

Theoretical Estimation of Cannulation Methods for Left Ventricular Assist Device Support as a Bridge to Recovery

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INTRODUCTION

Left ventricular assist devices (LVADs) have been widely used to help heart failure (HF) patients provide sufficient blood flow to peripheral organs, keeping patients alive as a bridge to transplantation. Additionally, LVADs unload failed ventricles and are used as a bridge to recovery.

Several studies have suggested how to increase the ventricular unloading effect with regard to pumping types and cannulation locations of the LVAD (1-4). Previously, we demonstrated that counter-pulsating LVAD is more beneficial in ventricular unloading and coronary perfusion, which are the main contributors to cardiac recovery (5). Timms et al. (6) compared the ventricular unloading effect according to cannulation locations: cannulation connected from the left ventricle to ascending aorta (LV-AA) and that from the left atrium to the ascending aorta (LA-AA), with continuous LVAD. They demonstrated experimentally that the LVAD support under LV-AA cannulation provided more ventricular unloading than that under LA-AA cannulation. They also showed that the LVAD support under LA-AA cannu-

lation developed an even higher afterload than that under the condition of HF without LVAD support (4), and suggested that the LV-AA cannulation method provided the best performance for unloading failed ventricles. However, when patients consider cardiac recovery, it is better not to connect the LVAD directly to the diseased ventricle to keep the ventricular muscle intact until the LVAD is weaned out. Thus, any cannulation method connecting the ventricle is unsuitable for LVAD therapy as a bridge to recovery. For this reason, the LA-AA cannulation method has been used alternatively in HF patients for whom cardiac recovery is expected with planned weaning off the LVAD in the future. However, as mentioned, LVAD support under the LA-AA method does not provide sufficient ventricular unloading, compared with that under LV-AA cannulation. Also, the ventricular ejection fraction in LVAD supported with LA-AA cannulation becomes very small or even zero. This may cause valve stenosis and blood thrombosis due to stagnated blood flow inside the ventricle (7). Shi et al. (8) suggested a new cannulation method that is connected in series to the failed heart and used a theoretical method to show that LVAD support with the in-series cannulation

Key Words: Left Ventricular Assist Device (LVAD); Cannulation Methods; Bridge to Recovery; Ventricular Unloading

method provided good performance for pumping blood to peripheral organs and ventricular unloading. However, they did not consider the effect on coronary perfusion during LVAD support or provide a direct comparison between LA-AA and the in-series method in terms of ventricular unloading effect. Experimental methods to record ventricular pressure and volume and coronary perfusion are hampered by low spatiotemporal resolution. Computational modeling represents an alternative approach to overcome this limitation. We have developed several computational models of cardiovascular system in order to obtain cardiovascular response according to various hemodynamic conditions (5, 9, 10).

In this study, the cardiovascular response during LVAD support with the in-series cannulation was compared with that of LVAD support with the LA-AA cannulation method theoretically. Here, the in-series cannulation represents a method in which LVAD is connected in-series with the ventricle from the ascending aorta to the descending aorta. We compared the ventricular unloading in terms of pressure and volume, ejection fraction, and coronary flow during LVAD support according to cannulation methods using a numerical model of a LVAD-implanted cardiovascular system. The model consisted of a time-varying elastance model of failed ventricle and atrium, a vascular system including coronary circulation, and LVAD functions. The effects of three different methods for cannulation were estimated: LA-AA, AA-DA, and LV-AA; the last method was considered here as a reference.

MATERIALS AND METHODS

Lumped model of a LVAD-implanted cardiovascular system

We modified Heldt’s lumped model of the cardiovascular system (11) and integrated it with left coronary circulation (12) and LVAD function. Right coronary circulation was neglected due to its low contribution to the total coronary flow compared with the left coronary circulation. The model was formulated with regard to an electric analog model, consisting of elements such as resistors, capacitors, and diodes. By mapping hemodynamic parameters into the electric elements, flow resistance to the electric resistors, vessel compliance to the capacitors, and the function of cardiac valves to the diodes, this model calculates the blood pressure and flow rate for each component of the body. Fig. 1 shows a schematic diagram of the cardiovascular system model (Fig. 1A) and three types of cannulation methods: LV-AA (Fig. 1B), LA-AA (Fig. 1C), and AA-DA (Fig. 1D).

