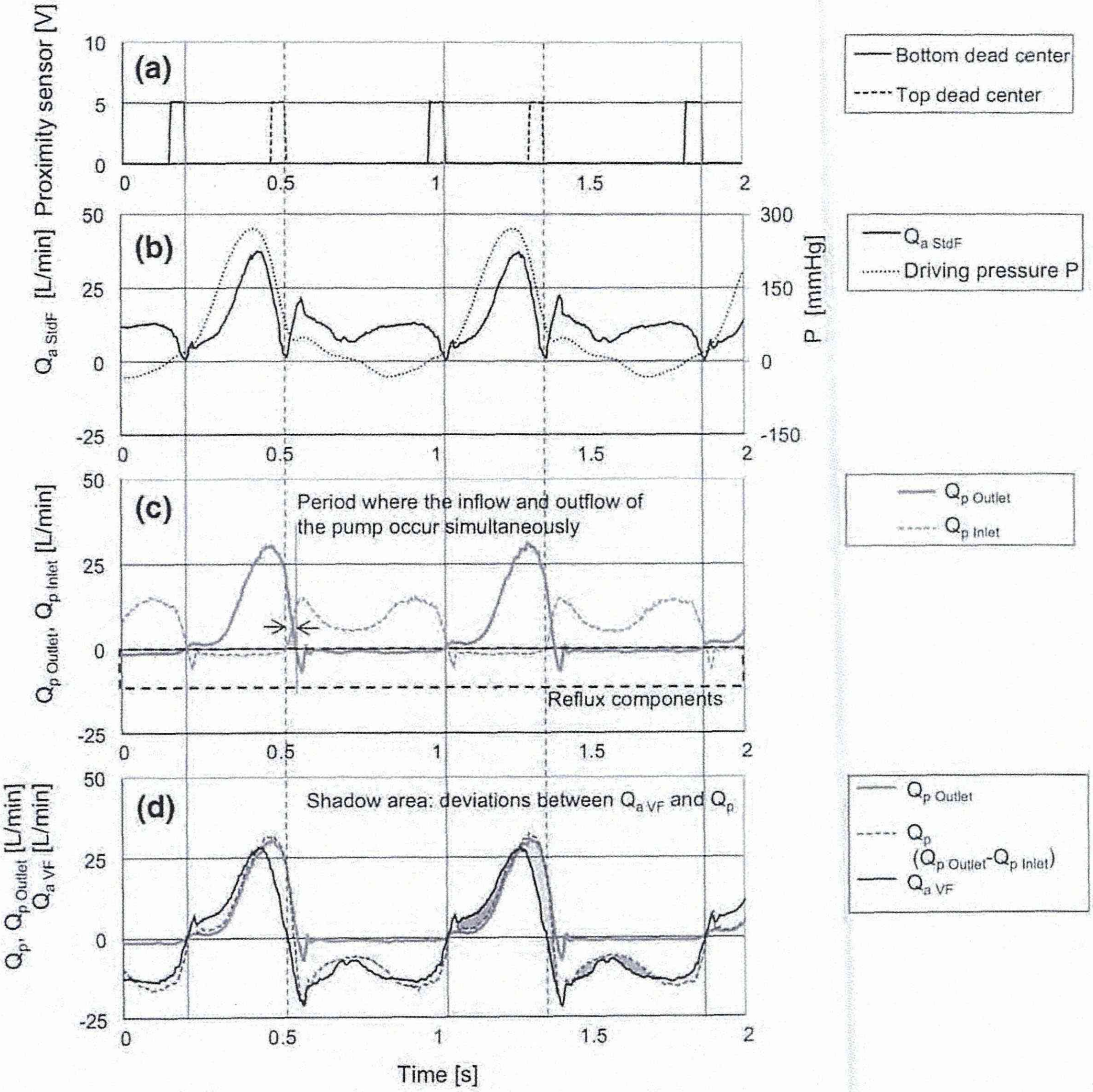


Fig. 3 Example of instantaneous waveforms when the blood pump was driven by WPD100-SD40 at 70 bpm, with an afterload of 100 mmHg. **a** Positions of the cylinder piston detected with proximity sensors, **b** measured air flow and driving pressure, **c** pump flow rate measured at the inlet and outlet sides of the pump, **d** converted volumetric flow rate of the air driveline, $Q_{a\ VF}$, and the flow rates into and out of the blood chamber of the pump, Q_p

Error factors that were not reflected in the air flow

Deviations between the air flow and blood flow could be attributed to several causes. For instance, there may be components that flow due to inertia during the period where the inflow and outflow of the pump occur simultaneously, as shown in Figs. 3c and 4b. This phenomenon is remarkable, especially at higher beating rates. The effect of this flow is not reflected in the air flow because it does not cause any volumetric changes in the blood pump chamber. However, any flow rate not generated by movement of the diaphragm has the range from 1.3 to 3.9 % under any test condition, so it was considered that these flow rates negligibly influence the estimation of flow rate. Similarly, reflux components generated by the mechanical valve are not reflected in the air flow rate (Figs. 3c, 4a). However, it was considered from Fig. 4a that the reflux components could be corrected using a constant term in the estimate of the pump flow rate.

The point that the room temperature was used when converting the volumetric air flow rate can be cited as another error factor. The air temperature in the driveline measured with the temperature sensor to be built into the air flow meter was up to 38 °C under all test conditions (response time of the sensor: 75 ms, room temperature: 25 °C). Compared with the volumetric air flow converted

