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Oxygen Distribution during Extracorporeal
Oxygenation for Acute Respiratory Failure
Comparison between Venoarterial
and Venovenous Bypass

MITSUHIKO MATSUDA

The 2nd Department of Surgery, Faculty of Medicine, Kyoto University
(Director : Prof. Dr. YORINORI HIKASA)
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Introduction

The development of membrane oxygenators has facilitated long-term heart-lung bypass, especially extracorporeal oxygenation. Clinical experiences³⁾⁴⁾⁵⁾⁹⁾¹⁰⁾¹³⁾¹⁷⁾²⁰⁾²⁵⁾³¹⁾³⁶⁾³⁸⁾³⁹⁾ with membrane oxygenators in recent years suggest that partial cardiopulmonary bypass offers a new supportive measure in the management of respiratory failure, and the value of this method is currently under investigation in many centers. The survival rate, however, is still low. There are many reasons for the failure to obtain good results: irreversible pulmonary lesions, hemorrhagic tendency, inadequate oxygen distribution through the body, cardiac failure, central nervous system damage, infection etc.²¹⁾

In this study, several types of bypass circuits were compared, in a search for satisfactory oxygenation by extracorporeal circulation of various hypoxic regions of the body. In order to investigate oxygen distribution in the whole body during heart-lung bypass, we used the model of acute pulmonary edema in dogs.

The proper positioning of cannulas to return oxygenated blood to patients with respiratory insufficiency on long-term membrane oxygenator support is not yet clinically clear. There are two kinds of systems for extracorporeal oxygenation: venoarterial (V-A) bypass and venovenous (V-V) bypass.

In this experiment, we studied four types of V-A circuits and one type of V-V circuit. (Fig. 1):

1. V-A bypass in which oxygenated blood returns to the right femoral artery.
2. V-A bypass in which oxygenated blood returns to the right subclavian artery.

Key words : Extracorporeal oxygenation, Respiratory failure, Oxygen distribution, Venoarterial bypass, Venovenous bypass

Present address : The 2nd Department of Surgery, Faculty of Medicine, Kyoto University, Sakyo-ku, Kyoto, 606, Japan.

