**Paul Dudley White International Lecture:
Cardiac Performance as Viewed Through the
Pressure-Volume Window**

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SUMMARY

Viewing canine left ventricular performance through the pressure-volume (P-V) window, I proposed a new index of ventricular contractility (Emax: end-systolic P-V ratio or maximum elastance) in my doctoral thesis at the University of Tokyo in 1969. After I joined Dr. Kiichi Sagawa (deceased in 1989) at Johns Hopkins University, we firmly established the Emax concept during 1971–1978. The concept was extended to derive the systolic P-V area (PVA) as a new measure of the total mechanical energy generated by ventricular contraction in 1978. Experiments have revealed that PVA closely correlates with cardiac oxygen (O_2) consumption (VO_2) under various loading conditions at a constant Emax, the VO_2 -PVA relation changes its elevation with Emax, and the O_2 costs of PVA and Emax characterize the mechanoenergetics of cardiac contraction under various normal and abnormal conditions in an innovative manner (Suga: *Physiol Rev* **70**: 247–277, 1990). Emax and PVA can also evaluate the ventriculo-arterial hydraulic and energetic matching in normal and failing hearts. Emax and PVA have thus widely opened the P-V window to the extent that human and animal normal and failing cardiac performance can be characterized in a physiologically sound manner. (*Jpn Heart J* **35**: 263–280, 1994)

Key words: Emax Time-varying elastance PVA Pressure-volume area Mechanoenergetics

MANY of you might doubt your eyes when you first look at the title of my lecture and are puzzled why pressure and volume are the current topics. You may think that this is 1993, not 1893! The famous Otto Frank¹⁾ is not present! The famous Ernest Henry Starling²⁾ is not present, either. Is there any recent discovery of genes expressing pressure and volume? No, that

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This named lecture was established in 1966 by the American Heart Association (AHA) after an eminent American physician Dr. Paul Dudley White for his leadership in the advancement of cardiology throughout the world. The lecturers have been elected as honorary fellows of the AHA Council on Clinical Cardiology. This, the 17th lecture, was given at the AHA 66th Scientific Session on November 9, 1993 in Atlanta, Georgia, USA. The abstract of the lecture was published in *Circulation* **88** (Suppl Part 2): I-C, 1993. This paper, which includes figures, is a slightly condensed version of the 45 min lecture.

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is not the case. Instead, I am going to review progress in our understanding of the ventricular P-V relationship over the past quarter century.³⁾

I am going to explain why the P-V relationship is very meaningful and important in today's cardiovascular physiology and cardiology. I hope that you will realize the power of pressure and volume variables for better understanding the performance of normal and diseased hearts.

Historical background

As shown in Figure 1, nearly a century ago, the German physiologist Otto Frank characterized ventricular contraction in a P-V diagram.⁴⁾ Panel A displays a P-V loop of a contraction, together with the end-diastolic and end-systolic P-V curves. He used the frog heart, which has an end-systolic P-V relationship that is both markedly nonlinear and sensitive to afterload conditions. The number of medical physiology textbooks that still show Frank's diagram has decreased⁵⁾ and major textbooks have already adopted the P-V relationship which has been established in mammalian hearts over the past two decades.⁶⁾

Nearly 70 years ago, a British physiologist Ernest Henry Starling extended Frank's concept of the ventricular P-V relationship to a canine pumping heart and studied the cardiac output-filling pressure relationship, as shown in Figure 1, Panel B.²⁾ You are familiar with Starling's law of the heart,²⁾ which is useful in

Figure 1. History of views on cardiac performance. Frank: Frank's pressure-volume (P-V) relationship. Starling: Starling's cardiac output (CO) curve as a function of filling pressure. Sarnoff: Sarnoff's ventricular function curve relating stroke work (SW) to end-diastolic pressure (EDP) of the ventricle. Sonnenblick: Sonnenblick's force-velocity curve with Vmax as an index of contractility. Suga: Emax as the slope of the end-systolic P-V relation.

cardiology. Starling's cardiac output curve and its modifications, such as Sarnoff's ventricular function curve (Figure 1, Panel C),⁷⁾ are categorized into this approach. Using these diagrams, inotropism or contractility changes can be visualized as a shift of the function curve.⁷⁾

