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Hemodynamic Effects of Pressure-Volume Relation in the Atrial Contraction Model on the Total Artificial Heart Using Centrifugal Blood Pumps.

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Abstract— **Hemodynamic effects of atrial contraction with centrifugal pump type total artificial heart is unknown. In this study, we simulated an atrial contraction in a mock model. By the driving condition with higher pressure in the mock atrial model, the load during atrial contraction increased. Based on these findings, we examined atrial contraction in the animal using adult goats. Prior to the measurement, we installed a centrifugal-type ventricular assist device (VADs), and then clamped both ventricles. We measured the hemodynamic data without ventricular contractile functions in order to obtain the effect of atrial contraction on hemodynamics under the condition of the total artificial heart (TAH) circulatory support model. We could estimate the heart rate by revolution number and voltage of pumps. There might be a possibility that we could regulate autonomic nervous response with the control of cardiac output.**

I. Introduction

The number of Japanese outpatients with left ventricular dysfunction is predicted to increase gradually with population growth and to be reached 1.3 million by 2030 [1]. There were 5.8 million people with heart failure (HF) in the United States in 2006 [2], and there were 0.2 million people with end-stage HF. The gold standard therapy for end-stage HF patient is the cardiac transplantation [3]. However, there are many cases that cannot get the cardiac transplantation because their age, complication or changing condition drops them from indication. VAD is the effective therapy for them [4]. In the United States and European countries, the purpose of VAD has changed rapidly from bridge-to-transplantation (BTT) to destination therapy (DT) [5]. Subsequent BiVAD installation may be necessary in about 5% of patients with VAD due to not only the left heart failure but also the right heart failure [6]. Total artificial heart (TAH) systems will be one of the viable alternatives, although there are functional differences between BiVADs and TAHs from the right or left ventricular physiological point of view.

As for the pulsatile TAH, which is commercially available at this moment, some critical issues on thrombosis and its durability are arising by the time of BTT, which is usually expected to be performed within 3 months [7]. Based on clinical evidences, the long-term follow up on the continuous-flow type VADs formed acceptable results for 2 years of awaiting period followed by DT [8]. Furthermore, Frazier, et al reported a trial with a continuous-flow TAH using axial blood pump [9].

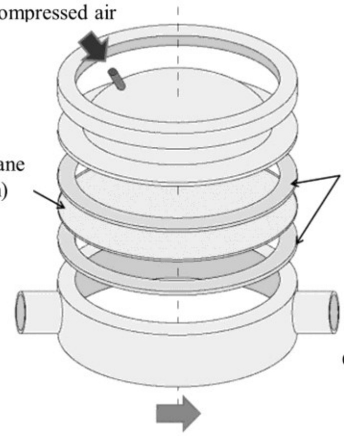

Fig. 1. Schematic illustration of the atrium model.

In this study, we designed a TAH support system which consisted of two centrifugal VAD devices. We preserved the functioning atriums. While some reports suggest that the atrial contraction may partly contribute to cardiac output promotion of the natural heart, the effect of atrial contraction for VAD with centrifugal pump system has not been known. Then, firstly, we performed simulation studies for the effectiveness of atrial contraction with a centrifugal-type TAH support in the mechanical circulatory system. Secondly, we examined the effectiveness of atrial contraction during the functional TAH support in the animal experiments.

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II. Mock Hemodynamic Examination

A. Atrium Model

We developed an atrium model which was capable of representing atrial contraction in the mock circulatory system. The chamber of the atrial model was made of an acrylic cylinder, the inner and outer diameters of which were 100 and 120mm, respectively. A dome-shaped acrylic casing was mounted on the cylinder, and a natural rubber membrane (Nippon Elaster, Ltd., Japan) was sandwiched, which separated the fluid and air chambers. Average height of the fluid chamber was 38 mm, and the maximum volume was designed to be 300mL. We used ePTFE gasket sheets (Japan Gore, Ltd., Japan) for sealing between the casing and cylinder. The schematic illustration of the atrial model developed in this study was shown in Fig. 1.