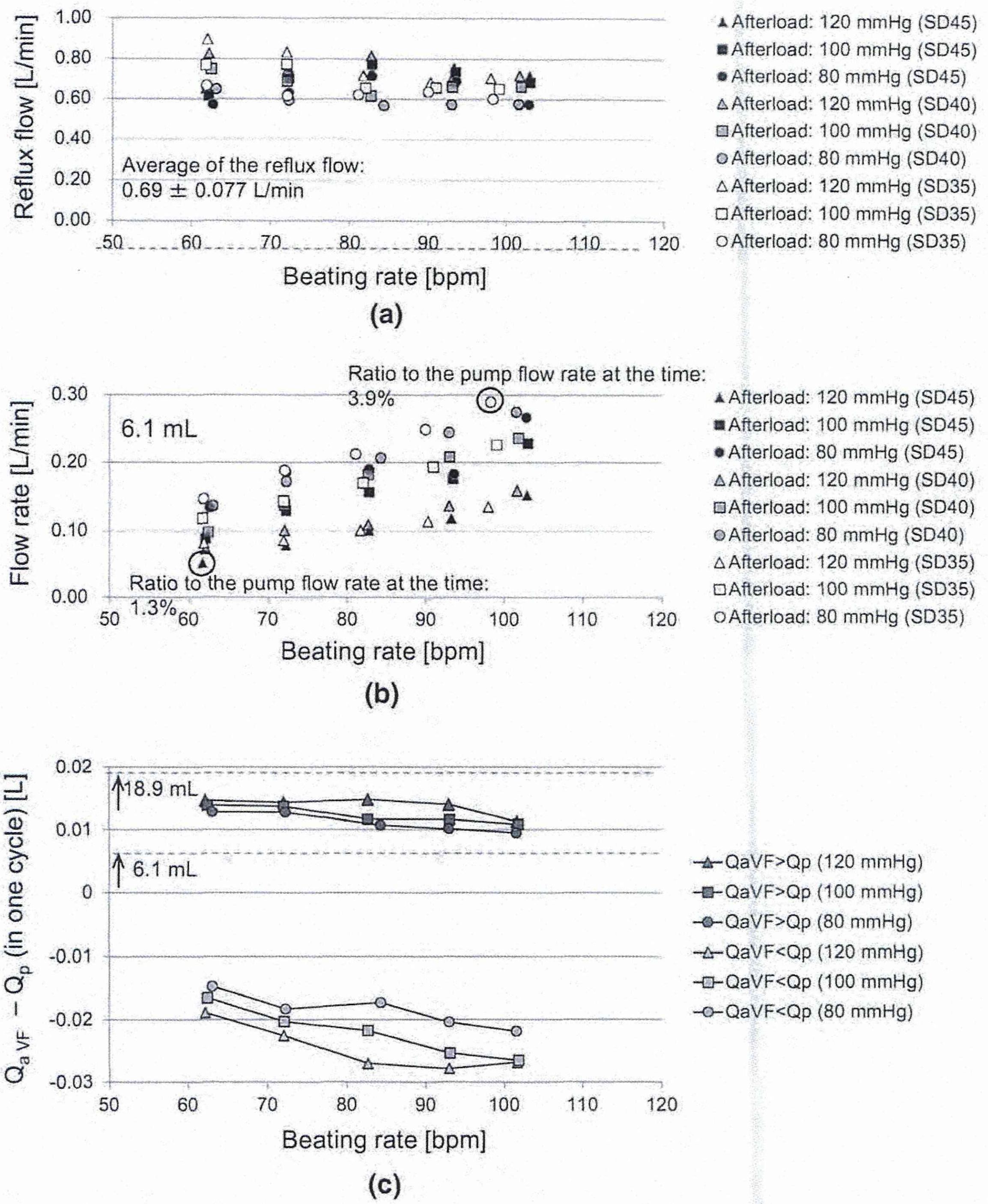
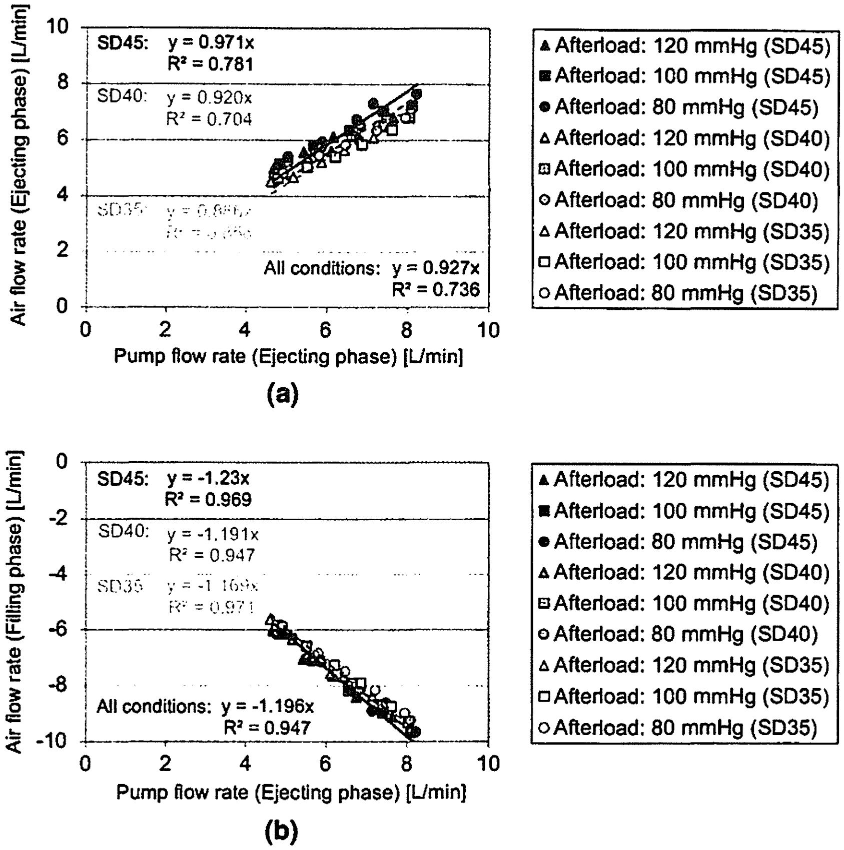


Fig. 4 Deviations between the air flow and blood flow. **a** Reflux components generated by the mechanical. **b** Flow components for a period during which the inflow and outflow of the pump occur simultaneously. **c** Example of differences between $Q_{a\ \mathrm{VF}}$ and Q_p during one cycle with WPD-100 SD40

with room temperature, the air flow converted with the air temperature in the driveline is increased up to 4.3 % from Eq. (1). The influence of the temperature is considered to be limited, the use of a higher responsive temperature sensor, however, will be able to contribute to improve the accuracy of the measurement of the volumetric air flow.

Deviation due to compressibility of the air

As shown in Fig. 3d, the deviation between the air flow rates and blood flow rates is apparently larger during the ejecting phase than during the filling phase. From the results shown in Figs. 3d and 4c, the capacity difference in



(a)

(b)

Fig. 5 Correlation between the average pump flow rate in the ejecting direction and the average air flow rate. **a** The air flow rates during the ejecting phase. **b** The air flow rates during the filling phase

the initial stage of ejection was found to be within the range of 6.1–18.9 mL. The deviation in the initial stage of ejection was considered to be mainly caused by the compression process of the air.

