# Effect of Right Ventricular Bypass Peak Flow-Rate on Intrapulmonary Shunt Ratio

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Abstract: The effect of total right ventricular bypass peak flow-rate on the intrapulmonary shunt ratio was quantitatively investigated in animal tests. To give variations in the peak flow-rate (from pulsatile to intermediate to nonpulsatile), three types of blood pump (piston-bellows, screw, and centrifugal) were applied to dogs. The intrapulmonary shunt ratio was calculated from blood oxygen content drawn every 30 min from the outlet of the right ventricular bypass pump and from the femoral artery, while the canine lung was ventilated with 100% oxygen gas by an artificial respirator. The results show that when the intrapulmonary shunt ratio ranged between 0.095 and 0.392 there is no clear relation to the peak-flow-rate index (which varied from  $1.1-17.0 \ 1 \ min^{-1} \ m^{-2}$ ) over the preceding 30 min. This study demonstrates that the intrapulmonary shunt ratio is able to be kept within the range of control values for 6 h even with a peak-flow-rate index of <4.0 l min^{-1} m^{-2}. Key Words: Right ventricular bypass— Intrapulmonary shunt ratio—Peak flow-rate—Piston-bellows pump—Screw pump—Centrifugal pump—Pulsatile flow.

In designing total ventricular bypass systems, e.g., a total artificial heart, the question of pulsatility as a design requirement for circulatory systems arises. For example, if a pulsatile pump is designed to imitate the natural heart, what is the minimum pulsatility required to maintain normal physiology?

To produce wide variations in the flow wave-form (and then study the resulting physiological effects), the authors used three types of blood pumps; i.e., (a) piston-bellows type (positive displacement pump), (b) screw type (intermediate pulsatility), and (c) centrifugal type (nonpulsatile). The first gives variable pulsatile flows which are controlled by the cyclic changes of a hydraulically driven artificial-ventricular volume. The second generates somewhat nonpulsatile flows which can be proportionally controlled by the rotor speed. The third is a completely nonpulsatile device which has recently been used clinically. To quantitate pulsatility, peak flow-rates resulting from each device were carefully controlled while mean flow-rates were maintained within the control range.

To examine some of the physiological effects of pulsatility, the authors focused on the pulmonary circulation; since it involves only one organ, the lungs, and since in its capillaries the control blood flow is pulsatile (1). A total right ventricular bypass was performed in animal experiments so that variable pulsatility could be applied to the lung vascular system. Evaluation of the effects of pulsatility on the pulmonary circulation was based on the efficiency of oxygen uptake, which was experimentally determined from the oxygen content in the blood by intrapulmonary shunt ratio equations. These equations have often been clinically used to evaluate pulmonary function and hypoxemia (2).

### MATERIALS AND METHODS

In the present study, three types of blood pump (piston-bellows type, screw type, and centrifugal type) have been manufactured to give variations in

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the peak flow-rate  $(Q_{peak})$ . The basic mechanism of each pump is described below.

## Piston-bellows pump

The piston-bellows pump consists of an artificial ventricle, a diaphragm driving chamber, a cylinder with bellows, two driving tubes (connecting the diaphragm driving chamber to the cylinder), a piston/ cam system, and an AC motor (Fig. 1).

A cyclic variation of V (artificial-ventricular volume) is generated by the mechanism as follows. A rotational motion of the AC motor (Fuji Electric, Japan) is converted to a reciprocating motion by the piston/cam system; a piston is pushed by a cylindrical cam in systole and pulled back by a coil-spring in diastole. This reciprocating motion is converted to cyclic variations in volume by the welded metal bellows (made of stainless steel, 45 cm<sup>2</sup> cross sectional area; Eagle Industry, Japan). Then, this variation of volume is transmitted to a variation of V through driving water; in other words, the diaphragm (silicon rubber. 1 mm thick) of the artificial ventricle (with polymethylmethacrylate housing) is hydraulically driven.

To smooth the flow of water, the driving system is provided with a one-way flow path; consisting of two tubes (made of polyvinylchloride stiffened by polyester fiber), of a one-way valve, and of a partition film (silicone rubber; 1 mm thick). This film partitions the driving water into two parts; that in the one-way flow path and that in the cylinder.

To convert this variation of V to pulsatile flow, the artificial ventricle is equipped with a couple of ball valves (nylon ball, 19.1 mm diameter; 15 mm orifice diameter) for the inlet and outlet.

