Ventriculo-arterial Coupling and the Areas under the End-systolic Pressure-volume Relation

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SUMMARY

Ventriculo-arterial coupling is expressed as the ratio $E_{\max}/e_{\text{am}}$ (maximum ventricular elastance/arterial elastance). Different areas under the end-systolic pressure-volume relation (ESPVR) are expressed in terms of $E_{\max}/e_{\text{am}}$. The explicit inclusion of the active force of the myocardium in the mathematical formalism describing the pressure-volume relation (PVR) leads to new insight into the mechanics of left ventricular contraction. Applications to experimental data related to stroke work area SW under ESPVR are discussed and provide further evidence for the consistency of the mathematical formalism used. (Jpn Heart J 1997; 38: 253–262)

Key words: End-systolic pressure-volume relation, Active force of the myocardium, Maximum elastance $E_{\max}$, Mechanics of left ventricular contraction, Ventriculo-arterial coupling

THERE has been some interest recently in studying ventriculo-arterial coupling, expressed by the ratio $E_{\max}/e_{\text{am}}$ (maximum elastance/corresponding arterial elastance).^{1–4)} The purpose of the present study is to review some basic equations used in the study of the end-systolic pressure-volume relation (ESPVR) with the aim of emphasizing the following concepts:

a) The mathematical formalism used to describe the pressure-volume relation (PVR) explicitly includes the active force of the myocardium.

b) Stroke work (SW), as well as other areas under ESPVR are used to express ventriculo-arterial coupling as a function of $E_{\max}/e_{\text{am}}$ (note that the corresponding notation $E_{\text{cs}}/E_{\text{a}}$ is also used).^{1–4)} Clinical applications of different areas under ESPVR as well as their significance for the study of left ventricular adaption to load have been discussed.^{12,13)} The following discussion stresses the point of view that the study of the mechanics of left ventricular contraction should be based on an integrated approach to the interrelation between different areas under ESPVR (Figures 3 and 4) rather than an isolated study of the stroke work area SW .

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Table I. Experimental Verification of Equations (7) and (8)

V_{ed} ml	V_m ml	E_{max} mmHg/ml	E_{max}/e_{am}	M mmHg	V_1 ml	V_{100} ml	V_{dm} ml	$M \times$ ($V_{ed}-V_1$)	SW Eq.(7)	$M/$ ($V_{ed}-V_1$)	$2m$ Eq.(8)
55.4	35.2	7.2	0.96	84.6	31.8	33.6	19.7	1997	2293	3.6	3.6
49.3	35.9	9.0	0.91	82.0	30.4	34.2	23.1	1550	1541	4.3	4.5
54.9	41.1	7.5	0.61	77.0	30.6	34.5	21.2	1871	2004	3.2	3.5
58.2	45.6	6.9	0.48	75.0	30.4	33.2	18.7	2085	2359	2.7	3.0
58.4	45.6	6.8	0.43	61.9	29.8	32.3	17.6	1770	2380	2.2	2.9
41.9	31.4	10.7	1.27	71.7	31.6	35.5	26.2	739	650	6.9	5.3
49.5	34.0	13.1	1.33	106.0	28.6	31.0	23.4	2215	2186	5.1	6.4
51.0	35.8	11.0	1.04	102.3	30.2	30.7	21.6	2128	2376	4.9	5.5
53.8	37.8	11.7	0.89	104.8	27.2	29.0	20.5	2788	3233	3.9	5.8
55.5	39.8	10.5	0.76	105.8	28.1	29.0	19.5	2899	3339	3.9	5.2
43.6	31.3	15.0	1.93	94.4	33.0	34.8	28.1	1001	810	8.9	6.7
mean								1913	2106	4.5	4.8
SD								654	847	1.9	1.3

V_{ed} =end-diastolic left ventricular volume; $V_m \approx V_{cs}$ =end-systolic left ventricular volume; E_{max} =maximum elastance, e_{am} =arterial elastance; $M(V_{ed} - V_1)$ =see eq. (9), $V_{100} = V_{dm} + 100/E_{max}$; values for V_{ed} , V_m , E_{max} , E_{max}/e_{am} , M , V_1 , V_{100} are taken from Table 1 of Little and Cheng³⁾.

