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Mechanical efficiency of the left ventricle as a function of preload, afterload, and contractility

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Summary. We have recently shown that the mechanical efficiency of the contractile machinery of the canine left ventricle is constant at 30%–50%, independent of its loading, heart rate, and inotropic conditions. In contrast, the conventional mechanical efficiency of the ventricle is known to vary between 0 and 30%, depending on these conditions. In this study, we derived an equation for the conventional mechanical efficiency as a function of ventricular preload, afterload, and contractility, based on the constant mechanical efficiency of the contractile machinery. In deriving this equation, we fully utilized our new concept of the total mechanical energy of the left ventricle, i.e., systolic pressure-volume area, and our recent findings of the linear relationship between left ventricular oxygen consumption and the systolic pressure-volume area as well as the dependence of this relation on the ventricular inotropic state. As a result, the conventional mechanical efficiency of the left ventricle was found to change between 0 and 25% as an explicit function of these cardiodynamic and inotropic conditions. Using this function, we obtained combinations of loading and inotropic conditions to maximize the conventional mechanical efficiency of the left ventricle.

Key words: Heart – Cardiac mechanics – Cardiac energetics – Oxygen consumption – Pressure-volume area.

The efficiency of energy conversion in a system is defined as the ratio of the useful energy delivered by the system to the energy supplied to it. In the heart, the conventional mechanical efficiency is the ratio of the external mechanical work to the energy supplied to the heart [1]. This mechanical efficiency of the heart is known to vary between 0 and 35%, depending on ventricular loading and inotropic conditions [1].

Recently, we have found that the mechanical efficiency of the contractile machinery is constant at 30%–50% (mean 40%) in the canine left ventricle regardless of the loading [2], heart rate [3], and inotropic conditions [4, 5]. We have also found that the oxygen consumption of the mechanically unloaded beating left ventricle, namely, oxygen consumption for both basal metabolism and the excitation-contraction coupling, sensitively increases with the contractile state [4].

In the present study, based on these new findings [5], we derived the relationship between the conventional mechanical efficiency of the left ventricle and the loading and inotropic conditions. As a result, we found that the conventional mechanical efficiency of the left ventricle changed as an explicit function of preload, afterload, and contractile state. This function is useful in predicting mechanical efficiency of the left ventricle under various loading and inotropic conditions as well as in searching for the loading and inotropic conditions to maximize the mechanical efficiency of the left ventricle.

Methods

All empirical data and relations that we used in this study had been obtained from our previous series of experiments on the left ventricular oxygen consumption and systolic pressure-volume area [2–5]. The experimental system in which we obtained the data was an *excised, cross-circulated canine heart preparation, in which the left ventricle was fitted with a water-filled balloon* [4]. Left ventricular pressure and volume were precisely controlled and accurately measured with the custom-made volume servo pump [5, 6].

Left ventricular systolic pressure-volume area (PVA) was used as a measure of the total mechanical energy generated by ventricular contraction [7]. As shown in Fig. 1, PVA is the area circumscribed by the end-systolic pressure-volume *(P-V)* line, the end-diastolic *P-V* curve, and the systolic segment of the *P-V* trajectory [7].

In the same heart, myocardial oxygen consumption (V_{O_2}) was measured as the product of coronary perfusion flow and arteriovenous oxygen content difference. Because the right ventricle was maintained in a collapsed state, we considered that the measured V_{O_2} represented V_{O_2} of the left ventricle [4].

The fundamental empirical relationship between PVA and V_{O_2} which we obtained in a previous series of experiments [2–4] is:

$$V_{O_2} = A \times \mathrm{PVA} + B \quad (1)$$

where the dimensions of V_{O_2} and B are ml O_2/beat/100 g, those of A are ml O_2/(mmHg ml), and those of PVA are mmHg ml/beat/100 g. A

is the regression (or slope) coefficient of the regression line of V_{O_2} on PVA, and B is the constant, or the V_{O_2} axis intercept of the regression line. B is identical to the V_{O_2} of unloaded contraction with zero PVA [2–4].

Our results have indicated that the coefficient A is constant regardless of the loading, heart rate, and inotropic conditions of each given left ventricle [2–4]. On average in 18 hearts [4].

$$A = 1.9 \times 10^{-5} \quad (2)$$

Standard deviation (SD) of A was 0.37×10^{-5} ml O_2/(mmHg ml).