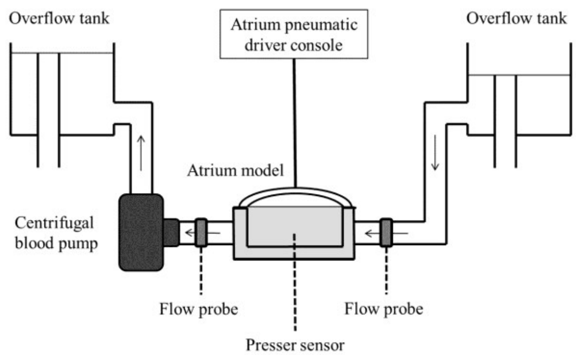

Fig. 2. Schematic illustration of the atrial mock circuit.

B. Controlling of Atrial Contraction Model

We also developed a pneumatic driver for the active contraction in the atrial model. Pressure in the upper air chamber was supplied and controlled by a regulator. We could control the period and timing of the contraction signal for the atrial model by a pulse controller using a microcontroller board (Arduino, MEGA 2590 R3, Italy). The system achieved the synchronous motion with ventricular driving signals in the atrial model, as well as its pumping rate and % systolic duration. During the systolic or diastolic phase, we supplied only pressure along with the passive dilatation of the atrial membrane without vacuum pressure.

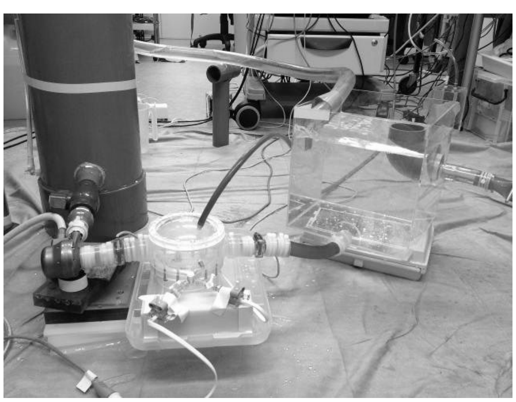

Fig. 3. Whole view of the atrial mock circuit.

C. A mock Circulatory System with the Contractive Atrium

We developed the simulator representing natural hemodynamics to examine the effects of atrial contraction on the function of the centrifugal pump type VAD. Figure 2 shows a schematic illustration of the atrial mock test circuit. The mock system consisted of reservoir tanks, overflow tanks, a VAD pump (EVAHEART^{TM}, Sun Medical Technology Research Corp., Japan) [10], the atrium model, the pneumatic driver. We measured pressure and flow rate at the pressure port and at the inflow and outflow portions of the atrium. Electromagnetic flow probes (Nihon Kohden, Japan) were used and the change of atrial volume was calculated by these data. We used 0.9% normal saline as circulatory media. As shown in Fig. 3, we installed the VAD pump at the outflow portion of the atrium in the mock circuit. We compared the pumping function of the VAD under the two different driving/ loading conditions, which simulated the systemic or pulmonary pressure loadings. We set the revolution number of the VAD under the driving conditions in the right or left heart circulations to be 1400 and 2400 rpm, respectively. We selected the pressure heads by changing the afterload as 80 – 100, and 10–30 mmHg for the left and right heart circulation, respectively. We varied the driving pressure in the atrial model from 5 to 20 mmHg in order to change the contraction force on the atrial membrane.

D. Results

Figure 4 shows pressure waveform obtained with the atrial contraction in the mock circulatory system. As shown in Fig. 5, the additional flow velocity peaks could be derived in the forward flow, whereas the inflow exhibited back flow from the atrial model.

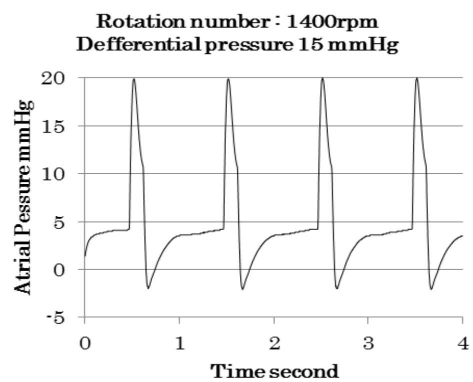

Fig. 4. Atrial pressure waveform in the mock loop.

