A Single-Beat Estimation Method for E_{max} Directly Based on Linearity of Ventricular Elastance

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Abstract—**This paper has derived a new method for estimating the maximum ventricular elastance E_{max} by assuming that the following two assumptions are simultaneously established in a certain part of the ejection period: the ventricular elastance $E(t)$ changes linearly with time and the dead volume V_0 does not change. The method can estimate E_{max} in a single beat without any change in the cardiac load by measuring the ventricular pressure and either the ventricular volume or outflow. The method does not need to previously assign the approximation range of $E(t)$ and does not include the recursive procedure to search for the peak time t_{max} that gives E_{max}. In an experiment *in vivo*, it could be ascertained that the method can derive the estimate of E_{max} roughly close to the true value.**

Keywords – **E_{max}, estimation, end-systolic ventricular elastance, ESPVR, cardiac function**

I. Introduction

The maximum value (E_{max}) of the ventricular elastance ($E(t)$) has been thought to be a good index for quantifying the ventricular contractile performance independently of the cardiac load. However, the conventional method for estimating E_{max} requires a change in the cardiac load during several beats. To promote clinical application of E_{max}, it is desirable to estimate E_{max} low-invasively on the basis of information acquired within a single heartbeat without any change in the cardiac load.

As one of such methods, the authors [1], [2] have proposed the parameter optimization method (POM). The POM can estimate E_{max} on the basis of ventricular pressure and either ventricular volume or outflow acquired only in a single beat. The POM does not need the normalized time-varying ventricular elastance curve ($E_N(t_N)$) used in Senzaki's method [3]. In the POM, however, it takes much computational time to search for the optimal parameters determining the linear function to approximate the elastance $E(t)$, and the approximation range must be given previously.

To overcome these defects of the POM, in this study, a new method for single-beat estimation of E_{max} has been developed by directly using linearity of ventricular elastance in the ejection period. In the proposed method, it is expected that the computational time can be reduced and that the problem of how to determine the approximation range of the elastance curve can be avoided.

II. Methods

A. Conventional Method

Let $P(t)$ and $V(t)$ denote ventricular pressure and volume, respectively. Ventricular contractility can be expressed by the ventricular elastance $E(t)$ calculated from

$$E(t) = \frac{P(t)}{V(t) - V_0} \tag{1}$$

where V_0 is the so-called *dead volume* defined as the volume axis intercept of the regression line of the end-systolic pressure-volume relation (ESPVR). Drastic change in preload or afterload is necessary to obtain sufficiently distinct end-systolic points to determine the ESPVR. E_{max} is equal to the maximum value of $E(t)$.

B. Assumptions

In this study, the following two assumptions are proposed.

Assumption I: $E(t)$ changes linearly with time in a certain part of the ejection period.

Assumption II: V_0 in the ejection period is constant.

C. Method I using Pressure $P(t)$ and Volume $V(t)$

First, consider the case where $P(t)$ and $V(t)$ can be measured directly, for example, with a pressure transducer and a conductance catheter, respectively.

Define the unbiased ventricular volume ($v(t)$) as

$$v(t) \stackrel{\text{def}}{=} V(t) - V_0 \tag{2}$$

Substitution of (2) to (1) yields

$$E(t) = \frac{P(t)}{v(t)} \tag{3}$$

Assumption I means that the second derivative of $E(t)$ is zero, that is,

$$\begin{aligned} \ddot{E}(t) &= \frac{2P(t)\dot{v}^2(t)}{v^3(t)} - \frac{2\dot{P}(t)\dot{v}(t)}{v^2(t)} - \frac{P(t)\ddot{v}(t)}{v^2(t)} + \frac{\ddot{P}(t)}{v(t)} \\ &= 0 \end{aligned} \tag{4}$$

Solving (4) with respect to $v(t)$ gives two solutions. However, the unbiased volume $V(t) - V_0$ must be positive in the

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Abstract

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ejection period, and therefore, the positive solution $v_p(t)$ is chosen as the feasible solution as follows:

$$v_p(t) = \frac{1}{2\ddot{P}(t)}\Big[2\dot{P}(t)\dot{v}(t) + P(t)\ddot{v}(t) - \sqrt{\{2\dot{P}(t)\dot{v}(t) + P(t)\ddot{v}(t)\}^2 - 8P(t)\dot{v}^2(t)\ddot{P}(t)}\Big] \quad (5)$$