c) Following experimental results presented by Burkhoff and Sagawa,⁵⁾ Asanoi et al,⁶⁾ Fourie et al,⁷⁾ the present study takes the position that under normal physiological conditions the left ventricle operates near maximum oxygen efficiency with $E_{max}/e_{am} \approx 2$, $E_{max}/e_{am} \approx 1$ (maximum SW) corresponds to a mildly depressed state of the heart while $E_{max}/e_{am} \ll 1$ corresponds to a severely depressed state. Based on experimental observations it has been reported by Burkhoff and Sagawa⁵⁾ that "... it does not seem possible to obtain simultaneously a physiological SV (stroke volume), end-diastolic volume, and end-systolic pressure with the condition $E_a = E_{cs}$. E_a must always be smaller than E_{cs} to obtain physiological conditions ...".

d) New applications to experimental data related to SW taken from Little and Cheng³⁾ are given in Table I and applications to simulation data related to SW taken from Takaoka et al¹⁾ are presented in Table II. The factor A introduced in Eq. (10) of Takaoka et al¹⁾ is derived again, and it is shown that $A = (1/2)(SW/TW)$, where SW =stroke work and TW =total area under ESPVR (Figure 3). These results provide further evidence for the consistency of the mathematical formalism used in the present study.

e) The concept of "preload recruitable stroke work" is reviewed. It is suggested that the apparent linearity between SW and the end-diastolic volume V_{ed} is only an approximation.

Although the ESPVR is slightly curvilinear, the linear model shown in Figure 2 is adopted. This model will simplify greatly the mathematical formalism to be developed, without affecting the basic concepts to be discussed.

MATHEMATICAL METHOD

The cross-section of a three-dimensional cavity of the left ventricle is shown in Figure 1. The helical structure of the fibre generates a radial active force/unit volume D , as explained by Shoucri.^{8,9)} In a quasi-static approximation (inertia and viscous forces neglected), the equilibrium of forces in the radial direction is given by^{8,9)}

$$\bar{D}h - P = E (V_{ed} - V) \quad (1a)$$

where $\bar{D}h = \int_a^b Ddr$ = radial active force/unit area developed on the inner surface of the myocardium

$h = b - a$ = thickness of myocardium

a = inner radius of the myocardium

b = outer radius of the myocardium

E = left ventricular elastance, slope of the P-V line in Figure 2

P = left ventricular pressure

V = left ventricular volume

V_{ed} = end-diastolic ventricular volume (when $dV/dt = 0$)

Near end-systole when E reaches its maximum value E_{max} , a suffix m is added to the variables

$$(\bar{D}h)_m - P_m = E_{max} (V_{ed} - V_m) \quad (1b)$$

Eq. (1a) can be separated into two equations

$$P = E (V - V_d) \quad (2a)$$

$$\bar{D}h = E (V_{ed} - V_d) \quad (2b)$$

Figure 1. Simplified cross-section of the left-ventricle, the helical muscular fibre of the myocardium is projected as a circle. D is the radial active force/unit volume of myocardium. $h = b - a$ is the thickness of myocardium, a = inner radius, b = outer radius, P = ventricular pressure, P_o = outer pressure assumed zero.

Figure 3. Areas under ESPVR. PE = potential energy absorbed by the internal metabolism of myocardial contraction, SW = stroke work delivered to systemic circulation, CW = contraction work absorbed by the passive medium of myocardium.

point d_4 corresponding to $(\bar{D}h)_m$ (Figure 2). In a quasi-static approximation (inertia and viscous forces neglected), the maximum active force $(\bar{D}h)_m$ is equal to the maximum isovolumic pressure P_{iso} represented by point d_3 in Figure 2, and in general $(\bar{D}h)$ is equal to P_{iso} by the symmetry of the lines d_2d_4 and d_1d_3 . Different notations have been used for the active force $(\bar{D}h)$ (ejecting contraction), and the isovolumic pressure P_{iso} (non-ejecting contraction) to emphasize that $\bar{D}h$ is a force and has magnitude and direction, whereas P_{iso} is a scalar quantity.

An immediate and interesting result that can be deduced from Figures 2 and 3 is that when d_1 moves along the ESPVR d_3V_{dm} , the stroke work SW represented by the area $V_{ed}d_2d_1V_m$ is maximum when d_1 coincides with d_3 (mid-point of the segment d_3V_{dm}) [note that d_1 and d_3 coincides when $E_{max}/e_{am} \approx 1$]. The condition $E_{max}/e_{am} \approx 2$ (maximum oxygen efficiency) corresponds to d_1 below d_3 on the line d_3V_{dm} , and the condition $E_{max}/e_{am} \ll 1$ corresponds to d_1 above d_3 . It is seen that when $E_{max}/e_{am} < 1$, SW decreases when P_m increases, creating cardiac insufficiency. Maximum oxygen efficiency as the normal physiological state of the myocardium has also been suggested by Burkhoff and Sagawa⁵⁾, Asanoi et al⁶⁾, Fourie et al⁷⁾ and Elzinga and Westerhof.¹⁵⁾ One can consequently see how the introduction of the active force $\bar{D}h$ in the formalism describing PVR has led to a simple and consistent description of some aspects of the mechanism of left ventricular contraction as summarized by the different areas under ESPVR in Figures 2 and 3. The application of these areas to the study of physiological adaption of the left ventricle to change of load as well as different clinical applications has been discussed^{12,13)}. Some aspects of the relation between SW and E_{max}/e_{am} are discussed below, as are possible relations with the areas CW and PE .