During the latter half of the ejection phase, the fluid flow on the blood chamber side of the pump generated by volumetric expansion of the air while releasing the driving pressure in the air chamber of the pump to push out the diaphragm after passing through the sensor section of the air flow meter (an element that is hardly reflected in the air flow meter) was considered to be the main factor causing the deviation.

During the filling phase, on the other hand, the magnitude of the negative pressure is relatively low, and the difference in the flow rate was smaller than that during the ejection phase.

Linearity of the average flow rate

As shown in Fig. 5a, b, the linearity of the average flow rate was higher in the air flow rate of the filling direction than that of the ejecting direction, because of the deviation with compressibility of the air during the ejecting phase and the volumetric air flow conversion with room temperature. The deviations from the blood flow meter were slightly low for the air flow rate of the ejecting direction. The estimation error of the average blood flow likely decreases under a wide range of driving conditions because of the high linearity when the air flow rate in the filling direction is used. Furthermore, estimation of the pump flow rate is considered stable and fully possible using our method because of high correlation with the pump flow and the air flow.

Practical application and availability

In the present study, the conversion from the standard air flow rate to the volumetric flow rate and the calculation of the average flow rate were performed offline. For practical applications, the estimate of the pump flow rate should be automatically calculated in real time, using the air flow of the filling direction. This is feasible using a general microprocessor because of the simple algorithm using the proximity sensors of the WPD and the linearity between the pump flow rate and the air flow rate. The air flow meter was installed in the driveline in this experiment. The flow meter should be installed into the WPD system not to impair the portability of the WPD. This problem was considered to be solved using a small embedded flow sensor.

It is possible, of course, to measure the blood flow rate in a pneumatic VAD using an ultrasonic flow meter, but the flow meter needs to be built into the system for a patient to be able to carry it around. It is necessary for the probe to be attached to the outflow tube crossing the skin. To date, various, indirect methods for measuring the blood flow rate in a pneumatic blood pump (or the internal capacity of the pump) have been attempted. While techniques that use electric impedance, capacitance, or ultrasonic waves [15–18] are useful for measuring the pump capacity in real time, these techniques require sensors or electrodes to be attached at positions near the blood chamber of the pump housing. Our method of measuring pump blood flow at the side of the drive unit from the air flow without modifying the existing blood pump may have disadvantage for the accuracy and the measurement of the instantaneous value because of estimating the pump flow rate indirectly. It, however, has an advantage of not disturbing the care of sites that the inflow and outflow conduits cross the skin. In addition, it has a sufficient measurement performance of the average pump flow rate.

Conclusion

A flow measurement method for the portable driver of a pneumatically driven VAD using an air flow meter for estimating the pump flow has been investigated. Limitations of this technique were indicated by the deviation between the air flow and blood flow resulting from compressibility of the air and the blood flow components that were not reflected in the air flow. A significant correlation was particularly recognized between the average blood flow rates and the air flow rates of the filling direction. It was demonstrated that the average pump flow rate was estimated exactly in a wide range of drive conditions using the air flow of the filling phase. This technique is useful for monitoring the pump blood flow in the case when a pneumatic VAD is driven by a WPD.

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Conflict of interest The authors declare that they have no conflict of interest.

References

1. Stewart GC, Givertz MM. Mechanical circulatory support for advanced heart failure: patients and technology in evolution. Circulation. 2012;125(10):1304–15.
2. Slaughter MS, Pagani FD, Rogers JG, Miller LW, Sun B, Russell SD, Starling RC, Chen L, Boyle AJ, Chillcott S, Adamson RM, Blood MS, Camacho MT, Idrissi KA, Petty M, Sobieski M, Wright S, Myers TJ, Farrar DJ. Clinical management of continuous-flow left ventricular assist devices in advanced heart failure. J Heart Lung Transplant. 2010;29(4S):S1–39.
3. Kirklin JK, Naftel DC, Kormos RL, Stevenson LW, Pagani FD, Miller MA, Baldwin JT, Young JB. The fourth INTERMACS annual report: 4,000 implants and counting. J Heart Lung Transplant. 2012;31(2):117–26.
4. Kirklin JK, Naftel DC, Kormos RL, Stevenson LW, Pagani FD, Miller MA, Baldwin JT, Young JB. Fifth INTERMACS annual report: risk factor analysis from more than 6,000 mechanical circulatory support patients. J Heart Lung Transplant. 2013;32(2):141–56.
5. Ishii M, Hamamoto M. Bioethics and organ transplantation in Japan. JMAJ. 2009;52(5):289–92.
6. Kyo S, Minami T, Nishimura T, Gojo S, Ono M. New era for therapeutic strategy for heart failure: destination therapy by left ventricular assist device. J Cardiol. 2012;59(2):101–9.
7. Shiga T, Kinugawa K, Hatano M, Yao A, Nishimura T, Endo M, Kato N, Hirata Y, Kyo S, Ono M, Nagai R. Age and preoperative total bilirubin level can stratify prognosis after extracorporeal pulsatile left ventricular assist device implantation. Circ J. 2011;75(1):121–8.
8. Takano H, Taenaka Y, Noda H, Kinoshita M, Yagura A, Tatsumi E, Sekii H, Umezu M, Nakatani T. Multi-institutional studies of the national cardiovascular center ventricular assist system: use in 92 patients. ASAIO Trans. 1989;35:541–4.
9. Takano H, Nakatani T, Taenaka Y. Clinical experience with ventricular assist systems in Japan. Ann Thorac Surg. 1993;55:250–5.
10. Saito S, Matsumiya G, Sakaguchi T, Fujita T, Kuratani T, Ichikawa H, Sawa Y. Fifteen-year experience with Toyobo paracorporeal left ventricular assist system. J Artif Organs. 2009;12:27–34.
11. Takatani S, Matsuda H, Hanatani A, Nojiri C, Yamazaki K, Motomura T, Ohuchi K, Sakamoto T, Yamane T. Mechanical circulatory support devices (MCSD) in Japan: current status and future directions. J Artif Organs. 2005;8:13–27.
12. Japanese Association for Clinical Ventricular Assist Systems. Japanese Registry for ventricular assist device. 2013. http://www.jacvas.com/VAS_registry2012.pdf. Accessed 28 May 2014. (in Japanese).
13. Nishinaka T, Taenaka Y, Tatsumi E, Ohnishi H, Homma A, Shioya K, Mizuno T, Tsukiya T, Mushika S, Hashiguchi Y, Suzuki A, Kitamura S. Development of a compact portable driver for a pneumatic ventricular assist device. J Airtif Organs. 2007;10:236–9.
14. Homma A, Taenaka Y, Tatsumi E, Akagawa E, Lee H, Nishinaka T, Takewa Y, Mizuno T, Tsukiya T, Kakuta Y, Katagiri N, Shimosaki I, Hamada S, Mukaibayashi H, Iwaoka W. Development of a compact wearable pneumatic drive unit for a ventricular assist device. J Artif Organs. 2008;11:182–90.
15. Gawlikowski M, Darlak M, Pustelny T, Kustosz R. Preliminary investigations regarding the possibility of acoustic resonant application for blood volume measurement in pneumatic ventricular assist device. Mol Quantum Acoust. 2006;27:89–96.
16. Gawlikowski M, Pustelny T, Kustosz R, Darłak M. Non invasive blood volume measurement in pneumatic ventricular assist device POLVAD. Mol Quantum Acoust. 2006;27:97–106.
17. Kamimura T, Homma A, Tsukiya T, Kakuta Y, Lee H, Tatsumi E, Taenaka Y, Kitamura S. Monitoring of diaphragm position in pulsatile pneumatic ventricular assisted device by ultrasound sensor (a new method for flow measurement in VAD). JSME Int J Ser C. 2004;47:1124–7.
18. Sasaki E, Nakatani T, Taenaka Y, Takano H, Hirose H. Novel method to determine instantaneous blood volume in pulsatile blood pump using electrical impedance. Artif Organs. 1994;18:603–10.

