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ORIGINAL ARTICLE

Development of a novel drive mode to prevent aortic insufficiency during continuous-flow LVAD support by synchronizing rotational speed with heartbeat

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Abstract Aortic insufficiency (AI) is a serious complication for patients on long-term support with left ventricular assist devices (LVAD). Postoperative aortic valve opening is an important predictor of AI. A system is presently available that can promote native aortic flow by reducing rotational speed (RS) for defined intervals. However, this system can cause a reduction in pump flow and lead to insufficient support. We therefore developed a novel "delayed copulse mode" to prevent AI by providing both minimal support for early systole and maximal support shortly after aortic valve opening by changing the RS in synchronization with heartbeat. To evaluate whether our drive mode could open the aortic valve while maintaining a high total flow (sum of pump flow and native aortic flow), we installed a centrifugal LVAD (EVAHEART®; Sun Medical) in seven goats each with normal hearts and acute LV dysfunction created by micro-embolization of the coronary artery. We intermittently switched the drive mode from continuous (constant RS) with 100 % bypass to delayed copulse mode with 90 % bypass. Total flow did not significantly change between the two modes. The aortic valve opened when the delayed copulse mode was activated. The delayed copulse mode allowed the aortic valve to open while maintaining a high total flow. This novel drive mode may considerably benefit patients with severe heart failure on long-term LVAD support by preventing AI.

Keywords Delayed copulse mode · Aortic valve opening · Aortic insufficiency · Continuous-flow LVAD · Synchronization with heartbeat

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Introduction

Left ventricular assist devices (LVAD) have become widely applied as a therapeutic option for patients with end-stage heart failure, and long-term LVAD support has become more important not only as a bridge to transplantation, but also as a destination therapy [1]. However, native aortic insufficiency (AI) can develop during long-term LVAD support [2–4]. Severe AI can lead to reduced forward cardiac output and increased LV preload due to recycling regurgitant blood flow from the LVAD outflow graft into the left ventricular inflow cannula, which in turn decreases the effectiveness of LVAD support and results in end-organ malperfusion. Survival rates are significantly worse for patients with, than without, AI [5]. Closure of the aortic valve after LVAD implantation is a significant predictor of AI [3–6]. Persistent closure of the aortic valve after LVAD implantation might promote reduced valve pliability and commissural fusion, consequently resulting in the occurrence or progression of AI. The aortic valve must be able to open on demand during LVAD support to prevent AI. The intermittent low-speed (ILS) mode promotes native aortic flow (AoF) by reducing rotational speed (RS) for a defined interval. However, this system is inappropriate for patients with severe heart failure because it can result in support flow that is insufficient to meet the requirements of patients. A methodology to resolve this issue is not available. Therefore, we developed a "delayed copulse mode" that can prevent AI by synchronization with the cardiac cycle in continuous-flow LVAD. The aim of this mode is to provide both minimal support during early systole to open the aortic valve and maximal support shortly after the valve has opened to maintain high pump flow (PF). Here, we compared the effects of this mode on aortic valve opening and PF with the ILS mode in animal models of normal and acute ischemic heart failure.

Materials and methods

Experimental preparation

We studied seven goats (52.6 ± 4.1 kg) with normal hearts and seven (52.3 ± 4.9 kg) with acute LV dysfunction created by coronary microsphere embolization of the left anterior descending coronary artery (LAD). All animals were sedated with an intramuscular injection of ketamine (10 mg/kg). General anesthesia was induced and maintained by isoflurane inhalation (1–3 vol/100 mL in oxygen). The animals were fixed in the right lateral recumbent position, intubated and mechanically ventilated. The fifth costal bone was resected via a left thoracotomy and the heart was approached through the left thoracic space. A centrifugal LVAD (EVAHEART; Sun Medical Technology Research Corporation, Nagano, Japan) was installed [7, 8] after heparinization (300 U/kg) by inserting the inflow cannula into the left ventricular apex and suturing the outflow graft to the descending aorta. Blood flow in the ascending aorta and LVAD was measured using electromagnetic (EMF-1000: diameter, 16–18 mm; Nihon Kohden, Tokyo, Japan) and ultrasonic (TS420: 16 mm; Transonic Systems) flow meters, respectively. Pressure lines for monitoring aortic (AoP) and central venous pressure (CVP) were established from the left internal thoracic artery and the left internal thoracic veins, and a pressure line for left ventricular pressure (LVP) monitoring was inserted into the left ventricle from the anterior wall. Pacing leads for ventricular electrocardiography were sutured onto the anterior wall of the right ventricle. The vital data described above were recorded using Labchart 5 software (ADInstruments, Bella Vista NSW, Australia). We calculated the instantaneous left ventricular-aortic pressure gradient (LV-Ao PG) by subtracting AoP from LVP. We evaluated aortic valve opening by echocardiography, and measured the aortic valve area (AVA) by echocardiographic planimetry.

The animals used in this study were maintained in accordance with the guidelines of the Committee on Animal Studies at the National Cerebral and Cardiovascular Center. This study was approved by the National Cerebral and Cardiovascular Center Animal Investigation Committee. Institutional guidelines for the care and use of laboratory animals were observed.

Making left ventricular dysfunction models

We created animal models of acute ischemic heart failure by micro-embolizing the LAD as described [9–11]. A multipurpose, 4 Fr Judkins catheter (Create Medic Co. Ltd., Yokohama, Japan) was introduced through a long sheath (4 Fr × 17 cm) into the left carotid artery towards the LAD under fluoroscopic guidance. We then injected $3.14 \pm 0.29 \times 10^4$ microspheres (diameter, 75 μm; 600/kg) into the LAD. We planned to reduce and then maintain cardiac output at about 60 % of the native heart function determined before creating the model of acute ischemic heart failure. After 30 min of observation, we collected data to assure stable optimal cardiac function. We stabilized the AoP and CVP throughout the experiment to ensure that heart afterload or preload remained constant, and that heart rate also remained constant by adjusting infusion volumes and changing the depth of anesthesia. Neither vasodilators nor catecholamines were used. Ventricular arrhythmias were prevented during the experiment using 2 % lidocaine (1 mg/kg/h).

Study protocol and drive mode

We previously described a novel pump controller in which the RS changes in synchrony with the cardiac cycle [12–18]. The controller can detect R waves from the ventricular ECG and momentarily change the RS to target speed. The RS was controlled using the delayed copulse mode in each of the early systolic, ejection period and diastolic phases of the cardiac cycle (Fig. 1). During early systole, LVP must exceed AoP to allow the aortic valve to open, and some left ventricular end diastolic volume (LVEDV) is needed to increase LVP. Therefore, we adjusted the RS of diastole to avoid inducing reverse flow. We set the RS of early systole at 700 rpm (the minimum RS for this LVAD) to minimize early systole support. Thereafter, we momentarily increased the RS of the ejection period and adjusted the RS to achieve the appropriate bypass rate to maintain high support flow. We defined early systole, ejection period and diastole as 11, 22 and 67 % of the RR interval, respectively and compared the following drive modes.

The first was the intermittent delayed copulse (IDCO) mode that was intermittently activated for every 10 of 80 cardiac beats with a triggered R wave. This means that for

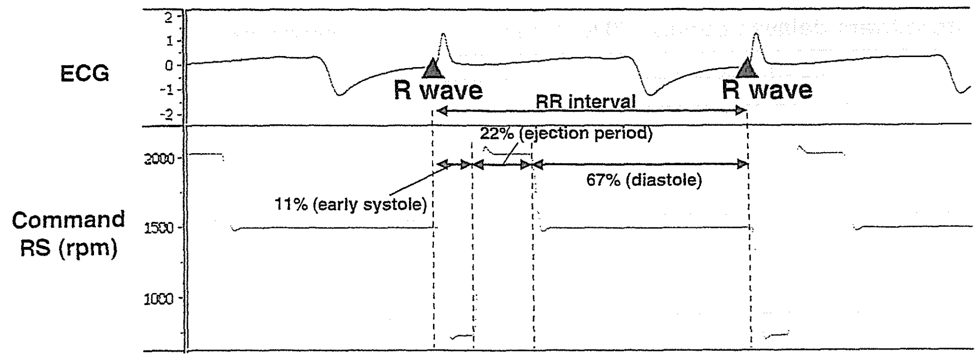

Fig. 1 Command rotational speed in delayed copulse mode. *ECG* electrocardiogram, *RS* rotational speed. Pumps were driven at early systolic RS of 700 rpm from R-wave input for 11 % of RR interval. Ejection period RS increased to target speed and was maintained for 22 % of RR interval. Diastolic RS instantly reduced to achieve diastolic PF of ~0 L/min, maintained RS for remaining 67 % of RR interval, and finally returned to initial early systolic RS of 700 rpm

70 beats we ran continuous mode (constant RS) and then switched to delayed copulse mode for the next 10 beats. The bypass rate (BR) was set at around 100 and 90 % in the continuous and delayed copulse modes, respectively. The second was the ILS mode using a Jarvik 2000 (Jarvik Heart Inc., New York, NY, USA) [19] as follows. We decreased the RS from 100 % bypass to low speed (1,200 rpm) for 10 of 80 heartbeats. We calculated BR by dividing PF by total flow (TF: sum of PF and AoF) and then assessed the effects of the delayed copulse and low-speed modes upon aortic valve opening, PF, AoF, and hemodynamic parameters. All data were compared with those generated using a circuit clamp (no pump support) as a control condition (Table 2; Figs. 3, 5).

Statistics

All numerical data are shown as averages ± standard deviation (SD). Groups were compared using a repeated-measures analysis of variance followed by Tukey's multiple comparison test. All analyses were two-sided, and a p value <0.05 was considered statistically significant. All data were analyzed using PASW Statistics ver. 20 (IBM SPSS).

Results

Table 1 shows the average RS in the continuous and delayed copulse modes. The RS required to achieve 100 % bypass in continuous mode was around 1,800 and 1,650 rpm in the animal models with a normal heart and in those with acute ischemic heart failure, respectively. The RS of the ejection period needed to achieve 90 % bypass in delayed copulse mode was ~2,100 and 2,000 rpm in the animals with a normal heart and in the models, respectively. The RS of diastolic phase required to avoid reverse flow in delayed copulse mode was 1,700 and 1,450 rpm in the animal models with a normal heart and with acute ischemic heart failure, respectively. Figure 2 shows typical waveforms of pressure and flow data when continuous mode with 100 % bypass was switched to either the delayed copulse or the low-speed mode in the models of acute ischemic heart failure. The AoF increased and the PF slightly decreased in delayed copulse mode. The AoF increased and the PF significantly decreased along with the RS reduction in the low-speed mode. Pulse pressure and the instantaneous maximum LV-Ao PG were increased in both the delayed copulse and low-speed modes when activated.