The model includes the left atrium and ventricle, ascending aorta, brachiocephalic arteries, upper body arteries and veins, superior vena cava, right atrium and ventricle, pulmonary arteries and veins, descending aorta, lower body arteries and veins, inferior vena cava, left coronary arteries, left circumflex artery, left anterior descending artery, coronary veins, and LVAD component. The pumping action of four cardiac chambers, the two ventricles and atria, was implemented by time-varying elastance, based on data adapted from experimental results (11). Heart rate was applied as 70 beats per minute.

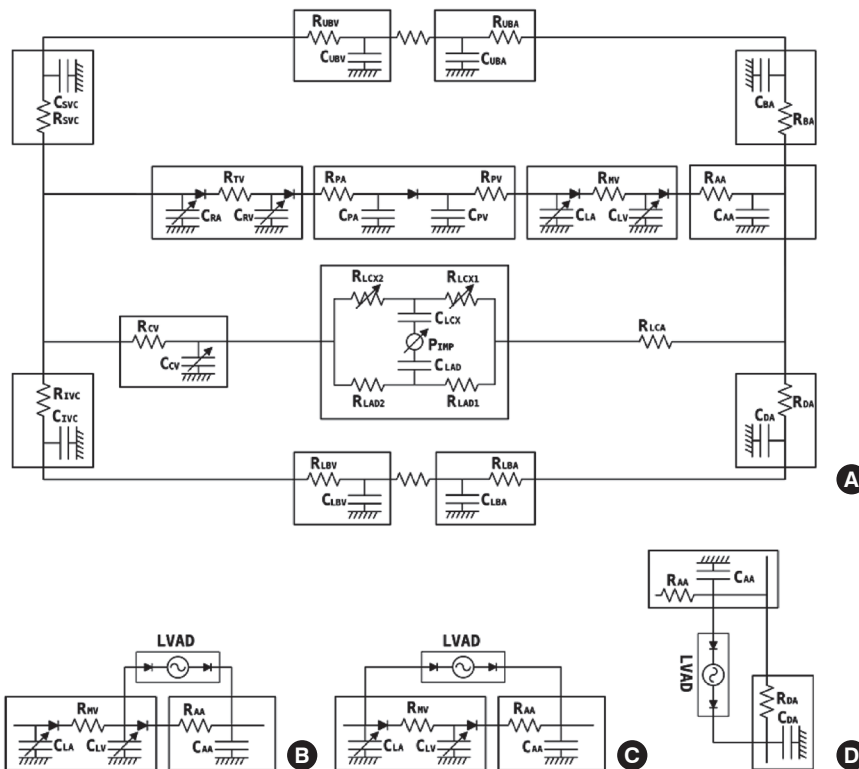


Fig. 1. Schematic of the LVAD-implanted cardiovascular model. Cardiovascular model (A) and three types of cannulation methods: LV-AA (B), LA-AA (C), and AA-DA (D). R, resistance; C, compliance; LA, left atrium; MV, mitral valve; LV, left ventricle; AA, ascending aorta; BA, brachiocephalic artery; UBA, upper body arteries; UBV, upper body veins; SVC, superior vena cava; RA, right atrium; TV, tricuspid valve; RV, right ventricle; PA, pulmonary arteries; PV, pulmonary veins; LCA, left coronary arteries; LCX, left circumflex; LAD, left anterior descending artery; CV, coronary veins; DA, descending aorta; LBA, lower body arteries; LBV, lower body veins; IVC, inferior vena cava, IMP, intra-myocardial pressure.