Figure 2 shows scatter diagrams plotting slope coefficient A in Eq. (1) against contractility index (E_{max}) in individual left ventricles. E_{max} was used as a sensitive index of the ventricular contractile state [8]. Figure 2 A shows the result when the contractile state was enhanced by administering epinephrine (1 μg/kg/min, iv) to the excised cross-circulated heart preparation. The result of enhancing the contractile state by administering calcium chloride (0.03 mEq/kg/min, iv) is shown in Fig. 2 B, and Fig. 2 C shows the pooled data from A and B. The correlation coefficients in all three cases are low and statistically insignificant ($P > 0.05$). Therefore, we assumed in the following theoretical derivations that the slope coefficient A in a given heart was constant at the mean value indicated in Eq. (2).

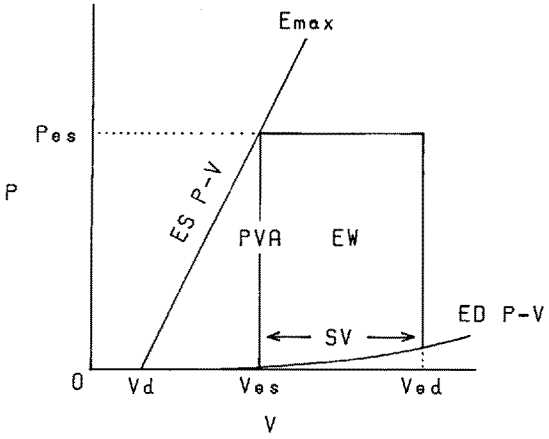

Fig. 1. Schematic illustration of the left ventricular pressure-volume loop trajectory, end-systolic pressure-volume line *(ES P-V)*, end-diastolic pressure-volume curve *(ED P-V)*, external mechanical work *(EW)*, and systolic pressure-volume area *(PVA)*. Ventricular pressure and volume variables used in the text are shown. P_{es} end-systolic pressure; V_{ed} end-diastolic volume; V_{es} end-systolic volume; V_d volume axis intercept of the end-systolic *P-V* line; *SV* stroke volume; E_{max} contractility index representing the slope of the end-systolic *P-V* line

In contrast, the constant B in Eq. (1) is sensitively dependent on the inotropic conditions of the left ventricle [4], although it is independent of the loading and heart rate conditions [2, 3]. Figure 3 shows scatter diagrams of B values plotted against E_{max} values in individual left ventricles subjected to the enhancement of contractility by epinephrine (A) and calcium (B). Figure 3 C shows the pooled data.

In Fig. 3 A, the linear regression line of B on E_{max} is:

$$B = 0.0032 \times E_{max} + 0.006 \quad (3)$$

where the dimensions of B and E_{max} are ml O_2/beat/100 g and mmHg/(ml/100 g), respectively. The correlation coefficient was 0.64, which is statistically significant at $P < 0.05$. The 95% confidence range of the slope coefficient of 0.0032 ml O_2/[mmHg/(ml/100 g)] is 0.0024–0.0040 ml O_2/[mmHg/(ml/100 g)].

Similarly, in Fig. 3 B, the linear regression line is:

$$B = 0.0019 \times E_{max} + 0.021 \quad (4)$$

The 95% confidence range of the slope coefficient of E_{max} of 0.0019 is 0.0013–0.0025 ml O_2/[mmHg/(ml/100 g)].

These two regression lines appear to differ slightly, but the analysis of covariance [9] shows that neither their elevations nor slope coefficients are significantly different to either epinephrine or calcium ($P < 0.05$). Therefore, we pooled both epinephrine and calcium data to obtain a common linear regression line in Fig. 3 C. As a result:

$$B = 0.0024 \times E_{max} + 0.014 \quad (5)$$

where the 95% confidence range of the slope coefficient was 0.0019–0.0029 ml O_2/[mmHg/(ml/100 g)], and the correlation coefficient was 0.61, statistically significant at $P < 0.05$. We consider that this slope coefficient is a parameter in determining the sensitivity of changes in B in response to changes in E_{max}. In the present study, we fixed this coefficient at the value of 0.0024 shown in Eq. (5).