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ORIGINAL ARTICLE

Artificial Lung / ECMO

Impact of bypass flow rate and catheter position in veno-venous extracorporeal membrane oxygenation on gas exchange in vivo

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Abstract The clinical use of veno-venous extracorporeal membrane oxygenation (VVECMO) in adult patients with respiratory failure is rapidly increasing. However, recirculation of blood oxygenated by ECMO back into the circuit may occur in VVECMO, resulting in insufficient oxygenation. The cannula position and bypass flow rate are two major factors influencing recirculation, but the relationship and ideal configuration of these factors are not fully understood. In the present study, we attempted to clarify these parameters for effective gas exchange. VVECMO was performed in eight adult goats under general anesthesia. The position of the drainage cannula was fixed in the inferior vena cava (IVC), but the return cannula position was varied between the IVC, right atrium (RA), and superior vena cava (SVC). At each position, the recirculation rates calculated, and the adequacy of oxygen delivery by ECMO in supplying systemic oxygen demand was assessed by measuring the arterial oxygen saturation (SaO_2) and pressure (PaO_2). Although the recirculation rates increased as the bypass flow rates increased, SaO_2 and PaO_2 also increased in any position of return cannula. The recirculation rates and PaO_2 were 27 ± 2 % and 162 ± 16 mmHg, 36 ± 6 % and 139 ± 11 mmHg, and 63 ± 6 % and 77 ± 9 mmHg in the SVC, RA and IVC position at 4 L/min respectively. In conclusion, the best return cannula position was the SVC, and a high bypass flow rate was advantageous for effective oxygenation. Both the bypass flow rates and cannula position must be considered to achieve effective oxygenation.

Keywords Veno-venous extracorporeal membrane oxygenation · Respiratory support · Cannulation · Bypass flow · Recirculation

Introduction

Extracorporeal membrane oxygenation (ECMO) is used for patients with severe pulmonary or cardiorespiratory failure. There are two basic types of ECMO veno-arterial ECMO (VAECMO) and veno-venous ECMO (VVECMO). VAECMO is particularly favored for severe cardiac or cardiorespiratory failure, while VVECMO is used for patients with severe respiratory failure who do not improve on mechanical support or do not respond to medical treatment [1].

Although VVECMO is widely utilized in neonatal and pediatric patients with severe respiratory failure [2], its usage is controversial in adults owing to their low survival rates [3]. In 2000, Bartlett et al. reported that the survival rate of discharged patients with progressive respiratory failure was 88 % in 586 neonates, 70 % in 132 children, and 56 % in 146 adults [4]. The number of adult ECMO patients with respiratory failure increased considerably in 2009 with the H1N1 influenza pandemic and the publication of the Conventional Ventilation or ECMO for Severe Adult Respiratory failure (CESAR) trial results. Since

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2011, approximately 400 cases yearly have been reported by the Extracorporeal Life Support Organization (ELSO) [5].

There are fewer complications associated with VVECMO than with VAECMO, which include systemic thromboembolism, limb ischemia, maldistribution of oxygen, and increased left ventricular wall tension [6]. Additionally, VVECMO offers the advantage of simple cannulation without requiring arterial puncture and, therefore, is easily implemented. However, because both the drainage and return cannulae are in a single vein in VVECMO, a variable proportion of oxygenated blood from the return cannula enters the drainage cannula, a condition known as recirculation. Recirculation during VVECMO may cause insufficient oxygenation. The four factors that can affect the magnitude of recirculation are cannula position, bypass flow rate, cardiac output (CO), and intravascular volume [7]. To date, the relationship between recirculation and effective oxygenation in VVECMO has not been thoroughly investigated in adults. In the present study, we attempted to clarify the effect of these variables on effective gas exchange.

Materials and methods

Animals

Eight adult goats with a mean body weight of 58.6 ± 0.6 kg were evaluated. They were maintained at the National Cerebral and Cardiovascular Center in accordance with the guidelines of the committee on animal studies. This study was approved by the Animal Investigation Committee of this institution.