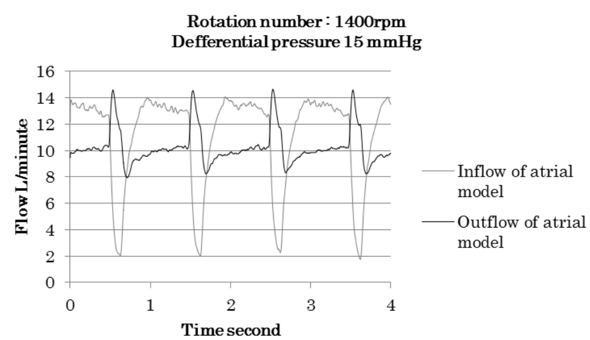

Fig. 5. Inflow and outflow waveforms obtained at the atrial model in the mock test.

Figure 6 shows the relationships between pressure and volume (P-V) calculated at the atrial model during the simulation of right heart circulation with the centrifugal VAD under the condition of active contraction of the atrial model. Figure 7 shows these P-V relations obtained from the mock circulatory system simulating the left heart circulatory conditions. We observed similar characteristics in both P-V loops under the different loading conditions in respect to the left or right ventricular support. The changes in the atrial stroke volume were 20mL, and the atrial pressures were 20/-2mmHg under the condition of 15mmHg supply at the atrium. These hemodynamic data resembled the natural heart functions. We investigated the negative pressure changes in the diastolic phase. By the elevation of driving pressure at the atrial model, the atrial pressure increased. There was no discernible difference in the cardiac output against the changes in the atrial driving pressure.

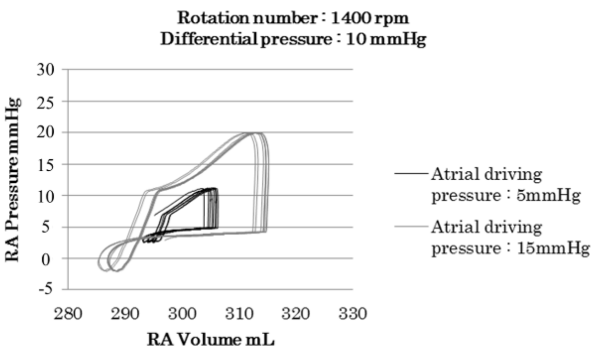

Fig. 6. Pressure-volume relations obtained in the right atrial model in the mock loop.

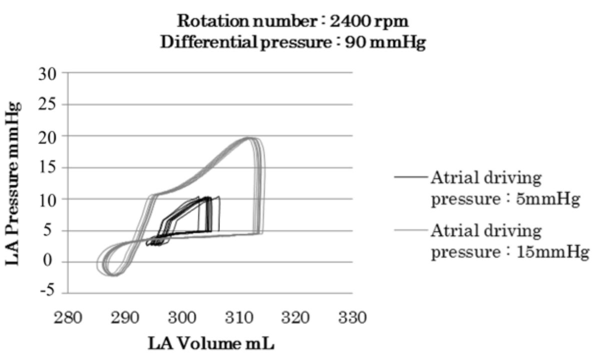

Fig. 7. Pressure-volume relations obtained in the left atrial model in the mock loop.

III. Animal Experiments

Based on the experimental results in the mock examination, we performed animal experiments. All the animal experimental procedure and related activities were reviewed and permitted by the Institutional Animal Use and Care Committee of the Tohoku University.