Experimental verification: The experimental application to be discussed first in this section is the relation between stroke work SW and V_{ed} . From Figure 3 and from Shoucri,^{11,12)} we obtain

$$\frac{SW}{TW} = 2 \frac{E_{\max}/e_{\text{am}}}{(1 + E_{\max}/e_{\text{am}})^2} \quad (5)$$

where TW is the total area under ESPVR. When d_1 moves along the line d_3V_{dm} (Figure 2), SW is maximum and equals $(SW)_{\text{max}} = TW/2$ when d_1 coincides with d_5 (d_5 is the middle point of the segment d_3V_{dm}). In this case $E_{\max}/e_{\text{am}} \approx 1$ and Figure 2 provides direct and simple proof of this result. The fact that $(SW)_{\text{max}}$ corresponds to $E_{\max}/e_{\text{am}} \approx 1$ has been experimentally observed by several authors (Asanoi et al,⁶ Burkhoff and Sagawa⁵) Sunagawa et al¹⁸) and Little and Cheng⁴). Equation (5) is equivalent to Eq. (7) of Little and Cheng⁴) and Eq. (2) of Little and Cheng.³) There is a difference of a factor of 2 because normalization in Eq. (5) with respect to TW , while Little and Cheng normalized with respect to $(SW)_{\text{max}} = TW/2$. By noting that the total area TW under ESPVR is given by

$$TW = \frac{1}{2} (\bar{D}h)_m (V_{\text{ed}} - V_{\text{dm}}) \quad (6)$$

Eq. (3b), (5) and (6) give

$$SW = m(V_{\text{ed}} - V_{\text{dm}})^2 \quad (7)$$

with

$$m = E_{\max} \frac{E_{\max}/e_{\text{am}}}{(1 + E_{\max}/e_{\text{am}})^2} \quad (8)$$

Eq. (7) is quadratic in $V_{\text{ed}} - V_{\text{dm}}$, and has been compared in Table I to the linear formula

$$SW_1 = M(V_{\text{ed}} - V_1) \quad (9)$$

given by Little and Cheng^{3,4}) where M is preload recruitable stroke work (Glomer et al¹⁷) and V_1 the axis intercept of the linear Eq. (9). The intercept V_{dm} of ESPVR (see Figure 2) has been calculated from the formula $V_{100} = V_{\text{dm}} + 100/E_{\max}$ given by Eq. (2) of Little and Cheng.³) The comparison between SW_1 (linear model) and SW (Eq. 7) in Table I is good. Note that data taken from Table I of Little and Cheng³) represent averages for experimental results for 8 animals and not data from a single experiment, so some fluctuation is expected. Since $SW_1 = (M/(V_{\text{ed}} - V_1))(V_{\text{ed}} - V_1)^2$ the values of $M/(V_{\text{ed}} - V_1)$ have also been compared in Table I with the values of $2m$ (Eq. 8). This comparison was also good, and factor 2 accounts for the fact that the slopes of a quadratic curve and a linear curve differ by a factor of 2. Statistical t-test of the means shown in Table I indicates that the difference is not statistically significant. The linear model (Eq. 9) appears to be an approximation and does not seem to reflect a basic characteristic of left ventricu-

lar contraction.

We shall now discuss the derivation of the quantity A introduced in Eq. (10) of Takaoka et al.¹⁾

A simple manipulation of Eq. (3b) and (6)–(7) gives

$$SW = E_{\max} (V_{\text{ed}} - V_{\text{dm}})^2 (E_{\max}/e_{\text{am}}) / (1 + E_{\max}/e_{\text{am}})^2 \quad (10)$$

Eq. (10) has been derived differently by Burkhoff and Sagawa⁵⁾ and Sunagawa et al.¹⁸⁾ One also has

$$SW = P_m (V_{\text{ed}} - V_m) = E_{\max} (V_m - V_{\text{dm}}) (V_{\text{ed}} - V_m) \quad (11)$$