The peak flow-rate can be varied independently from Q<sub>mean</sub> (mean flow-rate) by the following method. The eccentric radius of the cylindrical cam (ER) is set with variation between 2.5 and 15 mm to adjust the amplitude of the sinusoidal reciprocating motion of the piston. When ER is doubled, so is the maximum instantaneous piston-velocity, which determines Q<sub>peak</sub>. Then, the micrometer-head is positioned to adjust the stroke-length of the piston (SL) by cutting off a part of sinusoidal motion in the diastolic phase. This stroke-length proportionally determines the stroke-volume (SV).<sup>1</sup> The mean flowrate (max. 5.94  $| \min^{-1} \rangle$ ) is the product of SV (0-30 ml) and f (pulse rate;  $40-198 \text{ min}^{-1}$ ); the latter is controlled by the rotating speed of the motor. Thus, Q<sub>peak</sub> can be varied independently of Q<sub>mean</sub> by adjusting ER and SL separately.

The cyclic variations of V can be directly calculated from the piston-motion, which is electrically measured by the position sensor (potentiometer LP-10FB, Midori-precisions, Japan). The pulse-rate was fixed at  $120 \text{ min}^{-1}$  in the following animal tests.

# Screw pump

The screw pump consists of a rotor (made of stainless steel; Iwaki, Japan), a stator (nitrile rubber), a casing (polymethylmethacrylate), and a DC motor (Sawamura Denki, Japan) (Fig. 2). The pumping mechanism is as follows. The rotor (a single-threaded external screw) is inscribed in the stator (a double-threaded interior screw) with a space between them; in other words, the space is sealed between two spiral lines where the rotor contacts with the stator. The blood in this sealed space is transferred from inlet to outlet with one-way sliding motion of these spiral lines when the rotor is rotated by the DC motor. The mean flow-rate (0.26 to 6.76 l min<sup>-1</sup>) is proportional to the rotating speed of the rotor (100–2600 min<sup>-1</sup>).

## Centrifugal pump

The centrifugal pump consists of an impeller (made of polypropylene: lwaki, Japan), a front casing (polymethylmethacrylate), a rear casing (polypropylene), a driving magnet, and a DC motor (Sawamura Denki, Japan) (Fig. 3).

The pumping mechanism of this device is as follows. Blood is sucked into the inlet-port of the casing, impelled from the center to the fringe, and ejected through the outlet-port of the casing. This centrifugal effect is derived from the rotation of the impeller. The rotational motion of the impeller is driven by magnetic coupling from that of the DC motor (Fig. 3b).

The mean flow-rate is controlled by the rotating speed  $(100-3500 \text{ min}^{-1})$  of the impeller. When this is set at 3500 min<sup>-1</sup>, 22 l min<sup>-1</sup> water is pumped against a pressure difference of 200 mmHg between inlet and outlet.

#### Animal tests

Total right ventricular bypass was performed in 21 adult mongrel dogs (weighing between 15 and 31 kg) with three types of blood pump. That is, 21 dogs were divided into three groups as follows; (a) in 11 dogs with the piston-bellows type, (b) in three dogs with the screw type, and (c) in seven dogs with the centrifugal type. In the first group (with the piston-bellows type), ER was varied between 2.5 and 15 mm to produce variations in  $Q_{peak}$  according to the following three groups; (a-1) in five

<sup>&</sup>lt;sup>1</sup> In the strict sense, this is accurate when the regurgitant flow through the valves is ignored.





**FIG. 1.** Piston-bellows pump. External appearance **(A)** and diagram **(B).** B, bellows; T, driving tube; IV. inlet valve; OV, outlet valve.

dogs with 2.5 mm, (a-2) in five dogs with 7.5 mm, and (a-3) in one dog with 15.0 mm.

The animals were anesthetized with sodium pentobarbital (25 mg/kg body weight) and ventilated through an endotracheal tube with oxygen gas (including 0.5 vol. % halothane to keep the anesthetic state) by a positive-pressure respirator (breathing rate; 25 min<sup>-1</sup>). The fluid (heparinized saline solution)-filled catheters (attached to the pressure transducers) were introduced into the right femoral artery and into the vena cava via the right femoral vein to measure the femoral arterial pressure and the central venous pressure, respectively. These catheters were also used for drawing blood to measure oxygen contents of arterial blood (O<sub>2</sub>CTa) and of venous blood (O<sub>2</sub>CTv). Another catheter was introduced into the left femoral vein. Through this catheter, just enough volume of saline solution was supplied to maintain a proper circulating blood volume and hence a physiological central venous pressure during the animal experiments.