Animal preparation

Anesthesia was induced with 10 mg/kg of ketamine administered intramuscularly (Daiichi-Sankyo Pharmaceutical Products Ltd., Tokyo, Japan). The goats were then tracheotomized and ventilated to maintain normal blood gas values. During the preparation for VVECMO, the goats were ventilated at a FiO_2 of 0.4–1.0, respiratory rate of 10–20 breaths/min, and a tidal volume of 10 mL/kg; anesthesia was maintained with isoflurane (2 ± 0.5 vol/100 mL in oxygen). A 14-G catheter (Argyle, Covidien, Tokyo, Japan) was inserted into the left external jugular vein for drug infusion. A 7.5-Fr Swan-Ganz Oximetry catheter (CCOmbo Volumetrics Pulmonary Artery Catheter, model 741HF75, Edwards, Irvine, CA, USA) was inserted into the left external jugular vein with the tip positioned in the pulmonary artery (PA) and a second 14-G catheter was inserted into the carotid artery to obtain blood samples. CO was measured using a Vigileo Monitor (Edwards, Irvine, CA, USA) and a FloTrac sensor (Edwards, Irvine, CA, USA). The utility of the Vigileo Monitor has been reported previously [8–10]. Because the FloTrac sensor can predict the CO based on the standard deviation of the arterial blood pressure, it only needed to be connected to the existing arterial blood pressure line. The thermodilution method cannot be used directly for CO measurements during ECMO; therefore, a combination of the Vigileo monitor and the FloTrac sensor were utilized. Because Hb and CO influence oxygen consumption and delivery, these conditions were maintained at a constant level for the maximum time possible.

The rectal temperature was monitored using a thermistor thermometer (Type T, copper-constantan thermocouple) and maintained at 36.5 ± 1.0 °C using a warm water mattress and heat exchanger. The vital and bypass flow data were recorded using Labchart 5 (ADInstruments Pty Ltd., Bella Vista, Australia).

ECMO circuit

An ECMO system (Endumo® 6000, Heiwa Bussan, Tokyo, Japan) comprising a ROTAFLOW® centrifugal pump (Maquet, Rastatt, Germany), a heparin-coated circuit (T-NCVC® coating; National Cerebral and Cardiovascular Center, Osaka, Japan and Toyobo, Osaka, Japan), and an oxygenator (BIOCUBE 6000®, Nipro, Osaka, Japan) was used [1, 11, 12]. The system was primed with Lactated Ringer's solution.

The goats were administered 300 units/kg of heparin, and the 20-Fr return and drainage cannulae (PCKC-V-20, Toyobo Co., Ltd., Osaka, Japan) were inserted into the right external jugular vein and the inferior vena cava (IVC) using the surgical cutdown method.

Experimental protocol

First, recirculation was visualized by angiography by administering contrast media into the ECMO outflow. Second, to create baseline conditions before starting ECMO, the ventilator setting was adjusted appropriately. And the mixed venous oxygen saturation was maintained at 40 ± 5 % as the baseline condition. The blood sample at baseline was taken after the stable baseline condition was maintained at least 5 min. To investigate blood oxygenation using ECMO alone under the conditions of eliminated native respiration, the ventilator was discontinued, and ECMO was initiated. The oxygenator was ventilated with 100 % O_2, and the V/Q ratio ($V = O_2$ gas flow rate, Q = bypass flow rate) was set at 1.0. During VVECMO, anesthesia was maintained with intravenous propofol at 0.5 mL/kg/h (Mylan Pharmaceutical Products Ltd., Osaka, Japan). Third, to quantify the angiographic results, the recirculation rates were calculated under each condition by measuring the oxygen saturation as follows [13]:

$$\text{Recirculation rate} = \frac{\text{Oxygen saturation of the preoxygenator blood} - \text{Mixed venous oxygen saturation}}{\text{Oxygen saturation of the postoxygenator blood} - \text{Mixed venous oxygen saturation}}$$

This method is the gold standard of recirculation rate measurement in experimental settings [13]. Blood gas was measured with an automatic blood gas analyzer (Radiometer, ABL800 Flex Analyzer, Copenhagen, Denmark). Subsequently, the arterial oxygen saturation (SaO_2) and pressure (PaO_2) were measured under conditions of eliminated native respiration for 20 min. This experiment procedure was repeated in every cannula position and bypass flow rate, as shown below.

Position of the return and drainage cannulae, and bypass flow

The position of the return cannula was varied between the IVC, right atrium (RA), and superior vena cava (SVC), and the drainage cannula was fixed in the IVC (Fig. 1). Cannula positions were confirmed radiographically. The bypass flow rate was set from 1 to 4 L/min at each position. These data collection was taken 30–40 min after each change. Then, in consideration of existence of hysteresis, the order of the data collection in cannula positions and bypass flow rates was changed in every experiment.

Statistical analysis

All data are shown as mean ± standard error. Serial changes in recirculation rates, SaO_2, PaO_2, $PaCO_2$, Hb, and CO were analyzed by one-way analysis of variance (ANOVA). Bonferroni/Dunn's post hoc test was performed when a significant difference was detected in the one-way ANOVA. P values <0.05 were considered statistically significant. All data were analyzed using Statcel2 (the add-in forms on Excel).

