Total mechanical energy of a ventricle model and cardiac oxygen consumption

HIROYUKI SUGA
Department of Biomedical Engineering, The Johns Hopkins University School of Medicine, Baltimore, Maryland 21205

SUGA, HIROYUKI. *Total mechanical energy of a ventricle model and cardiac oxygen consumption.* Am. J. Physiol. 236(3): H498–H505, 1979 or Am. J. Physiol.: Heart Circ. Physiol. 5(3): H498–H505, 1979.—Mechanical energy (ENG) required by a time-varying elastance model of the ventricle was compared with oxygen consumption per beat (V_{O_2}) of the canine left ventricle contracting under a variety of loading conditions. ENG needed for this model to increase its elastance during systole is shown to be equal to the sum of the potential energy built in the elastance during systole plus the external mechanical stroke work. This ENG is equivalent to the area (PVA) bounded by the end-systolic and end-diastolic P-V curves and the systolic limb of the P-V loop trajectory in the P-V plane. There was a high correlation ($r = 0.89$) between V_{O_2}s documented in the literature and PVAs assessed by the author from the accompanying P-V data from both isovolumic and ejecting contractions in 11 hearts. A linear regression analysis yielded an empirical equation: V_{O_2} (ml O_2/beat) = $a \cdot$PVA (mmHg·ml/beat) + b, where $a = 1.37 \times 10^{-5}$ and $b = 0.027$, which can be used to predict V_{O_2} from PVA. A preliminary experimental study in my laboratory confirmed the validity of this empirical equation.

heart; time-varying elastance; potential energy; cardiac work; pressure-volume diagram

BECAUSE THE HEART relies almost exclusively on oxidative metabolism for energy generation, the rate of cardiac oxygen consumption can provide an adequate measure of its total energy utilization (3). Cardiac oxygen consumption has been experimentally correlated with various mechanical parameters of contraction. Tension-time index was proposed as a good index of cardiac oxygen consumption (27). But its usage is limited because it does not consider the ventricular volume or size factor. Recent studies showed that, besides the basal and activation metabolism for noncontractile activities, there are major determinants of oxygen consumption for contractile activities: ventricular pressure or muscle tension (24, 39), external work or muscle shortening work (5, 25), contractility or shortening velocity (30), and heart rate (2). Many empirical equations to relate one or more of these determinants to cardiac oxygen consumption have been proposed (4, 5, 13, 22, 39). However, agreement has not been reached as to which predicts best under a variety of cardiac loading conditions and contractile state.

Gibbs (12) has developed a phenomenological equation for cardiac muscle energetics based on a similar equation for skeletal muscle (14), but it is not easily applicable to the heart in a variety of loading conditions.

Ghista and Sandler (11) and Suga (31) proposed different empirical equations based on muscle models to predict cardiac oxygen consumption indirectly from ventricular pressure and volume data. Their equations were used to calculate cardiac oxygen consumption in their own recent theoretical studies (10, 32). However, their models require some overly simplifying assumptions on both ventricular geometry and muscle models. Besides, they involve complex calculations.

The present paper describes an entirely new approach to the equation to predict cardiac oxygen consumption. A simple mechanical model of the contracting left ventricle, based on recent physiological findings, was utilized. The mechanical energy needed to drive this ventricle model was correlated with cardiac oxygen consumption. A high correlation between them led to an equation for prediction of cardiac oxygen consumption from ventricular pressure and volume data. This method does not require any assumptions on ventricular geometry and muscle models nor any complex calculations. What is required is a planimetry of the pressure-volume area bounded by the end-systolic and end-diastolic pressure-volume curves and the systolic limb of the pressure-volume loop trajectory in a pressure-volume plane.

METHODS

First, a mechanical model of the contracting canine left ventricle was proposed from previous physiological findings on the canine left ventricular instantaneous pressure-volume (P-V) relationship. Second, I formulated the amount of mechanical energy needed for the ventricle model to contract along a P-V loop based on the theory of elasticity. Third, it was shown that the total amount of mechanical energy needed for the model can be calculated by planimetry of the pressure-volume area

bounded by the end-systolic and end-diastolic pressure-volume curves and the systolic pressure-volume trajectory. Finally, three studies on canine ventricular oxygen consumption were selected on the basis that they documented adequate data on the pressure and volume during contractions. The reported data of cardiac oxygen consumption were compared with the calculated amounts of the mechanical energy of the model in a variety of loading conditions.

Time-varying elasticity. As the left ventricle contracts under normal circumstances, intraventricular pressure (P) increases from a low diastolic level (e.g., 0–10 mmHg above atmospheric) to a high systolic level (70–150 mmHg) while intraventricular volume (V) first remains unchanged during the isovolumic contraction phase and then decreases during the ejection phase, as shown in Fig. 1*A*. The pressure-volume (P-V) data point moves with time counterclockwise in the P-V plane and draws P-V trajectory ABC. Then, the P-V point descends along CD during the isovolumic relaxation phase and moves along DA during the filling phase. Systole is represented by trajectory ABC and diastole by trajectory CDA.

