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Evaluation of cardiac function based on ventricular pressure-volume relationships during assistance with a rotary blood pump.

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***Abstract*— Nowadays, a rotary blood pump can be used as not only for a bridge to transplantation (BTT) but also for a bridge to recovery (BTR) and a destination therapy (DT). In such cases, evaluation of the recovery level of the native heart provides useful infomation to improve the clinical strategy and decide adequate timing for removing of the RBP. In contrast, the indices for cardiac function have been studied. However, most of them do not consider the assistance with the RBP. In this study, we aimed at evaluating whether E_{max}, which is an index for cardiac function based on the pressure-volume relationships, is still valid during assistance with the RBP from an animal experiment.**

In the acute animal experiment with an adult goat, we measured pressure-volume (P-V) loops while cardiac function was normal, augmented or diminished. The experimental results revealed that there were typical differences in the shapes of P-V loops when the cardiac function was altered, and E_{max} can still be used as an index for the cardiac function even if the assistance with the RBP is ongoing.

I. INTRODUCTION

A rotary blood pump (RBP) is a device to keep blood circulation of a cardiac patient instead of his/her weakened native heart. Clinical studies with the RBP have been performed widely, and they have revealed that the assistance with the RBP unloads a native heart and promotes its recovery. Nowadays, the RBP can be used as not only for a bridge to transplantation (BTT) but also for a bridge to recovery (BTR) and a destination therapy (DT)[1][2]. In such cases, evaluation of the recovery level of the native heart provides useful information to improve the clinical strategy and decide adequate timing for removing of the RBP. In addition, this information will be also helpful to realize the adaptive control algorithm for the RBP.

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In contrast, the indices for cardiac function have been studied; however, most of them do not consider the effect of the assistance with the RBP. For instance, ejection fraction (EF) is one of the indices, and given by

$$EF = \frac{SV}{\max(LVV)} \tag{1}$$

where, SV and LVV are stroke volume and left ventricular volume, respectively. $\max(LVV)$ can be altered by the operating point of the pump, thus, this index is not independent of the RBP. In other words, EF is not an accurate index to represent only cardiac function. Another index dP/dt that represents the maximum value of derivative of LVV, is also such a index and this value is also affected by the setting of the RBP.

Moreover, these two indices do not consider the effect of left ventricular pressure (*LVP*) or *LVV* respectively although the relationship between them is important to define cardiac function. The pitfall of these methods are in neglecting the bypass with the RBP, and cardiac function during assistance should be discussed considering the effect of the bypassing flow.

There are reports about the method in estimating *LVP* or other related value with electric current of the actuator[3][4]. As stated above, however, only pressure data is not enough to accurately represent cardiac function during the assistance.

The simulation studies for the interaction between the native heart and the RBP based on pressure-volume relationships have been also reported by some groups [5][6]. These studies are evidently important for cardiac function. However, the comparison between actual data and ideal ones is also necessary.

In this study, we aimed at clarifying whether E_{max}, which is an index for cardiac function based on the pressure-volume relationships, is still valid during assistance with the RBP from an animal experiment. In addition, we examined whether the index can represent the cardiac function independently of the setting of the pump. To measure the basic behavior of the pressure-volume (P-V) loops and E_{max} during the assistance, we performed an acute animal experiment and discussed about indices for cardiac function.

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II. MATERIALS AND METHODS

A. Ventricular pressure-volume relationship

The relationship between time-series data of *LVP* and *LVV* in one cardiac cycle can be translated as a P-V loop, as shown in Fig. 1 (a)[7].

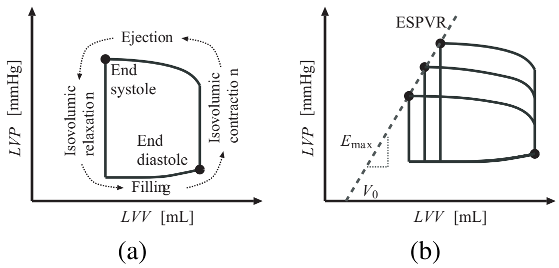


Fig. 1. P-V loop and ESPVR. (a) segmentation of the P-V loop, (b) definition of ESPVR and E_{max}.

The P-V loop is segmented to an isovolumic contraction phase (ICP), an ejection phase (EP), an isovolumic relaxation phase (IRP), and a filling phase (FP), based on the opening or closing of an aortic or a mitral valve. The ICP and the EP are included in systolic period and rest of them are included diastolic one. End point of systole and diastole is called end systole (ES) and end diastole (ED), respectively.