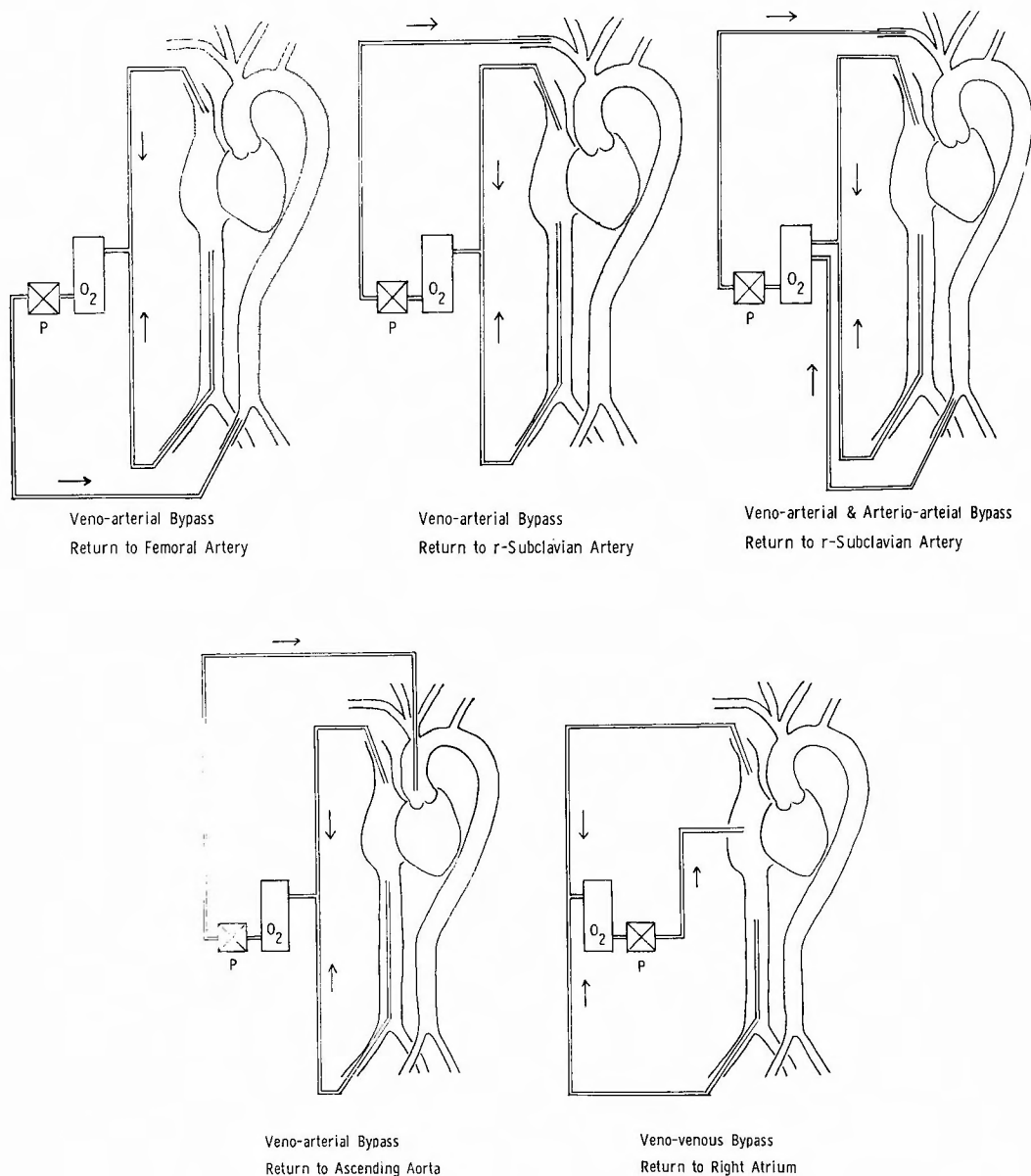


Fig. 1 Cannulation system of bypass circuits. P Roller pump, O_2 : Oxygenator.

3. V-A bypass in which oxygenated blood returns to the right subclavian artery, combined with arterioarterial (A-A) bypass.
 4. V-A bypass in which oxygenated blood returns to the ascending aorta.
 5. V-V bypass in which oxygenated blood returns to the right atrium.
- Dogs were assigned to these five groups.

Materials and Method

Mongrel dogs, weighing 8 to 21 kg, in apparent good health, were anesthetized with intravenous pentobarbital sodium (Nembutal®), intubated with a cuffed endotracheal tube, placed on a volume-cycled respirator (Harvard Apparatus Co. Inc. Model 614) and given room air with a tidal volume of 20 ml/kg at a respiratory rate of 15 breaths per minute.

A groin cutdown was performed and polyethylene catheter connected to a pressure transducer (Statham No. 18530) was inserted through the left femoral artery into the left ventricle, and then pulled back to the level of the aortic sinuses. This catheter was gradually withdrawn during bypass to sample blood for gas analysis at the levels of the aortic root, the aortic arch, the thoracic aorta, the abdominal aorta and the femoral artery and was utilized to monitor arterial blood pressure. Gas analysis was performed by Corning Gas Analyzer (Model 165).

The second catheter was inserted via the left femoral vein to the inferior vena cava for drip infusion and monitoring central venous pressure. The third catheter was located in the left external jugular vein without disturbing blood flow and was used for sampling the venous blood which returned from the brain and the head. Furthermore, the left axillary vein was exposed and a Swan-Ganz flow directed thermodilution catheter was advanced into the pulmonary artery. The tip of this catheter was positioned at a right or left pulmonary arterial branch for the injection of oleic acid. With this catheter, the cardiac output was also measured with a Kimray Thermodilution Cardiac Output Computer. The left subclavian and carotid arteries were cannulated to sample the arterial blood which perfused the upper half of the body during extracorporeal oxygenation.

Following thoracotomy, the other sampling catheters were inserted into the left atrium and the coronary sinus through the left appendage and the right atrial wall, respectively.

After completion of cannulation and baseline measurements, oleic acid (0.04 ml/kg) was injected slowly through the Swan-Ganz catheter into one lung to produce chemical pulmonary edema. The animals were thus rendered hypoxic. Arterial pressure was maintained by the intravenous infusion of lactated Ringer's solution and low molecular dextran. These dogs were placed on extracorporeal circulation when the PO_2 of left atrial blood fell below 40 mmHg. Prior to perfusion, 2 mg/kg of heparin was given intravenously and the heparin level was regulated with the use of activated coagulation time⁽⁴⁾ (Hemochron Time)⁽²⁸⁾⁽²⁹⁾ throughout the bypass period. One hundred per cent of oxygen was blown into the oxygenator, and the circuit was primed with donor blood freshly drawn in heparin and plasma expander.

Two cannulas of the largest possible size were advanced through the right femoral and the right jugular veins into the venae cavae until the tips were a few centimeters from the right atrium. Venous blood was drained directly from these cannulas into the oxygenator with a full gravity system. In clinical cases, membrane oxygenators must be used for a long-term extracorporeal oxygenation, however, in this experiment Temptrol

Q-110 bubble oxygenators (Bentley Inc.) were used. Oxygenated blood was returned to the animals with the use of a double roller pump (Pemco Co. Model 7350). The site of returning oxygenated blood was selected according to the method of bypass circuit.

In circuit 1, an arterial cannula was inserted for a few centimeters into the right femoral artery. The right subclavian artery was cannulated for oxygenated blood return in circuit 2. In circuit 3, arterial drainage to the oxygenator from the right femoral artery was added in order to increase the bypass flow, and the right subclavian artery was chosen as the site of arterial return. This system, then, consists of V-A and A-A bypass. With circuit 4, arterial return was by direct cannulation of the ascending aorta approximately 2 cm above the aortic valve. In circuit 5, oxygenated blood was released into the right atrium with the multiholed cannula which facilitated better mixing of oxygenated blood with venous blood (Fig.1).