Rewrite $v_p(t)$ as $v_p(P(t), \dot{P}(t), \ddot{P}(t), \dot{v}(t), \ddot{v}(t))$. From (2) and (5), the dead volume V_0 can be represented by

$$V_0 = V(t) - v_p(P(t), \dot{P}(t), \ddot{P}(t), \dot{v}(t), \ddot{v}(t)) \quad (6)$$

In addition to Assumption I, suppose that Assumption II is also established at least during a certain part of the ejection period, and then

$$\dot{v}(t) = \dot{V}(t) \quad (7)$$

$$\ddot{v}(t) = \ddot{V}(t) \quad (8)$$

hold. Thus, we have

$$V_0 = V(t) - v_p(P(t), \dot{P}(t), \ddot{P}(t), \dot{V}(t), \ddot{V}(t)) \quad (9)$$

It is true that if both Assumptions I and II hold, the right hand side of (9) will be constant. However, the time range in which both Assumptions I and II actually hold is not exactly equal to the whole of the ejection period, and then the right hand side of (9) must be the function of t in the whole of the ejection period. To avoid misunderstand, the left hand side of (9), V_0 should be rewritten as a time function $\tilde{V}_0(t)$ as follows:

$$\tilde{V}_0(t) \stackrel{\text{def}}{=} V(t) - v_p(P(t), \dot{P}(t), \ddot{P}(t), \dot{V}(t), \ddot{V}(t)) \quad (10)$$

An estimate ($\hat{V}_0$) of the dead volume V_0 can be obtained as the value of $\tilde{V}_0(t)$ at the time t when $\frac{\mathrm{d}}{\mathrm{d}t}\tilde{V}_0(t) = 0$, i.e., $\tilde{V}_0(t)$ is flat or a peak since Assumptions I and II are simultaneously established at that time. After substitution of $\hat{V}_0$ to (1), the estimate ($\hat{E}(t)$) of $E(t)$ can be defined as

$$\hat{E}(t) \stackrel{\text{def}}{=} \frac{P(t)}{V(t) - \hat{V}_0} \quad (11)$$

Finally, obtain the estimate ($\hat{E}_{max}$) of E_{max} as follows:

$$\hat{E}_{max} \stackrel{\text{def}}{=} \max_{t_{be} < t \leq t_{ee}} \hat{E}(t) \quad (12)$$

where t_{be} and t_{ee} are the beginning and the end time of ejection, respectively.

D. Method II using Pressure $P(t)$ and Outflow $i(t)$

Next, consider the different case where $V(t)$ cannot directly be measured but ventricular outflow ($i(t)$) can be measured with a flowmeter or an ultrasound Doppler image. Let $P(t)$ be still measurable.

Define the ejecting volume or the integrated value ($I(t)$) of the outflow $i(t)$ from t_{be} to t as

$$I(t) \stackrel{\text{def}}{=} \int_{t_{be}}^{t} i(t)\mathrm{d}t \quad (13)$$

Since $i(t) = 0$ for any t from the end-diastolic time (t_{ed}) to t_{be}, $V(t)$ can be represented as

$$V(t) = V(t_{be}) - I(t) = V(t_{ed}) - I(t) = V_{ed} - I(t) \quad (14)$$

where V_{ed} is the end-diastolic volume. The relation of (14) can transform (1) to

$$E(t) = \frac{P(t)}{V_{ed} - V_0 - I(t)} \quad (15)$$

Differentiating V(t) with respect to t, we have

$$\dot{V}(t) = -i(t) \quad (16)$$

$$\ddot{V}(t) = -\dot{i}(t) \quad (17)$$

Substitution of (14), (16) and (17) to (10) yields

$$V_{ed} - \tilde{V}_0(t) \stackrel{\text{def}}{=} I(t) + v_p(P(t), \dot{P}(t), \ddot{P}(t), -i(t), -\dot{i}(t)) \quad (18)$$

In the same way as Method I, let an estimate ($\widehat{V_{ed} - V_0}$) of $V_{ed} - V_0$ be the value of $V_{ed} - \tilde{V}_0(t)$ at the time t when $V_{ed} - \tilde{V}_0(t)$ is flat or a peak. Substitute $\widehat{V_{ed} - V_0}$ into (15) and we have $\hat{E}(t)$ as follows:

$$\hat{E}(t) \stackrel{\text{def}}{=} \frac{P(t)}{\widehat{V_{ed} - V_0} - I(t)} \quad (19)$$

Finally, obtain $\hat{E}_{max}$ according to (12).