The position and size of the P-V loop trajectory (ABCDA) in the P-V plane depend on ventricular loading conditions. Figure 1*B* displays three P-V loops for example: the middle loop (solid line) is obtained under normal loading conditions, the right one (dashed) with an increased arterial pressure, and the left one (dotted) with a decreased arterial pressure. The solid circles, one

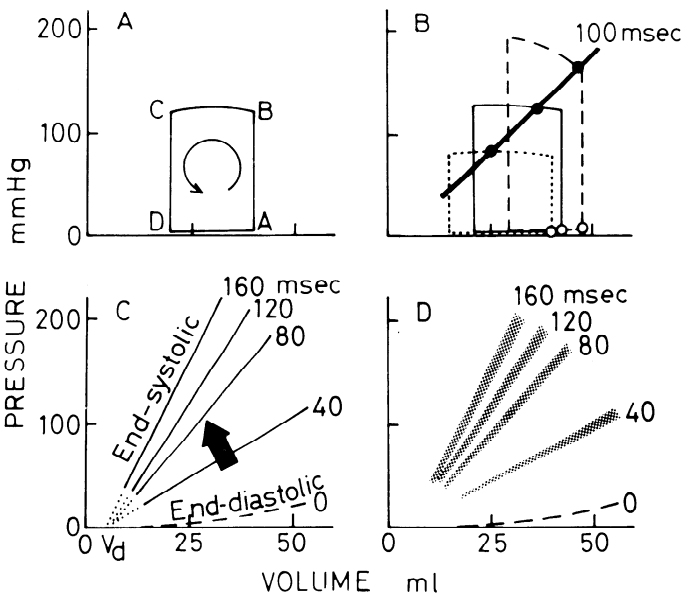

FIG. 1. *A*: pressure-volume (P-V) loop trajectory of a canine left ventricle. A P-V data point moves along ABC during systole and CDA during diastole in the direction of the arrow. *B*: three P-V loops under different loading conditions but a constant contractile state. Three solid circles are P-V data points at a specified time (100 ms) from onset of each contraction (*open circles*). Heavy line is the linear regression line for those 100-ms data points. *C*: instantaneous P-V regression lines for 40, 80, 120, and 160 ms from onset of contraction. P-V curve for 0 ms is end-diastolic P-V curve. V_d is the volume axis intercept of the end-systolic (160 ms) regression line. All instantaneous P-V regression lines converge on or near V_d. *D*: instantaneous P-V zones for 40, 80, 120, and 160 ms, which can approximate the real instantaneous P-V relationships better than the P-V lines in *panel C*. Width of zone is about 15% of corresponding pressure.

on each loop, correspond to the P-V data points at a specified time (e.g., 100 ms) from the onset of the individual contractions marked by the open circles. It has been shown that P-V data points at a specified time in systole fall close to a rectilinear line with a positive slope (34). A very high correlation coefficient ($r > 0.95$) has been obtained for the instantaneous P-V relationship at multiple instants of time during systole. Such a linear relationship was demonstrated as long as the ventricular loading conditions were within physiological ranges.

Figure 1*C* shows a representative family of the left ventricular instantaneous P-V relationship (regression) lines at 40-ms intervals in systole, together with an end-diastolic P-V relationship curve (dashed) (35). Each regression line was obtained experimentally from many P-V data points at a specified time in systole of both isovolumic and ejecting contractions in a given heart under a stable contractile state. These regression lines are known to converge closely on a relatively small positive value on the volume axis (5–10 ml in 60- to 100-g left ventricles). To explain in the other way, the P-V regression line rotates counterclockwise during systole as indicated by the heavy arrow, the slope of the line increasing with time. At the end of systole (160 ms in this case), the slope of the line becomes steepest. Then, the regression line rotates backward (clockwise) with progress of relaxation process during diastole, though not shown in the figure.

The findings described above means that the instantaneous P-V relationship during systole is reasonably well approximated by the following empirical equation (35)

$$P(t) = E(t)[V(t) - V_d] \quad (1)$$

where $E(t)$ represents the time-varying slope of the instantaneous P-V relationship lines, and V_d the volume-axis intercept of the end-systolic P-V regression line. Because this empirical equation provided the basis for a simple mechanical model of the left ventricle to be used, let me explain how well the equation can approximate the real ventricular P-V relationships.

First, the standard deviation of instantaneous pressure data of isovolumic and ejecting contractions from any of the multiple individual P-V regression lines was less than 10 mmHg (35). Second, the end-systolic pressure at a given volume was highest when the ventricle contracted isovolumically throughout and did decrease by up to about 15% as the ventricle contracted from greater end-diastolic volume, thus increasing stroke volume to 75% of the end-diastolic volume (34, 37). Studies from other laboratories also support this relative independence of the end-systolic P-V relationship from ventricular loading conditions (6, 40). Third, instantaneous pressure at a given volume was highest also in isovolumic contractions and did decrease by up to about 17% with increases in concomitant velocity of ejection to a relatively high level (33). Finally, the difference of the time courses of the time-varying slope of the instantaneous P-V line of isovolumic contractions (35) and of normally ejecting contractions (36) was as small as about 10% even at the time of peak velocity of ejection.