Table 1 Rotational speed

Mode (rpm)	Continuous mode	Delayed copulse mode
Normal heart		
Early systolic RS	1,800 ± 82	700 ± 0
RS of ejection period	1,800 ± 82	2,100 ± 129
Diastolic RS	1,800 ± 82	1,550 ± 87
Heart failure		
Early systolic RS	1,729 ± 76	700 ± 0
RS of ejection period	1,729 ± 76	2,050 ± 217
Diastolic RS	1,729 ± 76	1,471 ± 95

Data are shown as averages ± standard deviation

RS rotational speed

Table 2 shows numerical hemodynamic data. Changes in heart rate and mean AoP did not significantly differ between continuous and either delayed copulse or low-speed modes. Pulse pressure significantly increased in both delayed copulse and low-speed modes, compared with the continuous mode ($p < 0.05$). Left ventricular end systolic pressure (LVESP) and mean LVP tended to be higher in both delayed copulse and low-speed modes, than in the

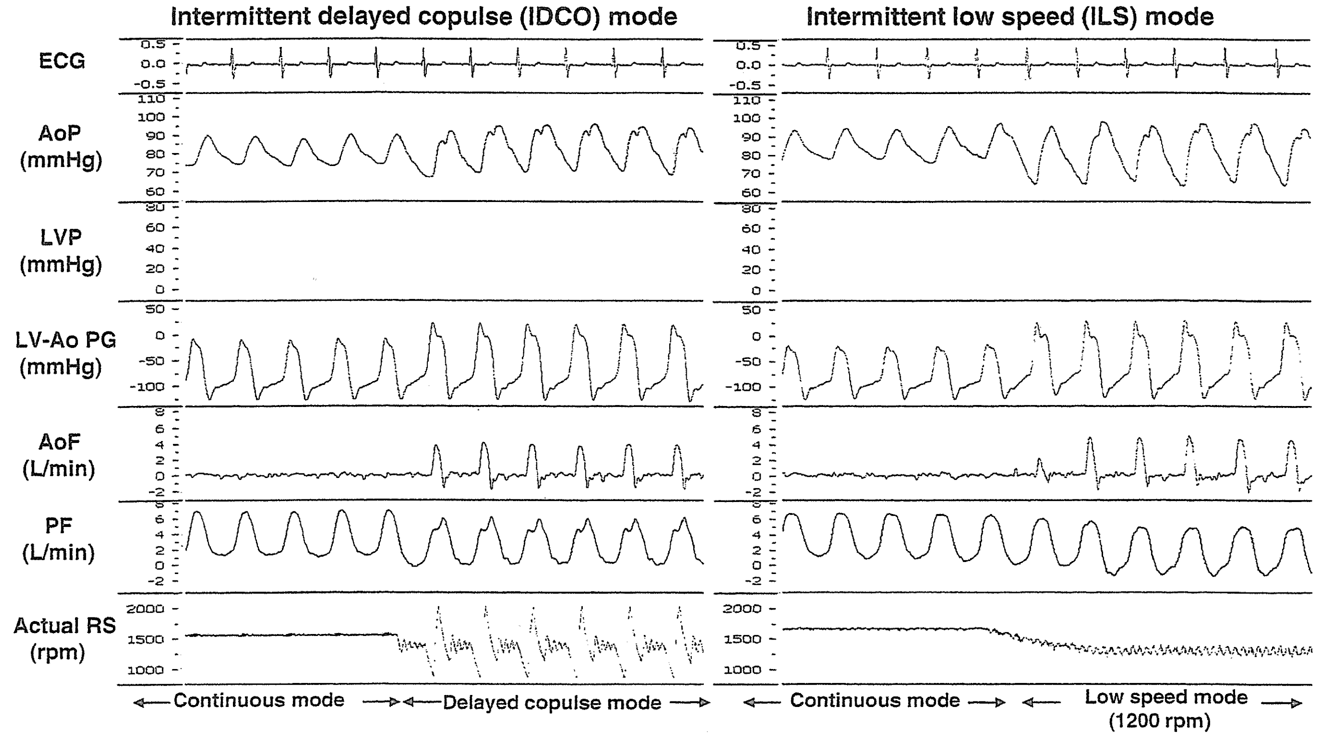

Fig. 2 Sample waveforms of pressure and flow data. *AoF* ascending aortic flow, *AoP* aortic pressure, *ECG* electrocardiogram, *IDCO* intermittent delayed copulse, *ILS* intermittent low speed, *LV-Ao* left ventricular-aortic pressure gradient, *LVP* left ventricular pressure, *PF* pump flow, *RS* rotational speed. Waveforms typical at the portion switched from continuous mode with 100 % bypass to either delayed copulse or low-speed (1,200 rpm) mode in animal models of acute ischemic heart failure. AoF increased and PF slightly decreased in delayed copulse mode. AoF increased and PF significantly decreased along with reduction of RS in low-speed mode. Pulse pressure and maximal LV-Ao PG were instantaneously increased in both delayed copulse and low-speed modes when activated

continuous mode. Instantaneous maximum LV-Ao PG was obviously increased in both delayed copulse and low-speed modes ($p < 0.05$). Left ventricular end diastolic pressure (LVEDP) significantly differed between the delayed copulse and low-speed modes in the models of acute heart failure. Delayed copulse mode activation improved pulsatility and LVEDP did not significantly change.

Figure 3a, b show the 80-beat average of TF in circuit-clamp, continuous, IDCO, and ILS modes. The TF in IDCO mode tended to be larger than that in the ILS mode, but the difference did not reach significance. Figures 3c, d show a 10-beat average of TF when the delayed copulse and the low-speed modes are activated, and in circuit-clamp, continuous mode. When the drive mode was switched from continuous to low-speed mode, PF significantly decreased, but the native heart could not keep up with it, and thus TF decreased ($p < 0.01$). The decreased ratio of TF was higher in the models (37.8 ± 8.8 %) than in animals with a normal heart (31.4 ± 10.3 %). On the other hand, TF in delayed copulse mode did not significantly change in animals with a normal heart and in the models of acute ischemic heart disease.

Figure 4 shows echocardiography in the short axis view of the aortic valve in models of acute ischemic heart failure. The aortic valve did not open in the continuous mode with 100 % bypass. Valve opening was better in the delayed copulse, than in the low-speed mode.

Figure 5 shows changes in AVA after the mode switch. The AVA significantly increased after switching the drive mode in both the delayed copulse and low-speed modes in the models ($p < 0.01$). In animal models of acute heart failure, the AVA in the delayed copulse mode was larger than in the low-speed mode ($p < 0.01$). These results indicated that the aortic valve opened in delayed copulse mode while high TF was maintained. However, TF decreased in the low-speed mode after the aortic valve opened.

Discussion

The REMATCH trial demonstrated that long-term mechanical cardiac support is clinically effective as destination therapy [20], and thus LVADs have become increasingly popular as long-term therapy for patients with end-stage heart failure. However, prolonged LVAD support remarkably alters cardiac and vascular physiology and function. The development of AI during long-term LVAD

Table 2 Pressure data

Mode	Circuit-clamp	Continuous	Delayed copulse	low-speed (1,200 rpm)
Normal heart				
Heart rate (bpm)	79.9 ± 19.1	80.2 ± 20.5	75.3 ± 23.0	80.9 ± 19.7
Mean AoP (mmHg)	62.9 ± 10.1	65.9 ± 7.2	59.6 ± 13.0	58.6 ± 9.8
Pulse pressure (mmHg)	35.4 ± 4.6	19.6 ± 7.2	28.3 ± 6.0*	36.3 ± 5.8*
Mean LVP (mmHg)	38.4 ± 10.2	24.1 ± 9.4	29.7 ± 9.0	36.8 ± 10.8
LVESP (mmHg)	89.2 ± 12.3	68.7 ± 9.0	82.8 ± 14.8	86.0 ± 13.6*
LVEDP (mmHg)	10.1 ± 5.4	7.07 ± 5.7	8.3 ± 4.4	12.0 ± 7.2
Max LV-Ao PG (mmHg)	32.2 ± 4.6	−0.9 ± 6.4	28.8 ± 5.2*	27.8 ± 7.6*
Bypass rate (%)[a]	0.0 ± 0.0	100.5 ± 1.9	90.0 ± 4.8*	36.0 ± 8.0*,†
Heart failure				
Heart rate (bpm)	76.1 ± 7.9	74.1 ± 9.0	71.9 ± 9.7	74.3 ± 8.6
Mean AoP (mmHg)	59.7 ± 12.9	62.9 ± 10.1	59.5 ± 10.9	58.4 ± 12.2
Pulse pressure (mmHg)	28.9 ± 4.8	17.2 ± 8.3	29.3 ± 8.0*	29.6 ± 4.7*
Mean LVP (mmHg)	37.5 ± 9.5	22.6 ± 8.7	31.1 ± 5.1	31.2 ± 7.8
LVESP (mmHg)	81.4 ± 15.6	58.6 ± 18.7	72.5 ± 11.4	72.0 ± 10.6
LVEDP (mmHg)	24.6 ± 3.1	18.5 ± 2.6	19.9 ± 1.9	25.3 ± 3.4*,†
Maximal LV-Ao PG (mmHg)	22.8 ± 4.5	−10.9 ± 13.9	20.4 ± 4.1*	13.2 ± 2.7*,†
Bypass rate (%)[a]	0.0 ± 0.0	107.5 ± 9.8	88.5 ± 4.4*	79.5 ± 8.0*,†

All data are shown as averages ± standard deviation

AoF Ascending aortic flow, *AoP* aortic pressure, *AVA* aortic valve area, *LVEDP* left ventricular end diastolic pressure, *LVESP* left ventricular end systolic pressure, *LVP* left ventricular pressure, *PF* pump flow, *PG* pressure gradient, *TF* total flow (sum of PF and AoF)

* $p < 0.05$ and † $p < 0.05$ compared with continuous and delayed copulse mode, respectively

[a] Bypass rate, calculated by dividing PF by sum of PF and AoF

is regarded as the most important complication, because survival is significantly worse for patients with, than without, AI due to insufficient LVAD support and end-organ mal-perfusion [5].