A. Animal Experiments

We examined the atrial contraction effects under the centrifugal blood pump support on hemodynamics in animal experiments using adult goats, which weighed 37.2–50.0kg. The heart was exposed by the left thoracotomy under general anesthesia. Prior to the measurement, we set up the functional TAH circulation by placing the clamps on both ventricles. Two centrifugal blood pumps (EVAHEART^{TM}) were installed for the systemic and the pulmonary circulation. We made end-to side anastomosis by the ePTFE vascular grafts to the descending aorta or the pulmonary artery, and connected to atriums via the atrial appendage for the inflow of each pump. Then we clamped both ventricles. Figure 9 shows overview of the functional TAH circulatory system. Then we examined the hemodynamic changes. We measured the ECG, the aortic, left atrial, right atrial, and pulmonary artery pressures. We also obtained the pump flow data by using two ultrasonic probes (ME16/19PXN, Transonic Systems Ltd., USA), and the revolution number and voltage in each pump simultaneously.

B. Results

Figure 8 shows an example of the hemodynamics obtained from the goat, which weighed 50.0kg. Atrial contraction wave in the ECG exhibited the synchronization with the atrial pressure changes. Hemodynamic parameters were obtained as follows: a) the right pump; the revolution number was 1250rpm, the pump flow was 2.51L/min, the atrial pressure was 19 / 6mmHg, the pulmonary artery pressure was 27mmHg, b) the left pump; 2370rpm, 2.21L/min, 30 / 10mmHg, respectively, and the arterial pressure was 105mmHg. As shown in the Fig. 8, we recognized the aortic and pulmonary arterial pressure increase by the atrial contraction, which was represented by P wave in the ECG, under the centrifugal blood pump support. By the blood flow through the pumps, the voltage and revolution number in each pump decreased during the atrial contraction phase under the pump control condition of the constant rotational speeds. We observed changes in responsive power consumption in each pump according to the variation of the flow velocity across the pumps by the atrial contractions.

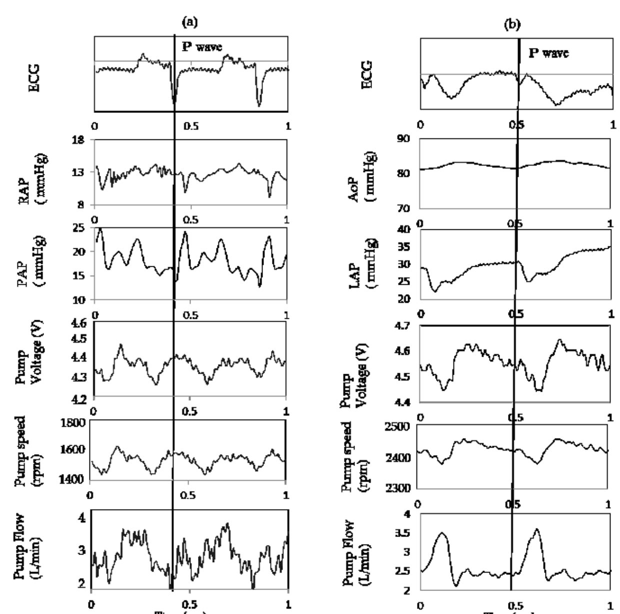

Fig. 8. Changes in parameters by the atrial contraction with the functional TAH support using two centrifugal blood pumps; (a) the right heart , and (b) the left heart circulations. ECG, electrocardiogram; RAP, right atrial pressure; PAP, pulmonary arterial pressure; AoP, aortic pressure; LAP, left atrial pressure.

IV. Discussion

In the mock test, we observed negative pressure changes during the active assistance by the atrial model. The elastic diaphragm might cause a kickback function in diastolic phase. Although the maximum pump flow rate was elevated by the atrial contraction, there was no discernible difference in the cardiac output due to the reciprocating flow at the atrial inflow portion in this mock experiment. As for the natural inflow characteristics of the atriums which are connected to veins, the impedance between the atriums and inflow vessels may change the flow characteristics consequently. We observed instantaneous flow velocity drops in the inflow waveforms as shown in Fig. 5. As the limitation of the mock test was in the calibration of the impedance matching of inflow of the atrium model was calibrated, the forward flow might increase under the optimized conditions with the centrifugal TAH, and we must update the atrium model to more sophisticated simulation of the natural heart.