If all these details are included, the instantaneous P-V

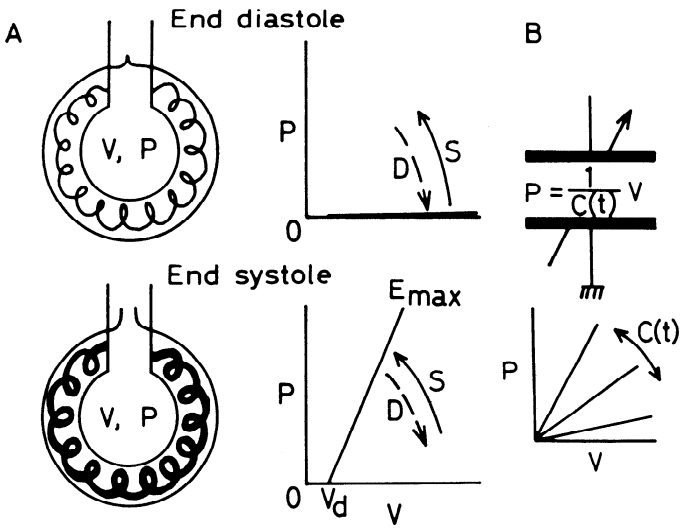

FIG. 2. *A*: elastic model of canine left ventricle and its P-V relationship lines at end of diastole (*top*) and end of systole (*bottom*). Stiffness of chamber wall increases with time from end of diastole to end of systole, and instantaneous P-V line rotates with time: counterclockwise during systole (S) and clockwise during diastole (D). *B*: time-varying capacitance model of left ventricle, which is similar in concept to the present mechanical model. $C(t)$ is the time-varying capacitance (or compliance). Its reciprocal is equivalent to $E(t)$. In this model, electric charge stored in the capacitor and electric voltage across the capacitor plates are analogous to ventricular volume and pressure, respectively.

relationships are characterized by a family of zones as shown in Fig. 1*D* instead of a family of lines in Fig. 1*C*. Because including all these details in the present model will complicate the structure of the model and lose the advantage of using the model in search for a better insight of the matter, I decided not to include them in the present model. However, errors to be caused by the exclusion were discussed later.

Ventricle model. The ventricle model proposed in this study is a chamber whose wall consists of elastic material with time-varying stiffness, as shown in Fig. 2*A*. The stiffness changes with time so that the instantaneous P-V relationships of this chamber can follow *Eq. 1*. In this ventricle model, $V(t)$ in excess of V_d is considered to be the effectively strained volume of the chamber, and $P(t)$ is the resultant stressing pressure. $E(t)$, or the slope of the instantaneous P-V line, is considered to be the time-varying volume elastance, which waxes with time during systole (in the direction of arrow S) and wanes during diastole (in the direction of arrow D). It attains a peak value, E_{max}, at the end of systole, and takes a minimal value at the end of diastole. $E(t)$ is a function of time only, independent of instantaneous and past pressure and volume under a stable contractile state.

This mechanical model of the left ventricle is essentially the same in concept as the time-varying capacitance (or compliance) models (Fig. 2*B*) of the ventricle proposed by other investigators (8, 28). Beneken and DeWit (1) arrived at a model similar to the present model in a simulation of ventricular contraction based on muscle contractile properties. Although the present model is therefore not entirely new in concept, the purpose of ventricular modeling in the present study was entirely different from that of those earlier studies. They used those models for simulation of cardiovascular hemodynamics, whereas I used the model to calculate mechanical energy associated with its contraction. Moreover, the present model was proposed based on the newer physiological findings not been available to those earlier modelers.

The present model was made perfectly elastic, i.e., nonviscous, because instantaneous pressure was assumed to be determined by the time and concomitant volume, but not affected by instantaneous velocity of ejection, according to *Eq. 1*. One may consider that such a nonviscous ventricle model is unrealistic. This is a reasonable objection to the present model in the light of the inverse force-velocity relationship of cardiac muscle (29) as well as skeletal muscle (14). The inverse force-velocity relation indicates the existence of a kind of viscosity in the contracting muscle in general, which is probably related to a net reaction rate of a family of chemical processes rather than literally viscous friction (15). However, as mentioned in the last section, the relatively small deviation of real P-V data from the present model and *Eq. 1* under physiological loading conditions supports the feasibility of the present nonviscous model under most of the normal circumstances.