Less frequent aortic valve opening significantly correlates with more severe AI [3–6], and Hatano et al. [4] reported that the incidence of AI is higher in patients with a continuous-flow than with a pulsatile-flow LVAD. Because almost all pulsatile devices function in asynchrony with the native cardiac cycle, the loading condition of the LV changes with each heartbeat. Therefore, the aortic valve is more likely to open in patients with pulsatile- than with continuous-flow LVADs. Among preoperative clinical parameters, a lower LV ejection fraction is an independent risk factor for the development of AI [4, 5]. Poor LV contractile function might contribute to inefficient aortic valve opening. Toda et al. [5] reported that preoperative functional mitral regurgitation (MR) is related to AI progression. This is because severe MR could lead to the aortic valve opening less frequently due to regurgitant blood flowing into the left atrium during LVAD support.

The loss of pulsatility caused by continuous-flow LVADs seems to closely correlate with AI development. A healthy aortic valve has a significantly redundant coaptation surface. The coaptation area of the normal aortic valve is directly related to the diameter of the aortic root, which is sensitive to root pressure [21]. We speculated that the same hemodynamic alterations induced by continuous-flow LVAD, loss of pulsatility and persistent elevation of aortic root pressure, cause aortic root dilation. Pressure in the ascending aorta is persistently higher than LVP in such patients and native aortic valves consequently do not open.

Mudd et al. [6] found evidence that a commissural fusion in eight of nine patients with continuous-flow LVAD correlated with decreased valve opening and an increasing prevalence of AI. Letsou et al. [22] identified some degree of commissural fusion in 51.5 % of patients on LVAD support, and a histopathological examination of areas of fusion revealed loose fibrous tissue between commissures. Pak et al. [3] identified significantly larger aortic root circumferences in patients with, than without AI.

From the above, we speculate that the main causes of AI are persistent aortic valve closure and elevated aortic root pressure. These can lead to commissural fusion, reduced valve pliability, and aortic root dilation, and consequently result in the occurrence or development of AI during long-term LVAD support. To open the aortic valve and improve pulsatility, pump flow should be reduced to promote the native AoF. However, this can reduce support flow and result in insufficient support to meet physiological requirements. Our delayed copulse mode can resolve these issues.

Our results showed that the delayed copulse mode could open the aortic valve and improve pulsatility while maintaining high bypass flow. The delayed copulse mode is characterized by minimal support of the early systolic phase and maximal support soon after the aortic valve has

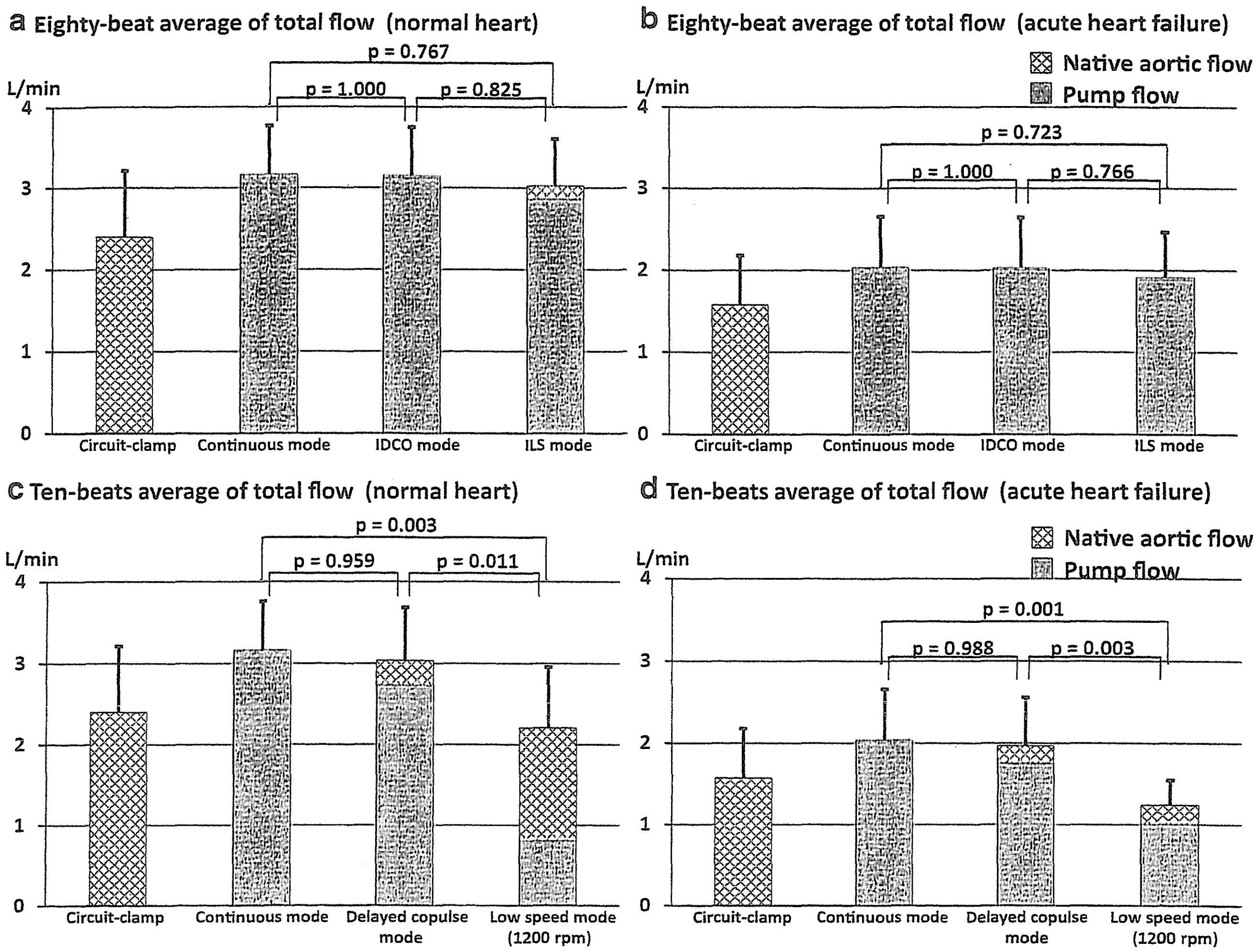

Fig. 3 **a**, **b** 80-beat average of total flow (TF) data in circuit-clamp (control condition), continuous, intermittent delayed copulse (IDCO) and intermittent low-speed (ILS) modes. TF, sum of pump (*blue*) and native aortic (*red*) flow. Continuous, IDCO and ILS modes did not significantly differ in normal animals (**a**) and in models of acute heart failure (**b**). Total flow in IDCO mode tended to be larger than in the ILS mode, but the two modes did not significantly differ between these two modes in both groups of animals. Figure 3c, d 10-beat average of total flow (TF) data in circuit-clamp (control condition), continuous, delayed copulse and low-speed (1,200 rpm) modes. *TF* sum of pump (*blue*) and native aortic (*red*) flow. During mode switch, TF did not significantly change between continuous and the delayed copulse modes in normal animals (**c**) and in models of acute heart failure (**d**). After mode switch, TF significantly decreased between continuous and low-speed modes in both groups of animals. Delayed copulse and low-speed modes also significantly differed in both groups of animals

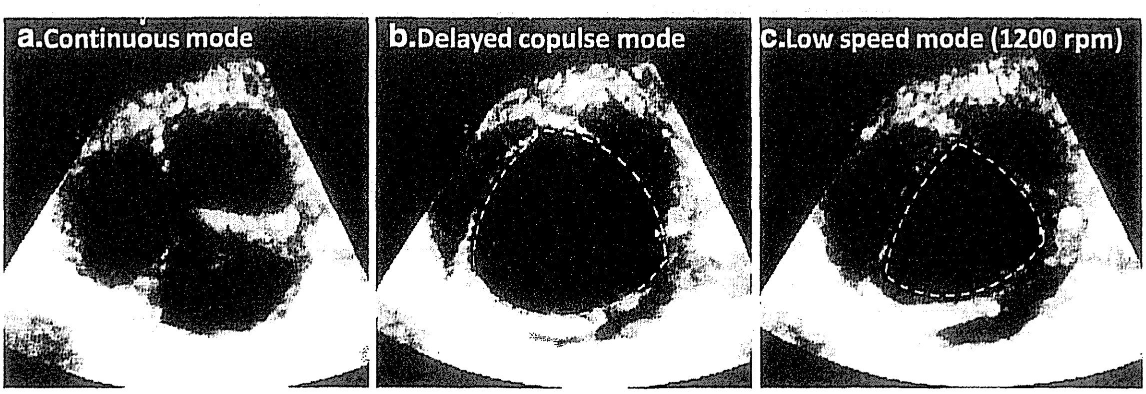

Fig. 4 Echocardiography in short axis view of aortic valve in animal models of acute ischemic heart failure (**a**, **b** and **c**, continuous, delayed and low-speed (1,200 rpm) modes, respectively), *Dotted line* maximal aortic valve area in each mode. Aortic valve did not open in continuous mode (**a**), but opened more efficiently in delayed copulse, than in low-speed mode (**b**, **c**)