The heart can also be viewed as an assemblage of myocardial fibers and characterized by the shortening velocity-force relationship (Figure 1, Panel D). This approach is analogous to the approach used for skeletal muscles, which were analyzed beautifully 50 years ago by A.V. Hill.⁸⁾ About 30 years ago, when I was a medical student, Edmund Sonnenblick⁹⁾ established $V_{\max}$ as an index of contractility (Figure 1, Panel D). $V_{\max}$ is the maximum unloaded shortening velocity. The $V_{\max}$ concept has been extended to ventricular circumferential shortening velocity (V_{cf}) for clinical use and is still used in cardiology.¹⁰⁾

When I started my doctoral research career in the late 1960s, I had some difficulty in accepting the $V_{\max}$ concept for cardiac muscle, because, unlike skeletal muscles, cardiac muscle does not normally contract in tetanus. I had a feeling that the characterization of ventricular contractile behavior was necessary for a better understanding of normal and diseased cardiac performance. Some of my colleagues said it was obsolete to study again the P-V relationship in the days of $V_{\max}$. This kind of comment discouraged me initially, but I was soon revived by my strong intuition that there must be some undiscovered concepts in the P-V diagram.

Then, one day, very fortunately, the central idea for exploring $E_{\max}$ occurred suddenly while I was serving once a week as a night dispensary doctor. Thereafter, $E_{\max}$ became the theme of my doctoral thesis in Tokyo.¹¹⁾ $E_{\max}$ is the key word in today's talk. $E_{\max}$ (or interchangeably E_{es}) denotes the slope of a linear end-systolic P-V relation, as shown in Figure 1, Panel E,¹²⁾ reopened the P-V window, which had been almost closed in those days. Since then, $E_{\max}$ has greatly facilitated our understanding of cardiac performance.¹³⁾

Advantages of pressure-volume window

Pressure and volume are the two most fundamental physical variables with which to describe the mechanical properties of any chamber, although the ventricle is actively contracting unlike ordinary manufactured chambers. The product of pressure and volume gives mechanical work. Cardiac mechanical work is given by the area within a P-V loop drawn in the P-V diagram (Figure 2, Panel A); this is well known from the fact that the P-V diagram used to be called the work diagram.¹⁾ The greater the area within the P-V loop, the greater the work. This is one of the main advantages of using the P-V diagram.

Another advantage of the P-V diagram is that a P-V relation curve reflects elastic properties of the chamber (Figure 2, Panel B). The steeper the curve, the

Figure 2. Information contained in the pressure-volume (P-V) window. A: Mechanical work is given by the area within a P-V loop. B: Volume elastance is given by the slope of a P-V relation. C: Elastic potential energy is given by the area under a P-V relation.

stiffer (or the more elastic) the chamber. Therefore, a P-V relation indicates the elastance of the chamber. When the P-V relation changes with time, it means that the chamber's elastance changes with time; this property is termed a time-varying elastance.¹²⁾ This is the basis of my discovery of the Emax concept.¹²⁾

Theoretically, the area under a P-V relation represents mechanical potential energy (Figure 2, Panel C). This is the third major advantage of using the P-V diagram, and it is the basis of my discovery of the cardiac energy concept in terms of PVA.¹⁴⁾

In these respects, the P-V diagram provides a better characterization of ventricular performance than Starling's cardiac output-filling pressure diagram,²⁾ Sarnoff's stroke work-end-diastolic pressure diagram⁷⁾ and Sonnenblick's Vmax-force diagram.⁹⁾

Although the volume and pressure variables are global, they are vector sums of the lengths of all the sarcomeres and the forces generated by crossbridges (CBs) within the wall of the ventricle. Figure 3 shows the correspondence of the P-V diagram to the sarcomere and CB behavior. Ventricular filling produces the horizontal P-V segment. During this period, sarcomeres are stretched and the number of available CBs increase, providing the basis of the Starling effect. Excitation causes contraction and the number of attached CBs increases, developing force and pressure, and forming the isovolumic contraction segment of the P-V loop. During ejection, attached CBs turn over and slide, producing external work and creating the ejection segment of the loop. During relaxation, the number of attached CBs and hence force decrease.