There is other supportive evidence of the time-varying elasticity model of the ventricle. Loeffler and Sagawa (20) and Templeton et al. (38) showed that the dynamic stiffness (= Δforce/Δlength) of contracting cardiac muscle increases with time in systole and decreases in diastole. The dynamic stiffness in a low frequency range (up to 1 Hz at 20°C) was equal to the static stiffness, i.e., the slope of the instantaneous force-length relationship curve (20). Saeki et al. (26) further showed that the dynamic stiffness of cardiac muscle (though in contracture) did not exceed the static stiffness up to a higher frequency (10 Hz) at 36°C, suggesting that the viscous effect is relatively small for muscle length changes in the frequency range below 10 Hz. Because the frequency power spectrum of the left ventricular volume changes dominates below 10 Hz (9), the viscous effect in the ventricular wall is probably small under most of the normal circumstances.

The present model is a phenomenological model of the contracting ventricular chamber. The reason that I did not begin with such constitutive muscle models as Huxley (15), Julian (18), Wong (41), and Huxley and Simmons (16) had proposed is that many unverified assumptions were used in these models, and some additional assumptions will have to be made in synthesizing a contracting ventricle from any of these muscle models. It means that the present model will not contribute to understanding of the fundamental process of muscle contraction. This does not matter at all in this study because the purpose of the present study is not an in-depth analysis of myocardial energetics but to find a formula with a reasonable mechanical basis correlating with actual oxygen consumption of the ventricle.

Despite the approximating nature of the present model, one of its greatest advantages for the present study is that mechanical energy needed for the ventricle model to change the wall's elastic state from a diastolic compliant level to an end-systolic stiff level can be easily formulated in an analytical manner based on the theory

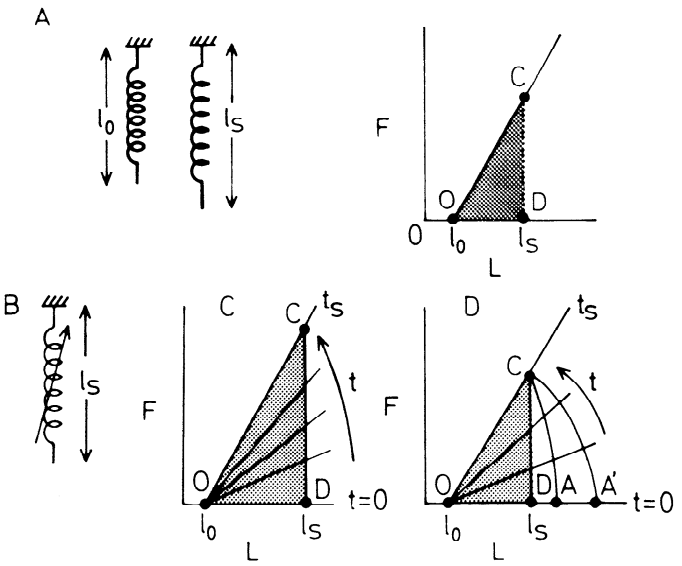

FIG. 3. *A*: a Hookean (i.e., linear) spring in the unstretched state at length l_o, and the same spring in a stretched state at length l_s. The force (F)-length (L) plane shows the force-length relationship line CO of the spring. Triangular shaded area DCO is equal to the mechanical potential energy of the stretched spring with length l_s. *B*: a time-varying Hookean spring in a stretched state at length l_s. *C*: Mechanical potential energy of the time-varying spring at a specified time $t = t_s$. DO is force-length relationship line for zero stiffness at $t = 0$. CO is force-length line for instantaneous stiffness specific for $t = t_s$. Three lines between DO and CO are instantaneous force-length relationship lines for three intermediate times between $t = 0$ and t_s. *D*: mechanical potential energy of the time-varying spring at $t = t_s$, independent of the past trajectory of a force-length data point (whether DC, AC or A'C).

of elasticity. This will be explained in the next section.

Mechanical energy. To simplify the explanation, let me first discuss the potential energy of a mechanical spring stretched from unstressed length l_o to a certain length l_s. Figure 3*A* shows a Hookean (i.e., linear) spring in the unstressed state (left) and the same spring in the stretched state (right). The figure also shows the force-length relationship (CO) of the spring. The theory of elasticity (for example, 17) indicates that the mechanical potential energy (or strain energy) of the spring at the stretched state at point C with length l_s is equal to the integration of the force as a function of length along the length from l_o to l_s. This integral is geometrically equal to the triangular area DCO (shaded) under the force-length line CO. This potential energy is equal to the amount of mechanical work that can be performed to the outside when the spring is shortened from l_s to l_o and the force-length data point moves from C to O along the force-length line CO.

Let me now discuss a special spring which has, as shown in Fig. 3*B*, a time-varying spring constant. It is still a Hookean spring in that its force-length relationship at any instant of time is linear. However, its stiffness gradually increases with time t from zero at $t = 0$ (therefore, the force-length line at this moment is DO on the abscissa) to the value corresponding to the force-length line CO at $t = t_s$ while its length is held constant at l_s. This is to say that the force-length data point of the spring will move vertically upward from D to C with the time-dependent increase in its stiffness, rather than along CO as in the previous discussion. With this, the potential energy in the spring will increase to an amount represented by the shaded area DCO in Fig. 3*C*. The reason is that the spring in this state at l_s and t_s performs a mechanical work to the outside that is equal to area DCO when it shortens from l_s to l_o and the force-length data point moves along the concomitant force-length line CO.