The regression constant of 0.014 ml O_2/beat/100 g in Eq. (5) can be considered the value for the unloaded V_{O_2} of the ventricle whose contractility measured by E_{max} is zero. Zero E_{max} signifies no mechanical contraction and no excitation-contraction coupling. Therefore, the above regression constant can be considered to indicate the basal metabolic V_{O_2}. Multiplying this value with an average heart rate of 162 beats/min gives 2.3 ml O_2/min/100 g. This value is in the middle of the reported range of 1–5 ml O_2/min/100 g for the basal metabolic V_{O_2} [10].

Our previous studies have revealed that the mechanical efficiency of the contractile machinery of the left ventricle is constant at 30%–50% (mean 40%) [4, 5]. Briefly, this efficiency (E_c) is the ratio of PVA to the excess V_{O_2} above the unloaded V_{O_2} [4, 5]. In other words, from Eq. (1):

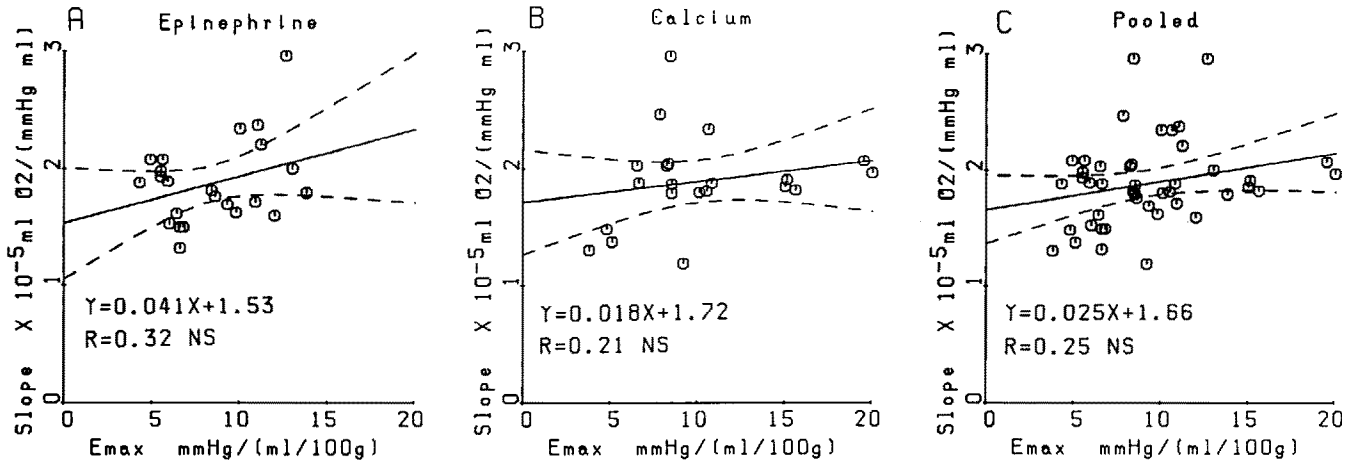

Fig. 2 A–C. Correlation and regression analysis of the relation between the slope coefficient of V_{O_2}-PVA regression line and E_{max} in nine different canine left ventricles. **A** epinephrine run; **B** calcium run; **C** pooled data from **A** and **B**. The *solid line* is the linear regression line of y values on x values. The paired *dashed curves* indicate the 95% confidence limits of the regression line. The *equations* indicate the linear regression equations. R correlation coefficient; *NS* statistically insignificant ($P > 0.05$)

