Suitable shunt size for regulation of pulmonary blood flow in a canine model of univentricular parallel circulations

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Objective: We examined the influence of shunt size on regulation of the pulmonary blood flow in a canine model of a univentricular heart because specific guidelines regarding suitable shunt size in the Norwood operation remain undetermined.

Methods: Beagle dogs ($n = 8$) 3 to 7 months old and weighing 3.0 to 5.0 kg were used. Atrial septectomy and patch closure of the tricuspid valve were performed, and a systemic–pulmonary arterial shunt was created by interposing a 3.5- or 4.0-mm graft between the right subclavian artery and main pulmonary artery. After cardiopulmonary bypass, hemodynamic variables including pulmonary and systemic blood flow were measured consecutively according to physiologically respiratory manipulations. The ratio of shunt size to body weight ranged from 0.80 to 1.33 mm/kg (1.08 ± 0.16 mm/kg).

Results: Each dog with a ratio of shunt size to body weight of 0.8 to 1.1 showed significant negative correlation between the pulmonary/systemic blood flow ratio and arterial PCO_2 , but those with a ratio of shunt size to body weight of 1.1 to 1.4 did not. Consequently each dog with a ratio of shunt size to body weight of 0.8 to 1.0 got adequate systemic flow, whereas a ratio of 1.0 to 1.4 resulted in inadequate systemic flow and acidic status. Similar phenomena were shown with the grouped data on relationship between the pulmonary/systemic blood flow ratio and inspired oxygen fraction.

Conclusions: These findings imply that when the ratio of shunt size to body weight is 0.8 to 1.1, the pulmonary/systemic blood flow ratio is controllable by physiologic respiratory manipulations. Larger shunts make pulmonary blood flow excessive and uncontrollable. We recommend that a ratio of shunt size to body weight of 0.9 to 1.0 be considered a useful index for suitable systemic–pulmonary arterial shunt in the Norwood operation.

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Since Norwood and colleagues' initial publication,¹ staged reconstruction for patients with hypoplastic left heart syndrome has been achieved according to several rationales and technical evolutions, and its outlook has dramatically improved with time.²⁻⁵ Contemporarily, however, the most problematic and controversial step in the staged-approach remains optimal pulmonary blood flow in the first stage of palliation.⁵⁻⁷ The size of the systemic–pulmonary arterial shunt, Paco_2 , and inspired oxygen fraction (FiO_2) may all play roles in controlling the pulmonary blood flow.^{2,6-11}

Generally speaking, the use of a smaller shunt in the first-stage palliative surgery is advocated clinically because larger shunts are associated with high incidence of acute cardiovascular collapse and mortality.^{2,6,7,12,13} However, the specific guide-

Figure 1. Preparation of canine model of univentricular heart. Atrial septectomy (A), patch closure of tricuspid valve annulus (B), and systemic-pulmonary arterial shunt (C) are performed to examine characteristics of pulmonary blood flow dynamics in univentricular parallel circulations. Note that right subclavian artery is third branch of first head vessel from aortic arch, unlike in human beings. For direct measurements of aortic and pulmonary blood flow, electromagnetic flowmeter probes are adjusted tangentially around ascending aorta and shunt graft, respectively.

lines for suitable shunt size remain undefined. Our aim was to elucidate the role of shunt size in regulation of the pulmonary blood flow and to determine a useful index for an optimal size of systemic-pulmonary arterial shunt in the first-stage palliative surgery with a canine model of the univentricular heart.

Material and Methods

Animal Preparation

Female beagle dogs ($n = 8$) 3 to 7 months old and weighing 3.0 to 5.0 kg were used. All animals received humane care in compliance with the "Guide for the Care and Use of Laboratory Animals" prepared by the Institutes of Laboratory Animal Resources, National Research Council, and published by National Academy Press, revised 1996.