LVAD function was modeled as a flow generator with a mean flow rate of 75 mL/s, which is enough pumping flow for 100% assistance. There are many types of pumping mechanisms for continuous and pulsatile LVADs. To apply a generalized waveform of continuous and pulsatile LVADs to the model, we used a constant flow rate for continuous LVAD and a harmonic profile of flow rate for pulsatile LVAD (Fig. 2). In the case of pulsa-

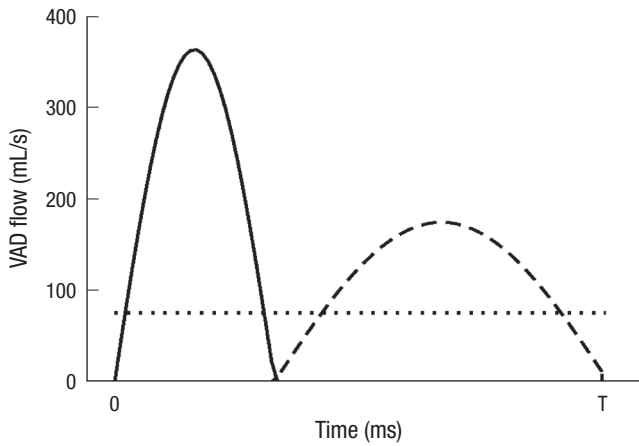


Fig. 2. Flow waveforms of pulsatile and continuous LVADs. LVAD flow waveforms during one cycle (T; 860 milliseconds) in continuous and pulsatile LVADs. Solid line, pulsatile LVAD inflow; dashed line, pulsatile LVAD outflow; dotted line, continuous LVAD flow.

tile LVAD, the pumping phase was synchronized with the failed ventricle as a counter-pulsation. The governing equations and solving methods of the integrated model, which is based on the windkessel method, have been described in detail (5, 11), and are described briefly in the Appendix section.

Heart failure condition

We applied the left heart failure condition to the model by reducing the end-systolic elastance of the left ventricle to 30% of the normal value. This produced hemodynamic results that were consistent with the data reported for systolic HF patients in clinical studies (13, 14). Fig. 3A depicts the time-varying elastance of normal and failed left ventricles. Fig. 3B shows the following pressure-volume curves for normal and failed left ventricles. The ejection fraction of the failed ventricle decreased, to 26%. Fig. 3C, D show the following pressure waveforms of the left atrium, left ventricle, and ascending aorta for the normal and HF conditions. The mean arterial pressure decreased to 59 mmHg under the HF condition.

Simulation protocol

Using the model of the LVAD-implanted cardiovascular system under the HF condition, we performed six independent simulations to compare hemodynamic effects with regard to cannu-