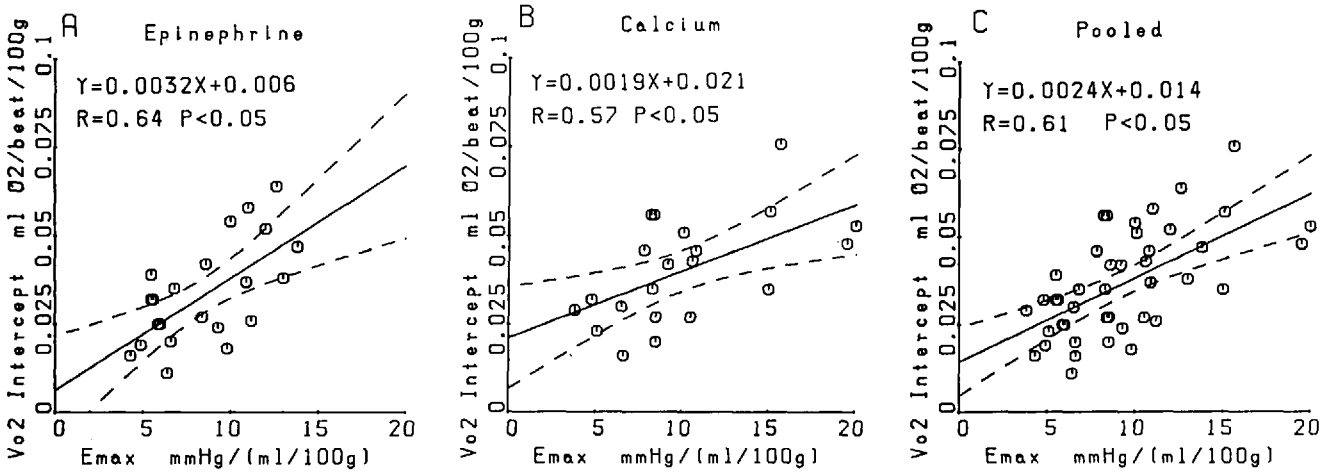

Fig. 3 A–C. Correlation and regression analysis of the relation between V_{O_2} intercept of V_{O_2}-PVA regression line on E_{max} in the same nine canine left ventricles as shown in Fig. 2 **A** epinephrine run; **B** calcium run; **C** pooled data from **A** and **B**. The *solid line* is the linear regression line of V_{O_2} intercept on E_{max}. The paired *dashed curves* indicate the 95% confidence limits of the regression line. The *equations* indicate the linear regression equations. *R* correlation coefficient. These correlations are statistically significant at $P < 0.05$

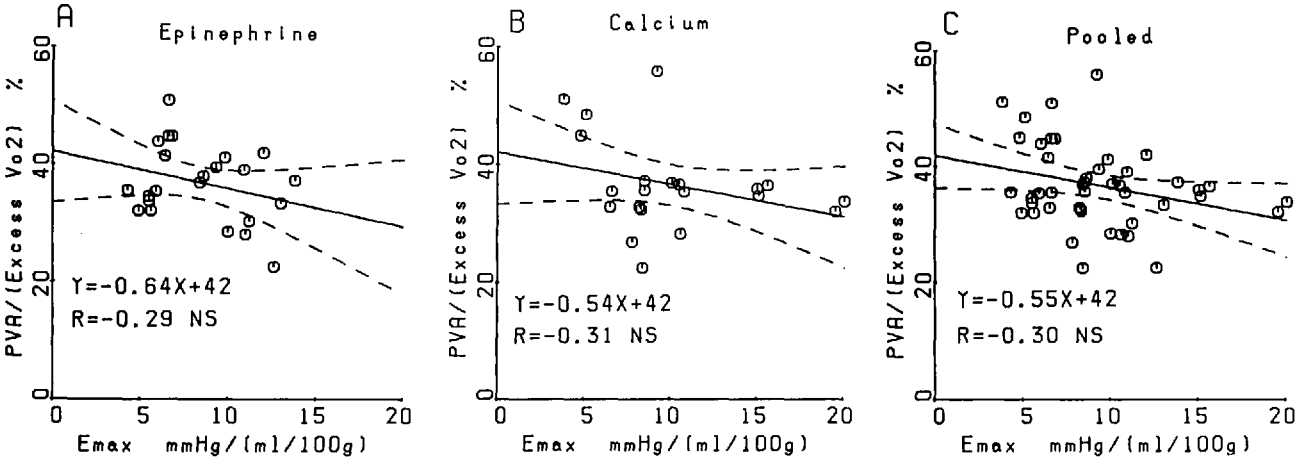

Fig. 4 A–C. Correlation and regression analysis of the relation between mechanical efficiency (E_c), PVA/(excess V_{O_2}), of the contractile machinery and E_{max} in nine differnet canine left ventricles. **A** epinephrine run; **B** calcium run; **C** pooled data from **A** and **B**. The *solid line* is the linear regression line. The paired *dashed curves* indicate the 95% confidence limits of the regression line. The *equations* indicate the linear regression equations. *R* correlation coefficient; *NS* statistically insignificant ($P > 0.05$)