Perfusion was started with a low flow, and the rate was changed at levels of 10, 20, 30, 40, 50, 55 and 75 per cent of the cardiac output obtained at a baseline measurement. Blood samples were taken from the arterial line from the oxygenator, venous drainage line, the left atrium, the aorta and its branches, the jugular vein, the coronary sinus and the pulmonary artery for pH, PO_2 , PCO_2 , total CO_2 , base excess and hematocrit. Oxygen saturation (SO_2) was calculated using BARTEL's nomogram²⁾. Systemic arterial pressure, central venous pressure and electrocardiogram were monitored throughout the experiments. Sodium bicarbonate was given to maintain a normal pH when oxygenator support was inadequate. Central venous pressure was maintained within normal limits and mean arterial pressure over 80 mmHg. The animal's body temperature usually remained stable at 34-37°C with the heat exchanger of the Temptrol oxygenator.

Postmortem examination was carried out when the animals died or were killed at the end of the experiment.

Result

I) Pulmonary insufficiency

The mean PO_2 in the PA (pulmonary artery) and LA (left atrium) prior to the injection of oleic acid was 47 and 84 mmHg, respectively. Arterial PO_2 gradually decreased and was below 45 mmHg about 2 hours after the oleic acid injection. At this point, bloody bronchial secretions, indicating the formation of pulmonary edema, were obtained by intrabronchial suction. The respiratory rate did not change because of controlled ventilation with the use of a muscle relaxant (Dialferin[®]). The change of PO_2 in the left atrium and the pulmonary artery when extracorporeal oxygenation was not provided is shown in Fig. 2.

II) Oxygen distribution during extracorporeal oxygenation

1) V-A bypass (return to the femoral artery)

Fig. 3 shows the partial oxygen tension at six sites of the body during femoral artery perfusion at rates of 30 and 50 per cent of cardiac output. The abdominal aorta (at the level of the renal artery) and the femoral artery had higher values of PO_2 than the carotid

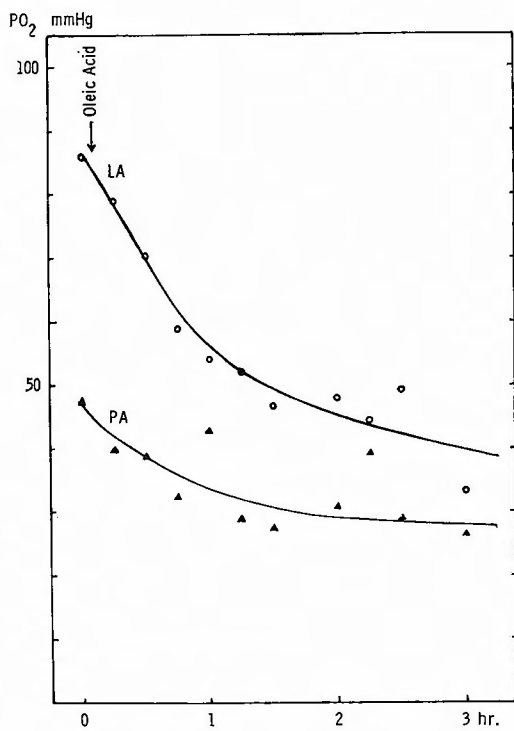


Fig. 2 Change of PO_2 after oleic acid injection

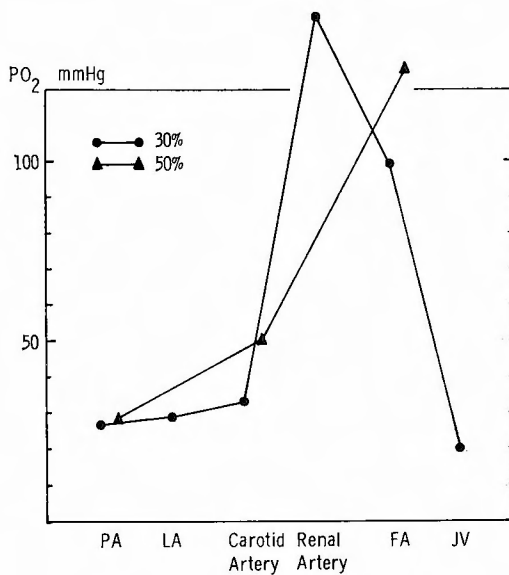


Fig. 3 PO_2 during V-A (FA) bypass

PA : Pulmonary artery, LA : Left atrium,
FA : Femoral artery, JV : Jugular vein.