Each dog was anesthetized with pentobarbital sodium (5 mg/kg intravenously), fentanyl (0.05 mg/kg intravenously), and pancuronium bromide (0.1 mg/kg intravenously). Mechanical ventilation

was instituted with initial settings of FiO_2 of 0.3, rate of 12 breaths/min, peak inspiratory pressure of 12 cm H_2O , and positive end-expiratory pressure of 3 cm H_2O (model IV-100B; Sechrist, Anaheim, Calif). Anesthesia was maintained with fentanyl (0.05 mg/[kg $\cdot$ h] intravenously) and pancuronium bromide (0.5 mg/[kg $\cdot$ h] intravenously).

A 4F plastic catheter was inserted into the descending aorta from the femoral artery for systemic arterial blood pressure monitoring and arterial blood gas sampling. Another 4F catheter was placed into the inferior vena cava from the femoral vein for central venous pressure monitoring.

With the animal in the supine position, the heart and great vessels were exposed through a midline sternotomy. A 4F catheter was inserted into the left atrium for left atrial pressure monitoring, and another catheter was placed into the main pulmonary artery from the infundibulum of the right ventricle for pulmonary arterial pressure monitoring.

The animal model of the univentricular heart was prepared in accordance with the procedure of Mora and colleagues⁹ (Figure 1). After systemic heparinization (0.3 mL/kg), a 3.5- or 4.0-mm microknitted Dacron polyester fabric graft (Golaski vascular prosthesis; Golaski Laboratories, Philadelphia, Pa) with 30 to 40 mm length was anastomosed end to side to the origin of the right subclavian artery. Cardiopulmonary bypass (CPB) was then initiated by placing the arterial cannula in the ascending aorta and placing the venous cannula into the right atrium. Pump flow was maintained between 100 and 150 mL/(kg $\cdot$ min), and mean arterial pressure was maintained between 40 and 70 mm Hg. While the animal was being cooled to a pharyngeal temperature of 18 to 20°C, another side of the graft was anastomosed to the main pulmonary artery. The shunt was clamped until the animal was halfway weaned from CPB. After completion of hypothermia, cardiac arrest was obtained by topical cooling with iced slush, and then the circulation was arrested. After a right atriotomy, an atrial septectomy and suturing of a patch to the annulus of the tricuspid valve were performed to exclude the right ventricle from the circulation. After the right atriotomy was closed, the animal was placed back on CPB and rewarmed to a pharyngeal temperature of 37°C. The heart was defibrillated as needed. During rewarming, hemoconcentration was performed by the extracorporeal ultrafiltration method until the hematocrit value was 35% to 45%. When pump flow was decreased to half after completion of rewarming, the clamp of the systemic-pulmonary arterial shunt was released and ventilation was resumed with FiO_2 of 1.0. When hemodynamics were satisfactory, the animal was weaned from CPB with the administration of dopamine in doses of 5 $\mu\text{g}/(\text{kg} \cdot \text{min})$.

This experiment constitutes a set of consecutive animal preparations with equal technical success. All animals were killed after data acquisition.

Data Acquisition

Arterial blood gas values, pH, base excess, and hematocrit were measured with a blood gas and hematocrit analyzer (GEM STAT; Mallinckrodt Inc, Ann Arbor, Mich). Pulmonary and systemic arterial, central venous, and left atrial pressures were measured with a polygraph system (AP-641G; Nihon Kohden Corporation, Tokyo, Japan). Mean pressure was obtained by electrical integra-

TABLE 1. Hemodynamic variables in all canine models after weaning from cardiopulmonary bypass

	Mean ± SD
Mean pulmonary arterial pressure (mm Hg)	16 ± 3
Mean systemic arterial pressure (mm Hg)	58 ± 10
Central venous pressure (mm Hg)	9 ± 3
Left atrial pressure (mm Hg)	8 ± 3
Qp (mL · kg ⁻¹ · min ⁻¹)	141.3 ± 35.0
Qs (mL · kg ⁻¹ · min ⁻¹)	126.2 ± 45.4
Qp/Qs	1.350 ± 0.81
Pulmonary vascular resistance (dyne · s · cm ⁻⁵ · kg)	4528 ± 2641
Systemic vascular resistance (dyne · s · cm ⁻⁵ · kg)	33,547 ± 12,950

tion. Pulmonary blood flow (Qp) and aortic blood flow were measured directly with the electromagnetic flowmeters (MFV-1200; Nihon Kohden) with flow probes placed around the graft as a systemic–pulmonary arterial shunt and the middle level of the ascending aorta, respectively. Systemic blood flow (Qs) was calculated as aortic blood flow minus pulmonary blood flow. Pulmonary and systemic vascular resistances were calculated by standard formulas.