$$E_c = 100 \times \text{PVA}/(\text{excess } V_{O_2}) = 100 \times \text{PVA}/(V_{O_2} - B) = 100 \times \text{PVA}/(A \times \text{PVA}) = 100/A \quad (6)$$

where A and B are the regression coefficient and constant, respectively, of Eq. (1). To determine E_c as a percentage, A must be dimensionless. In Eq. (1), the dimensions of A are ml O_2/(mmHg ml). Because 1 ml $O_2 = 20$ J and 1 mmHg ml $= 1.33 \times 10^{-4}$ J, A in ml O_2/(mmHg ml) is equal to $[20/(1.33 \times 10^{-4})] \times A$, i.e., $1.5 \times 10^5 \times A$ (dimensionless). Therefore,

$$E_c = 66.6 \times 10^{-5}/A \quad (7)$$

Substituting the average value of A, 1.9×10^{-5} ml O_2/(mmHg ml) in Eq. (2), for A in Eq. (7), we obtain:

$$E_c = 35.4 \quad (8)$$

indicating that E_c is 35% on average. This is the value for E_c that we obtained for the contractile machinery of the canine left ventricle.

Figure 4 shows the scatter diagrams of the E_c (i.e., PVA/excess V_{O_2}) efficiency plotted against E_{max} when E_{max} was increased by epinephrine (Fig. 4 A) and calcium (Fig. 4 B). Although there was a slight tendency for the efficiency to decrease with increases in E_{max} in both A and B, the correlation was statistically insignificant ($P < 0.05$) and the regression lines had no significant slope. The analysis of covariance [9] indicated no difference between these two regression lines. Therefore, we pooled all data and applied the linear regression analysis in Fig. 4 C. Again, the correlation was insignificant ($P < 0.05$) and the regression line had no significant slope, so we assumed that E_c is constant at 35% in the present study.

Next, we have to consider the theoretical relationship between the external mechanical work output (EW) of the left ventricle and PVA. Figure 1 illustrates schematically a *P-V* diagram in which a *P-V* loop trajectory of an ordinary ejecting contraction is drawn together with the end-systolic *P-V* line and the end-diastolic *P-V* curve. EW is the area within the *P-V* loop. PVA is the area circumscribed by the end-systolic *P-V* line, the end-diastolic *P-V* curve, and the systolic segment of the *P-V* trajectory. PVA comprises EW and the triangular area on the *P-V* origin side of the EW area. This triangular area is the elastic potential energy [7] that is generated during systole and is stored in the time-varying elastance at the end of systole [7].

This potential energy is part of the total mechanical energy generated by ventricular contraction that is unused for effective mechanical work output in either ordinary ejecting or isovolumic contractions [11]. Although there is a way to convert this potential energy into ef-

fective mechanical work, the method requires an additional ejection during ventricular relaxation [11]. Therefore, in the present study, we decided to consider EW of ordinary ejecting contractions whose *P-V* loop is rectangular and EW is performed only during systole.

The mathematical relation between EW (mmHg ml) and PVA (mmHg ml) is:

$$PVA = EW + 0.5 \times P_{es}^2/E_{max} - 0.00025 \times (P_{es}/E_{max})^4 \quad (9)$$

where EW = external work in mmHg ml or the area within the *P-V* loop, P_{es} = end-systolic pressure in mmHg, and E_{max} = slope of the end-systolic *P-V* line in mmHg/ml. The second term is the area for the end-systolic elastic potential energy.