We obtained the atrial contraction effects across the low-pressure loss centrifugal pump, such as EVAHEART^{TM} in the animal experiment without ventricular functions. During the functional TAH application, there was a difference between the right and left cardiac outputs. To determine the flow distribution patterns, we focused on venous return, coronary perfusion and other circulatory parameters. By monitoring pump power consumption, we might the atrial contraction non-invasively as well as the heart rate. We will be able to build a new feedback control and a co-pulse control to promote or lower the pump flow [11]. Leaving atriums may also be effective in preventing from sucking as a blood reservoir. Patients with chronic atrial fibrillation will be excluded explicitly in the purpose of those applications of pump control.

Fig. 9. Overview of the functional total artificial heart circulatory system in animal.

V. Conclusion

We measured hemodynamic effects of atrial contraction with two centrifugal type artificial hearts for the application as the functional TAH support. We examined the atrial contractile functions by using an originally designed atrial model as well as in animal experiments using goats. The atrial contraction might contribute to the increase of pulsatility during the centrifugal type TAH application without ventricular contractile functions.

References

[1] Y. Okura, M. M. Ramadan, Y. Ohno, et al., "Impending Epidemic Future Projection of Heart Failure in Japan to the Year 2055," *Circ J*, vol. 72, pp. 489–491, 2011.

[2] V. L. Roger, A. S. Go, D. M. Lloyd-Jones, et al., "Heart Disease and Stroke Statistics--2011 Update: A Report From the American Heart Association," *Circulation*, vol. 123, pp. e18–e209, 2010.

[3] M. R. Mehra, J. Kobashigawa, R. Starling, et al., "Listing criteria for heart transplantation: International Society for Heart and Lung Transplantation guidelines for the care of cardiac transplant candidates--2006," *J Heart Lung Transplant* : the official publication of the International Society for Heart Transplantation, vol. 25, pp. 1024–42, Sep. 2006.

[4] E. A. Rose, A. C. Gelijns, A. J. Moskowitz, et al., "Long-term use of a left ventricular assist device for end-stage heart failure," *N Engl J Med*, vol. 345, pp. 1435–43, Nov. 2001.

[5] J. K. Kirklin, D. C. Naftel, F. D. Pagani, et al., "Long-term mechanical circulatory support (destination therapy): on track to compete with heart transplantation?," *J Thorac Cardiovasc Surg*, vol. 144, pp. 584-603; discussion 597–8, Sep. 2012.

[6] J. K. Kirklin, D. C. Naftel, R. L. Kormos, et al., "The Fourth INTERMACS Annual Report: 4,000 implants and counting," *J Heart Lung Transplant* : the official publication of the International Society for Heart Transplantation, vol. 31, pp. 117–26, Feb 2012.

[7] K. Friedline and P. Hassinger, "Total artificial heart freedom driver in a patient with end-stage biventricular heart failure," *AANA journal*, vol. 80, pp. 105–12, Apr 2012.

[8] M. S. Slaughter, J. G. Rogers, C. A. Milano, et al., "Advanced heart failure treated with continuous-flow left ventricular assist device," The New England journal of medicine, vol. 361, pp. 2241–51, Dec 3 2009.

[9] O. H. Frazier, W. E. Cohn, E. Tuzun, et al., "Continuous-flow total artificial heart supports long-term survival of a calf," *Tex Heart Inst J*, vol. 36, pp. 568–74, 2009.

[10] K. Yamazaki, S. Saito, S. Kihara, et al., "Completely pulsatile high flow circulatory support with a constant-speed centrifugal blood pump: mechanisms and early clinical observations," *Gen Thorac Cardiovasc Surg*, vol. 55, pp. 158–62, Apr 2007.

[11] A. Tanaka, M. Yoshizawa, K. Abe, et al., "Open-loop analysis of transfer characteristics from blood pressure to heart rate using an effectively total artificial heart," *J Artif Organs*, vol. 28, pp. 109–14, Jan 2004.