The area within the P-V loop is external work. This work is equal to the integrated work that all CBs produce, according to the law of energy conservation.

Thus, although pressure and volume are global variables, they are closely related to CB behavior. Although their detailed relationships still remain to be elucidated, the P-V window has a fourth advantage: it contains information on

Figure 3. Correspondence of the P-V diagram to sarcomere and crossbridge (CB) behavior. Sarcomere length increases with volume. The number of attached CBs increases with contraction. Attached CB is shown by a myosin head (solid circle) on a thin filament.

the mechanoenergetically integrated CB behavior within the chamber wall. This advantage has reinforced the basis of the PVA concept.^{3,14)}

Experimental outcome

When I started to study the P-V relationship of the canine heart in Japan in 1967, the P-V diagram had been used occasionally only for quantifying heart size, the ejection fraction and external mechanical work. The power of the P-V diagram in revealing various mechanical and energetic aspects of cardiac performance was not suspected. However, I strongly believed that there must be something new and important undiscovered in the P-V diagram.

Figure 4 is taken from my doctoral thesis published in 1969.¹¹⁾ The left side shows left ventricular P-V loops of an *in situ* canine heart after cutting cardiac sympathetic nerves. Ventricular volume was measured by combining an electromagnetic flowmeter on the aorta and an indicator dilution technique. Therefore, there was some uncertainty regarding the absolute volume.

Nevertheless, the data revealed that the end-systolic P-V points of these P-V loops fell on a diagonal line. The P-V points at a given mid-systolic time also fell on a less steeper line. The slope of such a P-V line increased to the end-systolic peak value, E_{max} (initially termed e_{max}), and then fell to the diastolic level in each cardiac cycle.¹¹⁾ The curves on the right side of Figure 4 show that the slope changes $e(t)$ of these P-V relations and E_{max} (peak of e) of these 3 contractions under different loading conditions are similar. These curves marked the first

Figure 4. Left ventricular P-V loops of an *in situ* canine heart (A) and the slope changes of the P-V relations as a function of time under different loading conditions in a stable contractile state (B). (Modified from Figure 2 of Ref 11).

characterization of the time-varying elastic nature of a beating and ejecting ventricle.¹¹⁾

Pressure-volume loops and Emax

Figure 5 is also taken from my thesis.¹¹⁾ This shows that cardiac sympathetic nerve stimulation shifted the P-V loops upward and leftward. As the result, the slope of the end-systolic P-V relation became steeper and its slope Emax also increased markedly. Thus, Emax was suggested as a new index of ventricular contractility.

After I obtained a Doctorate of Medical Sciences at the University of Tokyo, I joined Dr. Kiichi Sagawa at Johns Hopkins University. He was intrigued by the Emax concept and encouraged me to develop the concept. I stayed with him for nearly six years in the 1970s, producing several original papers that established the Emax concept.^{12,15-17)} Our two Circulation Research papers^{12,15)} have been cited more than 1100 times and the total number of citations of my more than 100 papers on Emax and the P-V window numbers more than 3000, according to a recent Science Citation Index survey. Without Dr. Sagawa, I probably would not be speaking at this lectern.

In Baltimore, we confirmed the validity of Emax in canine hearts by im-

Figure 5. Left ventricular P-V loops under control (circles and solid lines) and cardiac sympathetic nerve stimulation with an augmented slope of the end-systolic P-V relation (triangles and dotted lines). (Modified from Fig. 4 of Ref 11).

Figure 6. Schematic drawing of P-V loops and the end-systolic P-V relation (ESPVR) in control (A) and an enhanced contractile state (B). The slope of the ESPVR line is E_{max} . E_{max} is largely independent of preload and afterload. The end-systolic P-V line has a positive volume intercept V_0 .

proving ventricular volumetric methods.^{12,18)} Figure 6 schematically summarizes representative P-V loops and the end-systolic P-V relation (ESPVR) in a stable contractile state (Panel A). We confirmed that E_{max} was largely independent of preload and afterload by refined measurements and load control. In addition, we discovered that the end-systolic P-V line had a positive volume intercept V_0 (which was initially called V_d).