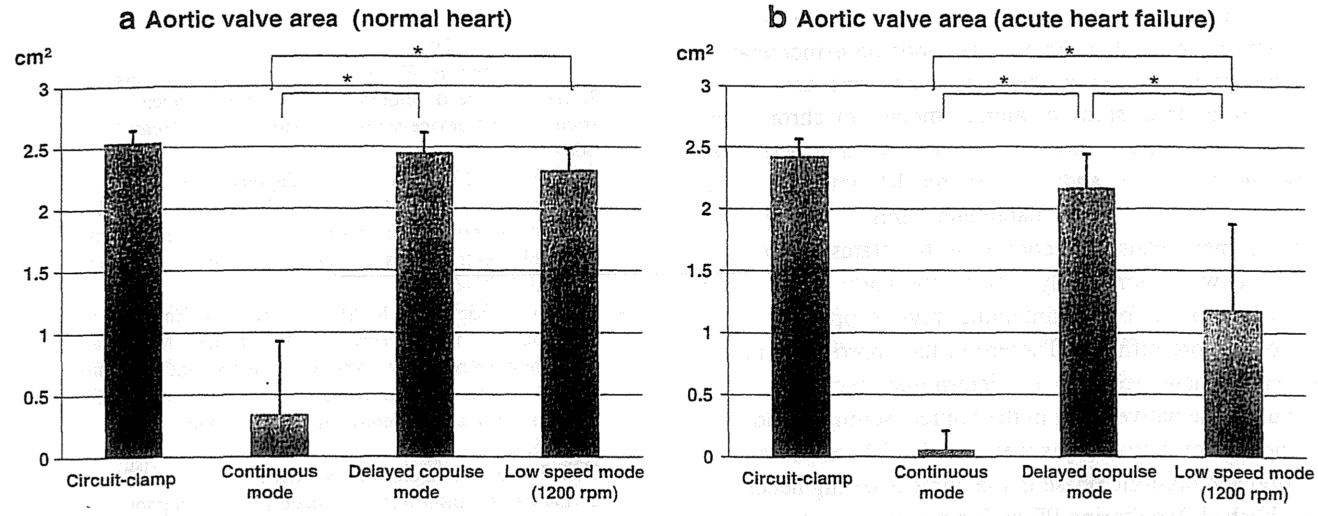

Fig. 5 Aortic valve area (AVA) in circuit-clamp (control condition), continuous, delayed copulse and low-speed (1,200 rpm) modes. *Asterisk* significant difference ($p < 0.01$). After switching, AVA significantly increased in both delayed copulse and low-speed modes (**a**, **b**) and these two modes significantly differed (**b**) in animal models of acute heart failure ($p < 0.01$)

opened. Therefore, this unique drive mode can open the aortic valve while maintaining high bypass flow. The delayed copulse mode could open the aortic valve without reducing the TF not only in the normal heart but also in the animal models of acute heart failure. These findings indicate that the delayed copulse mode will be effective for patients with low cardiac output. Furthermore, because LVEDP did not significantly change between continuous mode and delayed copulse modes, the latter might be able to maintain adequate LV unloading.

We demonstrated that the 80-beat average of TF in the ILS mode tended to be smaller than that in the continuous mode, and that the two modes did not significantly differ (Fig. 3a, b). However, TF significantly decreased when the low-speed mode was activated (Fig. 3c, d). This tendency was evident in animal models of acute heart failure with LV dysfunction compared with animals with a normal heart. We speculate that preprogrammed intermittent reduction of pump speed can maintain TF for long periods, but this also has a risk of not providing sufficient support to meet physiological requirements at slow pump speeds. From this perspective, we believe that the delayed copulse mode carried an extremely small risk of insufficient support that could result in transient ischemic attacks.

The EVAHEART is an implantable centrifugal blood pump with a flat pressure-flow curve that can provide a significantly high PF rate. This feature can provide higher flow during systole and lower flow during diastole, thus providing pulsatile high-flow, which can solve the current clinical problems with the continuous-flow LVAD [7, 8]. With respect to AI, higher flow during systole might interfere with aortic valve opening. In contrast, high pulsatility might prevent AI development because of a lower pressure effect during diastole. Therefore, we speculate that the EVAHEART confers both an advantage and a disadvantage against AI. The concept of the delayed copulse mode is to overcome the disadvantage by opening the aortic valve and to enhance the advantage by improving its pulsatility.

The delayed copulse mode has some possible negative aspects. First, it might elevate hemolysis levels due to high shear stress caused by a momentary increase in the RS. The effects on blood should be evaluated using hemolysis tests in vitro and by long-term studies of animal models of chronic heart failure. The long-term effects on device durability should be similarly evaluated. The delayed copulse mode might increase regurgitant blood flow during early diastole in patients with extant mild AI, because the pressure effect caused by an increase of the RS during the ejection period can be slightly delayed. However, even if patients have mild AI before LVAD implantation, the likelihood that LV preload increases in the delayed copulse mode is hardly conceivable. This is because we adjusted the RS of diastole to avoid inducing reverse flow in delayed copulse mode, and thus regurgitant blood flow can be reduced during the mid- and late-diastole as compared with continuous mode.

The present study has several limitations. Our results are based on animals with a normal heart and an animal model of acute ischemic heart failure. Thus, to determine whether or not the same results would apply to chronic heart failure in the clinical setting is difficult. We have not yet examined the effectiveness of the long-term application of the delayed copulse mode, or its effects on pathological changes of the aortic valve. We have started to evaluate the effects of delayed copulse mode on the native heart in animal models of chronic heart failure. We aim to assess the effects of the delayed copulse mode on hemodynamics, pathological changes in the aortic valve and device durability in a larger study of animal models of chronic heart failure. We defined early systole, the ejection period, and diastole as 11, 22, and 67 % of the RR interval, respectively. However, these parameters might widely differ among individuals or according to the status of the native heart. If we prolong early systole, the aortic valve will be easier to open, but maintaining high support flow will become more difficult. Therefore, the appropriate interval of each phase needs to be determined according to the status of the native heart in the clinical setting. In addition, a method of actual adjustment of the RS of the ejection period and diastolic phase in the clinical setting needs to be established. Monitoring PF during pump support is difficult with the current system and BR needs to be estimated in the clinical setting by echocardiography. The delayed copulse mode was intermittently activated for every 10 out of 80 cardiac beats with a triggered R wave. However, it is not possible to determine whether this intermittent interval is optimal for preventing AI during long-term LVAD support from experiments on animals with acute conditions. Delayed copulse mode should perhaps be activated throughout sleep. However, the optimal method for preventing AI remains unclear.

Conclusions

Our delayed copulse mode allowed aortic valve opening while maintaining high pump flow in goats with normal and acute ischemic hearts. This novel drive mode might confer considerable benefits upon patients with chronic heart failure on long-term LVAD support by preventing AI. Further investigation is currently underway in models of chronic heart failure.

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Conflict of interest The authors have no conflicts of interest to disclose.

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ORIGINAL ARTICLE

Development and evaluation of endurance test system for ventricular assist devices

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Abstract We developed a novel endurance test system that can arbitrarily set various circulatory conditions and has durability and stability for long-term continuous evaluation of ventricular assist devices (VADs), and we evaluated its fundamental performance and prolonged durability and stability. The circulation circuit of the present endurance test system consisted of a pulsatile pump with a small closed chamber (SCC), a closed chamber, a reservoir and an electromagnetic proportional valve. Two duckbill valves were mounted in the inlet and outlet of the pulsatile pump. The features of the circulation circuit are as follows: (1) the components of the circulation circuit consist of optimized industrial devices, giving durability; (2) the pulsatile pump can change the heart rate and stroke length (SL), as well as its compliance using the SCC. Therefore, the endurance test system can quantitatively reproduce various circulatory conditions. The range of reproducible circulatory conditions in the endurance test circuit was examined in terms of fundamental performance. Additionally, continuous operation for 6 months was performed in order to evaluate the durability and stability. The circulation circuit was able to set up a wide range of pressure and total flow conditions using the SCC and adjusting the pulsatile pump SL. The long-term continuous operation test demonstrated that stable, continuous operation for 6 months was possible without leakage or industrial device failure. The newly developed endurance test system demonstrated a wide range of reproducible circulatory conditions, durability and stability, and is a promising approach for evaluating the basic characteristics of VADs.

Keywords Endurance test · Circulation circuit · Ventricular assist devices (VADs) · Pulse duplicator · Field: artificial heart (basic)

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Introduction

Ventricular assist devices (VADs) are widely used in patients with serious heart failure [1–4]. VADs require validity, safety and reliability; therefore, it is necessary to conduct animal experiments and pump performance tests, hemolysis tests and endurance tests, and the performance of VADs must be fully evaluated in order to extract and analyze potential problems in preclinical studies [5–9]. In particular, implantable VADs have become mainstream in recent years; therefore, durability and reliability are required for VADs that will be used in the body for long periods of time. Therefore, it is necessary to evaluate VADs over long periods of time under physiologically relevant pulsatile load conditions using test equipment that can reproduce the circulatory conditions of the living human body [10].

Test equipment using a pulse duplicator with a flexible diaphragm or sac similar to a ventricle has been proposed in order to generate pulsatile flow similar to circulatory conditions [11–13]. There was a report that the diaphragm which was used as pulse duplicator of the endurance test had to be exchanged because a crack occurred in the diaphragm [11]. Additionally, breakage of the diaphragm of a pneumatic pulsatile VAD was also reported at the 17th Japanese association for clinical ventricular assist systems, held in 2011. Thus, diaphragms or sacs made from flexible materials have the possibility of fatigue or fracture after long-term continuous operation. The evaluation of VADs may possibly be influenced when diaphragm breakage in the test equipment occurs during the process of the durability test. Therefore, the test equipment requires durability and stability that can be continually driven for long periods of time without device failure.

In addition, the development of VADs for children has been promoted in recent years [14–17]. It is necessary to evaluate these devices on each target specification because the circulatory conditions of the living human body are not uniform. Therefore, it is necessary that the test equipment is versatile and can simulate various circulatory conditions for a range of devices.

There is an industrial pulsatile pump which has an active filling mechanism as a pulsatile pump with durability. However, since this industrial pulsatile pump is a constant volume pump, there is no compliance in this pulsatile pump. It is difficult to simulate a ventricle with compliance using this pulsatile pump. Therefore, we recently proposed giving compliance to the industrial pulsatile pump with durability by connecting a closed chamber to the pulsatile pump in order to simulate a circulatory condition similar to that of hemodynamics in the living human body. In addition, various circulatory conditions can be quantitatively simulated by varying the compliance of the pulsatile pump. Thus, we developed a novel endurance test system which can simulate various circulatory conditions with durability and stability by applying the industrial pulsatile pump and the closed chamber. The present study describes the evaluation of the reproduction of pulsatility due to the effect of the closed chamber connected to the pulsatile pump and an investigation into the range of reproducible circulatory conditions by the developed endurance test system. In addition, a long-term continuous operation experiment was carried out in order to assess the durability and stability of the endurance test system.