Experimental Protocol

After about 30 minutes of observation with stable univentricular hemodynamics, respiratory interventions for the change of the pulmonary/systemic resistance ratio were begun. The hemodynamic variables (systemic arterial blood pressure, pulmonary arterial pressure, central venous pressure, left atrial pressure, Qp, and Qs) were measured consecutively, and systemic arterial blood gas analysis was performed simultaneously during voluntary changes in the respiratory conditions (Fio₂, respiratory rate, peak inspiratory pressure). Fio₂ was intermittently set at 0.21, 0.4, 0.5, 0.7, 0.8, and 1.0. The respiratory rate and peak inspiratory pressure were changed between 12 and 30 breaths/min and between 11 and 18 cm H₂O, respectively, then Paco₂ was changed between 25 and 70 mm Hg.

Data Analysis and Statistics

The values obtained within 15 minutes of changing the respiratory conditions were excluded from the data analysis. StatView (version 4.5; SAS Institute, Inc, Cary, NC) was used to calculate analytic statistics. Linear regression analysis was used to determine the correlation between the ratio of Qp to Qs and Paco₂, hematocrit, and base excess. One-way analysis of variance was used to analyze the relationship between the ratio of Qp to Qs and Fio₂.

Results

The measured and calculated hemodynamic variables after weaning from CPB in all canine models under all respiratory conditions are shown in Table 1. We considered them to fall within a reasonable range as the univentricular hemodynamics of beagle dogs compared with those of a similar previous animal model.⁹

TABLE 2. Group characteristics using shunt size/body weight ratio

	Body weight (kg)	Shunt size (mm)	SS/BW ratio
Small shunt group (group S)			
	3.6	3.5	0.97
	3.7	4.0	1.08
	4.0	4.0	1.00
	5.0	4.0	0.80
Large shunt group (group L)			
	3.0	4.0	1.33
	3.4	4.0	1.81
	3.5	4.0	1.14
	3.5	4.0	1.14

SS/BW, Shunt size/body weight.

The ratio of shunt size (in millimeters) and body weight (in kilograms; SS/BW ratio) was used to assess the influences of shunt size on the regulation of the pulmonary blood flow. We used a 3.5-mm graft in one dog and 4.0-mm graft in 7 dogs at random, and the body weight of each animal scattered SS/BW ratio from 0.80 to 1.33 (1.08 ± 0.16) (Table 2). We divided all canine models into two groups according to SS/BW ratio. The group of animals in which the SS/BW ratio was 0.8 to 1.1 was defined as the small shunt group and consisted of 4 dogs. The group of animals in which the SS/BW ratio was 1.1 to 1.4 was defined as the large shunt group and also consisted of 4 dogs.

We drew the actual curves of Qp/Qs ratio versus Paco₂ for each of the 8 animals, and the composite results by group are shown in Figure 2. When the SS/BW ratio was less than 1.1, there was a significant negative correlation between Qp/Qs ratio and Paco₂ of each dog. When SS/BW ratio was larger than 1.1, however, there was no correlation between Qp/Qs ratio and Paco₂ of each dog. The regulation of Qp with ventilatory manipulations in each of the animals with the SS/BW ratio less than 1.0 resulted in adequate Qs (Figure 3). The smaller the SS/BW ratio became, the more the value of Qs changed with the value of Paco₂. When SS/BW ratio was greater than 1.0, however, there was no significant correlation between the Qs and Paco₂ of each animal.

The influence of Fio₂ on the Qp/Qs ratio is shown in Figure 4. In the small shunt group, as Fio₂ became higher from 0.21 to 0.7, the Qp/Qs ratio increased significantly from 1.31 ± 0.20 to 1.76 ± 0.13 (P < .01). In the large shunt group, however, no correlation was found.