E. Experimental Protocols and Data Processing

In vivo experiments were carried out by using an adult goat weighing 50kgs in an open chest. An conductance catheter (Leycom; Sigma 5) was inserted into the left ventricle via the apex to measure left ventricular volume $V(t)$. Aortic flow $i(t)$ was measured at the ascending aorta with an electromagnetic flow meter (Nihon Kohden; MFV-3100), and left ventricular pressure $P(t)$ was measured with a catheter-tip pressure transducer (Camino; 420).

In our calculation, a mathematical processing language *Mathematica* (Wolfram Research Inc.) was employed for sampled data of $P(t)$, $V(t)$ and $i(t)$ with the sampling interval of $\Delta t = 10$ms. In particular, its curve fitting function *Fit* was used to yield polynomial functions $P(t)$, $V(t)$ and $i(t)$ in the ejection period for eliminating measurement noises. This is because the first and the second derivatives of $P(t)$, $V(t)$ and $i(t)$, which are very sensitive to noise, are required in calculation of (10) and (18).

III. Results

Fig. 1 shows an example of pressure-volume loops (PV-loops) obtained in our experiment. The PV-loops are depicted during successive five beats after manually clamping

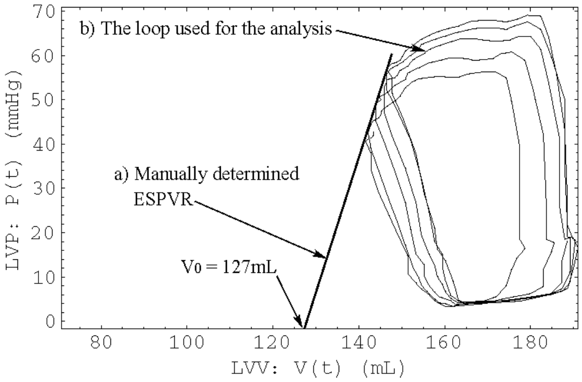

Fig. 1. An example of pressure-volume loops in manually clamping the pulmonary artery.

the pulmonary artery. The line a) is an ESPVR manually determined on the basis of the end-systolic points. In this example, the corresponding dead volume V_0 can be obtained as $V_0 = 127$mL.

The sampled values of $P(t)$, $V(t)$ and $i(t)$ corresponding to the ejection period of the loop b) in Fig. 1 are depicted as dots in Figs. 2, 3 and 4, respectively. The sampled values were approximated by the solid curves shown in these figures. The orders of the polynomials were 3, 3 and 6 for $P(t)$, $V(t)$ and $i(t)$, respectively.

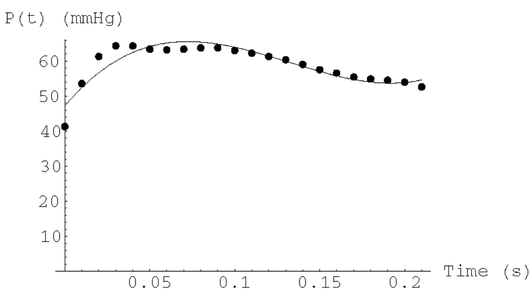

Fig. 2. Sampled values (dots) of left ventricular pressure $P(t)$ corresponding to Fig. 1b) and its approximation (solid curve).

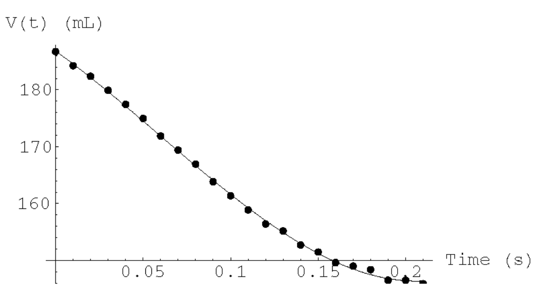

Fig. 3. Sampled values (dots) of left ventricular volume $V(t)$ corresponding to Fig. 1b) and its approximation (solid curve).