More generally, the instantaneous potential energy that a spring with a time-varying stiffness has at an instant of time (t_s) is equal to area DCO (shaded) under the concomitant force-length line DO specific for that instant (Fig. 3*D*). This amount of energy is not affected by how the present state of stiffness and length has been reached. As examples in Fig. 3*D* illustrate, the amount of energy is identical whether the spring reached point C along DC, AC or A'C. The instantaneous force-length curves before t_s could be even nonlinear, because the potential energy of the spring at t_s is determined by the concomitant force-length line CO.

One may wonder how the potential energy can be supplied to the spring when the spring stayed at a constant length. There is no mechanical work performed on the time-varying spring from the outside because the spring was not stretched when it developed force. Instead, the potential energy was produced entirely within the spring by the increase in its stiffness. What the actual mechanism for the time-varying stiffness is is not a matter in the present study where only the resultant potential energy is of interest. Whatever it is, some form of energy has to be converted into the mechanical potential energy in the spring when its stiffness increases.

By the same principle as in the time-varying spring, one can obtain the elastic potential energy in the present model of the ventricle. In the model, the effective strain is the volume $V(t)$ in excess of V_d and stressing force is the pressure $P(t)$. Figure 4*A* shows the end-systolic P-V relationship line. When the end-systolic P-V data point is at C, the potential energy of the ventricle model at this moment is equal to triangular area DCO (shaded) under the end-systolic P-V line CO. This amount of energy is equal to the amount of mechanical work the elastic chamber can do to the outside when its volume decreases from D to O and the P-V point moves from C to O along CO. Because this amount of mechanical work is dependent only on the present P-V line and the present volume, it is constant no matter what trajectory (whether DC, AC, or A'C) has been taken by the P-V point before this final state at C is reached (Fig. 4*B*). It should also be noted that as long as the end-systolic P-V line (CO) is known, other instantaneous P-V lines during systole, i.e., $E(t)$, are not necessary for the determination of the end-systolic potential energy of the ventricle model.

When the ventricle model reduces its internal volume in the same way that the real ventricle does from end-diastolic volume to end-systolic volume during systole as shown in Fig. 4*C*, it performs mechanical work to the outside equal to the integration of the P-V trajectory ABC along volume change AD. This external work is equal to the shaded rectangular area ABCD. The potential energy that the ventricle model maintains at the end of this systole is equal to the shaded triangular area DCO, which is not affected by the past pathway of the P-V data point during systole. Therefore, the total

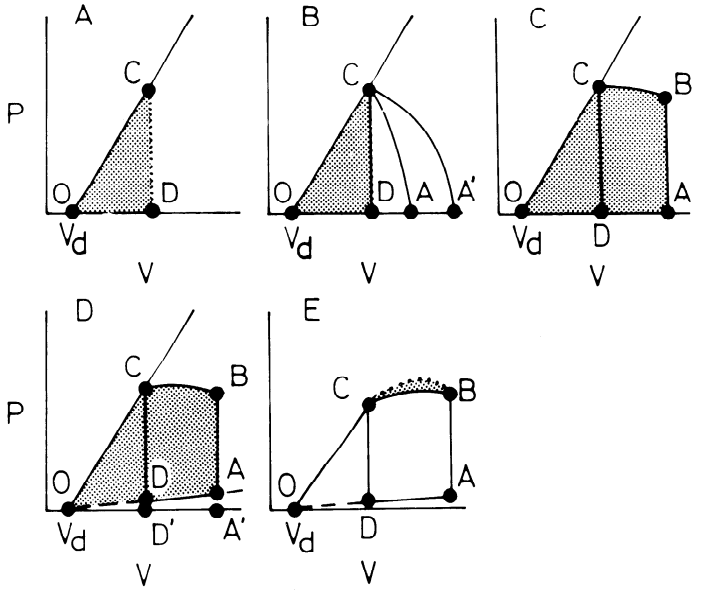

FIG. 4. *A*: mechanical potential energy of ventricle model at end of systole. CO is end-systolic P-V Line. *B*: independence of end-systolic potential energy from past trajectory of a P-V data point (whether DC, AC or A'C). *C*: end-systolic potential energy (DCO) and external mechanical work (ABCD) in an ejecting contraction. *D*: end-diastolic P-V curve (*dashed line* ADO) and total mechanical energy of interest (ABCD). *E*: difference of mechanical energy between the nonviscous ventricle model and a reasonable viscoelastic model. Solid curve BC is the real measured P-V trajectory during ejection phase. Dotted curve BC is the hypothetical P-V trajectory that the viscoelastic model would take if the viscosity is eliminated and the model becomes nonviscous. In the viscoelastic model, the energy corresponding to the shaded area is converted into heat.

amount of the mechanical energy needed for this ventricle model to contract along the trajectory ABC is the sum of the external mechanical energy (or stroke work) ABCD and the end-systolic potential energy DCO. This combined area is equal to the P-V area bounded by the end-systolic P-V line, the systolic limb of the P-V loop trajectory and the volume axis. This area ABCO can be determined by planimetry on the P-V plane.