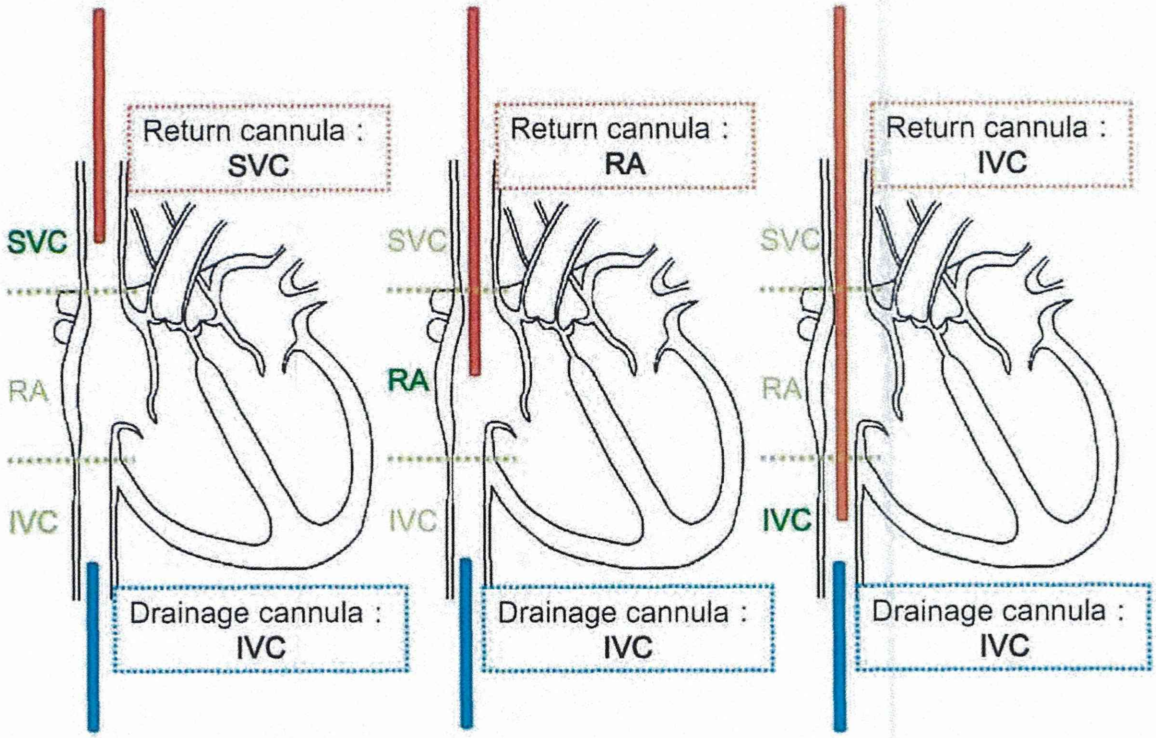

Fig. 1 Position of return and drainage cannulae. Schematic of heart and position of return and drainage cannulae. The *orange cannula* represents the return cannula; the *blue cannula* represents the drainage cannula. *IVC* inferior vena cava, *RA* right atrium, *SVC* superior vena cava

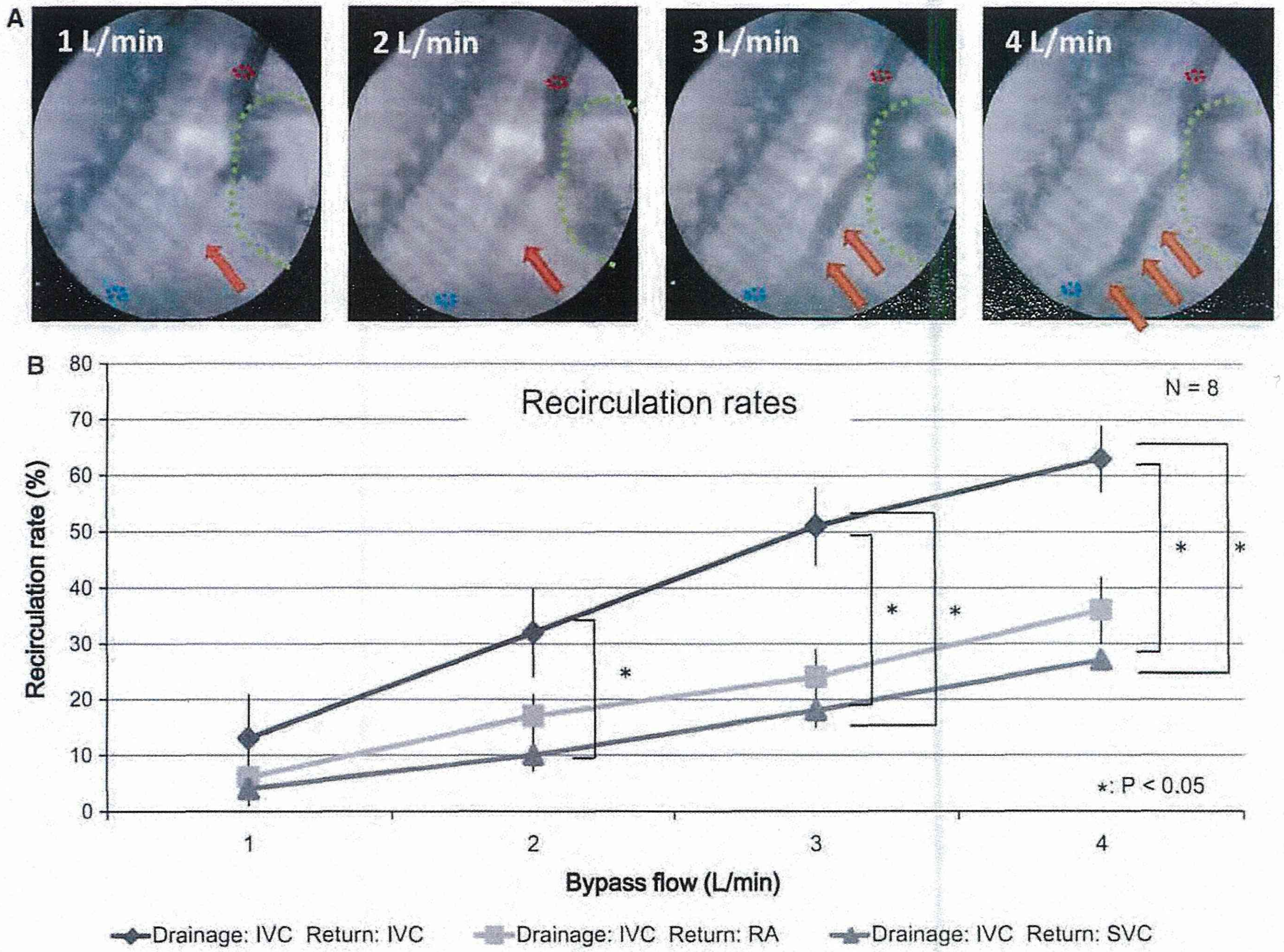

Fig. 2 Recirculation (angiography and recirculation rates). **a** Angiography on each bypass flow in the SVC return cannula position. The *red oval* represents the tip of return cannula in the SVC; the *blue oval* represents the tip of drainage cannula in the IVC; the *green section* represents the heart; the *orange arrow* indicates where recirculation occurs. The blood in the area indicated by the *orange arrow* flows from the return cannula to the drainage cannula. The contrast medium appears darker as the bypass flow rate increases. **b** The recirculation rates on each bypass flow. The return cannula positions are indicated by: *diamond markers* for IVC, *square markers* for RA, and *triangular markers* for SVC. The recirculation rates in the SVC and RA return cannula positions at 3 and 4 L/min were significantly lower than those in the IVC return cannula position ($P < 0.05$). *IVC* inferior vena cava, *RA* right atrium, *SVC* superior vena cava

Results

Recirculation

A representative angiogram showing the return cannula positioned in the SVC is shown in Fig. 2a. With the return cannula in this position, it is easy to understand the phenomenon of recirculation variation. Most of the blood exiting the return cannula flowed toward the PA. However, a small volume of blood entered the drainage cannula (Fig. 2a, arrows). The contrast medium gradually darkened as the bypass flow rate increased, and the increased recirculation was visually confirmed as the bypass flow rate increased.