By making $k = e_{\text{am}}/E_{\max}$ and by equating Eq. (10)–(11) we obtain, using Eq. (6)–(7)

$$k/(1+k)^2 = (1/2) (SW/TW) = A \quad (12)$$

The dimensionless quantity A is given in Eq. (10) of Takaoka et al.¹⁾ and was used by them to calculate e_{am} (or E_a), but its relation to the curve for SW/TW given in Figure 4 is not derived. One should note how the mathematical model used in the present study allows a simple derivation of an expression for A . Moreover, by writing $K = 1/k$ we obtain $SW/TW = 2K/(1+K)^2$. Derivation with respect to K gives $(d/dK) (SW/TW) = 2/(1+K)^2 - 4K/(1+K)^3$, which is zero when $K = 1$, or $E_{\max}/e_{\text{am}} = 1$. This corresponds to the maximum of the curve SW/TW in Figure 4. For $K = 1$, $(SW)_{\text{max}} = TW/2$, which is the maximum value of the stroke volume (d_1 and d_5 in Figures 2 and 3).

A further validation of Eq. (7) and (8) is provided by the results of Table II. The values of V_{dm} , $E_{\max}/e_{\text{am}}$ and V_{ed} are taken from Figure 6A of Takaoka et al.¹⁾ (with an obvious change in notation, for instance Takaoka et al.¹⁾ use $E_a/E_{\max}$

Figure 4. Relations between SW/TW , CW/TW , PE/TW , and $E_{\max}/e_{\text{am}}$.

Table II. Verification of Equations (7) and (8) from Simulation Data

V_{dm} ml	E_{max} mmHg/ml	E_{max}/e_{am}	m mmHg/ml Eq. (8)	V_{ed} ml	SW mmHg/ml Eq. (7)
7	7	1/3	1.313	20	222
				30	695
				40	1430
7	7	1/2	1.556	20	263
				30	823
				40	1695
7	7	1	1.750	20	296
				30	926
				40	1906
7	7	2	1.556	20	263
				30	823
				40	1695
7	7	3	1.313	20	222
				30	695
				40	1430

V_{dm} = intercept of ESPVR with volume axis; V_{ed} = end-diastolic volume; E_{max} = maximum slope of ESPVR; e_{am} = corresponding arterial elastance. Values for V_{dm} , V_{ed} , E_{max} , E_{max}/e_{am} are taken from Figure 6A of Takaoka et al.¹⁾ with an obvious change in the notation.

while the ratio E_{max}/e_{am} is used in the present study). In Table II, m is calculated using Eq. (8) and SW using Eq. (7). The values obtained for SW compare very well with the corresponding values of SW that can be measured from Figure 6A of Takaoka et al.¹⁾ In particular note the equality of the values of m for $E_{max}/e_{am} = 1/3$ and 3, or for $E_{max}/e_{am} = 1/2$ and 2, that results by applying Eq. (8), and the equalities of the corresponding values of SW as shown in Table II and verified by the corresponding values of SW in Figure 6A of Takaoka et al.¹⁾ Here again, Eq. (7) and the results of Table II suggest that the linear dependence of SW on V_{ed} given by Eq. (9) is an approximation.

Other areas appearing under ESPVR are CW and PE . CW seems to be related to the energy absorbed in the contraction of myocardium (see appendix A of Shoucri¹¹⁾). The area PE appears to be related to the energy absorbed by the internal metabolism of the heart. For example Takaoka et al.¹⁶⁾ observed that the area PE increases in cardiomyopathy cases. Variations of areas SW/TW , CW/TW , PE/TW , with E_{max}/e_{am} based on previous theoretical relations¹²⁾ are shown in Figure 4. Experimental verification of these curves can be found in Figure 5 of Shoucri.¹²⁾ The curve for SW/TW is similar to Figure 2 of Little and Cheng,⁴⁾ Figure 7 of Fourie et al.,⁷⁾ and Figure 4 of Takaoka et al.¹⁾ The interrelation between these different areas comes from the fact that $SW/TW + CW/TW + PE/TW = 1$. No experimental investigation of this interrelation has yet been undertaken.