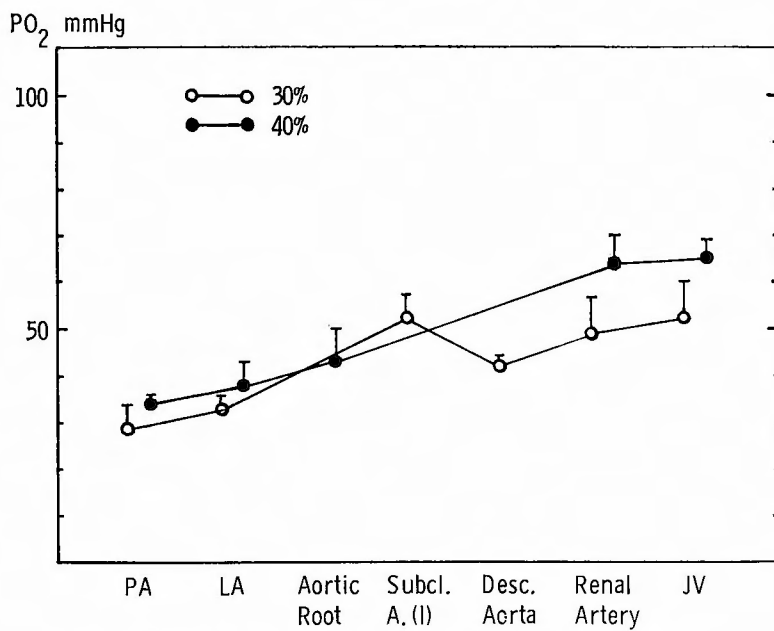


Fig. 4 PO_2 during V-A (r-Subclavian Artery) bypass

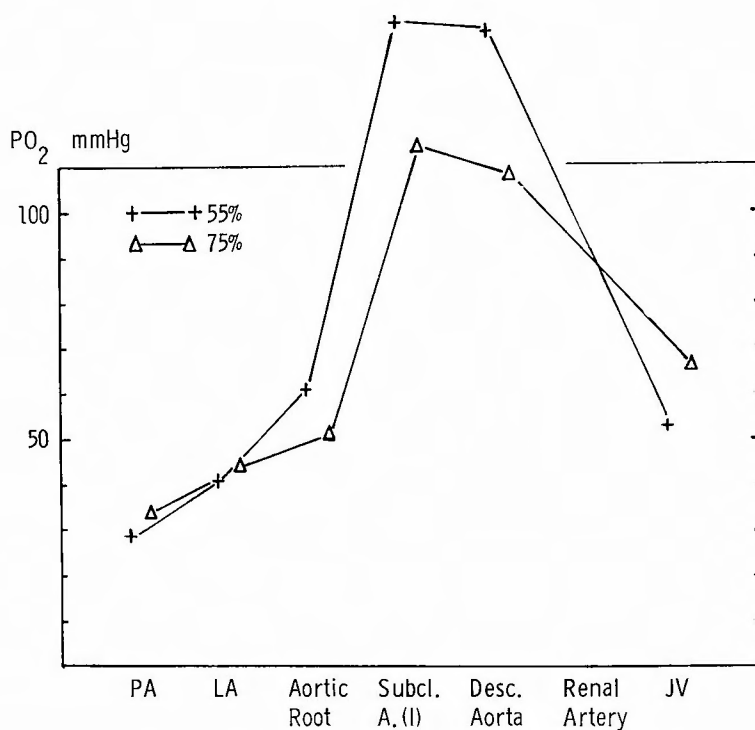


Fig. 5 PO₂ during V-A (r-Subclavian Artery) bypass combined with A-A bypass

artery, and the PO₂ in the jugular vein was very low. These findings show that the upper half of the body could not be perfused sufficiently with oxygenated blood.

2) V-A bypass (return to the right subclavian artery)

Fig. 4 shows the value of PO₂ at various sites of the body during right subclavian artery perfusion with flow rates of 30 and 40 per cent. The oxygen tension of jugular venous blood was higher than that of arterial blood in the aortic root. Thus, oxygenated blood delivered to the right subclavian artery was directed mainly to the head.

3) V-A and A-A bypass (return to the right subclavian artery)

With the addition of A-A bypass (blood withdrawal from the right femoral artery), the perfusion rate could be increased to 75 per cent of the cardiac output. In this system, the PO₂ in the left subclavian artery and in the descending aorta was above 100 mmHg, but that in the blood from the aortic root remained below 60 mmHg (Fig. 5).

4) V-A bypass (return to the ascending aorta)

As seen in Fig. 6, the PO₂ in the aortic root, aortic arch and femoral artery was maintained evenly but at relatively low values. Furthermore, the PO₂ and SO₂ of coronary sinus blood remained low (Fig. 7) at 30 and 40 per cent of the flow rate. With 50 per cent bypass, these two values still could not reach baseline measurements. This fact is presumably due to inadequate mixing of oxygenated blood in the aortic root at low bypass