Figure 2b summarizes the recirculation rates. At each return position, the recirculation rates increased as the bypass flow rates increased. The recirculation rate in the IVC return cannula group was higher than those in the SVC and RA groups. When the bypass flow rates were 3 and 4 L/min, the recirculation rate in the IVC position was significantly higher than the recirculation rates in the SVC and RA positions ($P < 0.05$).

Blood oxygenation

Figures 3 and 4 illustrate the SaO_2 and the PaO_2 values according to the cannula positions at bypass flow rates from 1 to 4 L/min. The SaO_2 and PaO_2 increased as the bypass flow rates increased. When the bypass flow rates were higher than 2 L/min in the SVC and RA positions, the SaO_2 was maintained at greater than 80 %. When the bypass flow rate was 4 L/min in the SVC and RA positions,

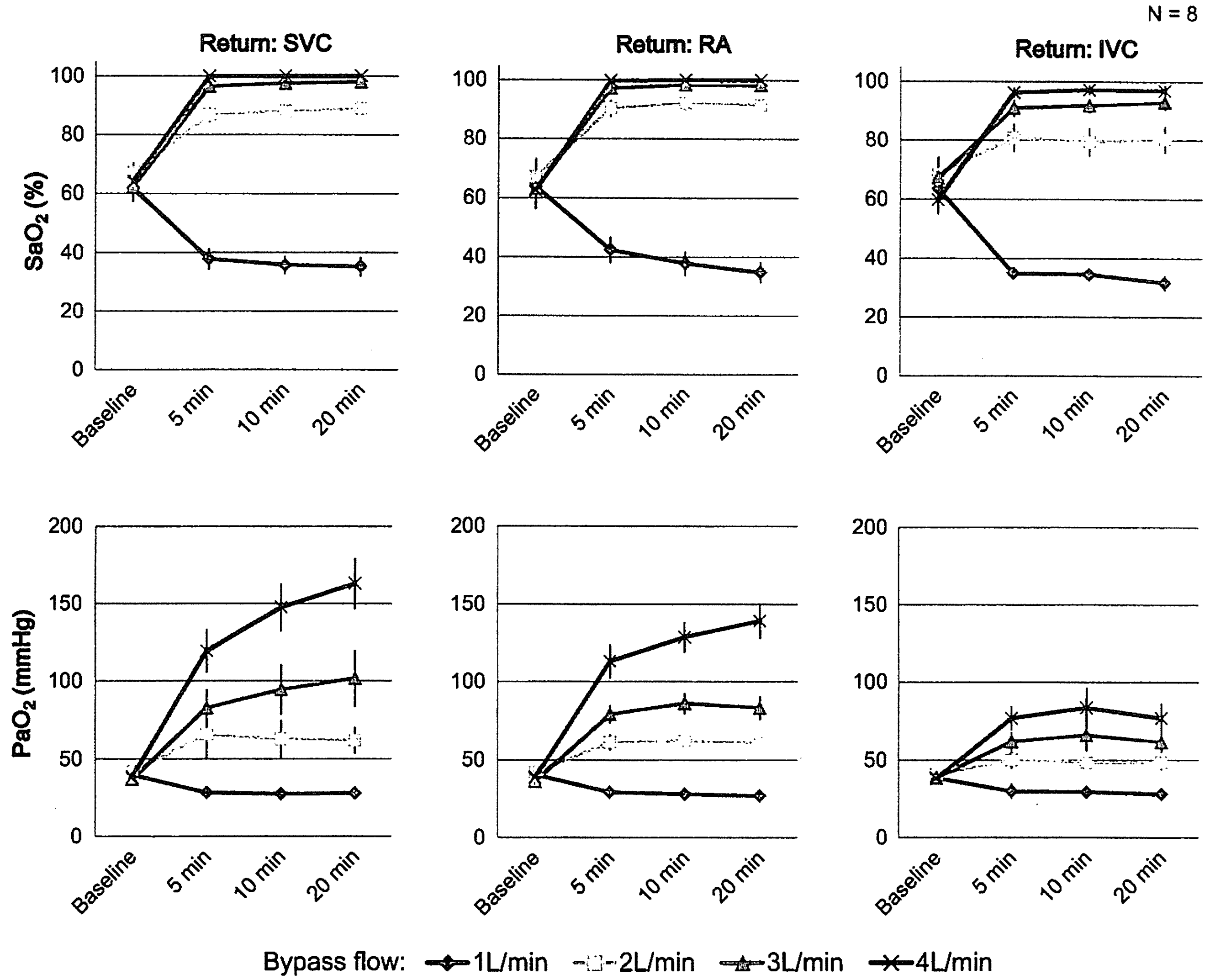

Fig. 3 Variation of oxygenation: arterial oxygen saturation (SaO_2) and pressure (PaO_2). The variation of the SaO_2 and the PaO_2 before VVECMO (in baseline condition) and during VVECMO for 20 min ($n = 8$). The SaO_2 showed no significant difference in any position at each bypass flow. The PaO_2 was significantly higher in the SVC position at 3 and 4 L/min than that in the IVC position ($P = 0.02$ and $P < 0.01$). *IVC* inferior vena cava, *RA* right atrium, *SVC* superior vena cava

the SaO_2 was 100 %. Interestingly, at 20 min, the PaO_2 was higher in the SVC position than in the RA position (162.9 ± 16.6 vs 139.0 ± 11.5 mmHg), although the difference was not statistically significant ($P = 0.15$). The PaO_2 in the SVC return cannula position 20 min after initiating ECMO support was significantly higher than that in the IVC return cannula position (162.9 ± 16.6 vs 77.0 ± 9.2 mmHg, respectively, $P < 0.01$). The SaO_2 and PaO_2 values in the IVC return cannula group were lower than those at the other two return cannula positions.