The last term of Eq. (9) is the area between the end-diastolic *P-V* curve and the volume axis. This term was derived assuming that the end-diastolic *P-V* curve can be approximated by a third-power function of the ventricular volume exceeding V_d [12], i.e.:

$$P_{ed} = a \times (V_{ed} - V_d)^3 \quad (10)$$

where P_{ed} = end-diastolic pressure, V_{ed} = end-diastolic volume, V_d = volume axis intercept of the end-systolic *P-V* line, or the ventricular volume at which peak systolic pressure is zero. In the 75-g left ventricle of a 15-kg dog, $a = 0.001$ is a reasonable value, because Eq. (10) with this value of a gives $P_{ed} = 0$, 2, 12, 36, 80 mmHg at $V_{ed} = 10$, 20, 30, 40, 50 ml, respectively. The definite integral of Eq. (10) between V_d and V_{ed} is $(a/4) \times (V_{ed} - V_d)^4 = 0.00025 \times (V_{ed} - V_d)^4$, and that between V_d and V_{es} ($= P_{es}/E_{max} + V_d$) is $(a/4) \times (P_{es}/E_{max})^4 = 0.00025 \times (P_{es}/E_{max})^4$, which is the last term in Eq. (9).

Similar to PVA:

$$EW = P_{es} \times SV - 0.00025 \times [(V_{ed} - V_d)^4 - (P_{es}/E_{max})^4] \quad (11)$$

where SV = stroke volume in milliliters. The last term subtracted from $P_{es} \times SV$ is equal to the area between the end-diastolic *P-V* curve and the volume axis under EW. We assumed that ventricular pressure during ejection is equal to P_{es} and the ejection stops at end systole, so that the *P-V* trajectory is rectangular, as shown in Fig. 1.

Since

$$SV = V_{ed} - V_{es} \quad (12)$$

and

$$V_{es} = P_{es}/E_{max} + V_d \quad (13)$$

we obtain from Eqs. [11–13]:

$$EW = P_{es} \times (V_{ed} - P_{es}/E_{max} - V_d) - 0.00025 \times [(V_{ed} - V_d)^4 - (P_{es}/E_{max})^4] \quad (14)$$

To obtain the energy conversion efficiency from V_{O_2} to EW as a percentage, we converted the dimensions of both EW and V_{O_2} into common dimensions of J/beat/100 g. Again, 1 mmHg ml = 1.33×10^{-4} J. From Eq. (14):

$$EW = 1.33 \times 10^{-4} \times \{P_{es} \times (V_{ed} - P_{es}/E_{max}33 - V_d) - 0.00025 \times [(V_{ed} - V_d)^4 - (P_{es}/E_{max})^4]\} \quad (15)$$

and because 1 ml O_2 = 20 J, from Eqs. (1) and (8):

$$V_{O_2} = 20 \times (A \times PVA + B) = 20 \times \{1.9 \times 10^{-5} \times [P_{es} \times (V_{ed} - P_{es}/E_{max} - V_d) + 0.5\, P_{es}^2/E_{max} - 0.00025 \times (P_{es}/E_{max})^4] + 0.0024 \times E_{max} + 0.014\} \quad (16)$$

From Eqs. 15 and 16, we obtain:

$$EW/V_{O_2} = (1.33 \times 10^{-4}/20) \times \{P_{es} \times (V_{ed} - P_{es}/E_{max} - V_d) - 0.00025 \times [(V_{ed} - V_d)^4 - (P_{es}/E_{max})^4]\} / \{1.9 \times 10^{-5} \times [(P_{es} \times (V_{ed} - P_{es}/E_{max} - V_d) + 0.5\, P_{es}^2/E_{max} - 0.00025 \times (P_{es}/E_{max})^4] + 0.0024 \times E_{max} + 0.014\} \quad (17)$$

Note that this equation describes the conventional mechanical efficiency as a function of preload (V_{ed}), afterload (P_{es}), and contractile state (E_{max}), which are the three basic parameters that are known to affect left ventricular performance independently.

We set this equation in a microcomputer and analyzed numerically how preload, afterload, and contractility affect the mechanical efficiency of the left ventricle.

Results

Figure 5 shows how the conventional mechanical efficiency, i.e., EW/V_{O_2} efficiency, is affected by ventricular preloaded end-diastolic volume, afterloaded ventricular pressure, and the contractile state index. Six surfaces are shown for representative E_{max} values. These E_{max} values cover the reported normal working range in 15-kg dogs [13].

The general tendency is that the mechanical efficiency increases with increases in preloaded end-diastolic volume. It also increases with increases in afterloaded ventricular pressure, but reaches a maximal efficiency at an intermediate pressure and then decreases with further increases in pressure. The surface tends to become higher and extend to the right with increases in E_{max}.