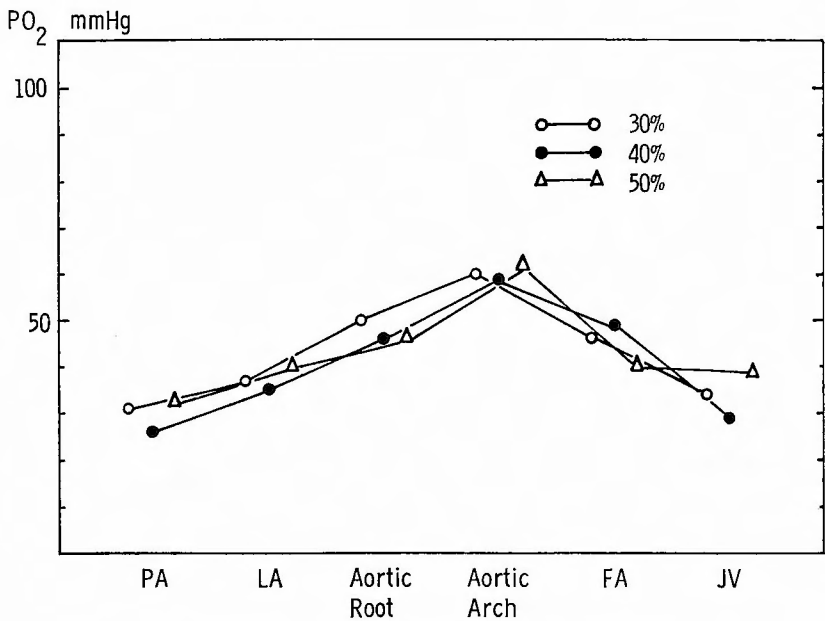


Fig. 6 PO₂ during V-A (Ascending Aorta) bypass

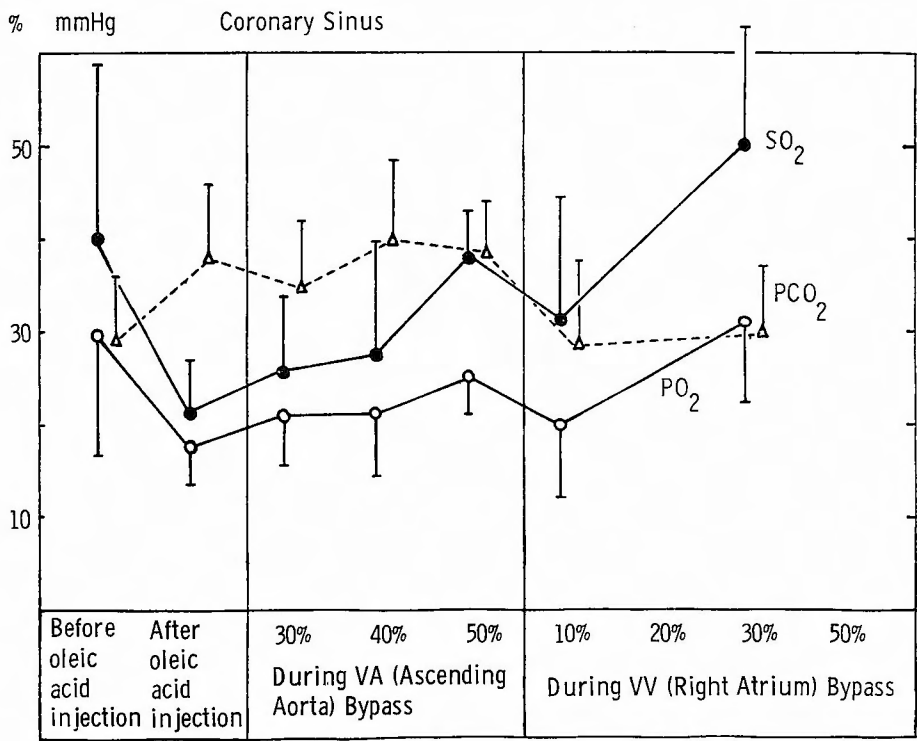


Fig. 7 PO₂, SO₂ and PCO₂ of the coronary sinus. Comparison between venoarterial and venovenous bypass.

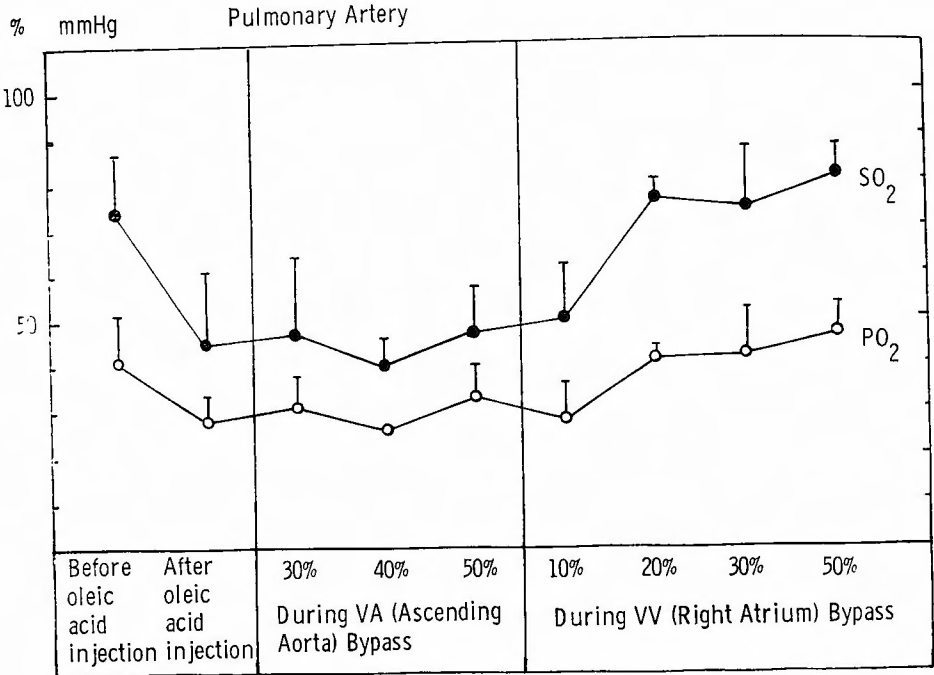


Fig. 8 PO₂ and SO₂ of the pulmonary artery.