When ventricular contractility was enhanced by administration of epinephrine, we confirmed that the P-V loop grew markedly during positive inotropism.^{12,15)} The end-systolic P-V relation became steeper and E_{max} in-

creased (Figure 6, Panel B) in a similar manner to Figure 5, but V_o was unaffected. We obtained similar results with other positive inotropic interventions.¹³⁾ Negative inotropic interventions produced the opposite results.¹³⁾ Thus, it became our contention that Emax, defined as the end-systolic maximum elastance of the ventricle, could indicate the contractile state of the chamber.^{12,13,15)}

Limitations

However, as more investigators in various laboratories studied Emax experimentally and clinically, they encountered various problems. Some are fundamental and others are practical and clinical. Emax is not an exception to "Murphy's law" that "Every Solution Breeds New Problems." One main limitation is that Emax is slightly dependent on loading conditions. For example, isovolumic Emax may be different from ejecting Emax depending on ejection fraction.¹⁹⁾ In addition the end-systolic P-V relation is not always linear. For example, it tends to be concave downward at a high Emax and upward at a low Emax.²⁰⁾ Finally, normalization of Emax for heart size is not simple.²¹⁾ These are very interesting issues, but they are beyond the scope of this lecture.

Clinical application

After Emax was publicized by our 1973 and 1974 Circulation Research papers,^{12,15)} cardiologists began to apply Emax to patient care. The first cardiologist was Myron Weisfeldt at Johns Hopkins. He presented his work, under the title of "Emax as a new contractility index in man", at the 1976 meeting of the AHA.²²⁾ The second one was William Grossman at Harvard.²³⁾ End-systolic P-V relations were compared in three patient groups with normal and moderately and severely failing hearts. Evidently, the Emax line shifted to the right as cardiac failure became severe. Many similar results in patients have been reported by different groups over 15 years and Emax has helped cardiologists assess the degree of heart failure. After Jan Baan developed a volumetric conductance catheter in 1980,²⁴⁾ ventricular volumetry became much easier in both animal experiments and clinical settings.²⁵⁾

Discovery of PVA

When I started my research career, I was taught the adage: "Make your own work important." This motto motivated me to expand the Emax concept beyond an index of contractility. This extension of the framework for Emax, first developed in 1977, resulted in the PVA concept.¹⁴⁾

The contracting ventricle has a time-varying elastic nature (Figure 7, Panels A and B). The increasing slope of the P-V relation and hence the increasing elastance during systole, is symbolized by a thickening spring within the ventricu-

Figure 7. The time-varying P-V relation (A and B) and time-varying elastance model (C) of the ventricle. The increasing slope of the P-V relation and hence the increasing elastance during systole are symbolized by a thickening spring within the ventricular wall as shown in Panel C. This varying-elastic spring is an analogy to the increasing number of attached CBs within the ventricular wall during contraction. Each attached CB has elasticity and the overall elasticity is considered proportional to the total number of attached CBs although the detailed relation remains to be determined.

The new idea from the time-varying elastance model of the heart is that mechanical energy must be increased within the time-varying elastance when the elastance increases within the ventricular wall. This is analogous to the elastic energy stored in a stretched spring. Physics tells us that such an elastic energy can be assessed in the stress-strain diagram. Therefore, ventricular elastic energy can be quantified in the P-V diagram.

lar wall (Figure 7, Panels C and D). This variable-elastic spring is analogous to the increasing number of attached CBs within the ventricular wall during contraction. Each attached CB has elasticity and the overall elasticity is assumed to be proportional to the total number of attached CBs.

The new idea was that mechanical energy must be increased within the time-varying elasticity when the elasticity increases within the ventricular wall.¹⁴⁾ This is analogous to elastic energy stored in a stretched spring. Physics tells us that such an elastic energy can be assessed in a stress-strain diagram. Therefore, I proposed that ventricular elastic energy can be quantified in the P-V diagram as shown in Figure 7.¹⁴⁾

Figure 7, Panel E shows an isovolumic contraction. The elastic energy is given theoretically by a triangular area under the E_{max} line. This is the elastic potential energy generated during systole and stored at the end of systole in the ventricle. Figure 7, Panel F shows an ejecting contraction. The elastic energy is

given by a triangular area under the $E_{\max}$ line. This is also the elastic potential energy generated during systole and stored at end systole in the ventricle. On top of this potential energy, an ejecting ventricle has performed external work by end systole. This work is given by the area within the P-V loop. The sum of the external work and the potential energy is the total mechanical energy. Therefore, the sum of these two areas gives the total mechanical energy that the ventricle generates during each contraction. The isovolumic contraction is a special case where external work is zero. Therefore, I called this specific area "P-V area" and abbreviated it as "PVA".¹⁴⁾ Thus, PVA is a new measure of total mechanical energy generated by each contraction of the ventricle. This PVA concept is an epoch-making extension of the $E_{\max}$ concept.