We limited ventricular pressure to less than 200 mmHg and ventricular volume to less than 50 ml, which are the upper limits of the normal working range

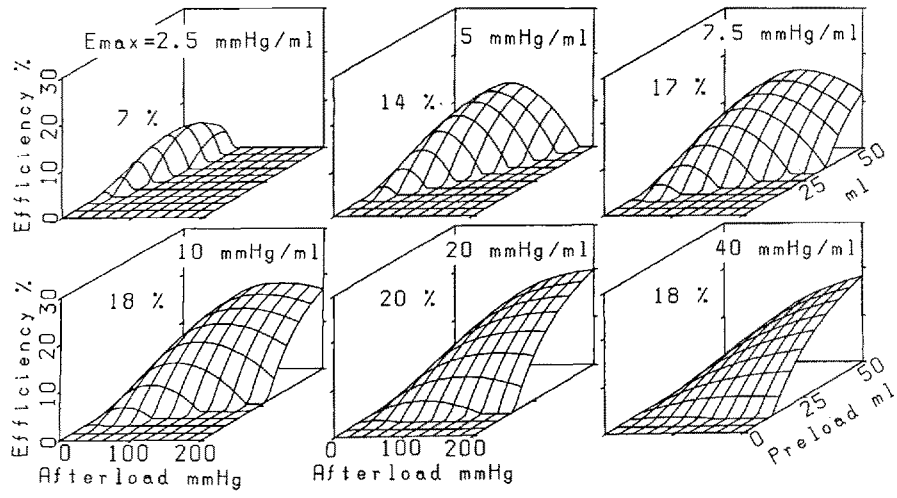

Fig. 5. Three-dimensional surfaces of the mechanical efficiency of the ventricle on the vertical coordinate as a function of end-diastolic volume (preload) and ejection pressure (afterload) on the two horizontal coordinates. The six *parts* show the surfaces for six different E_{max} values. Efficiency value in percentage in each *part* indicates the maximal efficiency value for each E_{max} value

in normal canine left ventricles of a 15-kg dog. Therefore, although the surface continues into higher preload and afterload regions, we limited its display to less than 200 mmHg and 50 ml. By extrapolation of the surfaces, we can recognize that the general shape of the surface is unchanged with different E_{max} levels and the major differences among them are their locations and magnitudes.

The maximal efficiency obtained below 200 mmHg and 50 ml increases with E_{max} until E_{max} reaches 20 mmHg/ml, and then decreases as E_{max} further increases. Below 15 mmHg/ml of E_{max}, the maximal efficiency is reached below 200 mmHg. For example, the afterload pressures for maximal efficiency is 30 mmHg at $E_{max}=2.5$ mmHg/ml, 60 mmHg at $E_{max}=5$ mmHg/ml, 110 mmHg at $E_{max}=7.5$ mmHg/ml, and 140 mmHg at $E_{max}=10$ mmHg/ml. However, at $E_{max}=15$ mmHg/ml, the maximum efficiency is reached at 200 mmHg, which is equal to the upper end of the afterload range. Above 15 mmHg/ml of E_{max}, the efficiency is still increasing at 200 mmHg, and the extrapolated true maximal efficiency would be reached at a pressure above 200 mmHg, out of the afterload range.

Although the maximal efficiency is reached at 50 ml of preload for E_{max} levels above 5 mmHg/ml, it is reached at lower preloads for E_{max} below 5 mmHg/ml. For example, the preloaded volumes for maximal efficiency are 30 ml at $E_{max}=1$ mmHg/ml, 35 ml at $E_{max}=1.5$ mmHg/ml, 40 ml at $E_{max}=2$, 2.5, and 3 mmHg/ml, and 45 ml at $E_{max}=4$ mmHg/ml. The efficiency at greater volumes for low E_{max} levels decreases because the fraction of EW in PVA at low E_{max} cannot increase in proportion to preloaded end-diastolic volume because end-diastolic pressure sharply increases due to the downward convex end-diastolic P-V relation curve.