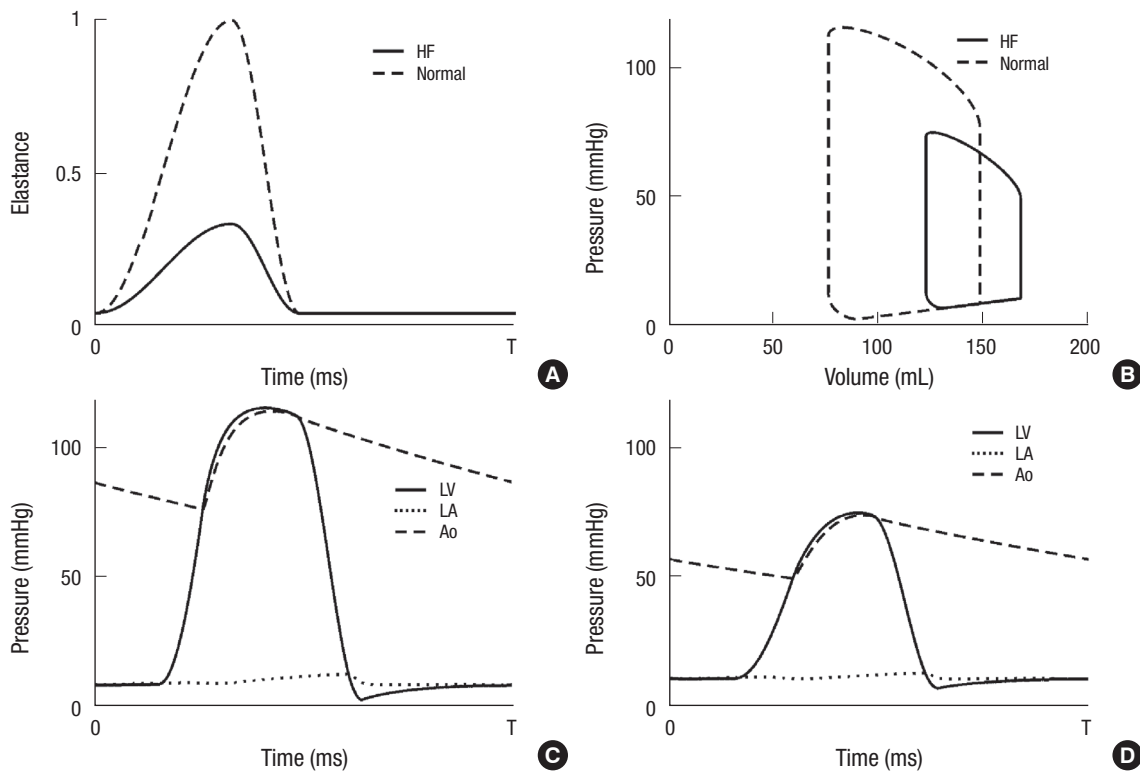


Fig. 3. Comparison of cardiovascular characteristics between normal and heart failure patient. Relative value of time-varying elastance of the left ventricle under HF condition compared with normal condition (A) and following hemodynamic responses: pressure and volume curves for normal and HF conditions (B); pressure waveform of the left ventricle, left atrium, and aorta for normal (C) and HF condition (D). HF, heart failure; LV, left ventricle; LA, left atrium; Ao, aorta; T, cycle length (860 milliseconds).

lation methods of the LVAD. Three cannulation methods, LV-AA, LA-AA, and AA-DA, were simulated under the conditions of continuous and pulsatile LVADs. The pulsatile LVAD pumps blood synchronously with the failed ventricle as counter-pulsation in the model. Each simulation was performed for 20 s to obtain a steady-state response of the cardiovascular system.

RESULTS

Fig. 4 illustrates the simulated pressure waveforms in the left ventricle and atrium and systemic artery according to three cannulation methods, LV-AA, LA-AA and AA-DA, for the LVAD-implanted HF model operating in continuous flow (A-C) and counter-pulsating flow (D-F) mode. In both modes, the cannulation method, LV-AA, showed the lowest ventricular peak pressure (36 and 12 mmHg in continuous and pulsatile mode, respectively), as expected based on previous results (15). As mentioned,

the direct cannulation into the ventricle is not suitable for LVAD support as a bridge to recovery because it results in the injury of the myocardium. The Cannulation method, LA-AA, showed 87 and 76 mmHg left ventricular peak pressure with continuous and pulsatile LVADs, respectively. The in-series cannulation method, AA-DA, showed 75 and 62 mmHg left ventricular peak pressure, respectively. Between the two methods that are not connected directly to the diseased ventricle, the in-series cannulation method provided 14% and 19% less ventricular pressure than the LA-AA method in continuous and pulsatile LVAD modes, respectively.