The morphology and position of the P-V loop are changed by altering afterload or preload, as shown in Fig. 1 (b). For example, if the aorta is occluded then aortic pressure (*AoP*) increases, and afterload become higher. Meanwhile, it is known that ES follows a linear equation called end systolic pressure-volume relationship (ESPVR) and its slope is called E_{max}, which is possible to evaluate cardiac function independently of preload and afterload. E_{max} is given by (2) as follows:

$$LVP_{\mathrm{ES}} = E_{max}(LVV_{\mathrm{ES}} - V_0) \quad (2)$$

where, LVP_{ES} and LVV_{ES} are *LVP* and *LVV* at end systole, respectively. V_0, which is the intercept of the ESPVR, responds to the dead volume of the left ventricle.

B. Experimental setup

Experimental setup for an acute animal experiment with an adult goat (female, 50kg) is shown in Fig. 2. We attached NEDO PI-710 gyro pump[8] to the circulatory system. The inlet and outlet of the pump were connected to the left apex and the aorta with cannula, respectively. The conductance catheter (Sigma-5, Leycom, US) was inserted into the left ventricle through the left atrium to measure *LVP* and *LVV*. Left pump flow (*LPF*) and aortic flow (*AoF*) were measured with ultrasound flow probes (Transonic Inc., US). Left atrium pressure (*LAP*) and *AoP* were also measured with the pressure transducers as references.

C. Measurement conditions

We measured P-V loops while cardiac function was (a) normal, (b) augmented (positive inotropic intervention) or (c) diminished (negative inotropic intervention). To imitate the positive and negative inotropic intervention, we injected

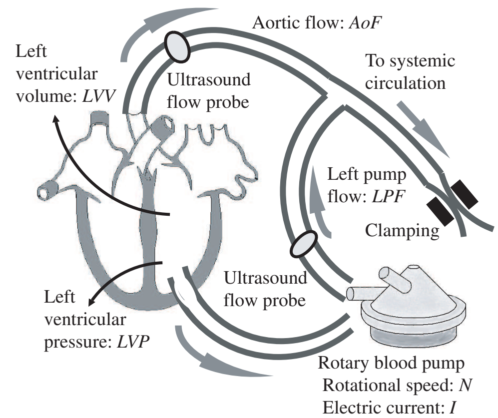


Fig. 2. Experimental setup

0.3mg of Epinephrine and 0.5 mg of Propranolol, respectively. In each condition, we altered the rotational speed of the pump (N) from 1600rpm to 2000rpm per 100rpm, or clamped the outlet of the pump to measure P-V loops during no assistance with the RBP.

Each measurement was performed 60 seconds while afterload was altered by narrowing the aorta manually to obtain ESPVR. The data while the aorta clamping was not performed were also collected, to obtain the basic P-V loops.

End systole points were chosen from each cardiac cycles as follows:

1) Find the median of *LVP* and *LVV*.
2) Neglect points larger than median of *LVV* or smaller than median of *LVP*.
3) Find the point with the largest slope at a certain point in third quadrant of a *LVV*-*LVP* plane. Regard the point as ES.

III. RESULTS

A. P-V loops

Figs. 3 (a) to (c) show the P-V loops while the cardiac function was normal, augmented and diminished, respectively. In these results, all data were collected while afterload was not altered.

B. ESPVR and E_{max}

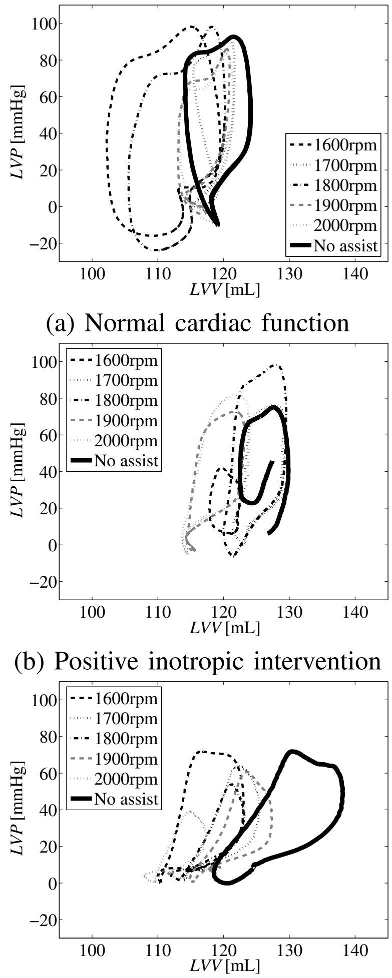
Figs. 4 (a) to (c) show the ES and ESPVR while cardiac function was normal, augmented and diminished, respectively. In these figures, the measurement was performed while afterload was varied by clamping the aorta manually. In Fig. 4, each loop is average of 5 cardiac cycles.