The maximal efficiency values at different E_{max} levels range between 2% at $E_{max}=1$ mmHg/ml and 20% at $E_{max}=20$ mmHg/ml. The maximum value of the maximal efficiency, 20%, is only 57%, or about two-thirds, of the mechanical efficiency (E_c) of the contractile machinery, 35%.

Discussion

The present study has revealed that the mechanical efficiency, i.e., EW/V_{O_2}, of the left ventricle varies as an explicit function of preloaded end-diastolic volume, afterload pressure during ejection, and contractility index E_{max}, although the mechanical efficiency E_c, i.e., PVA/(excess V_{O_2}), of the contractile machinery is constant.

To the best of our knowledge, the present study is the first that elucidates a quantitative relationship of the mechanical efficiency of the heart as a function of preload, afterload, and contractility. Although mechanical efficiency of the heart under pressure and volume loads was studied quantitatively and systematically by Evans and Matsuoka [14] and Sarnoff et al. [15], their results yielded empirical relations of cardiac mechanical efficiency as a function of external mechanical work in a given contractile state. Other investigations reported individual values for cardiac mechanical efficiency under different cardiovascular conditions [1, 16]. According to these reports, cardiac mechanical efficiency, i.e., ratio of external mechanical work to total myocardial oxygen consumption, ranges between 0 and 35%, with a normal functioning value of 10%–25%. Our present data fall within this range.

Our data in Fig. 5 show that the maximal efficiency is 20% at most, and does not reach the extreme maximal values of 25%–35% mentioned above. We consider that this discrepancy probably comes from the variations in coefficient A, which appears in Eqs. (1, 2, 6, 7), and constant B, which appears in Eqs. (1, 3–6), among individual canine left ventricles [2–5]. The variations of A and B affect several coefficients and constants in Eq. (17) and, in turn, EW/V_{O_2} values for given sets of preload, afterload, and E_{max}. Generally, the maximal efficiency values for given E_{max} values decrease as either A or B increase. An increase in A is equivalent to a decrease in the mechanical efficiency of the contractile machinery and an increase in B is equivalent to an increase in the oxygen consumption for basal metabolism and excitation-contraction coupling.

If PVA/(excess V_{O_2}) efficiency is 50%, a maximum extreme in the canine left ventricle [5], our present study indicates that EW/V_{O_2} efficiency will be 30%, or two-thirds of 50%, which is close to the maximum extreme value for the mechanical efficiency of the heart [1, 16]. Therefore, we consider that our present values for the mechanical efficiency of the left ventricle are generally consistent with the range reported in the literature [1, 16].

This substantial reduction of the mechanical efficiency from the contractile machinery level to the ventricular level is due to the existence of energy utilization for both basal metabolism and excitation-contraction coupling as well as to the existence of the end-systolic elastic potential energy. The basal metabolism and excitation-contraction coupling are nonmechanical activities of the myocardium that are prerequisite to mechanical contraction in normal myocardium. The elastic potential energy is always associated with mechanical contraction and remains unused in ordinary contractions. Therefore, we consider that under normal conditions the significant (about one-third) reduction of the mechanical efficiency from the contractile machinery level to the ventricle level is inevitable.

The new finding that the maximal efficiency increases with E_{max} up to a level of 20 mmHg/ml is intriguing in the following ways. The physiological data in our previous studies indicate that left ventricular oxygen consumption for the excitation-contraction coupling significantly increases with E_{max}. Therefore, left ventricular oxygen consumption for a given total me-

chanical energy, i.e., PVA, increases and the efficiency from oxygen consumption to PVA decreases with E_{max} [4]. However, the present analysis indicates that the efficiency from oxygen consumption to external mechanical work increases with E_{max}. We believe that this improvement of the mechanical efficiency with E_{max} is due to the accompanying increases in both PVA itself and the fraction of external work in PVA due to the counterclockwise rotation of the end-systolic P-V line [8]. The decrease in the maximal efficiency above E_{max} of 20 mmHg/ml is due to the limitation of preload at 50 ml and afterload at 200 mmHg.

To summarize, the present study has provided the relationship of the mechanical efficiency of the left ventricle as an explicit function of preload end-diastolic volume, afterload ejection pressure, and contractility index, E_{max}. The mechanical efficiency is maximized at an appropriate combination of preload, afterload, and contractility.

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