Fig. 5 presents the simulated pressure-volume curves of the left ventricle according to cannulation methods, LV-AA, LA-AA and AA-DA, for the LVAD-implanted HF model operating in continuous flow (A) or counter-pulsating flow (B) mode. The LV-AA cannulation method showed the lowest end-diastolic ventricular volume among the three methods tested, under both contin-

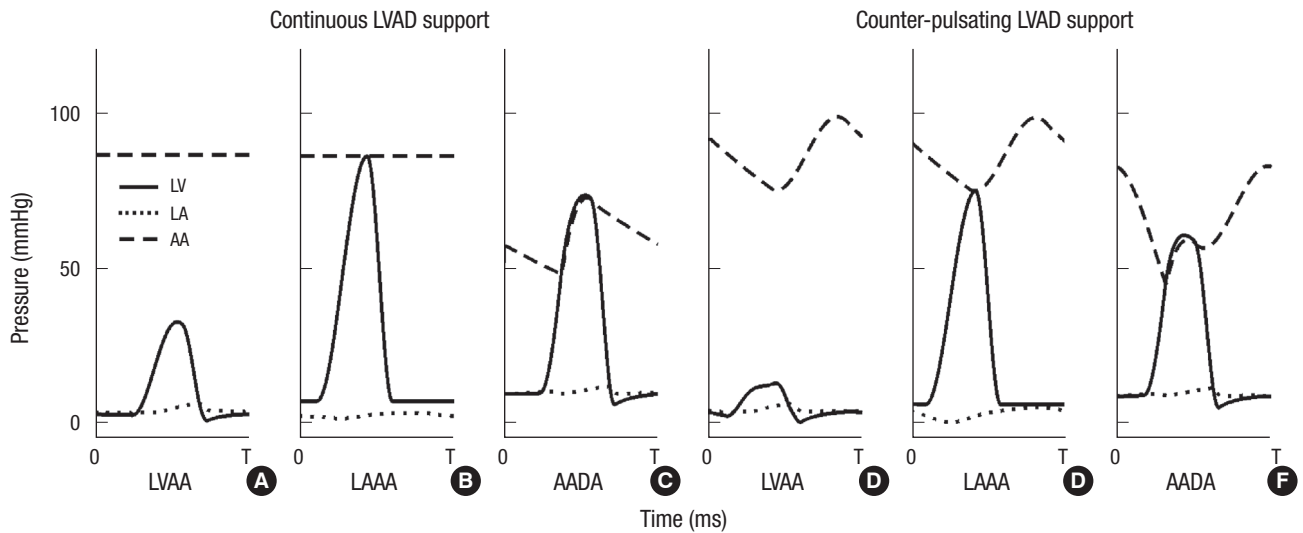


Fig. 4. Cardiovascular pressure waveforms according to LVAD cannulation type. Simulated pressure waveforms in the left ventricle (LV) and atrium (LA) and ascending aorta (AA) according to cannulation locations, from left ventricle to ascending aorta (LV-AA), from left atrium to ascending aorta (LA-AA), and ascending aorta to descending aorta (AA-DA), for the LVAD-implanted HF model operating in continuous flow (A, B, and C) and counter-pulsating flow (D, E, and F) modes. T, cycle length (860 milliseconds).