Myocardial ATPases

Figure 8 shows major energy consuming activities of myocardium. Most O_2 is consumed to produce ATP. ATP is a primary substrate for three ATPases. The first is Na/K ATPase, which is related to membrane excitation. The next is Ca pump ATPase, which is related to Ca handling in the excitation-contraction (E-C) coupling. The third is myosin ATPase, which causes CB cycling to develop force, exhibit $E_{\max}$, elicit shortening, produce PVA and perform work.

We studied the correlation between PVA and myocardial O_2 consumption (VO_2), because VO_2 is the input to the cardiac bioengine and PVA is the output. Although PVA is one of the mechanical measures integrating CB mechanics, the law of energy conservation implies that it measures the total mechanical energy

Figure 8. Three major energy consuming processes of myocardium. MT=mitochondria; SR=sarcoplasmic reticulum. ATPases are shown by solid circles.

of CBs.

Cardiac O_2 consumption versus PVA

In our experiments on PVA, we used the same canine heart model as in our Emax studies, except for the addition of an oximeter to measure Vo_2 . We measured PVA and Vo_2 of the left ventricle in a stable contractility, namely at a constant Emax. Figure 9, Panel A shows a linear regression of Vo_2 on PVA in isovolumic contractions with increased volume loading. Ejecting contractions produced similar results (Figure 9, Panel B). Superimposing these isovolumic and ejecting results produced Figure 9, Panel C. Both isovolumic and ejecting contractions produced virtually identical Vo_2 -PVA relationships. Based on these results, we concluded that in a given stable contractility, Vo_2 is correlated linearly with PVA.^{26,27)} We also confirmed this tight relation between Vo_2 and PVA under various loading conditions in a stable contractile state.²⁷⁾

We studied the effects of positive inotropism on the Vo_2 -PVA relation. Epinephrine was given in this case. We found that epinephrine increased Emax and simultaneously elevated the Vo_2 -PVA relation in a parallel manner (Figure 10).^{27,28)} We obtained similar results with many positive inotropic agents including various new cardiotoxic agents.²⁷⁾ Negative inotropic agents lowered the Vo_2 -PVA relation in a parallel manner.²⁷⁾ These results were confirmed by other investigators.

Figure 9. Linear regression of Vo_2 on PVA in isovolumic contractions with increased volume loading (Panel A), in ejecting contractions (Panel B), and in both contractions pooled together (Panel C).

Figure 10. Linear regression of Vo_2 on PVA in contractions in control contractile state (Panel A) and in contractions in an enhanced contractile state with epinephrine (Panel B). Panel C is a superimposition of A and B.

Figure 11. Macro and micro correspondence of PVA-dependent and PVA-independent Vo_2 , dividing Vo_2 at the Vo_2 intercept. CB=crossbridges; SR=sarcoplasmic reticulum.

PVA-independent and PVA-dependent Vo_2

Figure 11 shows schematically how the Vo_2 -PVA relation at the macro-level corresponds to the micro-level myocardial activities. The Vo_2 -PVA relation can be divided into two components by a horizontal line at the level of the Vo_2 intercept at zero PVA. We call the lower fraction of Vo_2 "PVA-independent Vo_2 " because this fraction remains even when PVA is reduced to zero. We call the upper Vo_2 fraction "PVA-dependent Vo_2 " because this fraction increases with increases in PVA. We assume that the PVA-independent component is related to

non-mechanical activity of the myocardium, consisting primarily of Ca^{2+} ion handling in E-C coupling and basal metabolism.²⁷⁾ We also assume that the PVA-dependent component is related to the mechanical activity of myocardium, namely CB cycling.²⁷⁾ Based on these considerations, we can estimate the effects of inotropic interventions on Ca^{2+} handling from a change in the elevation of the Vo_2 -PVA relation or its Vo_2 intercept (=PVA-independent Vo_2).²⁷⁾