CONCLUSION

Important features of this study are as follows:

a) The inclusion of the radial active force of the myocardium $\bar{D}h$ in the mathematical formalism describing ESPVR;

b) The possibility of using the ratio $E_{\max}/e_{\text{am}}$ to distinguish between normal ($E_{\max}/e_{\text{am}} \approx 2$), mildly depressed ($E_{\max}/e_{\text{am}} \approx 1$) (maximum SW), and severely depressed states of the heart ($E_{\max}/e_{\text{am}} \ll 1$);

c) It is suggested that the interrelation between different areas under ESPVR (summarized in Figures 3 and 4) plays a fundamental role in understanding cardiac mechanics. The linear equation Eq. (9) for SW_1 for instance does not represent a fundamental aspect of cardiac contraction, but rather appears simply to be an isolated approximation. Figure 4 shows that there is a need for an integrated approach for the modelling of different areas under ESPVR. For instance in Figure 2, the study of the area $V_{\text{ed}} d_2 d_4 V_{\text{m}}$ (or by symmetry $V_{\text{ed}} d_3 d_1 V_{\text{m}}$) which represents the work of the active force $\bar{D}h$, when $\bar{D}h$ moves from d_2 to d_4 , has not received any attention.

d) An important aspect of this interrelation between different areas under ESPVR, not discussed in this study, is the relation between oxygen consumption and the different areas of PE , SW , CW under ESPVR. This problem has been discussed^{11,12)} and requires further experimental as well as theoretical study.

The possibility of non-invasive implementation of the results of this study for clinical work using M-mode echocardiography for example is another challenge for experimentalists and has been discussed.¹²⁾ Finally, it should be mentioned that an interesting review of cardiac mechanics based on PVR has been given by Suga.¹⁹⁾

REFERENCES

1. Takaoka H, Suga H, Goto Y, Hata K, Takeuchi M. Cardiodynamic conditions for the linearity of preload recruitable stroke work. *Heart and Vessels* 1995; 10: 57-68
2. Nevo E, Marmor M, Lanir Y, Weiss TA, Marmor A. A new methodology for non-invasive clinical assessment of cardiovascular performance and of ventricular-arterial coupling during stress. *Heart and Vessels* 1995; 10: 24-34.
3. Little WC, Cheng CP. Left ventricular-arterial coupling in conscious dogs. *Am J Physiol* 1991; 261: H70-H76.
4. Little WC, Cheng CP. Coupling of the left ventricular and arterial system. *Med Biol Eng Comput* 1994; 32: 205-9.
5. Burkhoff D, Sagawa K. Ventricular efficiency predicted by an analytical model. *Am J Physiol* 1986; 250: R1021-R1027.
6. Asonoi H, Sasayama S, Kamegama T. Ventriculo arterial coupling in normal and failing heart in humans. *Circ Res* 1989; 65: 483-93.
7. Fourie PR, Coetzee AR, Bolliger CT. Pulmonary artery compliance: its role in right ventricular-arterial coupling. *Cardio Res* 1992; 26: 839-44.

8. Shoucri RM. The pressure volume relation and the mechanics of left ventricular contraction. *Jpn Heart J* 1990; 31: 713-29.
9. Shoucri RM. Theoretical study of pressure-volume relation in left ventricle. *Am J Physiol* 1991; 260: H282-H291.
10. Shoucri RM. Non-linear pressure-volume relation in left ventricle. *Jpn Heart J* 1991; 32: 337-46.
11. Shoucri RM. Theoretical study related to left ventricular energetics. *Jpn Heart J* 1993; 34: 403-17.
12. Shoucri RM. Possible clinical applications of the external work reverse of the myocardium. *Jpn Heart J* 1994; 35: 771-87.
13. Shoucri RM. Clinical application of end-systolic pressure-volume relation. *Ann Biomed Eng* 1994; 22: 212-7.
14. Shoucri RM. The active force of the myocardium, In: Power H, Hart RT, editors. *Computer Simulations in Biomedicine*. Boston: Computational Mechanics Publications, 1995: 19-26.
15. Elzinga G, Westerhof N. Matching between ventricle and arterial load, an evolutionary process. *Circ Res* 1991; 68: 1495-500.
16. Takaoka H, Takeuchi M, Odake M, et al. Depressed contractile state and increased myocardial consumption for non-mechanical work in patients with heart failure due to old myocardial infarction. *Cardiov Res* 1994; 28: 1251-7.
17. Glower DD, Spratt JA, Snow ND, et al. Linearity of the Frank-Starling relationship in the intact heart: the concept of preload recruitable stroke work. *Circulation* 1985; 71: 994-1009.
18. Sunagawa K, Maughan WL, Sagawa K. Optimal arterial resistance for maximal stroke work studied in isolated canine left ventricle. *Circ Res* 1985; 56: 586-95.
19. Suga H. Paul Dudley White International Lecture: Cardiac performance as viewed through the pressure-volume window. *Jpn Heart J*. 35: 263-80.