Surgical access was gained through the left fourth interspace. After the lung was exposed, the strokevolume of the respirator was increased so that the canine lung was fully inflated with no collapsed lobes (no visible atelectatic areas). Under this condition, control values of the intrapulmonary shunt ratio (s) were calculated from the oxygen content in blood drawn from the femoral artery ( $O_2CTa$ ) and femoral vein ( $O_2CTv$ ). The computations were done using the equation-set explained in the following section, titled "intrapulmonary shunt ratio calculation."

Before cannulation, a control wave-form of flowrate (Q) at the pulmonary trunk was measured using an electromagnetic flow-meter (MFV-1100, Nihon-kohden, Japan) with a cuff-type probe. The fluid-filled catheters attached to the pressure transducers were then inserted into the pulmonary trunk and into the left atrium to measure pulmonary-arterial (PAP) and left-atrial (LAP) pressures, respectively.

After systemic heparinization (2.5 mg/kg body weight), cannulae (made of polyvinylchloride, 9 mm internal diameter) were introduced into the pulmonary trunk and into the right atrium via the right ventricle (Fig. 4). These cannulae were connected to the pump (primed with heparinized saline solution) by connectors (polymethylmethacrylate) and tubes (polyvinylchloride, 15 mm internal diameter). On the connector in the outflow-path of the pump was a catheter for drawing blood to measure oxygen content. The electromagnetic flow probe (FF-160T, Nihon-kohden, Japan) was incorporated



FIG. 2. Screw pump. External appearance (A) and diagram (B). M, flow-meter; I, inlet; O, outlet.

A C M D



**FIG. 3.** Centrifugal pump. External appearance **(A)** and diagram **(B).** C, controller; M, flow-meter; I, inlet; O, outlet.

into the blood outflow-path of the pump for measuring the wave-form of Q. A thermometer was also incorporated there to measure blood temperature (T). Partial right ventricular bypass was started, followed immediately by total right ventricular bypass. This was accomplished by tightening with the snare which occluded the proximal side of the pulmonary trunk (Fig. 4).

For 30 min,  $Q_{mean}$  was kept constant (a constant value had been selected between 0.8 and 2.5 l min<sup>-1</sup> m<sup>-2</sup>) by controlling circulating blood volume with the aid of saline solution. At the same time, pump drive conditions, namely, the stroke-length of the piston (piston-bellows pump), the rotating speed of the impeller (centrifugal pump), or the rotating speed of the rotor (screw pump), were kept fixed for 30 min.

The flow-rate index (QI) is the quotient of flowrate (Q) divided by surface-area of the canine body (SA)

$$QI = Q/SA \tag{1.1}$$

SA was calculated as

$$SA = 0.12 W^{\frac{2}{3}}$$
 (1.2)

where W is the canine body weight (3).

The pulmonary vascular resistance (R) is calculated from  $PAP_{mean}$ ,  $LAP_{mean}$ , and  $Q_{mean}$  by

$$R = (8.0 \times 10^6)(PAP_{mean} - LAP_{mean})/Q_{mean} \quad (1.3)$$

During these 30 min, the Q wave-form (pumpoutput) was recorded, and  $QI_{peak}$  (the peak-flow-



**FIG. 4.** Cannulation method of the total right ventricular bypass. RA, right atrium; RV, right ventricle; PA, pulmonary artery; LA, left atrium; LV, left ventricle; AO, aorta.



FIG. 5. Intrapulmonary shunt ratio calculation.

rate index),  $QI_{mean}$  (the mean-flow-rate index), and R were calculated. Then representative values for each index, shown in Figs. 9, 10, and 13, were determined by averaging for 30 min. Additionally, the wave-forms of Ql were quantitated by Fourier analysis explained as follows.