Fig. 5 shows $\tilde{V}_0(t)$ and $V_{ed}-\tilde{V}_0(t)$. The upper curve $\tilde{V}_0(t)$ was calculated from (10) substituted by approximated time functions $P(t)$, $V(t)$ and their derivatives corresponding to Figs. 2 and 3. In the same way, the lower curve $V_{ed}-\tilde{V}_0(t)$ was calculated from (18) substituted by $P(t)$, $i(t)$ and their derivatives corresponding to Figs. 2 and 4. In Fig. 5, the parts a) and b) of $\tilde{V}_0(t)$ satisfy $\frac{\mathrm{d}}{\mathrm{d}t}\tilde{V}_0(t) = 0$. However, the part b) corresponds to the peak time t_{max} that maximizes $E(t)$. Then, the estimated dead volume $\hat{V}_0$ can be given as the value of $\tilde{V}_0(t)$ of the part a). In this case, we have $\hat{V}_0 = 126$mL. In the same way, the part d) of $V_{ed} - \tilde{V}_0(t)$ can be chosen as the estimated value $\widehat{V_{ed} - V_0}$, because the part d) is the closest to the part a). Thus, we have $\widehat{V_{ed} - V_0} = 60$mL.

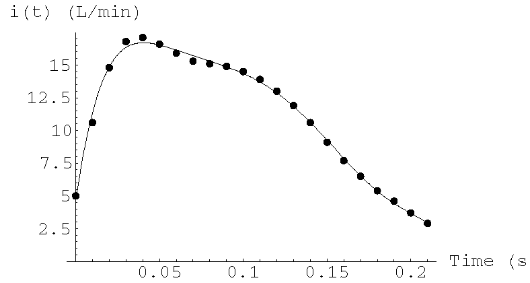

Fig. 4. Sampled values (dots) of aortic flow rate $i(t)$ corresponding to Fig. 1b) and its approximation (solid curve).

Substitutions of $\hat{V}_0$ and $\widehat{V_{ed} - V_0}$ to (11) and (15) yielded the estimates $\hat{E}(t)$ as shown in Figs. 6 and 7, respectively. In both figures, the shape of $\hat{E}(t)$ is nearly linear. The maximum value of each $\hat{E}(t)$ gives the estimated maximum elastance $\hat{E}_{max}$, and thus, we have $\hat{E}_{max} = 2.62$mmHg/mL using pressure and volume shown in Fig. 6, and $\hat{E}_{max} = 2.76$mmHg/mL using pressure and flow rate shown in Fig. 7.

The above process was applied to each ejection period of the five PV-loops shown in Fig. 1. Table 1 shows mean values and standard deviations of estimates $\hat{V}_0$ and $\hat{E}_{max}$ averaged over the five beats. The ESPVRs can be depicted as shown in Fig. 8 using the estimates of a) and b) of Table 1. The Table 1 and Fig. 8 indicate that the proposed methods could yield the estimated values roughly close to the true values.

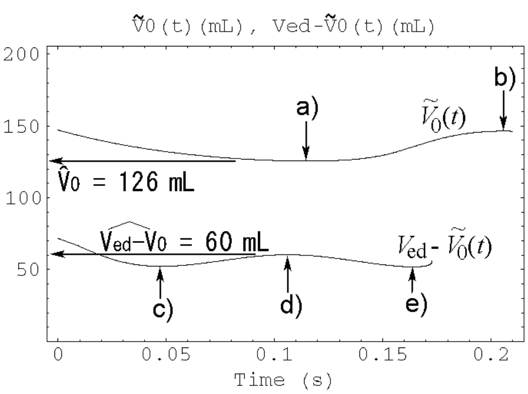

Fig. 5. $\tilde{V}_0(t)$ and $V_{ed} - \tilde{V}_0(t)$ calculated from (10) and (18), respectively. The peak values a) and d) give the estimates, $\hat{V}_0$ and $\widehat{V_{ed} - V_0}$, respectively.

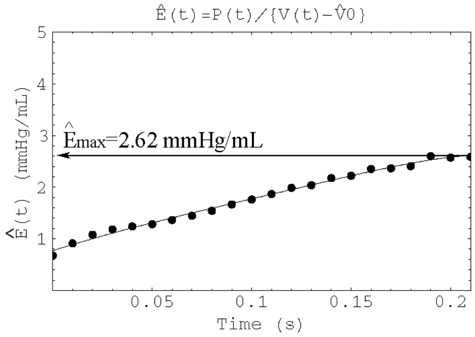

Fig. 6. Estimate $\hat{E}(t)$ of the left ventricular elastance $E(t)$ calculated from (11) on the basis of approximated $P(t)$ and $V(t)$ (solid curve), and their measured values (dots).