Oxygen costs of PVA and E_{max}

Based on these experimental studies, we obtained an empirical equation^{27,29)}: $\text{Vo}_2 = a \cdot \text{PVA} + b = a \cdot \text{PVA} + c \cdot E_{\text{max}} + d$. This relates Vo_2 to PVA and E_{max} . $a \cdot \text{PVA}$ corresponds to the PVA-dependent Vo_2 and b corresponds to the PVA-independent Vo_2 . Since b changes with E_{max} , b can be written as the sum of $c \cdot E_{\text{max}} + d$. Then, a indicates the O_2 cost of PVA and c indicates the O_2 cost of E_{max} . These concepts are illustrated in Figure 12.

We obtained a , b , c and d values for various positive and negative inotropic interventions. As a result, we found that both the O_2 costs of PVA and E_{max} were stable for most conventional inotropic interventions in normal hearts.²⁷⁻²⁹⁾

Abnormal hearts, though, exhibit different behavior. Hyperthyroidism in the rabbit heart increased the O_2 cost of PVA.³⁰⁾ This may be related to the

Figure 12. Relations among cardiac oxygen consumption (Vo_2), PVA and E_{max} . A: PVA=external work (EW) + elastic potential energy (PE). B: Oxygen cost of PVA as the slope a of the Vo_2 -PVA relation at a given E_{max} . C: Vo_2 -PVA relations at three E_{max} levels. Vo_2 intercept b increases with E_{max} without changes in slope a . D: Oxygen cost of E_{max} as the slope c of the PVA-independent Vo_2 - E_{max} relation. d =PVA-independent Vo_2 at zero E_{max} .

massive isomyosin shift from β to α type. Such an isomyosin shift was hardly observed in the hypothyroid dog heart, resulting in the absence of an increase in the O_2 cost of PVA.³¹⁾ Acute failing hearts tended to have a slightly decreased O_2 cost of PVA, although the underlying mechanism remains to be elucidated.^{32,33)}

The O_2 cost of E_{max} increased in stunned myocardium and acidotic myocardium.^{32,33)} This seems to reflect a malfunction of the E-C coupling. We speculated that futile Ca^{2+} cycling in the sarcoplasmic reticulum and a decreased Ca^{2+} sensitivity of the contractile machinery underlie the pathophysiology. Thus, we consider that analyses of cardiac energetics by the E_{max} and PVA concept are helpful to characterize normal and diseased hearts and differentiate their pathophysiology and the underlying mechanisms.^{27,29)}

E_{max} and PVA have been shown to be powerful indices for assessing the mechanoenergetic effects of pharmacologic agents, including the Ca^{2+} sensitizer EMD 53998,³⁴⁾ the plant alkaloid ryanodine,³⁵⁾ the phosphatase 2,3 BDM³⁶⁾ and a variety of new cardiostonic agents (OPC-8212, UDCG 115 BS, DPI 201-106, milrinone).^{37,38)}

Pump function and pressure-volume window

In addition to its value as an index of contractility, E_{max} is also a useful measure for associating ventricular chamber contractile properties with cardiac pump performance.¹³⁾ Figure 13 (Panel A) shows that stroke volume is defined as the end-diastolic volume minus end-systolic volume. The end-systolic volume

Figure 13. Stroke volume (SV) as a function of end-diastolic volume (V_{ed}), dead volume (V_0), end-systolic pressure (P_{es}) and contractility (E_{max}). A: SV, V_{ed} , V_0 , P_{es} and E_{max} in the P-V diagram. B: SV as an increasing function of V_{ed} . C: SV as a decreasing function of P_{es} . D: SV as a nonlinearly increasing function of E_{max} .

minus V_0 is equal to the ratio of end-systolic pressure divided by $E_{\max}$. These relations are described by the inset equation. This equation, though simple, is meaningful. For example, if preloaded end-diastolic volume alone is changed, stroke volume is an increasing function of end-diastolic volume V_{ed} (Figure 13, Panel B); i.e., it displays the Starling effect. If afterloaded end-systolic pressure alone is changed, stroke volume is a decreasing function of afterload P_{es} (Figure 13, Panel C). This shows the afterload effect. If $E_{\max}$ alone is changed, stroke volume is a nonlinearly increasing function of $E_{\max}$ (Figure 13, in Panel D). Interestingly, stroke volume is sensitive to changes in $E_{\max}$ in its low range, namely, failing hearts. Stroke volume is insensitive to $E_{\max}$ changes in its normal range (normal hearts). These theoretical predictions are consistent with experimental results.