The expression of a periodic QI function as a Fourier series is given by the following formula

$$QI = A_0 + \sum_{n=1}^{\infty} (A_n \cos n \omega t + B_n \sin n \omega t)$$
(1.4)



**FIG. 6.** Blood sample drawing. a, arterial blood sample drawing port; v, venous blood sample drawing port; RA, right atrium; RV, right ventricle; PA, pulmonary artery; PV, pulmonary vein; LV, left ventricle.

where  $A_0$  is  $QI_{mean}$ , n is the harmonic number,  $A_n$ and  $B_n$  are the Fourier coefficients,  $\omega$  is the fundamental angular frequency, and t is time. The coefficients  $A_n$  and  $B_n$  are resolved into a single rotating vector. That is,

$$QI = A_0 + \sum_{n=1}^{\infty} C_n \cos(n \ \omega \ t + \phi_n) \quad (1.5)$$

When  $C_n = \sqrt{A_n^2 + B_n^2}$  and  $\phi_n = \tan^{-1} (-B_n/A_n)$ . In Fig. 8,  $A_0$  and  $C_n$  ( $n \le 15$ ) are shown. In the case of nonpulsatile flow,  $2 \text{ s}^{-1}$  (=120 min<sup>-1</sup>) is substituted for F (fundamental frequency:  $F = \omega/(2\pi)$ ) in Figs. 8C and 8D.

At the end of 30 min pumping, blood samples were drawn from the outlet of the pump and femoral artery. From the oxygen content in these samples, intrapulmonary shunt ratio (s) was calculated. Thus the relationships between  $QI_{peak}$ ,  $QI_{mean}$ , the pulse flow ratio,<sup>2</sup> and s could be studied.

The 30 min experimental process was then repeated after the operating factor of the pump was reset to maintain the newly selected  $Q_{mean}$ , which depends on the canine left heart function and on the control of circulating blood volume. When the hematocrit (Ht) decreased below 60% of control values, due to saline inflation and bleeding, right ventricular bypass pumping was halted. Thus, 21 experiments were performed with pumping lasting from 1–6 h.

To evaluate the relationships between variables, regression lines and the correlation coefficient ranges for 99% confidence limits were statistically calculated from experimental data (Figs. 9, 10, 11, and 13).

#### Intrapulmonary shunt ratio calculation

The intrapulmonary shunt ratio (s) was calculated from oxygen contents in the blood by the following method (Fig. 5).

The values of Hb, pH, PO<sub>2</sub>, and PCO<sub>2</sub> were measured in blood samples. To measure pHv, PvO<sub>2</sub>, and PvCO<sub>2</sub>,<sup>3</sup> the blood sample was drawn from the outlet (v in Fig. 6) of the right ventricular bypass pump (or from the vena cava through the catheter introduced via the femoral vein before pumping). To measure pHa, PaO<sub>2</sub>, and PaCO<sub>2</sub>,<sup>3</sup> the blood sample was drawn from the femoral artery (a in Fig. 6). PO<sub>2</sub>, PCO<sub>2</sub>, and pH were measured by the electrode-method in a blood-gas analyzer (Model 168, Corning-Medical, U.S.A.).

In this blood-gas analyzer, the base excess (BE) is calculated from Hb, pH, and  $[HCO_3^{-}]^4$  with the following equation suggested by Siggaard-Andersen (4)

$$BE = (1 - 0.0143 \text{ Hb})([\text{HCO}_3^-]) - (9.5 + 1.63 \text{ Hb}) (7.40 - \text{pH}) - 24.0)$$
(2.1)

Accordingly, BEa and BEv are calculated from "pHa, PaCO<sub>2</sub>, Hb" and from "pHv, PvCO<sub>2</sub>, Hb" by Eq. 2.1, respectively.

Then the fractional oxygen saturation of hemoglobin  $(SO_2)$  is calculated from BE, pH, PO<sub>2</sub>, and T (blood temperature) using the following equation suggested by Thomas (5)

$$SO_2 = (n^4 + A n^3 + B n^2 + C n)/(n^4 + A n^3 + D n^2 + E n + F) (2.2)$$

Where n =  $-PO_2 \exp(\ln 10 \ (0.48 \ (pH - 7.4) - 0.024 \ (T - 37) - 0.0013 \ BE))$ , A = 15, B = 2.045 × 10<sup>3</sup>, C =  $-2 \times 10^3$ , D = 2.4 × 10<sup>3</sup>, E = 3.11 × 10<sup>4</sup>, and F = 2.4 × 10<sup>6</sup>. That is, SaO<sub>2</sub> and SvO<sub>2</sub> are calculated from "pHa, BEa, PaO<sub>2</sub>, T" and from "pHv, BEv, PvO<sub>2</sub>, T" by Eq. 2.2, respectively.