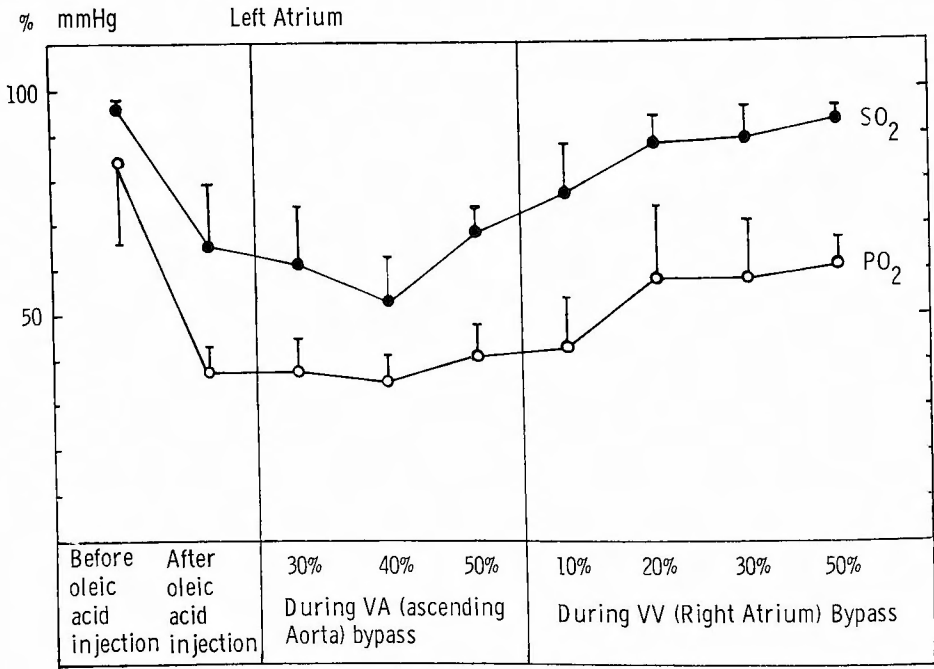


Fig. 9 PO₂ and SO₂ of the left atrium.

Table 1 PO₂, SO₂ and PCO₂ of the pulmonary artery, left atrium, coronary sinus and jugular vein before and after oleic acid injection and during bypass.

Probability by t test with the value after oleic acid injection.

	Before oleic acid injection	After oleic acid injection	During VA (Ascending Aorta) Bypass			During VV (Right Atrium) Bypass			
			30 %	40 %	50 %	10 %	20 %	30 %	50 %
Pulmonary Artery	41.3±10.0	27.0± 7.1	30.9± 8.1	26.7± 1.5	32.9± 7.8*	28.2± 9.5	41.4± 3.3*	42.3± 9.7*	46.7± 7.6*
	73.6±13.5	45.1±16.7	46.0±18.6	39.3± 5.4	46.5±10.9	49.5±14.3	75.5± 4.8*	73.6±14.1*	80.8± 7.5*
	26.7± 8.9	33.5± 9.9	38.2±10.3	43.9± 4.5	45.6± 5.7	26.9± 8.5	25.1± 4.9*	31.5± 8.5	38.4± 2.4*
Left Atrium	83.9±18.0	36.8± 6.7	37.3± 7.5	35.0± 6.1	40.9± 7.4	42.3±12.4	58.0±16.1*	58.1±13.6*	60.9± 7.3*
	95.8± 2.5	66.2±12.9	60.9±13.5	57.3± 9.9	67.8± 6.1	76.7±13.6	88.1± 7.7*	89.4± 6.5*	92.6± 3.5*
	22.6± 9.2	31.1± 6.6	32.3± 5.3	35.0± 5.7	36.1± 6.4	23.5± 6.6	22.0± 5.4*	26.6± 7.5*	32.7± 1.4
Coronary Sinus	29.4±12.9	17.2± 3.6	20.8± 5.3	20.9± 7.6	24.7± 3.5*	20.4± 8.3		30.9± 9.0*	
	40.0±19.1	20.8± 6.5	25.4± 8.8	26.8±13.3	37.5± 5.5	30.8±13.9		49.8±13.7	
	29.5± 6.7	38.3± 8.9	35.3± 6.7	37.9± 8.7	38.6± 5.3	28.8± 8.8		29.5± 7.6	
Jugular Vein			34.0± 8.1	28.6± 4.8	40.1± 7.9	PO ₂ mmHg			
			52.6±18.1	43.0±14.1	60.5±10.8	SO ₂ %			
			34.0± 5.3	43.0± 6.3	40.7± 8.5	PCO ₂ mmHg			
						Mean±SD			
						* = P<0.05			

rates. Only a small elevation of PO₂ in the left atrium was observed in this group.