Materials and methods

Description of endurance test system

The newly developed endurance test system for evaluating the durability and reliability of VADs consists of a circulation circuit, a measurement device, several sensors and a control device. The system specifications are shown in Table 1. Figures 1 and 2 show a schematic drawing and an image of the circulation circuit. The circulation circuit consists of the pulsatile pump with a small closed chamber (SCC), a closed chamber, a reservoir, an electromagnetic flow meter and an electromagnetic proportional valve. Each component is connected to pipes by a ferrule that is simple to maintain. The pipes are made of stainless steel and are 35.7 mm inner diameter. The pulsatile pump (AXA-120; Iwaki Co., Ltd., Tokyo, Japan), which approximates the left ventricle (LV), has an active diaphragm-type filling mechanism. The pulsatile pump consists of a diaphragm, a drive shaft and a motor as a driving source. The drive shaft directly connects the diaphragm and the motor, and the position of the diaphragm creates a back and forth motion in the shape of a sine wave by the motor. The pulsatile pump has a variable heart rate (HR) and stroke length (SL); HR can be regulated from 0 to 120 bpm; and SL, which can change the stroke volume of the pulsatile pump, can be adjusted quantitatively between 0 and 100 %, with 100 % SL being about 84 ml in the stroke volume, and 0 % SL being 0 ml in the stroke volume. Also, the pulsatile pump has a fixed systole ratio of 50 %. The SCC, which is small in volume compared with the closed chamber, is connected to the pulsatile pump and contains a mixture of air and fluid. The compliance of the pulsatile pump can be adjusted by changing the air volume in the SCC. The duckbill valves are made of synthetic rubber and are mounted as inlet and outlet valves in the pulsatile pump. The working fluid is then circulated in one direction. The closed chamber approximates the aorta (Ao) and contains a mixture of air and fluid, with the compliance of the Ao adjusted by air volume. The reservoir, which approximates the left atrium (LA), is opened to the atmosphere in order to remove the effect of arterial pulsatility and to give an established pressure; and adjusting the water level alters the pre-load of the pulsatile pump. The electromagnetic proportional valve (RDH124-2; KITZ, Chiba, Japan), which approximates the peripheral resistance (PR), is connected to change the fluid resistance of the circulation circuit. The fluid resistance can be changed quantitatively by varying a gate opening of the electromagnetic proportional valve from 0 to 100 %; and 100 % gate opening is fully opening and 0 % gate opening closes almost completely. Test objects such as VADs are connected to the

Table 1 Endurance test system specifications

Flow range (l/min)	0 to 10
Pressure range (mmHg)	−200 to 300
Heart rate range (bpm)	0 to 120
Wetted material	SUS304, PVC, synthetic rubber
Size ($W \times D \times H$) (mm)	1000 × 1000 × 1500
Weight (kg)	250

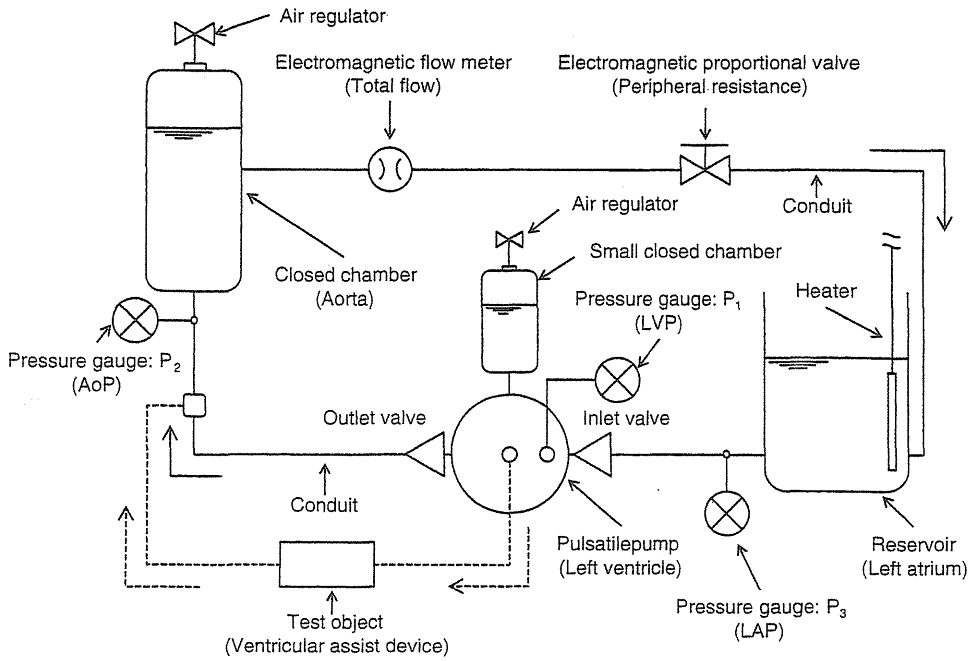


Fig. 1 Schematic diagram of the circulation circuit

pulsatile pump upstream of the closed chamber, and its durability and reliability can then be evaluated. The features of the developed circulation circuit are as follows: (1) the components of this circulation circuit consist of optimized industrial devices, with rigid piping made from stainless steel being used, thereby ensuring durability for the long-term operation of VADs; (2) the pulsatile pump can vary HR and stroke volume, as well as its compliance using the SCC, which ensures that the endurance test system can quantitatively simulate various circulatory conditions.

In terms of sensors, pressure transducers (PA-500; Nidec Copal Electronics Corporation, Tokyo, Japan) were attached to measure the pressures generated by the circulation circuit, and the range of these pressure gauges was between −200 and 300 mmHg. Pressure measurements for parts P1, P2 and P3 of the circulation circuit in Fig. 1 were considered to approximate left ventricle pressure (LVP), aortic pressure (AoP) and left atrium pressure (LAP), respectively. The electromagnetic flow meter (MGS11U; Azbil, Tokyo, Japan) was attached between the closed chamber and the electromagnetic proportional valve in order to measure total flow (TF). A heater and a thermocouple were installed in the reservoir and could be controlled such that the working fluid reaches a preset temperature. The pressure sensors were selected in consideration of the range of pressure in the living human body. The electromagnetic flow meter, heater and the thermocouple were selected from industrial devices in consideration of durability.

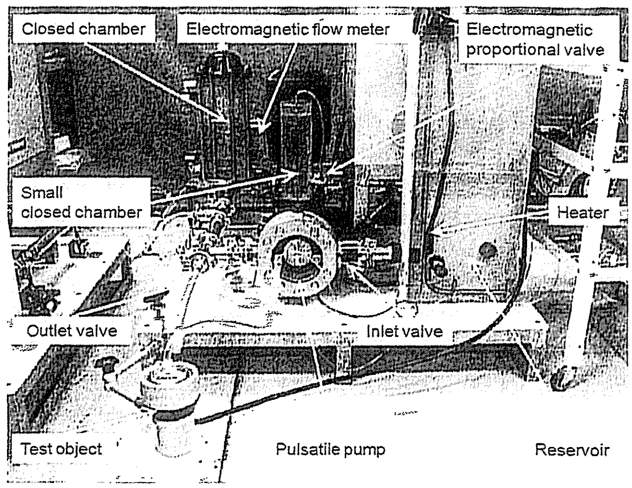


Fig. 2 Image of the circulation circuit

In terms of control, the endurance test system can regulate the HR and SL of the pulsatile pump, and the resistance of the electromagnetic proportional valve electronically using a liquid crystal display controller (GT1150-QLBD; Mitsubishi Electric Corporation, Tokyo, Japan). Moreover, for the prolonged test, automatic operation is possible for a life pattern (awake, sleep, exercise, etc.) which incorporates the circulatory conditions and time schedule, which are set up beforehand.

For measurement, a multi-unit PC data acquisition system (NR-600; Keyence, Osaka, Japan) was used. With 2 GB of storage, approximately 1 month of data collection is possible for a maximum of eight channels at a sampling frequency of 100 Hz.

Specific targets of the endurance test system

The pre-load and after-load of VADs are LVP and AoP at the circulation circuit. LVP and AoP in the adult condition are reported as 120–0 mmHg, 120–80 mmHg [18]. In addition, it is reported that the ranges of AoP and HR in children (0–18 years) are approximately 120–60 mmHg and 80–140 bpm [19, 20]. Therefore, in order to verify whether it is possible to observe the pulsatile load equivalent to a living human body in our circulation circuit, we defined the pressure values of LVP and AoP for the cardiac cycle, the TF and HR values in normal adults and children (Table 2).

According to the guidelines of the Ministry of Economy, Trade and Industry of Japan, endurance testing for at least 6 months or more must be carried out in preclinical studies in Japan [21]. In this article, a target for the period of durability test of our system decided on 6 months.

Effect of SCC and reproduction of pulsatility of pressure wave forms

In this study, the SCC was added in order to vary the compliance of the pulsatile pump. First, static characteristics between the pressure and the fluid volume in the SCC were investigated in order to evaluate the compliance in each air volume of SCC. Figure 3a shows a measuring method of static characteristics of SCC. Experiments were conducted using the SCC alone. The SCC was filled with fluid and constant air volume (air volume of SCC = 250, 500 and 750 ml). Then the fluid was injected into the SCC at 10 ml intervals using a syringe quantitatively and the pressures of fluid inside the SCC were measured using the pressure gauge. Figure 3b shows a static relation between the pressure of fluid inside the SCC and the injected fluid volume in each air volume of SCC, and an elastance (reciprocal of the compliance) was found from each characteristic (Table 3). It is reported that the elastance of the living human body is approximately 3 mmHg/ml [22]. Therefore, the initial air volume of SCC was decided on 250 ml.