The oxygen content  $(O_2CT)$  is calculated from Hb, SO<sub>2</sub>, and PO<sub>2</sub> by

$$O_2CT = (1.34 \times 10^{-2})Hb SO_2 + (3 \times 10^{-5})PO_2$$
(2.3)

And as before,  $O_2CTa$  and  $O_2CTv$  are calculated from "SaO<sub>2</sub>, PaO<sub>2</sub>, Hb" and from "SvO<sub>2</sub>, PvO<sub>2</sub>, Hb" by equation 2.3, respectively. That is

$$O_2CTa = (1.34 \times 10^{-2})Hb SaO_2 + (3 \times 10^{-5})PaO_2$$
(2.4)  
$$O_2CTv = (1.34 \times 10^{-2})Hb SvO_2$$
(2.5)

+  $(3 \times 10^{-5})$ PvO<sub>2</sub> (2.5)

 $O_2CTc$  is given by

$$O_2CTc = (1.34 \times 10^{-2})Hb ScO_2 + (3 \times 10^{-5})PcO_2$$
 (2.6)

where  $ScO_2 = 1$ , and  $PcO_2$  is calculated by the following equation

$$PcO_2 = (760 - P_AH_2O - P_ACO_2)(100 - HA)/100$$
(2.7)

and  $P_AH_2O = 47$  mmHg,  $P_ACO_2 = 40$  mmHg, and HA = 0.5 vol. % in the present study.

The intrapulmonary shunt ratio (s) is given by

$$s = Q_s / Q_T \tag{2.8}$$

 $<sup>^2</sup>$  Pulse flow ratio is the quotient of  $Q_{\text{peak}}$  divided by  $Q_{\text{mean}}.$  This value is unity when the flow is steady.

 $<sup>^3</sup>$  Suffixes "a" and "v" denote arterial and venous blood, respectively.

 $<sup>^4</sup>$  [HCO3-] is derived from pH and PCO2 by the Henderson-Hasselbach's equation.

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The total blood flow (flow-rate,  $Q_T$ ) is the mixture of the oxygenated blood flow (flow-rate,  $(Q_T - Q_S)$ ) and the nonoxygenated blood flow (flow-rate,  $Q_S$ ) (Fig. 6). Then

$$(Q_{T} - Q_{S})(O_{2}CTc) + Q_{S}(O_{2}CTv) = Q_{T}(O_{2}CTa)$$
(2.9)

Combining Eqs. 2.8 and 2.9,

$$s = (O_2CTc - O_2CTa)/(O_2CTc - O_2CTv)$$
 (2.10)

## RESULTS

Some typical traces of PAP, LAP, QI (of pumpoutput), and V (shown only for the positive displacement pump) during total right ventricular bypass with three types of blood pump are shown in Fig. 7. The harmonic contents of QI for each corresponding case are shown in Fig. 8, along with the control QI. In Fig. 8, the height of each bar represents the average magnitude of the harmonic. The 0-harmonic represents the average of  $QI_{mean}$ . These figures show quantitatively that the waveform of QI truly varies with each of the three types of blood pump. In the piston-bellows pump,  $QI_{peak}$ is varied with ER (compare A with B in Fig. 7). The harmonic contents of QI in B of Fig. 8 resembles those of the control (E of Fig. 8). Figures 7A and 7B show (i) the back flow and (ii) the inertial flow due to mobility of the valves: the latter makes the minor (second) peak of OI in 7A. Figures 7C and 8C show the notches with small amplitude and with high frequency in QI which are generated from the vibration of the rotor. The pulse pressure of PAP and the pulse flow (the difference between peak and trough flow-rates) of QI are markedly decreased with the screw pump and with the centrifugal pump, as the records in C and D of Fig. 7 demonstrate. These results are quantitatively expressed by the small magnitudes of harmonic content (harmonic number > 1) in C and D of Fig. 8. Especially in the centrifugal pump, every magnitude (harmonic number > 1) was under the noise level of the system.

From animal experiments in these 21 dogs, 92 data points were recorded and are shown in Figs. 9, 10, and 11. The mean flow-rate was controlled to within 10% variation of the target value in the preceding 30 min for these data, where  $PAP_{mean}$ , LAP<sub>mean</sub>, T, and Ht were 18  $\pm$  6 mmHg, 7  $\pm$  5 mmHg, 33  $\pm$  2°C, and 30  $\pm$  8% (mean  $\pm$  1 standard error), respectively.