Values of E_{max} and V_0 in each cardiac function and rotational speed are shown in Table. I.

IV. DISCUSSION

A. P-V loops

1) Morphology of P-V loop: Fig. 3 shows that the basic shapes of the P-V loops were the same as the ones when the assist was off. However, there were typical differences in these shapes when cardiac function was altered.

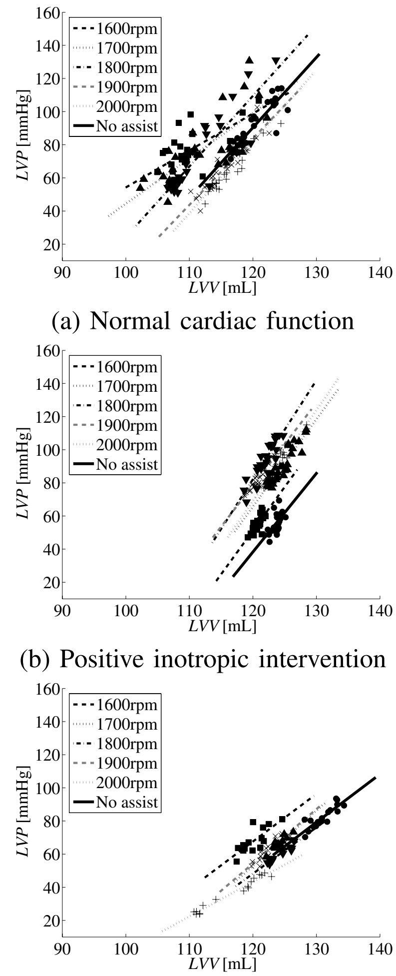


(a) Normal cardiac function

(b) Positive inotropic intervention

(c) Negative inotropic intervention

Fig. 3. Averaged P-V loops while the cardiac function was normal, augmented or diminished.



(a) Normal cardiac function

(b) Positive inotropic intervention

(c) Negative inotropic intervention

Fig. 4. ESPVR while the cardiac function was normal, augmented or diminished. (points: end systole points, line: ESPVR)

Especially, in Fig. 3 (c), shapes of P-V loops were different from (a) and (b). In this case, the slopes in the ICP and IRP were relatively modest, and the curve in the EP was short.

In the isovolumic contraction or relaxation phases, *LVV* is literally constant if the bypass does not exist. However, it is not correct when the assistance with the RBP is performed, because the RBP keeps draining blood from the left ventricle even if the aortic valve is closed. As a result, *LVV* reduces in these isovolumic phases, and then, the slope of the isovolumic part is not vertical. In addition, the assist with the RBP causes higher *AoP*, thus the opening of the aortic valve tends to be later because the aortic valve opens when the *LVP* is higher than *AoP*. In consequence, the curve in the EP becomes short because of the longer ICP. The case of the IRP is also explained as the ICP.

The morphological difference indicates the changes in cardiac function. Thus, this information would be useful to evaluate the elastance of the ventricular wall. In particular, the elastance in isovolumic contraction or relaxation phases is possibly different each other, and it might realize more appropriate evaluation of the elastance.

2) Other issues: Figs. 3 (a) to (c) show that the P-V loops tend to shift left during the assistance. This result indicates that ejection fraction became different from the cases where the assist was off, as stated in the introduction.

In particular, when the rotational speed was set to 1600rpm and 1800rpm in Fig. 3 (a), negative pressure can be found in the filling phase, which is never seen without the bypass with the RBP. In these cases, the difference in *LVV* between the ICP and the IRP became large. Thus, ejection fraction was also quite different from other cases. It also suggests conventional methods fail to explain this effect.