Table 2 Physiological conditions

	Adults	Children
LVP (mmHg)	120–0	120–0
AoP (mmHg)	120–80	120–60
Mean AoP (mmHg)	100	90
HR (bpm)	70	120
Total flow (l/min)	5	3

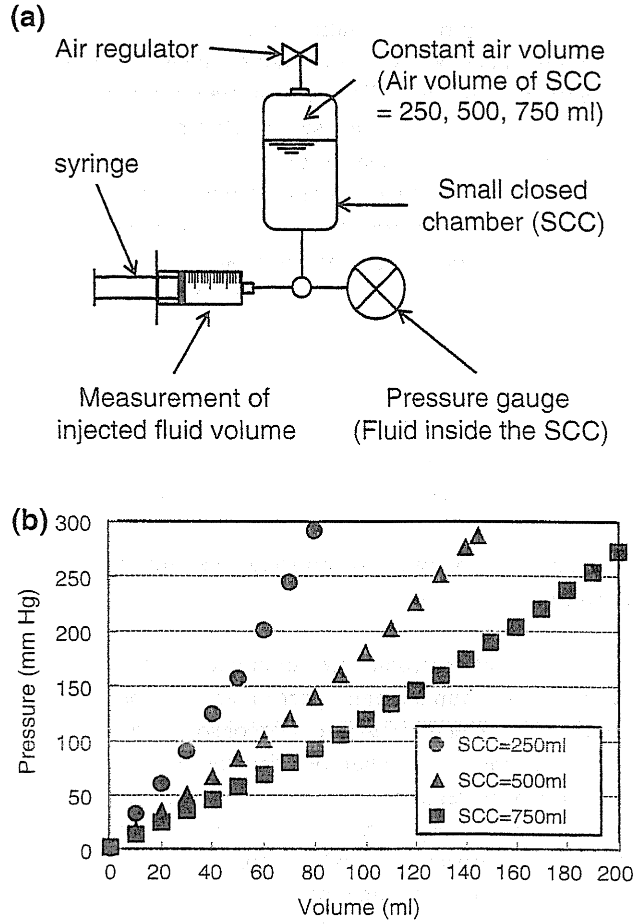


Fig. 3 **a** Measuring method of static characteristics of SCC. **b** Static relation between the pressure of fluid inside the SCC and the injected fluid volume in each air volume of SCC

Table 3 Elastance values in each air volume of SCC

Air volume of SCC (ml)	Elastance (mmHg/ml)
250	3.58
500	1.96
750	1.37

Next, in terms of the effects of SCC, the relationship between the air volume in SCC and output of the pulsatile pump in the circulation circuit were examined. Experiments were conducted using the circulation circuit alone without the test object. As an initial condition for the circulation circuit, the air volume of SCC, HR and SL of the pulsatile pump were set at 250 ml, 70 bpm and 100 %. After the circulation circuit was initiated, the electromagnetic proportional valve, the air volume in the closed chamber and the water level of the reservoir were regulated such that the AoP and LAP were set at 120–80 mm Hg (mean AoP = 100 mmHg) and 20 mmHg, respectively, while operating the circulation circuit, and the air volume of closed chamber was maintained constant. Here, the negative pressure of LVP was indicated in the preliminary test. Therefore, LAP was set at 20 mmHg in order to reduce the negative pressure of LVP as much as possible. After operation of the circulation circuit stabilized, the air volume of SCC was regulated at 50 ml intervals from 0 to 750 ml while operating the circulation circuit, and the maximum and minimum values for LVP (max LVP and min LVP), mean AoP and mean TF were measured. Particularly, the wave forms for LVP and AoP, and the mean value of TF were compared when the air volume of SCC was adjusted to 0, 250 and 500 ml. Here, these conditions of air volume of SCC were decided in order to compare eliminated and increased compliance against 250 ml.

Evaluation of the range of reproducible circulatory conditions

The range of reproducible circulatory conditions was examined as a fundamental performance of the circulation circuit. The electromagnetic proportional valve, the air volume in the closed chamber and the water level of the reservoir were regulated such that AoP and LAP were set to 120–80 mmHg (mean AoP = 100 mmHg) and 20 mmHg, respectively, while operating the circulation circuit when the air volume of SCC was 0, 250 and 500 ml. Under these conditions, the fixed SL was 100 %. The fluid resistance of the circulation circuit was changed by varying the gate opening of electromagnetic proportional valve from 100 % to 20–60 % (pressure measurement range is under 300 mmHg) in order to vary the TF in each given HR for each air volume of SCC. Here, since the fluid resistance of the electromagnetic proportional valve was not linear with respect to the gate opening, the gate opening was therefore regulated at 20 % intervals from 100 to 60 % and was regulated at 5–10 % intervals under 60 %. In addition, the max LVP, min LVP, mean AoP and mean TF were recorded, and the same experiments as previously described were conducted when the pulsatile pump SL was adjusted to 50, 75 and 100 %. Under these conditions, the fixed air volume of SCC was 250 ml. The air volumes of SCC and SL were readjusted while stopping the circulation circuit.

Long-term continuous operation experiment

A long-term continuous operation experiment was conducted for 6 months in order to evaluate the durability and stability of the endurance test system. The experiment was conducted under fixed conditions, and the circulatory conditions and control parameters were as shown in Table 4. Several factors, including industrial device failure,

Table 4 Parameters for long-term operation

Air volume of SCC (ml)	250
HR (bpm)	70
AoP (mmHg)	120–80 (100)
LAP (mmHg)	20
Total flow (l/min)	4.5
PR (%)	44

fluid leakage and changes in pressure wave form, which are attributed to long-term continuous operation, were evaluated.

Experimental conditions

The viscosity of the working fluid had a possibility of changing due to evaporation during the experiments because the reservoir used in our circulation circuit was open to the atmosphere. Therefore, in all experiments, tap water (viscosity, 0.001 Pa s) at 37 °C was used as the working fluid.

In terms of data acquisition, in all experiments, the sampling frequencies for the three pressure channels and the TF and temperature of the working fluid channels were set at 100 and 10 Hz, respectively.

Results

Effect of SCC and reproduction of pulsatility of pressure wave forms

The characteristic max and min LVP, mean AoP, and mean TF when the SCC air volume was varied from 0 to 750 ml are shown in Fig. 4. Then the LAP in each condition was 20 mmHg. The max and min LVP, mean AoP, and mean TF showed nonlinear characteristics against the air volume in SCC, and each absolute value decreased with increasing air volume in SCC. LVP and AoP wave forms when the air volume of SCC was 0, 250 and 500 ml are shown in Fig. 5. The max and min LVP, as well as pulse pressure, decreased when the air volume of SCC was increased from 0 to 250 or 500 ml. The mean and pulse pressure of AoP also decreased. The mean TFs at SCC air volumes of 0, 250 and 500 ml were 5.6, 4.4 and 3.8 l/min, respectively. Although pressure wave forms with a spike were observed when the air volume of SCC was 0 ml, there was no spike in the wave forms when the air volume of SCC was 250 and 500 ml. The defined pressure ranges were observed when the air volume of SCC was 250 ml. Therefore, a pulsatility similar to that in the living human body was qualitatively achieved in the present circulation circuit. However, negative pressure was shown at the LVP, and reductions in the

Fig. 4 SCC characteristics

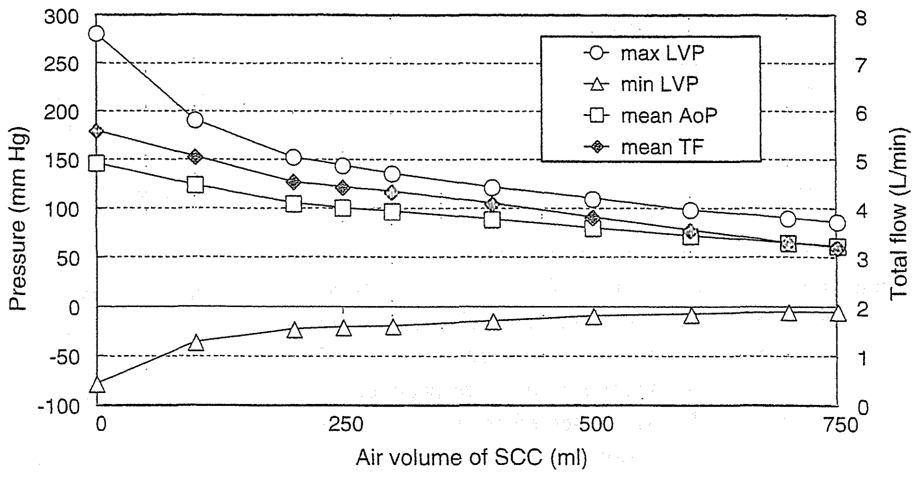
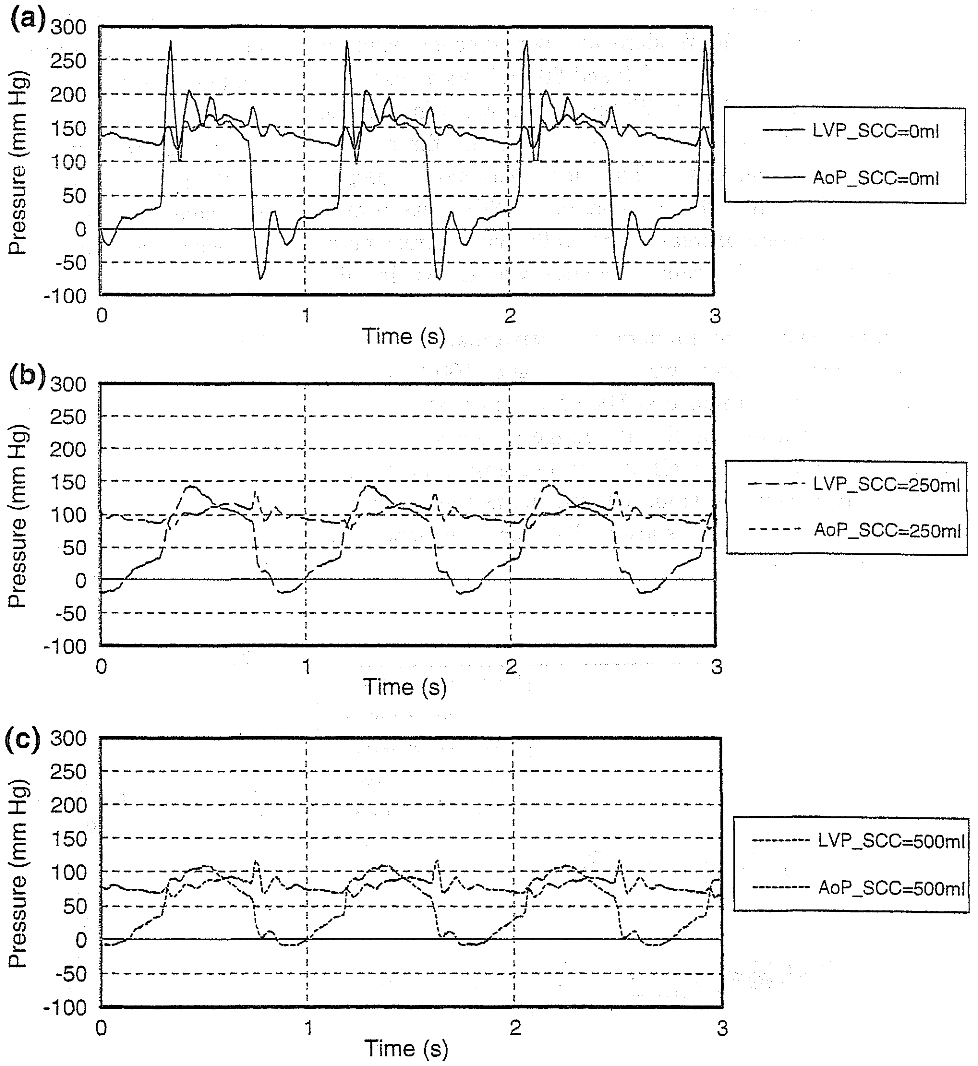


Fig. 5 LVP and AoP waveform when air volume of SCC is 0, 250 and 500 ml. **a** SCC = 0 ml. **b** SCC = 250 ml. **c** SCC = 500 ml



maximum value and phase lag in AoP against the LVP were shown, as compared with pressure wave forms in the living human body.