5) V-V bypass (return to the right atrium)

The experiences and results mentioned above indicate that V-V bypass might be necessary for well oxygenated blood to be distributed to the whole body. As shown in Fig. 7, 8 and 9, with 10 per cent V-V bypass, the PO₂ in the PA and LA did not increase enough, but with 20, 30 and 50 per cent bypass, PO₂ and SO₂ values showed significant increase in the PA, LA and coronary sinus. PCO₂ values in the coronary sinus were lower than those of V-A bypass (Fig. 7). The values of PO₂, SO₂ and PCO₂ in the PA, LA, coronary sinus and jugular vein before and after oleic acid injection and during bypass were shown in Table 1. The differences in oxygen saturation values between samples from the drainage cannula to the oxygenator and those from the PA suggest that oxygenated blood was returned to the heart from the extracorporeal circuit without being wasted in the drainage cannulas. The mean pulmonary artery pressure and the right atrial pressure did not increase during V-V bypass.

Optical microscopic observation of the lungs perfused with V-V bypass showed parenchymal changes similar to those seen with V-A bypass.

Discussion

Progressive pulmonary insufficiency and resulting hypoxia necessitate the use of toxic levels of inspired oxygen and unphysiologic mechanical ventilation. Extracorporeal oxygenation diminishes the requirement for mechanical ventilation and allows reduced concentrations of inspired oxygen. Many investigators have described the effect of extracorporeal oxygenation experimentally²⁷⁾³³⁾³⁷⁾ and clinically. In order to make experimental pulmonary failure models, KRANSA, SOETER, HANSON, KOLOBOW and others lowered the oxygen concentra-

tion of inspired gas¹⁶⁾²⁴⁾²⁶⁾. However, the effect of extracorporeal oxygenation during V-V bypass could not be determined in their models because of oxygen elimination from oxygenator blood during pulmonary circulation. AWAD¹⁾ lowered the ventilation rate and BRANDT⁷⁾ used a chemical agent (0.1N HCL) to make the animals hypoxic. In the present study, pulmonary edema was induced by oleic acid⁶⁾ as described by KING and ASHBAUGH²²⁾. GEMER and KOJA selected the right atrium as the site of injection of oleic acid¹⁵⁾²³⁾, but in our experience that method caused severe dysfunction of all lobes; and large bleeding from bronchi and unstable hemodynamics made the following experiments difficult. Therefore, we chose one of the pulmonary arterial branches as the injection site via a using Swan-Ganz catheter. This provided a suitable experimental model.

With extracorporeal V-A bypass in respiratory failure, regional tissue hypoxia develops because of inadequate distribution of oxygenated blood. The site chosen for cannulation and the rate of perfusion are more important factors in prolonged extracorporeal oxygenation. V-A bypass provides cardiovascular as well as pulmonary support, and arterial cannulation via the femoral artery has no difficulty. However, oxygenated blood returned to the femoral artery is distributed only to the kidneys, the mesenteric beds and the lower limbs. ESATO¹²⁾ investigated the distribution of oxygenated blood in V-A bypass via the femoral and carotid arteries and concluded that more than 75 per cent of cardiac output was required for femoral artery perfusion to achieve satisfactory oxygenation of the upper body. In other investigations 70 to 85 per cent bypass was required for that purpose¹⁴⁾. Our experimental data confirmed these findings.

The major flaw of V-A bypass is the inappropriate distribution of arterialized blood, depending upon the position of the arterial cannula. HILL showed that even small amount of cardiac output precluded perfusion of the thoracic aorta and proximal aortic branches by oxygenator efflux from a catheter tip in the femoral artery. Therefore, attempts to improve proximal aortic saturation by extracorporeal means are of great importance. Some workers have used brachial artery perfusion to obtain adequate oxygenation in the aortic region¹⁹⁾. DERKS¹¹⁾ investigated the oxygen supply to the myocardium and the brain, and concluded that both heart and brain received adequate oxygenation when the bypass was large and the carotid and femoral arteries received a share of arterialized blood. SOETER³⁵⁾ showed that brachial perfusion required a much lower (45 per cent) bypass to achieve high PO_2 levels in the upper aorta, and stability of the system was evident. We chose the right subclavian artery perfusion system, but could not obtain adequate oxygen at the aortic root. To correct this failure to oxygenate the aortic root, additional arterial drainage was used to increase the bypass rate. In our experiment, with a V-A and A-A bypass we were unable to obtain a satisfactory PO_2 at the aortic root despite 75 per cent bypass.

MCENANY³⁰⁾ indicated that perfusion of the upper extremity is not ideal since the size of the upper extremity arteries is small. Therefore, in order to supply more flow to the proximal aorta, he suggests the use of a large, steerable thin-walled cannula introduced through the femoral artery and passed retrograde to the root of the ascending aorta.

COOPER and ZAPOL also reported⁸⁾⁴⁰⁾ that they performed retrograde cannulation of the ascending aorta and the oxygenated blood returning through this cannula was completely mixed with blood in the ascending aorta. In this study, instead of retrograde cannulation, direct ascending aorta cannulation was done and the tip of the cannula was directed to the aortic valve, but the PO_2 of the coronary sinus blood remained low and the PCO_2 high. The myocardium was partly perfused with venous blood flowing out of the nonfunctioning lungs. SECKER-WALKER³⁴⁾ suggested that the coronary arterial blood was hypoxic except in those animals with zero left ventricular output. With partial V-A bypass, it is difficult to obtain a high flow rate (more than 85% bypass), and such a high flow makes hemodynamics and homeostasis unstable.