Figure 9 shows s as a function of QI<sub>peak</sub>. The in-



**FIG. 7.** Some examples of simultaneous traces of pressure and flow during total right ventricular bypass with three types of pumps. **A** and **B**, piston-bellows type (A. ER = 7.5 mm; B, ER = 2.5 mm); **C**, screw type; **D**, centrifugal type.



**FIG. 8.** Harmonic contents of QI from A, B, C, and D of Fig. 7 are shown in **A**, **B**, **C**, and **D** in this figure, respectively. The height of each bar represents the mean magnitude of each harmonic. Vertical lines around the mean represent the standard error of the mean over the 30 min period. The harmonic contents of QI control values are shown in **E**, where vertical lines around the mean represent the standard deviation. The noise level of the system is indicated by the horizontal broken lines.

trapulmonary shunt ratio ranges between 0.095 and 0.392 with no clear relation (-0.3 < r < 0.3) to  $QI_{peak}$ , which varied between 1.1 and 17.0 l min<sup>-1</sup> m<sup>-2</sup>.

Figure 10 shows s as a function of  $QI_{mean}$ . The intrapulmonary shunt ratio does not increase as  $QI_{mean}$  decreases from 2.5 to 0.8 l min<sup>-1</sup> m<sup>-2</sup>, and reveals no clear difference among the three group of data (divided according to the pump types) even in the range of small  $QI_{mean}$ .

Figure 11 shows s as a function of the pulse flow ratio. Again, s ranges with no clear relation (-0.3 < r < 0.2) to the pulse ratio, which is varied between 1.0 and 13.6.

Figure 12 shows s as a function of pumping time where data are divided into two groups. One is the pulsatile flow group, in which  $(Q_{peak}/Q_{mean}) \ge 2.5$ and  $QI_{peak} \ge 4.0 \ \text{I} \ \text{min}^{-1} \ \text{m}^{-2}$ ; and the other is the nonpulsatile flow group, in which  $(Q_{peak}/Q_{mean})$ <2.5 and  $QI_{peak} < 4.0 \ \text{I} \ \text{min}^{-1} \ \text{m}^{-2}$ . The former group includes data with the piston-bellows pump, and the latter group includes data with the centrifugal pump or with the screw pump. The intrapulmonary shunt ratio is kept within the range of control values for 6 h, even in the nonpulsatile flow group.

Figure 13 shows R as a function of the pulse flow ratio. This figure shows that in several cases R remains very small even when  $Q_{peak}/Q_{mean}$  is approximately unity (which means quasi-steady flow), although a faint trend is shown that R increases with  $Q_{peak}/Q_{mean}$  decrease.

In Figs. 9, 10, 11, 12, and 13, each control value of s,  $QI_{peak}$ ,  $QI_{mean}$ ,  $Q_{peak}/Q_{mean}$ , or R is shown adjacent to the y axis by the closed circle (mean) and the bar ( $\pm 1$  standard deviation), respectively.

#### DISCUSSION

The effects of pulsatile or nonpulsatile blood flow on circulatory systems have been previously discussed based upon the cardiopulmonary bypass

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**FIG. 9.** Intrapulmonary shunt ratio (s) as a function of  $Ql_{peak}$ . -0.3 < r < 0.3 (the correlation coefficient range with 99% confidence limit; the same kind of range is shown in Figs. 10, 11, and 13).  $\bigcirc$ , piston-bellows pump;  $\triangle$ , centrifugal pump;  $\blacktriangle$ , screw pump.

and isolated organ perfusion experimental preparations (6). The possible effects of pulsatile blood flow on circulatory systems are (a) the control of distribution of the blood flow (including anastomotic and lymphatic flows) and (b) the enhancement of metabolites-transfer (7). The former might be derived from visco-elastic properties of blood vessels, from non-Newtonian behaviour of blood, and from the vasomotor tone controlled by the nervous system. The latter might be related to a mixing effect, which reduces the diffusion resistance of metabolite pathways. These effects have been studied in animal tests using right ventricular, left ventricular, or biventricular bypass. Some studies have reported that the blood flow distributions in organs (e.g., in the kidney) are more physiological under pulsatile than under nonpulsatile flow along with organ (e.g., renal) functions, and also that the peripheral resistance is smaller under pulsatile than under nonpulsatile flow (8, 9). On the other hand, a calf's total circulation had been maintained in good physiological status for 99 days under nonpulsatile conditions (10). In other words, some data from these studies demonstrate advantages to pulsing the blood flow, while others do not.