Evaluation of the range of reproducible circulatory conditions

Figure 6 shows the fundamental performance when the fluid resistance was changed from 100 % to 20–60 % in each given HR at SCC air volume of 250 ml. The max and min LVP and mean AoP were plotted against the TF for every HR and are shown in Fig. 6a, b, respectively. In each HR, the highest TF was observed in the gate opening of 100 %. When the gate opening was reduced, the decrease in the TF and increase in each pressure were observed. The same characteristic was found in every HR. The maximum range for each pressure and TF was near 300 mmHg and 10 l/min, respectively.

Figure 7 shows the fundamental performance when the air volume of SCC was 0, 250 and 500 ml. As an example, the performance at HR of 70 bpm is shown. When the air volume of SCC increased to 250 or 500 ml, the pressure and TF ranges decreased. The slope was nearly perpendicular to TF when the air volume of SCC was 0 ml.In contrast, the slope decreased gradually with increasing air volume of SCC. The same tendency was shown in other HR.

Figure 8 shows the fundamental performance when SL of the pulsatile pump was 50, 75 and 100 %. As an example, the performance at HR of 120 bpm is shown. In terms of decreasing the SL, the range of pressure and TF decreased with SL, as well as with decreasing air volume of SCC. However, the slope was maintained and a shift to the low TF region was shown. The same tendency was shown in other HR.

Long-term continuous operation experiment

Figure 9 shows the result for the long-term continuous operation experiment. Each plot shows the mean values for LVP, AoP, LAP, TF and temperature of working fluid, averaged for 1 h each day under steady circulatory conditions. Although pressure and TF decreased with human errors (failure of air valve closing in closed chamber) after 90 days, average values were almost constant over the six-month experiment. Continuous operation of the endurance test system was possible for 6 months without leakage or industrial device failure.

In terms of the diaphragm of the pulsatile pump, fatigue, fractures and leakage along its circumference were not observed. In addition, each sensor used in the rated range was also able to measure the data for 6 months without failure. However, it was necessary to adjust the air volume of SCC and closed chamber in order to maintain the initial condition twice a week over the experimental period, and replenishment of tap water due to evaporation was also necessary.

Figure 10 shows the LVP and AoP pressure wave forms on the first day and after 6 months. Although pulsatility did not change, spikes and oscillating components increased for each wave form.

Discussion

Effect of SCC and reproduction of pulsatility of pressure wave forms

The pressure wave forms generated in the present endurance test system had a pulsatility similar to that in the living human body because the range of pressures was

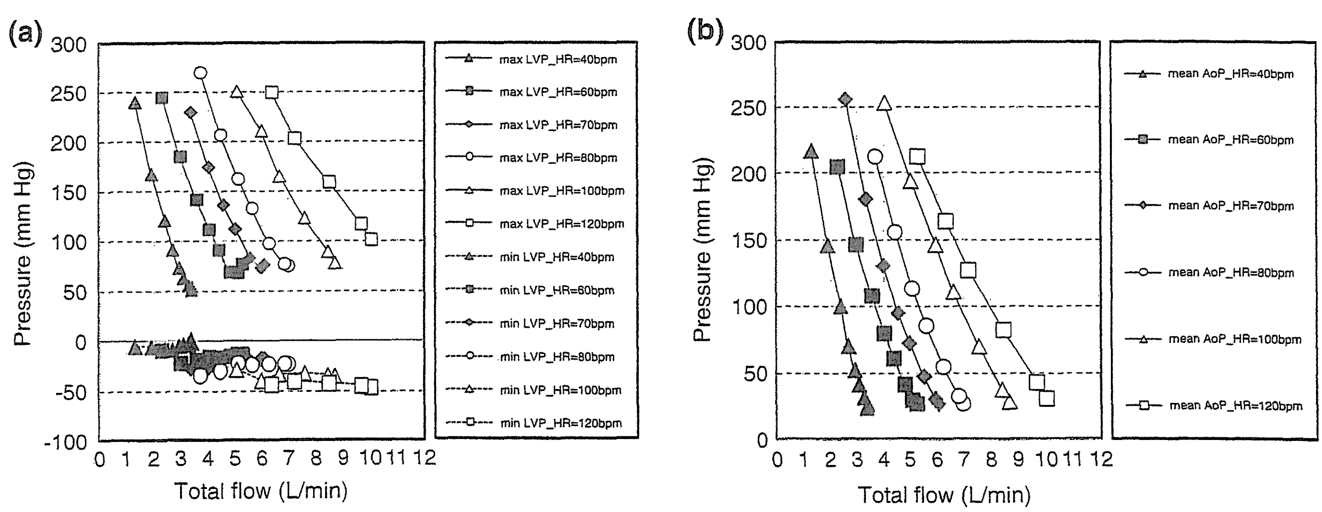


Fig. 6 Pressure-TF characteristics (SCC = 250 ml, SL = 100 %). **a** Max LVP, min LVP-TF characteristics. **b** Mean AoP-TF characteristics

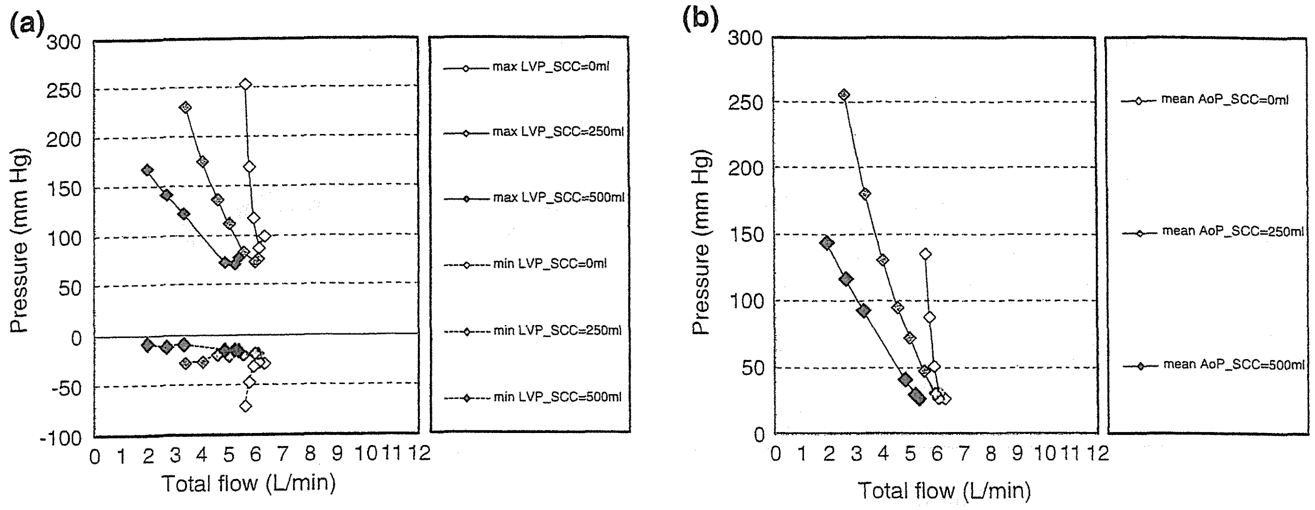


Fig. 7 Pressure-TF characteristics (SCC = 0, 250, 500 ml, SL = 100 %, HR = 70 bpm). **a** Max LVP, min LVP-TF characteristics. **b** Mean AoP-TF characteristics

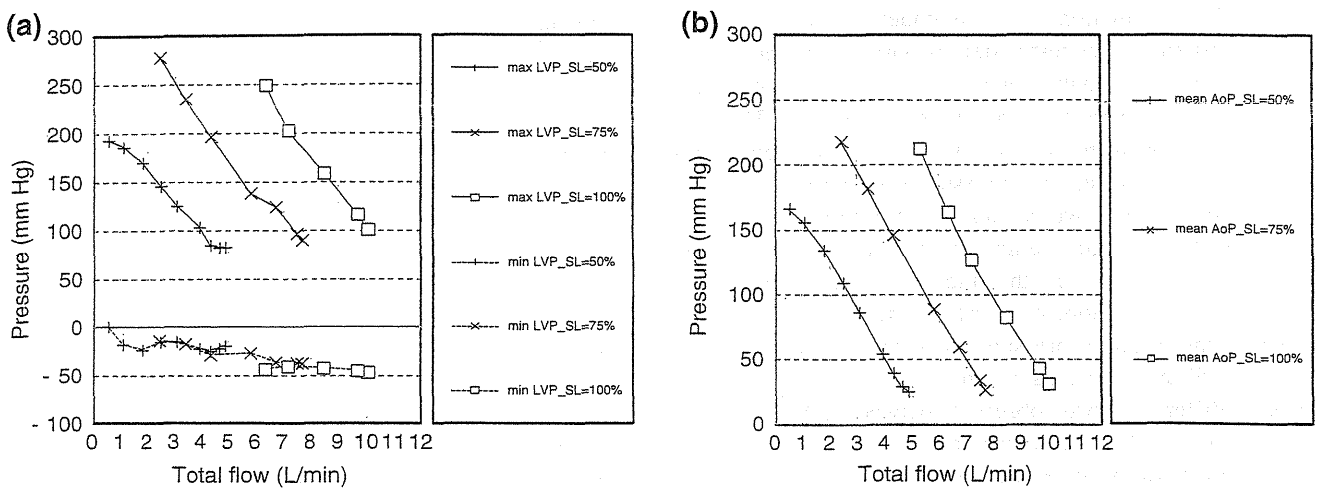
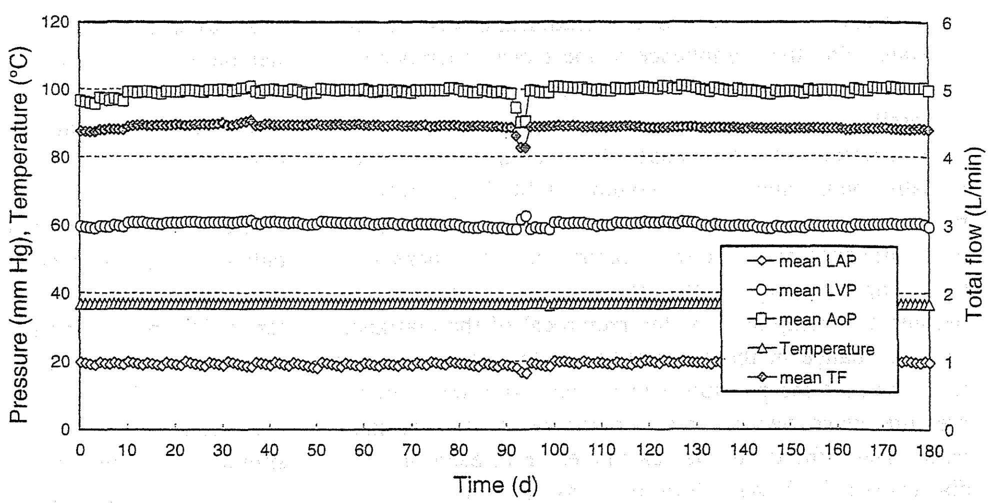