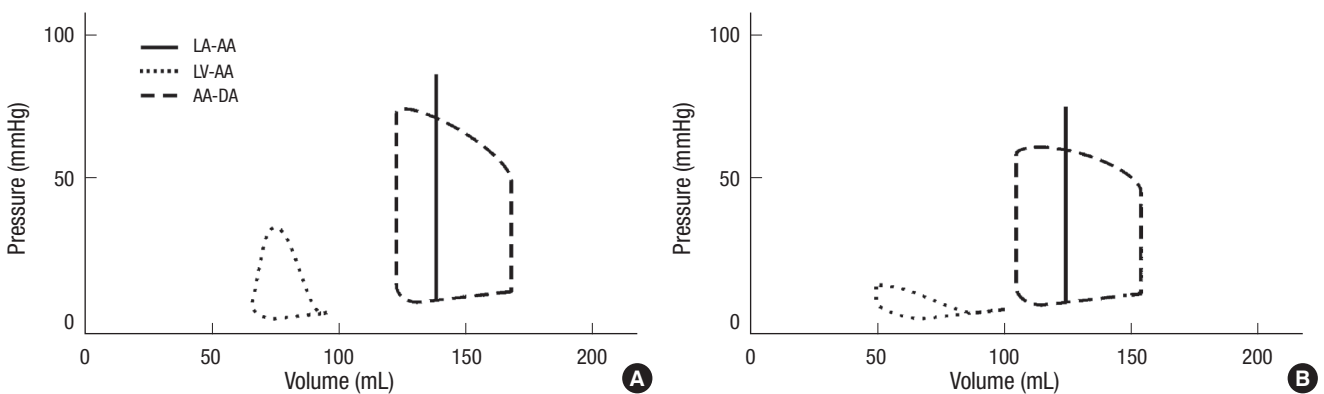


Fig. 5. Pressure-volume diagram according to LVAD cannulation type. Simulated pressures-volume curves of the left ventricle according to cannulation locations, from left ventricle to ascending aorta (LV-AA), from left atrium to ascending aorta (LA-AA), and ascending aorta to descending aorta (AA-DA), for LVAD-implanted HF model operating in continuous flow (A) and counter-pulsating flow (B) mode.

Table 1. Cardiac responses during pulsatile and continuous LVAD supports: total cardiac output, ventricular ejection fraction, and recirculation during different types of LVAD supports

	No LVAD	LV-AA		LA-AA		AA-DA	
		CLVAD	PLVAD	CLVAD	PLVAD	CLVAD	PLVAD
TCO (mL/s)	51	75	75	75	75	51	56
EF	27%	31%	50%	0	0	27%	32%
Recir.	0	0	0	0	0	32%	25%

CLVAD, continuous left ventricular assist device (LVAD); PLVAD, pulsatile LVAD; LV-AA, cannulation method connected from left ventricle to ascending aorta; LA-AA, cannulation method connected from left atrium to ascending aorta; AA-DA, cannulation method connected from ascending aorta to descending aorta; TCO, total cardiac output; EF, ventricular ejection fraction; Recir., recirculation.

uous and pulsatile LVAD support (95 mL in continuous LVAD and 99 mL in pulsatile LVAD). The ejection fraction was 31% with continuous LVAD and 50% with pulsatile LVAD support (Table 1). The LA-AA cannulation method showed an ejection fraction of zero and maintained a constant ventricular volume of 138 mL in continuous LVAD and 124 mL in pulsatile LVAD support. The in-series cannulation method showed 168 mL of end-diastolic ventricular volume and 27% ejection fraction under continuous LVAD support, compared with 154 mL and 32% under pulsatile LVAD support.

Under the condition of the in-series cannulation, the total cardiac output, sum of flows out of LV and LVAD, was less than the LVAD outflow. This means that the bulk of blood in the descending aorta from the LVAD outflow ran back to the ascending aorta and LVAD inlet. This recirculation occurred only in the in-series cannulation (AA-DA). The recirculated blood volume was 32% of the LVAD outflow with continuous LVAD support and 25% with pulsatile LVAD support (Table 1).

Finally, coronary perfusion was compared among the three cannulation methods under continuous and pulsatile LVAD supports. Fig. 6 shows the relative value of coronary flow to the value calculated under the condition of HF without LVAD support. All LVAD supports improved coronary flow. The LA-AA cannulation method demonstrated the most significant improvement of coronary flow under both continuous and pulsatile LVAD support (152% and 162%, respectively). The AA-DA cannulation method showed a slight improvement of coronary perfusion under continuous LVAD support (103%), and better performance under pulsatile LVAD support (123%).

DISCUSSION

Although the LV-AA cannulation is being used for LVAD support, its use has a critical disadvantage for HF patients who need a LVAD support as a bridge to recovery. Left ventricular muscle injury is inevitable during the cannulation. For the purpose of bridge to recovery, it is better not to connect the LVAD directly to the failed ventricle to keep the ventricular muscle intact until