So far, the end-diastolic P-V curve has been neglected for the sake of simplicity of the above explanations. Because the P-V area below the end-diastolic P-V curve represents mechanical energy that does not seem to be actively supplied (23), it had better be eliminated from the total amount of mechanical energy under consideration. Therefore, area ABCD (shaded) in Fig. 4*D* is the external mechanical work of interest and area DCO (shaded) is the potential energy of interest in the present study.

Thus, by knowing the P-V trajectory during systole and both the end-systolic and end-diastolic P-V relationship curves of a real ventricle, one can determine the total amount of mechanical energy needed for the contraction of the ventricle model along the same P-V trajectory as the real one, by planimetry of the pressure-volume area on the P-V plane.

The potential energy stored in the model at the end of systole was assumed to be totally converted into heat during isovolumic relaxation phase (i.e., CD in Fig. 4*D*). This is a reasonable assumption because cardiac muscle contracting isometrically was reported to consume energy at the highest rate (7) and dissipate heat also at the highest rate (12). Under the above assumption, the mechanical energy (work plus potential energy) needed during systole can be equal to the total mechanical energy needed for one entire contraction of the model. Without this assumption, the potential energy at the end of systole would be converted back into some form of energy other than heat and might be reused for the next contraction. This situation sounds unrealistic from the physiological knowledge (7, 12). The assumption of the 100% conversion of the residual potential energy into heat during diastole can hold regardless of the mechanism of this energy conversion. Therefore, I did not include any specific mechanism of this energy conversion in the present model.

The mechanical energy thus calculated from a given P-V trajectory in the present ventricle model will not be the total amount of mechanical energy needed for the model if the pure elasticity of the model is replaced with a viscous elastic property to better approximate the real P-V relationship. The reason is that part of the mechanical energy will be converted into heat during the volume change and the remainder can be converted into the effective external work. Therefore, the pressure-volume area planimetered on the P-V plane can underestimate the total amount of mechanical energy needed for the contraction of the model by the amount of energy equal to the dissipated heat. Because the above physiological data have shown that the pressure deficit in ejecting contractions was up to about 15% of instantaneous isovolumic pressures at the same instantaneous volume, the actual P-V trajectory during ejection phase would be lower by as little as 15% than a hypothetical P-V trajectory that a nonviscous elastic model could produce from a given amount of mechanical energy, as shown in Fig. 4*E*. Therefore, the planimetered pressure-volume area can still be a very close approximation for the total amount of mechanical energy in a reasonable viscoelastic model of the ventricle.

Pressure-volume area. To evaluate whether the total mechanical energy (ENG) calculated in terms of the present ventricle model correlates with cardiac oxygen consumption per beat (V_{O_2}) measured in a variety of loading conditions, I examined other investigators' experimental data documented in literature. Because the P-V data necessary for the planimetry of the pressure-volume area (PVA) were not always documented in reports on V_{O_2}, the number of the reports appropriate for the comparison reduced to only three: studies by Monroe and French (24), by Graham et al. (13), and by Burns and Covell (5). Monroe and French (24) documented P-V trajectories on the P-V plane in their Figs. 9 and 12. PVA was determined directly by planimetry after V_d was determined by extrapolating their end-systolic P-V regression line. Graham et al.'s (13) contractions were all isovolumic. Their Tables 1 and 2 list isovolumic volume, peak isovolumic pressure, and end-diastolic pressure as well as V_{O_2}. Because there was no way to assess V_d from their data alone, it was assumed to be zero. Thus PVA was calculated simply as (isovolumic volume) × (peak pressure − end-diastolic pressure)/2. Burns and Covell (5) provided sets of end-diastolic volume, stroke