To make any discussion clear on this subject, pulsatility of blood flow has to be quantitated and the effect of pulsatility has to be quantitatively related to each point of the circulatory system. For example, Jacobs et al. (9) looked at the initial phase



**FIG. 10.** Intrapulmonary shunt ratio (s) as a function of  $QI_{mean}$ . -0.03 < r < 0.5.  $\bigcirc$ , piston-bellows pump;  $\triangle$ , centrifugal pump;  $\blacktriangle$ , screw pump.

of rapid ejection as an important element of pulse. In the present study,  $Q_{peak}$  is picked up to quantitate pulsatility with f fixed at 120 min<sup>-1</sup>. As stated before, in total ventricular bypass,  $Q_{mean}$  was equal to the cardiac output, while  $Q_{peak}$  could be varied to produce various pulsatile conditions depending on which pump was used. The harmonic contents of QI in Fig. 8B resemble those of a control dog with



**FIG. 11.** Intrapulmonary shunt ratio (s) as a function of  $Q_{peak}/Q_{mean}$ . -0.3 < r < 0.2.  $\bigcirc$ , piston-bellows pump;  $\triangle$ , centrifugal pump;  $\blacktriangle$ , screw pump.



**FIG. 12.** Intrapulmonary shunt ratio (s) as a function of pumping time.  $\bigcirc$ , pulsatile flow;  $\bullet$ , nonpulsatile flow.

natural heart, which also were reported by Patel (11).

Although the distinction between pulsatile and nonpulsatile groups was not quantitatively defined in previous studies, authors arbitrarily classified these two groups according to the pulse flow ratio  $(Q_{peak}/Q_{mean}): Q_{peak}/Q_{mean} \ge 2.5$  in the pulsatile group, and  $Q_{peak}/Q_{mean} < 2.5$  in the nonpulsatile group. Especially, nonpulsatile flow should be dis-



**FIG. 13.** Pulmonary vascular resistance (R) as a function of  $Q_{\text{peak}}/Q_{\text{mean}}$ . -0.6 < r < -0.04.  $\bigcirc$ , piston-bellows pump;  $\triangle$ , centrifugal pump;  $\blacktriangle$ , screw pump.

tinguished carefully, because the perfectly steady flow is hardly realized in general fluid circulation, much less in blood circulations. Peripheral flows with  $Q_{peak}/Q_{mean} < 2.5$  are estimated to be quasisteady, because vibrations of small amplitude (or of high frequency) at the pump outlet are smoothed by the viscoelastic compliance of blood vessels (12). According to this classification, the Q wave-forms from either the centrifugal or screw pump are classified into the nonpulsatile group.

In the present study,  $Q_{mean}$  is controlled not by the transfusion of homogeneous blood but by the supply of the saline solution, in order to minimize the other biological effects on the intrapulmonary shunt ratio. In the present experiments, data indicate no clear relation between s and Ht (17–50%), which means that this transfusion does not have much effects on s.

The results in the present study show that even in the nonpulsatile flow,  $1.0 < (Q_{peak}/Q_{mean}) < 2.5$ , the blood is well oxygenated so that the intrapulmonary shunt ratio is within the control value (Fig. 11), while pulsatility enhances gas transfer in the membrane oxygenator (the artificial lung) (13). These results do not completely negate the possibility that pulsatility enhances gas transfer in the pulmonary microcirculation, where pulsatile condition might exist owing to the backward propagation of the pulse from the left atrium, due to the bronchial pulse or the respiratory pulse in the present experiments. These results may be attributed to the large allowances of the natural lung, of which gastransfer-membrane is much thinner and larger than that of artificial lung which is available today. This tendency does not change when QI<sub>mean</sub> is small in Fig. 10, although the former studies have shown that the pulse has good effect on systems when  $QI_{mean}$  is small (6). Small value of  $QI_{mean}$  in Fig. 10 (which might indicate heart failure) does not adversely affect the experimental design, because the blood oxygenation is measured in relation to QI<sub>peak</sub> which is mechanically controlled by right heart bypass pumping. The result in Fig. 13 also indicates that pulmonary vascular resistance is able to be kept small even under nonpulsatile flow, which does not agree with Clarke's study (8).

This study demonstrates that the intrapulmonary shunt ratio is able to be held in the range of control value even with the peak-flow-rate index smaller than 4.0 l min<sup>-1</sup> m<sup>-2</sup>, and that nonpulsatile pump are available for the total right heart bypass pumps.

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