Fig. 8 Pressure-TF characteristics (SCC = 250 ml, SL = 50, 75, 100 %, HR = 120 bpm). **a** Max LVP, min LVP-TF characteristics. **b** Mean AoP-TF characteristics

Fig. 9 Long-term continuous operation experiment for 6 months



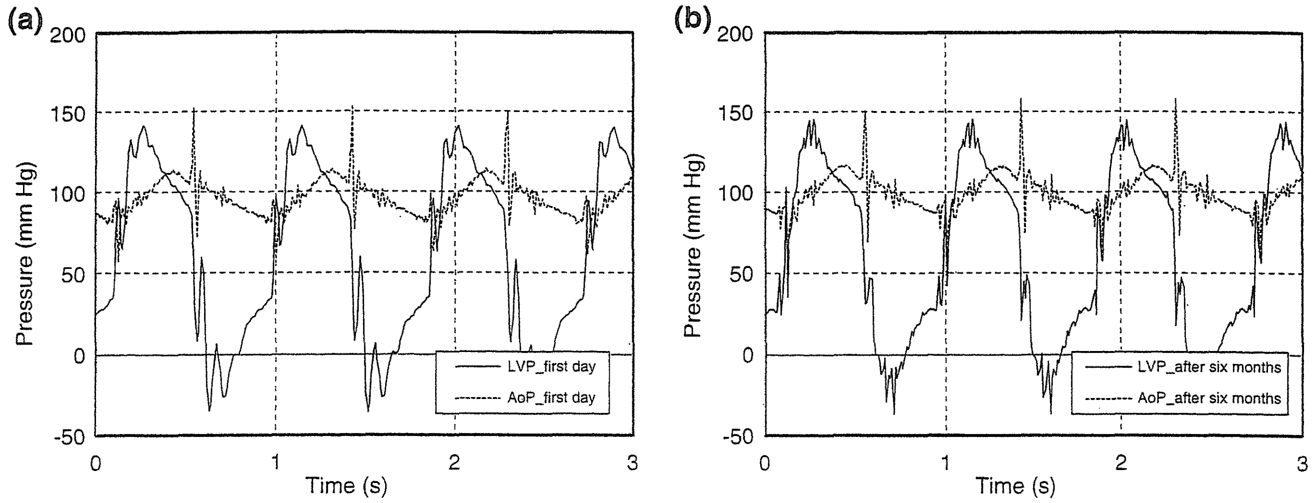


Fig. 10 LVP and AoP waveform on first day and after 6 months in long-term continuous operation experiment. **a** First day. **b** After 6 months

comparable compared with defined pressure values in Table 2. Examination of VADs under pulsatile conditions using this endurance test system is possible. In general, it is thought that the negative pressure of LVP does not occur in normal hemodynamics in the living human body. However, a negative pressure of LVP in the diastolic phase was shown. And this negative pressure was causally related to the pulsatile pump, which had an active filling mechanism. Because the pulsatile pump had more than 10 years operational experience in the industry, this active filling mechanism was adopted in order to give better durability. Hence, the negative pressure could be eliminated using a passive filling mechanism, similar to the native heart. A phase difference was observed between LVP and AoP wave forms. This was attributed to the resistance of the pipe which was attached between the outlet valve and the closed chamber and the compliance of the closed chamber. If the phase difference is large, the pressure load condition (pressure difference) to VAD changes even if the values of LVP and AoP are equivalent to the living human body. Therefore, an investigation of the relationship between pipe resistance and the compliance of the closed chamber will be necessary in order to make the phase difference as small as possible.

As a result of the relationship between the output of the pulsatile pump and the air volume of SCC, the pulsatile pump output could be quantitatively adjusted by changing the compliance of the pulsatile pump. Here, the increase in the compliance equals the decrease in the contractility because the compliance is the reciprocal of the elastance. Thus, a change in the contractility of the pulsatile pump forms against the pressure wave occurs as a result of the pressure wave varying the compliance of the pulsatile pump. Here, the dP/dt was calculated from each one cardiac cycle at LVP wave form that was measured for 1 min and expressed as a mean value with its standard deviation. The dP/dt at SCC air volumes of 0, 250 and 500 ml were 7313.0 ± 140.3, 1786.3 ± 48.2 and 1778.0 ± 40.0 mmHg/s, respectively. It is reported that the dP/dt in normal are approximately 1600 mmHg/s [23]. The dP/dt comparable to a living human body was shown when the air volume of SCC was 250 and 500 ml. However, a comparison of the dp/dt in each air volume of SCC showed that, although the dP/dt was decreased when the air volume of SCC was increased from 0 to 250 ml, changes in the dP/dt were not seen when the air volume of SCC was 250 and 500 ml. This may be due to the motion of the diaphragm in the shape of a sine wave in the pulsatile pump. In future studies, in order to reproduce further wide range circulation conditions like the reappearance of further low dP/dt, it is necessary to examine the motion of the diaphragm in the pulsatile pump or the SCC capacity; nonetheless, the present endurance test system showed pulsatility which can evaluate the VADs. Subsequently, the contractility of the pulsatile pump will be examined in order to obtain a pressure wave form more similar to that of hemodynamics in the living human body.

Evaluation of the range of reproducible circulatory conditions

In the measurement of fundamental performance, the circulation circuit was able to produce a wide range of pressure (maximum range, 300 mmHg) and TF (maximum range, 10 l/min) conditions. There is no compliance of the pulsatile pump when the air volume of SCC is 0 ml. Hence, even if the PR varied, the TF were not changed. TF were dependent on HR (Fig. 7). In addition, it is difficult to simulate the conditions containing compliance like the living human body because an excessive spike or negative pressure occurred without compliance in Fig. 5 (air volume of SCC = 0 ml). The increase of air volume in the SCC allowed a decrease of pulsatile pump output, and the change in slope in the case of fundamental performance of SCC originated in the change in pulsatile pump compliance. Thus, the pulsatile pump became the condition containing the compliance (Fig. 7), and pressure wave forms could be generated without the excessive spike in Fig. 5 (air volume of SCC = 250, 500 ml). It was thought that our endurance test system which used industrial devices allowed the simulation of circulatory conditions by using the SCC, as well as the test equipment which used a flexible diaphragm or sack. In addition, although the range of pressure and TF became narrow when decreasing the proportion of SL, simulation of a low flow domain ($\leq$3 l/min) became possible (Fig. 8). As a result, defined pressure ranges within the children circulatory condition were observed when the SL was 50 %. Therefore, it is thought that this equipment will be applicable to endurance testing of VADs for children because the above circulatory conditions of children can be reproduced using this equipment. The endurance test system can be thought to generate not only adult but also children circulatory conditions by combining both SCC and SL function.

Long-term continuous operation experiment

The selected components of the endurance test system showed durability and stability for 6 months. However, when comparing the LVP and AoP data from the first day and after 6 months, some augmentation of spikes and oscillations was observed. This was thought to be caused by the valves mounted in the pulsatile pump; fatigue of the duckbill valves probably resulted from the pressure load of the pulsatile pump when opening and closing the valves. Progression of valve fatigue would affect the valve opening and closing performance, resulting in an insufficient closure and an increase in back-flow. Although there was no influence of the valves on mean TF for 6 months, back-flow might probably increase in long-term evaluation periods beyond 6 months. Therefore, it may be necessary to improve the valve design and materials in order to improve durability for further long-term evaluation.

The diaphragm of the pulsatile pump was made of rubber, as well as the valve, it was 1 cm in thickness, and although the rigidity was high, its compliance was low. The compliance of the pulsatile pump could be adjusted without affecting durability by connecting the SCC to the pulsatile pump. If the diaphragm was thin, it could fracture due to fatigue. Therefore, the use of the SCC was thought to be effective for maintaining diaphragm durability. In terms of the reservoir which is open to the atmosphere, water refilling was necessary due to evaporation, and this was disadvantageous for a long-term continuous operation experiment. Therefore, it may be necessary to attempt a closed chamber which approximates the LA in our endurance test system. Although it is necessary to improve the valves and the reservoir, the present endurance test system showed durability and stability and allowed 6 months evaluation. This time the 6 months continuous experiment was performed supposing the minimum period of the endurance test in the guideline [21]. Hence, more than 6 months continuous operation experiment was not carried out. In addition, a practical examination of VADs was not performed. In future studies, evaluation of more than 6 months continuous operation and durability testing of VADs will be necessary in order to validate the usefulness of the present endurance test system.

Conclusions

We developed a novel endurance test system and evaluated its basic performance and long-term durability and stability. The developed endurance test system showed a wide range of reproducible circulatory conditions, durability and stability through the use of an SCC and industrial devices. This endurance test system is potentially useful for evaluating the basic characteristics of VADs.

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