$E_a/E_{\max}$ ratio

A new concept, the effective arterial elastance (E_a), was added to the P-V window in 1983 by Kenji Sunagawa.³⁹⁾ It is the slope of the line connecting the end-diastolic volume and the end-systolic P-V point (the left upper corner) of the P-V loop as shown in Figure 14. Combining E_a with $E_{\max}$ yields very important information on the mechanical and energetic matching of ventriculo-arterial coupling.⁴⁰⁾

When E_a is comparable to or slightly smaller than $E_{\max}$, the ventriculo-arterial coupling is matched because external work and its efficiency are maximum or near maximum. The situation is found in normal hearts. However, as E_a

Figure 14. Ventriculo-arterial coupling in terms of $E_a/E_{\max}$ ratio. EF=ejection fraction; E_a =effective arterial elastance; $E_{\max}$ =end-systolic maximum ventricular elastance. A: $E_a/E_{\max}$ ratio is comparable to 1 in normal hearts with a high EF. B: $E_a/E_{\max}$ ratio increases from 1 as heart failure proceeds with a decreasing EF.

increases relative to $E_{\max}$, the degree of matching deteriorates because external work and its efficiency decrease. This situation is found in failing hearts. Therefore, the P-V diagram is very helpful for understanding the normality and abnormality of the ventriculo-arterial mechanoenergetic coupling.^{25,40)}

The $E_a/E_{\max}$ matching concept has been applied to cardiology.^{25,41)} In a normal heart with an EF above 60%, $E_{\max}$ was large and comparable to or slightly greater than E_a . In a moderately failing heart with an EF above 40%, $E_{\max}$ decreased and E_a increased with a decreased stroke volume, increasing the $E_a/E_{\max}$ ratio. In a severely failing heart with a further decreased EF below 40%, $E_{\max}$ further decreased and the E_a further increased, increasing the $E_a/E_{\max}$ ratio considerably.

The $E_a/E_{\max}$ ratio is very helpful in the treatment of heart failure because the treatment can be designed to shift the $E_a/E_{\max}$ ratio to approach unity. One method is to decrease E_a by decreasing the heart rate. Another method is to decrease E_a by decreasing the afterload. A third method is to increase $E_{\max}$. By appropriately combining these three methods, heart failure will be effectively treated so that its ventriculo-arterial coupling is corrected or normalized. Therefore, the P-V diagram is very helpful to better understand the ventriculo-arterial coupling and to decide the strategy of cardiological treatment.

Summary and conclusion

- 1) $E_{\max}$ can serve as an index of ventricular contractility.
- 2) $E_{\max}$ is the slope of the ventricular end-systolic P-V relation.
- 3) $E_{\max}$ represents ventricular end-systolic maximal elastance.
- 4) $E_{\max}$ characterizes ventricular pump performance.
- 5) PVA is a measure of the ventricular total mechanical energy generated by contraction.
- 6) PVA correlates linearly with $\dot{V}O_2$. Its slope is the O_2 cost of PVA.
- 7) Changes in $E_{\max}$ shift the $\dot{V}O_2$ -PVA relation. Its sensitivity is the O_2 cost of $E_{\max}$.
- 8) O_2 costs of PVA and $E_{\max}$ characterize myocardial energetics under various conditions.
- 9) $E_{\max}$ and PVA, together with E_a (effective arterial elastance), determine cardiac efficiency and load matching.
- 10) Thus, despite some limitations, the $E_{\max}$ and PVA concepts are useful to characterize abnormalities of diseased hearts.

Therefore, cardiac mechanoenergetic performance of normal and failing hearts has been better understood through the widely opened P-V window.

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