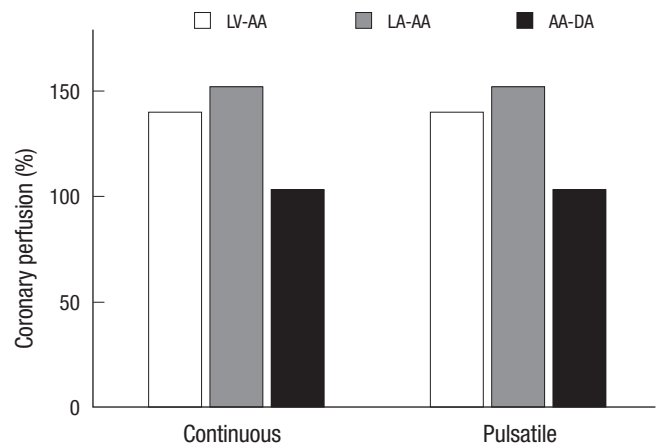


Fig. 6. Coronary perfusion according to LVAD cannulation type. Simulated coronary perfusion according to cannulation locations, from left ventricle to ascending aorta (LV-AA), from left atrium to ascending aorta (LA-AA), and ascending aorta to descending aorta (AA-DA), for LVAD-implanted HF model operating in continuous flow and counter-pulsating flow mode.

the LVAD is weaned out. For this reason, the LA-AA cannulation instead of LV-AA is used in HF patients for whom cardiac recovery is expected with planned weaning of the LVAD in the future. However, it has been reported that LVAD therapy with the LA-AA cannulation method shows poor performance in ventricular unloading and has some problems, including valve stenosis and blood thrombosis due to the small ejection fraction.

As an alternative method to overcome the problems of LA-AA cannulation, we theoretically examined the previously described in-series cannulation method (15). We developed a theoretical model of a LVAD-implanted cardiovascular system and quantitatively compared the ventricular unloading effect, ejection fraction, and coronary perfusion during LVAD support according to three different cannulation methods, LV-AA, LA-AA and AA-DA, under continuous and pulsatile LVAD.

The in-series cannulation method showed better performance in ventricular unloading in terms of pressure (Fig. 4) and volume (Fig. 5) compared with that of LA-AA cannulation under both continuous and pulsatile LVAD supports. In particular, the ventricular unloading effects were more significant in counter-pulsating LVAD support; the advantage of counter-pulsating LVAD on ventricular unloading was also demonstrated theoretically in our previous paper (5).

However, with the in-series cannulation method, the bulk of blood in the descending aorta that comes from the LVAD ran back to the ascending aorta due to reduced pressure in the ascending aorta. Recirculation occurred only in the AA-DA cannulation method because there was no valve between the LVAD inflow site (ascending aorta) and the LVAD outflow site (descending aorta). The pulsatile LVAD showed less amount of recirculation than the continuous LVAD did. This is because the temporal periods of LVAD inflow and outflow under pulsatile conditions are totally separate, whereas under continuous conditions,

they are not (Fig. 2). Thus, it is recommended to choose pulsatile LVAD when the AA-DA cannulation method is applied.

The LA-AA cannulation method showed an ejection fraction of zero and maintained a constant large volume of the left ventricle. In this case, both the mitral and aortic valve remained closed during LVAD support and no blood passed through either valve. This situation would lead to blood thrombosis and valve stenosis. Even in the case of the LV-AA cannulation method, the aortic valve remained closed and no blood passed through the valve because the aortic pressure remained higher than the left ventricular pressure throughout the cardiac cycle. Thus, the LV-AA cannulation method also carries the possibility of aortic stenosis. However, in the case of the AA-DA cannulation method, the mitral and aortic valves opened and closed regularly and positive ejection fraction was provided, so it would not be expected to have such problem as valve stenosis and blood thrombosis.

Use of the LA-AA cannulation method improved coronary perfusion most significantly among the three different cannulation methods tested; coronary perfusion was lowest in the in-series cannulation method, but it did show an improvement of coronary perfusion compared with that in the HF patient without LVAD support. Counter-pulsating LVAD demonstrated better performance than continuous LVAD, which was also demonstrated in our previous study (5). Although this was a simulation study, our results may be used as reference data when considering the clinical use of a LVAD to increase ventricular unloading when expecting cardiac recovery.