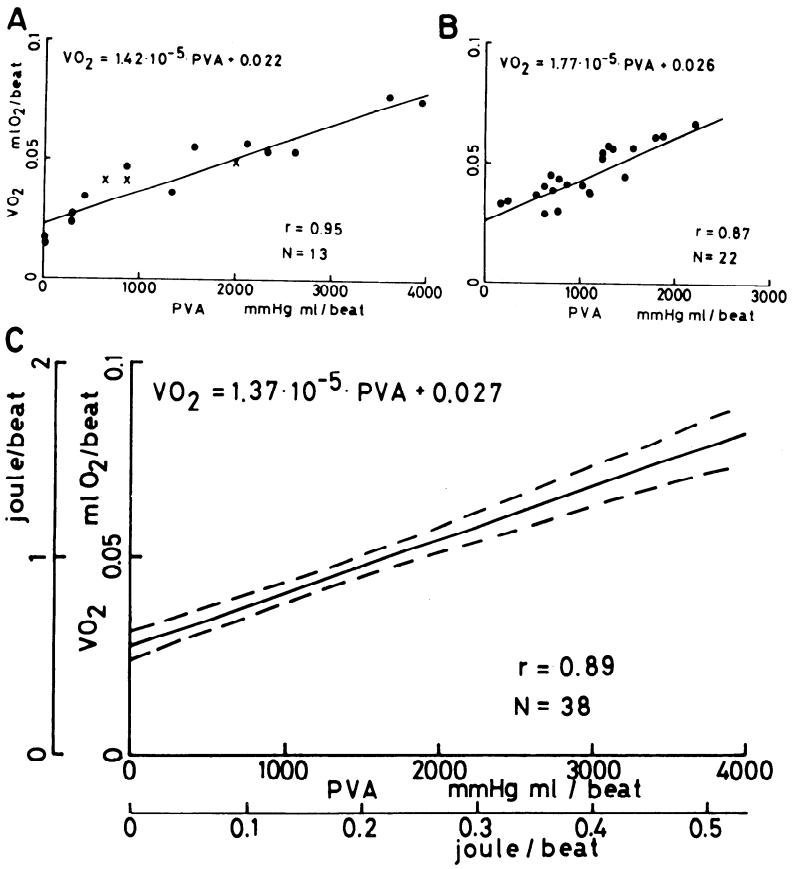

FIG. 5. *A*: correlation between Vo_2 and PVA (= ENG) for data from Ref. 24 (*solid circles* only). Rectilinear line is linear regression line for these solid circle data. ×'s are three additional data from Ref. 13, which are not included in the regression analysis of the solid circle data. *B*: correlation between Vo_2 and PVA for data from Ref. 5. *C*: linear regression line and 95% confidence zone of this regression line, calculated from all the above data points pooled together (N = 38). Vo_2 and PVA in ml O_2 and mmHg·ml, respectively, are converted into a common unit of energy, the joule.

volume, and peak pressure in their Table 1. V_d was assumed to be zero because it was impossible to assess it from their data. PVA was geometrically obtained as the sum of (peak pressure × stroke volume = external work) and [(end-diastolic volume − stroke volume) × peak pressure/2 = potential energy)], assuming that systolic pressure and end-systolic pressure were equal to the documented peak pressure value. The contour of their ventricular pressure tracing supports this assumption.

RESULTS

Figure 5*A* shows the correlation between PVA (=ENG) and Vo_2 pooled from seven isovolumic contractions in one canine left ventricle (88 g in weight) and six ejecting contractions in another canine left ventricle (101 g) taken from Figs. 9 and 12 of Ref. 24. Correlation coefficient was 0.947 ($P < 0.01$). Linear regression analysis by least-squares fit yielded the following formula

$$Vo_2 \text{ (ml } O_2\text{/beat)} = 1.420 \times 10^{-5} \times \text{PVA (mmHG·ml/beat)} + 0.0223 \quad (2)$$

Figure 5*B* shows the correlation between PVA and Vo_2 pooled from 11 isovolumic contractions and 11 ejecting contractions in seven canine left ventricles (82–98 g, mean 88 g) taken from Table 1 of Ref. 5. The correlation coefficient was 0.872 ($P < 0.01$) and the linear regression line was

$$Vo_2 = 1.769 \times 10^{-5} \times \text{PVA} + 0.0255 \quad (3)$$

Because the two regression lines were relatively close to each other in spite of the different sources, both sets of data were pooled together in Fig. 5*C*. Three more data points, taken from Tables 1 and 2 of Ref. 13, were also pooled in the analysis. The correlation coefficient was 0.885 ($P < 0.01$). A linear regression line fitted to the data was

$$Vo_2 = 1.373 \times 10^{-5} \times \text{PVA} + 0.0272 \quad (4)$$

Furthermore, the sample standard deviation of the regression coefficient of *Eq. 4* (1.373×10^{-5}) was as small as 0.120×10^{-5} (less than 10%), and the 95% confidence interval of this regression coefficient was from 1.130 to 1.617×10^{-5}. The sample standard deviation from the regression was as small as 0.0067 ml O_2/beat. The 95% confidence zone of the regression line is shown by the two dashed curves in Fig. 5*C*.

DISCUSSION

A highly linear correlation has been found between the cardiac oxygen consumption per beat (Vo_2) measured in the canine left ventricles and the pressure-volume area (PVA), which is equivalent to the total mechanical energy (ENG) needed for the equivalent contraction of the ventricle model. The feasibility of the empirical equation (*Eq. 4*) was recently confirmed by a series of dog experiments in my laboratory and reported (19). Although the details of this experiment will be described elsewhere, I would add here that the results from five canine left ventricles (45–90 g, mean 69 g) yielded an average empirical equation

$$Vo_2 \text{ (ml } O_2\text{/beat)} = 1.18 \times 10^{-5} \times \text{PVA (mmHg·ml/beat)} + 0.016 \quad (5)$$

with correlation coefficient of 0.88 ± 0.05 (SD). The regression coefficient of this equation had a standard error of the mean of 0.10×10^{-5} (less than 10%) and is not significantly different ($P > 0.1$) from the regression coefficient of *Eq. 4*. The Vo_2-axis intercept of *Eq. 5* is about 60% of that of *Eq. 4*. This seems to be explained by the difference of the left ventricular weights in the two studies because the Vo_2-axis intercept largely reflects the basal metabolism (39).