Blood carbon dioxide removal ($PaCO_2$ and pH)

Figure 4 shows the partial pressure of carbon dioxide in the arterial blood ($PaCO_2$) and the blood pH. The mean pH, $PaCO_2$, HCO_3, and BE before VVECMO were 7.24 ± 0.01, 58.3 ± 0.9, 23.6 ± 0.3, and −3.4 ± 0.2, respectively, and respiratory acidosis was induced in all the goats. After initiating VVECMO, the $PaCO_2$ decreased as the bypass flow rates increased, except at 1 L/min. When the bypass flow rate was maintained at 1 L/min, the $PaCO_2$ tended to increase over a 20-min period after initiating VVECMO. The $PaCO_2$ approached the normal level of 45 mmHg at a bypass flow rate of 2 L/min in the SVC or RA return cannula position and at a bypass flow of 3 L/min in all return cannula positions. The $PaCO_2$ and pH showed no significant differences between the return cannula positions at each bypass flow. When the bypass flow rate was maintained at greater than 3 L/min for 20 min, the pH approached the normal range. The mean HCO_3 during

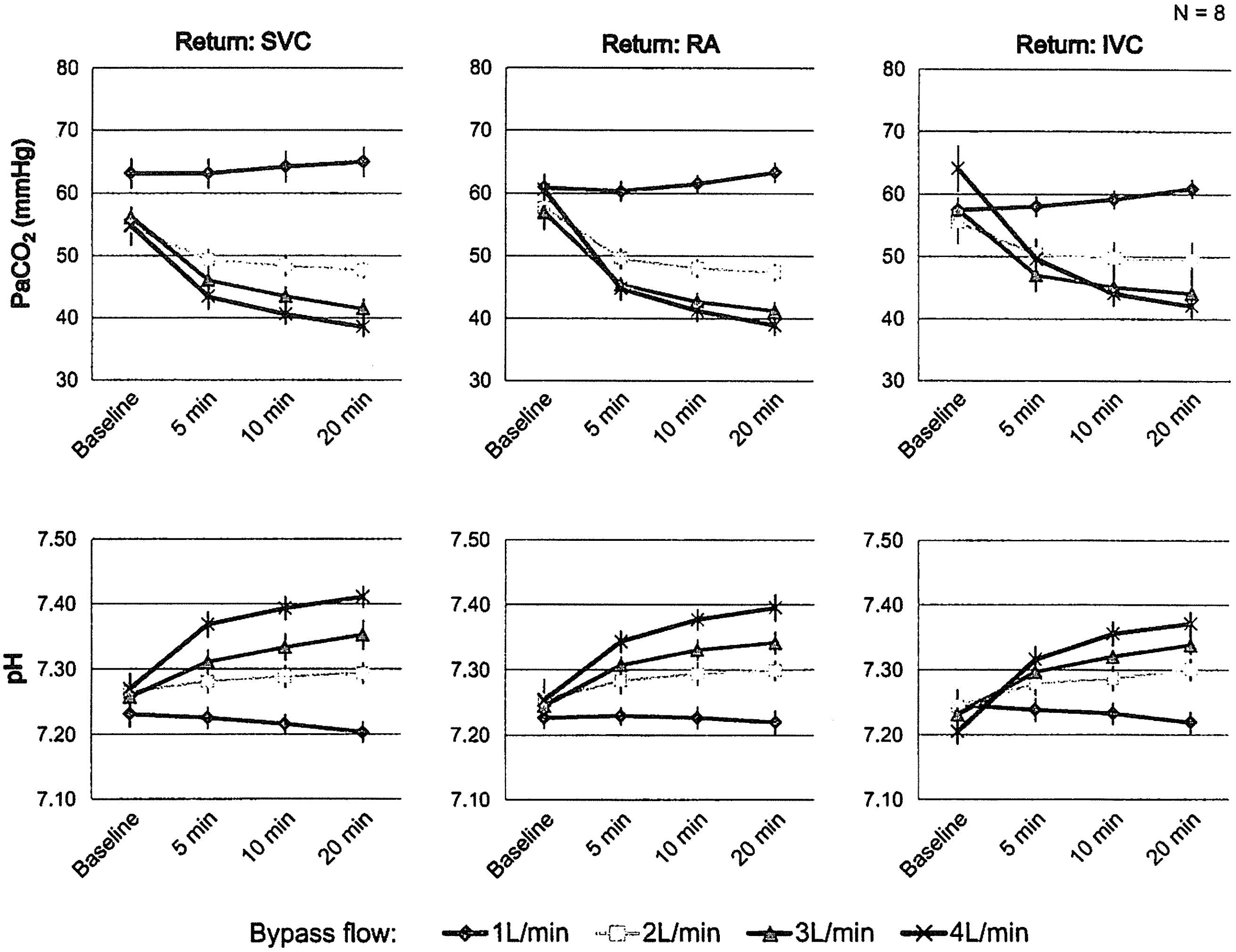

Fig. 4 Variation of carbon dioxide removal: Partial pressure of carbon dioxide in arterial blood ($PaCO_2$) and pH. The $PaCO_2$ and pH before VVECMO (in baseline condition) and during VVECMO ($n = 8$). $PaCO_2$ and pH showed no significant difference in any position at each bypass flow. *IVC* inferior vena cava, *RA* right atrium, *SVC* superior vena cava

VVECMO was 22.5 ± 0.2 and were close to the normal range.

Measurement conditions

The mean hemoglobin (Hb) was 9.8 ± 0.1 mg/dL, and the mean CO was 4.9 ± 0.1 L/min. These values showed no significant differences among the positions at each bypass flow rate.

Discussion

This study determined the recirculation and blood oxygenation rates in VVECMO under several conditions. We demonstrated that it is preferable to position the return cannula in the SVC, and a high bypass flow is better for effective oxygenation than a low bypass flow.

VVECMO can cause recirculation, which results in inadequate oxygenation and should be minimized. Heard et al. also reported that the cannula position, bypass flow rate, CO, and intravascular volume influence recirculation [7]. Of these four factors, CO and intravascular volume are passive factors that vary primarily due to the patient's condition. In the present study, we focused on the cannula position and bypass flow rate because these are measurable active factors.

VVECMO is inserted using two techniques: dual cannulation with return and drainage cannulae, and single cannulation comprising one cannula with a double-lumen catheter (DLC) that allows both return and drainage [1, 14]. The use of single cannulation has increased in several countries, though it has not yet been approved by Japanese regulatory authorities. The combined return and drainage cannulae sites are often used: the femoral vein (FV) drainage/internal jugular vein (IJV) return, IJV drainage/