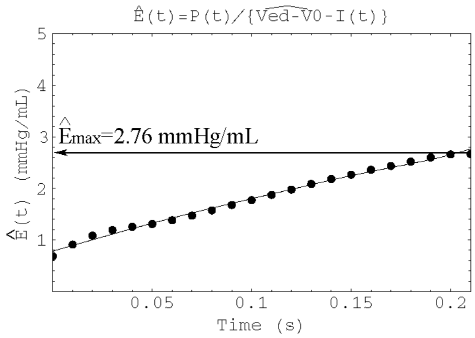

Fig. 7. Estimate $\hat{E}(t)$ of the left ventricular elastance $E(t)$ calculated from (19) on the basis of approximated $P(t)$ and $i(t)$ (solid curve), and their measured values (dots).

IV. Discussion

The result of Table 1 and comparison between Fig. 1 and Fig. 8 imply that the proposed method (Methods I and II) can estimate E_{max} beat by beat with reasonable accuracy without any change in the cardiac load. However, the standard deviation of each estimate is not so small. This is because the method depends strongly on the waveform of the time series data and is sensitive to noise. To cope with this defect, the time series data such as $P(t)$, $V(t)$ and $i(t)$ should be averaged over several beats which have almost the same cardiac cycle as one another in the steady state or under a constant cardiac load.

The proposed method does not need the procedure for optimizing unknown parameters as the POM does, and then the proposed method requires much less computational time for estimation than the POM. Moreover, the POM must previously assign the approximation range where the elastance $E(t)$ can be regarded as a line. On the other hand, in the proposed method, the adequate part in which both Assumptions I and II hold can automatically be given as the time when $\tilde{V}_0(t)$ or $V_{ed} - \tilde{V}_0(t)$ is flat or a peak.

Senzaki's method [3] also does not need the optimizing procedure but needs the normalized ventricular elastance curve $E_N(t_N)$ and the recursive procedure for searching for the peak time t_{max}. In this paper, unfortunately, the estimation accuracy has not yet been compared among the proposed method, the POM and Senzaki's method.

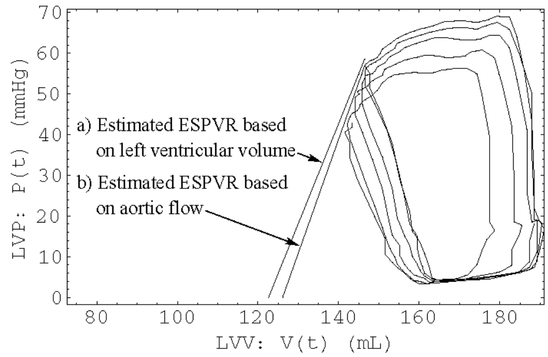

Fig. 8. ESPVRs depicted by means of the estimates of a) and b) of Table 1.

Table 1 Estimates $\hat{V}_0$ and $\hat{E}_{max}$ averaged over the five beats shown in Fig. 1 or Fig. 8.

	True value	a) Estimate using $P(t)$ and $V(t)$	b) Estimate using $P(t)$ and $i(t)$
$\hat{V}_0$ (mL)	127	123(±5.3)	126(-)
$\hat{E}_{max}$ (mmHg/mL)	2.9	2.5(±0.54)	2.8(±0.50)

V. Conclusions

The present study has derived a new method for estimating the maximum ventricular elastance E_{max} by assuming that the following two assumptions are simultaneously established in a certain part of the ejection period: 1) the ventricular elastance $E(t)$ changes linearly with time; 2) the dead volume V_0 does not change. The method can estimate E_{max} in a single beat without any change in preload or afterload by measuring the ventricular pressure and either the ventricular volume or outflow. The method does not need to previously assign the approximation range of $E(t)$ and does not include the recursive procedure to search for the peak time t_{max} that gives E_{max}. In the experiment *in vivo*, it could be ascertained that the method can give the estimate of E_{max} roughly close to the true value obtained from the conventional method.

In further studies, the estimation accuracy of the proposed method should be compared with that of other single-beat estimation methods.

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