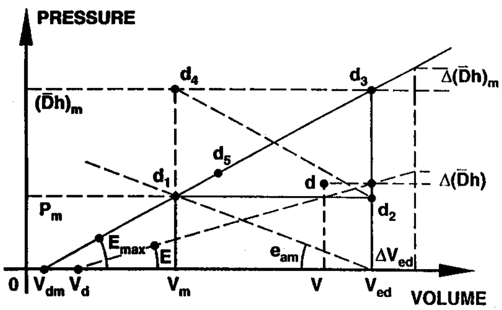

Figure 2: Schematic drawing representing the pressure-volume relation. The *espvr* is represented by the line d_3V_{dm}, d_5 is the middle point of d_3V_{dm}. During an ejecting contraction $V_{ed}d_2d_1V_m$ represents the pressure volume loop in a simplified way. The change $\Delta(\bar{D}h)_m$ corresponds to ΔV_{ed} according to the Frank-Starling mechanism. It is assumed that $V_m \approx V_{es}$.

The total area under the *espvr* is designated by $TW \approx V_{ed}d_3V_{dm}$, the area $PE \approx V_md_1V_{dm}$ seems to correspond to the energy absorbed by the internal metabolism of the myocardium, the area $CW \approx d_2d_3d_1$ seems to correspond to the energy absorbed by the passive medium of the myocardium, the area $SW \approx V_{ed}d_2d_1V_m$ is the energy delivered to the systemic circulation called stroke work. Relations giving the variation of *SW/TW*, *CW/TW* and *PE/TW* with E_{max}/e_{am} have been derived and verified by experimental data published in the literature [4, 6]. It has been suggested in [13] that the area *SW* can be used as a measure of the ventriculo-arterial coupling. It is clear from what precedes that the ventriculo-arterial coupling is determined by all the areas under the *espvr*.

As can be seen from Fig. 2, the stroke work *SW* reaches its maximum value $(SW)_{max}$ when d_1 and the mid-point d_5 of the line d_3V_{dm} coincide. Consequently one can distinguish between normal physiological state (maximum efficiency for oxygen consumption by the myocardium) with $E_{max}/e_{am} \approx 2$ or $P_m/(\bar{D}h)_m \approx 1/3$, mildly depressed state of the heart with $E_{max}/e_{am} \approx 1$ or $P_m/(\bar{D}h)_m \approx 1/2$ (d_1 and d_5 coincide), and severly depressed state of the heart with $E_{max}/e_{am} < 1$ or $P_m/(\bar{D}h)_m > 1/2$ (d_1 above d_5, in this region an increase in P_m results in a decrease of *SW* creating cardiac insufficiency). Experimental results that confirm these theoretical results can be found in the literature [14, 15]. These results show the importance of considering the interaction between the three areas *SW*, *CW* and *PE* when studying cardiac mechanics.

3.2. Stroke work reserve

The horizontal area delimited by the points d_1 and d_5 under the *espvr* is the stroke work reserve $SWR = (SW)_{max} - SW$, this area is a measure of the ability of the heart to respond to change in load condition when P_m increases by increasing the stroke work. The stroke work reaches its maximum value $(SW)_{max}$ when d_1 and d_5 coincide. Possible mechanism of short term or long-term adaptation of the heart to change in load condition by changing the slope E_{max} of the *espvr* in order to maintain or to create a stroke work reserve has been suggested in [4, 5].

3.3. Stress induced in the myocardium

By modeling the active force of the myocardium as described in this article, it has been possible to express the stress induced in the myocardium as the sum of two components, a stress induced by *P* and a stress induced by $\bar{D}h$ as expressed by Eqs. (4)-(6). Application of this formalism to experimental data has given consistent results [7-9]. The implication of these results for the study of cardiac hypertrophy still needs further investigation.

It should be noted that these consistent results [7-9] have been obtained by using the linear theory of elasticity. Previous applications of the linear theory of elasticity to the calculation of the stress in the myocardium have given inconsistent results [10], and assumptions made to close the gap between measured and calculated stress have added to the confusion of the problem.

3.4. Preload recruitable stroke work

The relation between stroke work *SW* and end-diastolic volume V_{ed} is known as preload recruitable stroke work *PRSW*. Several results have been published in the literature that shows the apparent linearity of this relation expressed in the form

$$SW \approx M(V_{ed} - V_I) \tag{7}$$

where the slope *M* and and the intercept V_I are supposed to be constant [13]. It has been shown in [11, 12] that Eq. (7) is in fact non-linear and can be identified with the following expression for the area $V_{ed}d_2d_1V_m$ in Fig. 2

$$SW \approx P_m(V_{ed} - V_m) \tag{8}$$

By comparing Eqs. (7) with (8) we can establish the relations $M \approx P_m$ and $V_I \approx V_m$, which have been verified by experimental data in [11, 12]. Consequently the study of the *PRSW* should be directly linked to the study of the *espvr*.

4. Discussion and conclusions

The wide range of results discussed in this study is an indication of the consistency of the mathematical formalism used. New results have been introduced that include: 1) a new mathematical way to express the active force of the myocardium [1]; 2) new mathematical expressions for the *pvr* (Eqs. (1),(2)); 3) a new way to formulate the Frank-Starling mechanism, the larger the initial stress of the myocardium, the stronger the active force of contraction (see Fig. 2) [6]; 4) a new method to asses the condition of the heart based on the *espvr* and the ratio E_{max}/e_{am} as discussed in section 3.1 [6]; 5) a new suggested mechanism to predict long term or short term adaptation of the ventricle to changes in load condition [4, 5]; 6) new indexes to discriminate between different clinical groups based on the study of interrelation between the areas under the *espvr* [4]; 7) a new relation between oxygen consumption and the total area under the *espvr* [3]; 8) possibility to apply the same formalism to the four chambers of the heart [2]; 9) possibility to implement some of these results in a non-invasive way by using for instance M-mode echocardiography as discussed in [16]. A recent review of the properties of the pressure-volume relation with possible future orientation can be found in [17].

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Address for correspondence

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