B. ESPVR and E_{max}

From Fig. 4, it was revealed that the ESPVR in each cardiac condition was not unique. However, the difference was found mainly on the intercept and E_{max} was almost constant. In addition, E_{max} was basically larger when the cardiac function was higher, and vice versa. And E_{max} during no assistance was not so different from the one during assistance.

The exceptions can be seen in at N = 1600rpm and 1700rpm in Fig. 4 (a), and we guess this was caused by

TABLE I
VALUES OF E_{max} AND V_0 IN VARIOUS CARDIAC CONDITIONS.

	E_{max}[mmHg/mL]			V_0[mL]		
N [rpm]	N	PII	NII	N	PII	NII
1600	2.23	5.26	2.87	75	110	96
1700	2.74	5.28	3.35	84	107	104
1800	4.26	5.98	2.80	94	106	102
1900	4.01	4.98	3.29	99	104	103
2000	4.32	5.50	2.08	101	107	99
No bypass	4.24	4.75	2.90	97	111	102

(N: Normal, PII: positive inotropic intervention, NII: negative inotropic intervention.)

instability in the beginning of the experiment. It is possible that actual cardiac function was different from other cases.

From these results, we can conclude that E_{max} can be used as an index for the cardiac function even if the assistance with the RBP is ongoing. Theoretically, E_{max} is the index which represents the elastance independently of changes in preload and afterload. Although the assist with the RBP can alter afterload *AoP* widely, E_{max} was not affected by that because of its independency. Thus, we can use E_{max} as the index for cardiac function during assistance. In addition, negative *LVP* found in Fig. 3 did not affect evaluation of the cardiac function.

C. Comparison with the related studies.

Vandenberghe *et al.* [9] reported how time-varying elastance curve can be altered during assistance with the RBP. In the literature, the trajectory of the normalized elastance curve was different when the outflow of the pump was varied. However, their results suggest the elastance at the end systole point was almost constant. This result supports our conclusion that E_{max} is almost constant when the cardiac function can be considered as constant. And our results revealed that this characteristic is also correct when the cardiac function is augmented or diminished, and afterload was altered.

In their research, the dead volume V_0 was obtained with an iterative calculation, and it was revealed that V_0 can be altered by the RBP. Meanwhile, our experimental results showed that the differences in the averaged value of *LVV* was obvious, especially in (c) negative inotoropic intervention. However, significant difference in V_0 was not observed though they fluctuated. V_0 is determined not only by the cardiac function but also blood volume, systemic regulation or other factors in the circulatory system.

In our study, V_0 was determined in a fundamental way with altering afterload, and we consider this is more appropriate. The accuracy of V_0 is quite important because it will strongly affect the calculation for E_{max}.

D. Limitation

1) Instability of cardiac function: Elastance of the ventricular wall is apparently time-varying, and it is possible that E_{max} during no assistance was not entirely equal to the one during assistance. Strictly speaking, actual E_{max} at each operating point of the pump might be different each other. In addition, this experiment was performed acutely and circulatory system was not always stable because of the invasive surgery. Even though, our results imply that such a fluctuation is not so dominant as the injection of the medicine, excepting N = 1600 and 1800rpm in Fig. 3 (a).

2) Difficulty in the measurement: Our current testing method needs insertion of the conductance catheter and alternation of afterload. The insertion of the catheter is not so special in clinical case. However, it is still invasive and desired to be omitted.

It is necessary to sophisticate the measurement system and procedure against this problem. For example, it is possible to replace the measurement of *LVP* and *LVV* with the estimated pressure or flow rate. As stated in introduction, we should develop an estimation method for the ventricular pressure with the pump parameters. A method to estimate flow rate with these data is also developed, which will be helpful to estimate *LVV*.

Afterload can be altered with the intra-aortic balloon pumping (IABP), injection of medicine for the peripheral resistance, or continuous measurement. Especially, to achieve continuous monitoring for cardiac function, we need to sophisticate the measurement system with estimation or non-invasive sensors.

V. CONCLUSIONS

In this study, we revealed that there was typical difference of the P-V loops in the isovolumic contraction or relaxation phases when cardiac function was diminished and the RBP was assisting the blood circulation. We also showed E_{max} is still a useful index for cardiac function to represent the elastance of the ventricular wall independent of the preload and afterload.

We should develop a more sophisticated system for monitoring cardiac function with the integration of the estimation methods, non-invasive sensors, and conventional methods to measure E_{max}.

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