To examine different cannulation methods for LVAD support as a bridge to recovery, we theoretically compared cardiovascular response during LVAD supports with LA-AA and AA DA cannulation methods. The effects of the cannulation method on ventricular unloading, ejection fraction of diseased ventricle and coronary perfusion were delineated using a mathematical model of a LVAD-implanted cardiovascular system under HF conditions. The LA-AA cannulation method provided more coronary perfusion than the AA-DA cannulation method, though both methods improved the coronary flow rate compared with that under HF without LVAD support. Indeed, the AA-DA cannulation method provided better performance in ventricular unloading and generated a greater ejection fraction than the LA-AA cannulation method. Each cannulation method had its own advantages and weak points in this study. Thus, these results comprise basis data for the selection of a specific type of cannulation according to the state of the patient when LVAD implantation is needed as a bridge to recovery. In conclusion, the LA-AA method is more advantageous to the increase of ventricular unloading and the AA-DA method is better in the aspect of coronary perfusion.

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AUTHOR SUMMARY**Theoretical Estimation of Cannulation Methods for Left Ventricular Assist Device Support as a Bridge to Recovery**

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Left ventricular assist device (LVAD) support under cannulation connected from the left atrium to the aorta (LA-AA) is used as a bridge to recovery in heart failure (HF) patients. However, it sometimes has serious problems, such as valve stenosis and blood thrombosis. Using mathematical simulation model, we estimated the effect of the in-series cannulation, connected from ascending aorta to descending aorta (AA-DA), on ventricular unloading as an alternative to the LA-AA method. It was predicted that the AA-DA method provided better scores than the LA-AA method.

■ Appendix ■

The time derivative of the eighteen-compartmental volume can be expressed as

$$\frac{dV_i}{dt} = Q_{i,in}(t) - Q_{i,out}(t) \quad (1)$$

where V indicates volume, Q is blood flow rate, t indicates time, i means each compartmental index, in means inflow to i node, and out means outflow from i node.

Each compartmental pressure is calculated as:

$$P_i(t) = \frac{V_i(t) - V_{i,d}}{C_i} \quad (2)$$

where P indicates pressure and $V_{i,d}$ indicates dead volume in the i compartment.

In the compartment of coronary circulation, pressure is calculated as:

$$P_i(t) = P_{i,IMP}(t) + \frac{V_i(t) - V_{i,d}}{C_i} \quad (3)$$

IMP indicates intra-myocardial pressure, which is shown below.

$$P_{i,IMP}(t) = \gamma_{norm} P_{LV}(t) \quad (4)$$

where γ_{norm} is the proportionality factor for left ventricular squeezing.

Compliance of the coronary vein is defined in terms of volume-dependent compliance, as in the equation below. This explains the characteristic of increasing vessel stiffness with progressive distension.

$$C_{CV}(V_{CV}) = \chi [1 - \sigma V_{CV}(t)]^{-1} \cdot \exp[-\sigma(V_{CV}(t) - V_{CV,d})] \quad (5)$$

where CV indicates coronary vein, and χ and σ are derived coefficients for the equation.

Flow resistance of left circumflex artery is not constant but has a volume-dependent value as in the equations below.

$$R_{LCX1}(t) = \begin{cases} R_{LCX} & \text{when } P_{bif} - p_{cap} > 0 \\ R_{LCX} + \beta / (V_{LCX}(t))^2 & \text{when } P_{bif} - p_{cap} < 0 \end{cases} \quad (6)$$

$$R_{LCX2}(t) = \begin{cases} R_{LCX} + \beta / (V_{LCX}(t))^2 & \text{when } P_{cap} - p_{ven} > 0 \\ R_{LCX} & \text{when } P_{cap} - p_{ven} < 0 \end{cases} \quad (7)$$

A detailed explanation of the governing equations and parameters are presented in Heldt et al. (11) and Schreiner et al. (12).