Therefore, I conclude from the present study that ENG measured as PVA is a promising candidate for the practical predictor of Vo_2 of the canine left ventricle. However, in this study, Vo_2 and PVA were taken only from ventricles contracting under control contractile state without any intentional inotropic interventions such as administration of catecholamines and calcium and sympathetic stimulation. It has been reported that contractile state per se is an independent determinant of cardiac oxygen consumption (3). Therefore, the regression coefficient and the Vo_2-axis intercept of the empirical equation may vary with changes in contractile state. This remains to be studied.

So far, the energy units of PVA and Vo_2 were mmHg·ml and ml O_2, respectively. These units can be converted into a common unit of energy, the joule (J), utilizing the following conversions: 1 mmHg·ml = 1.333×10^{-4} J. 1 ml O_2 = 20.2 J, because 1 ml O_2 has a caloric equivalent of 4.86 cal in normal cardiac muscle (3) and 1 cal = 4.16 J. With these conversions, the PVA and Vo_2 coordinates in Fig. 5*C* were changed to joules, and *Eq. 4* was rewritten as

$$Vo_2 \text{ (J/beat)} = 2.08 \times \text{PVA (J/beat)} + 0.549 \quad (6)$$

This equation indicates that energy consumption of the real left ventricle is about twice as much as the calculated mechanical energy (ENG = PVA) of the present model of the ventricle, plus the constant energy for the basal metabolism. This constant term, which is considered to be required by the heart even when the left ventricle is not developing any pressure nor performing any external mechanical work, can be considered the energy needed mainly for the noncontractile activities such as maintenance of ionic environment, protein synthesis, electrical activation of the membrane, and release and uptake of calcium by sarcoplasmic reticulum (3). Total Vo_2 minus this unloaded Vo_2 can be considered the energy needed by the contractile activities of the heart. From *Eq. 6*, PVA/(Vo_2 − unloaded Vo_2) = 0.48. This suggests that, if the real ventricular wall were made of such time-varying nonviscous elastic material as considered in the present model, 48% of Vo_2 used for contractile activities could be converted into mechanical energy (work plus potential energy) and the rest (52%) eventually dissipated as heat. Of the 48%, part could be converted into external mechanical work when ejection occurs against pressure. The rest of the 48% would remain as potential energy in the wall at the end of systole and be converted into heat during diastole. Whether this suggestion holds in the real ventricle remains to be studied.

Without the guide provided by the present ventricle model, the empirical equation (*Eq. 4*) might not have been obtained except by a coincidence. The PVA exclusive of external work is meaningful as the potential energy of the elastic wall in the present model, but is difficult to conceive as representing potential energy in other types of muscle model (14–16, 18, 41). PVA is obviously different from the potential energy stored in the series elasticity of muscle at the end of systole. Because the stiffness of the series elasticity of cardiac muscle is greater than the static stiffness, i.e., the slope of the instantaneous force-length relationship curve (20), the potential energy stored in the series elasticity is much smaller than PVA. It seems worthwhile to attempt to understand the present results in terms of those constitutive models. However, it seems still too early to attempt this since much remains to be known about the time course of the number of crossbridges contributing to the force generation and shortening in cardiac muscle contracting under a variety of loading conditions (21). For the same reason, it is also too early to conclude from the present study alone whether the present equation for the PVA-Vo_2 relationship is the physiological reality or a merely fortuitous empiricism.

Quantitative comparison of the present equation with previously proposed ones in their predictability of Vo_2 is not within the scope of the present study. However, let me compare correlation coefficients between Vo_2 and major predictors of other investigators with those between Vo_2 and PVA. The correlation coefficients of Vo_2 with PVA (0.95, 0.87, and 0.89) seem comparable to those with contractile element work (0.91, Ref. 4), with peak developed tension times heart rate (0.87, Ref. 22), and with time integral of systolic force (0.92 and 0.87, Ref. 39). However, reliable evaluation of the superiority of one to the other can be obtained only by new, appropriately designed experiments where all the relations of interest are compared simultaneously.

If the present method is capable to predict Vo_2 in a degree similar to others, major advantages of the present method over them will be the following. *1*) Only a planimetry of the specified pressure-volume area (PVA) is necessary to use the empirical equation. *2*) No assumptions are necessary on the shape of the ventricle, structure of the ventricular wall, and mechanical model of cardiac muscle.

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H. Suga's present address is National Cardiovascular Center Research Institute, Suita, Osaka 565, Japan.

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