V-A perfusion decreases pulmonary blood flow. HILL has reported that V-A perfusion decreases the mean pulmonary artery pressure, but this was rarely observed during V-A or V-V-A (venovenous and venoarterial) perfusion in ZAPOL's study⁴⁰⁾. BRANDT⁷⁾ and HILL have pointed out the advantages of using V-A bypass as opposed to V-V bypass, but V-A bypass also has some disadvantages. It does not supply the pulmonary artery with saturated blood and therefore may impede healing of the pulmonary parenchyma. It may lower pulmonary artery pressure and decrease perfusion of areas of high resistance, possibly causing further necrosis or injury. HILL and McENANY indicated that the problem of potential embolization with thrombi formed in the left side of the heart or pulmonary veins is troublesome with V-A perfusion³²⁾.

On the other hand, several investigators believe that exposure of the pulmonary vasculature to more oxygenated venous blood helps to support the healing process of lung¹⁹⁾. Cerebral and cardiac dysfunction, frequently seen in patients with severe respiratory failure, is in part due to perfusion of the carotid and coronary arteries with unsaturated blood. V-V perfusion has the advantage of allowing the arterial tree to distribute oxygenated blood in a uniform pattern via the left ventricle and is more effective in delivering oxygen to the myocardium than are several kinds of V-A perfusion at a low flow rate.

Clinically, there are practical advantages in using the lowest pump rate and the least number of cannulation sites to achieve satisfactory perfusion of the vital organs in the upper body. Thus, it is necessary to deliver oxygenated blood directly into the right heart. V-V bypass is a relatively simple method of perfusion, is more physiological and presents fewer technical problems in regard to cannulation and pumping.

From our experimental results, V-V bypass is thought to be better than V-A bypass for oxygen distribution. The control of high flow bypass which must be carried on for a long period is difficult to keep stable, because of the unphysiologic state during extracorporeal circulation. V-V bypass distributes oxygen in a uniform pattern through the whole body and makes the oxygen tension in the aortic root effectively higher than any type of V-A bypass at a relatively low flow rate.

In addition to the oxygen distribution, there are some problems⁵⁾³²⁾ in the treatment of respiratory failure with extracorporeal oxygenation; for example, infection, hemorrhage,

long-term control of bypass etc⁴⁾¹⁸⁾³⁹⁾. Although these problems must be solved at the same time, we intend to apply these results to clinical practice in the future.

Summary

Venoarterial (V-A) and venovenous (V-V) bypass were compared in regard to their ability to provide adequate oxygen distribution during extracorporeal oxygenation.

- 1) With V-A bypass, adequate oxygen supply at the aortic root could not be obtained.
- 2) V-V bypass was able to deliver satisfactory oxygen to the heart at a relatively low flow rate.
- 3) No significant change occurred in pulmonary artery pressure and right atrial pressure under V-V bypass.
- 4) Parenchymal changes in the lung after V-V bypass were similar to those seen with V-A bypass.

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和文抄録

急性呼吸不全における体外補助循環時の 酸素分配について (V-A バイパスと V-V バイパスの比較)

京都大学医学部外科学教室第2講座 (指導: 日笠頼則教授)

松 田 光 彦

膜型人工肺の開発は長期体外循環を可能にし、呼吸不全における治療の手段として、その有効性が実験的、臨床的に報告されている。しかし、体外補助循環を用いた呼吸不全症の救命率はまだ低い。その原因として、原疾患の病態が大きな要素をしめているが、長期補助循環中にみられる出血傾向、心不全、中枢神経系機能低下、感染、生体内酸素分配の不適當など問題は多い。なかでも、酸素分配の不均衡は、心不全、中枢神経系機能抑制を招来する可能性が大きいため、安全かつ効果的な体外循環を行うことが必要とされる。

本実験では、オレイン酸投与により惹起せしめた呼吸不全犬に、4種類のV-Aバイパス及び右心房環流V-Vバイパスを行い、生体内各部、特に大動脈起始部、心筋への酸素分配を比較した。オレイン酸は、スワンガンツカテーテルを用いて、左右いずれか一方の

肺動脈内に注入し、部分的肺水腫を惹起せしめこれを実験に供した。

比較検討を行ったバイパス回路は、1)大腿動脈環流V-Aバイパス、2)右鎖骨下動脈環流V-Aバイパス、3)大腿動脈脱血を加えた右鎖骨下動脈環流V-A、A-Aバイパス、4)上行大動脈環流V-Aバイパス、5)右心房環流V-Vバイパスの5回路であった。

V-Aバイパス群はいずれの回路を用いても、大動脈起始部における酸素分圧の上昇が不充分であり、長期間のバイパスでは、心機能低下の発生が予想された。それに比してV-Vバイパスでは、右心系、肺動脈圧の上昇をみることなく均等な酸素分配が得られ、肺組織にもV-Aバイパスと著変なく、効果的であることが示された。