The change of hematocrit between 35% and 45% did not produce any significant difference in the Qp/Qs ratio in either group. That is to say, usual hemoconcentration was of weak significance as a regulator of pulmonary blood flow despite the augmented viscosity and should be expected to increase oxygen supply in the limited pulmonary blood flow of the univentricular hemodynamics.

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Figure 2. Relationship between arterial carbon dioxide tension ($Paco_2$) and pulmonary/systemic blood flow ratio (Qp/Qs) of each dog. There is a significant negative correlation in group S (A, SS/BW ratio of 0.8-1.1). Triangles, $Qp/Qs = 2.262 - 0.019 \times Paco_2$ ($P = .0251$); diamonds, $Qp/Qs = 2.874 - 0.036 \times Paco_2$ ($P < .0001$); circles, $Qp/Qs = 4.585 - 0.081 \times Paco_2$ ($P < .0001$); squares, $Qp/Qs = 3.415 - 0.072 \times Paco_2$ ($P = .0006$). Particularly, the most valuable negative correlation is observed in the dogs with an SS/BW ratio of 0.97 or 1.0. There is no significant correlation in group L (B, SS/BW ratio of 1.1-1.4).

There was no correlation between the $\dot{Q}p/\dot{Q}s$ ratio and base excess in either group. In the small shunt group, however, the base excess ranged from -8 to $+6$ and was

distributed within the physiologically homeostatic range, whereas in the large shunt group it ranged from -12 to -2 and was distributed within the severely acidic range (Figure 5).

Figure 3. Relationship between arterial carbon dioxide tension (P_{aCO_2}) and systemic blood flow (Q_s) of each dog. There is a significant positive correlation and tendency in the dogs with an SS/BW ratio of 0.80, 0.97, and 1.0, respectively. *Squares*, $Q_s = -97.809 + 7.751 \times P_{aCO_2}$ ($P = .0038$); *diamonds*, $Q_s = -21.334 + 3.599 \times P_{aCO_2}$ ($P < .0001$); *circles*, $Q_s = 40.849 + 1.866 \times P_{aCO_2}$ ($P = .0989$). The most valuable correlation is observed in the dog with an SS/BW ratio of 0.97. There is no significant correlation in other dogs with a shunt larger than an SS/BW ratio of 1.0.

Discussion

In a univentricular heart with systemic and pulmonary parallel competing circulations after first-stage Norwood pal-

liative surgery, the pulmonary blood flow depends on a systemic-pulmonary arterial shunt, which is surgically created. Current knowledge regarding the regulation of the

Figure 4. Relationship between inspired oxygen fraction (FiO_2) and pulmonary/systemic blood flow ratio (Qp/Qs ratio) among group S (A, SS/BW ratio of 0.8-1.1) and group L (B, SS/BW ratio of 1.1-1.4). Data are presented as mean $\pm$ SD.

Figure 5. Relationship between base excess and pulmonary/systemic blood flow ratio (Qp/Qs ratio) among group S (A, SS/BW ratio of 0.8-1.1) and group L (B, SS/BW ratio of 1.1-1.4).

pulmonary blood flow has derived not only from clinical experience^{2,6-8,14} but also from animal experiments^{9-11,15,16} and hydromechanical studies.^{14,17,18} According to these investigations, it has become obvious that the pulmonary blood flow in the univentricular hemodynamics is influenced by the change of the pulmonary/systemic resistance ratio, which could be controlled by FiO_2 , $Paco_2$, and inotropic interventions.^{2,7,14-16} However, it is true that the excessive pulmonary blood flow caused by an unreasonably large or proximal systemic-pulmonary arterial shunt could not be regulated simply by changes in such physiologic factors and would result in cardiovascular collapse or death during the first postoperative day.^{2,7,14}

Mosca and colleagues⁷ suggested from their clinical experience that the major restriction to pulmonary blood flow after a Norwood operation occurs within the innominate-pulmonary artery shunt, and pulmonary vascular resistance itself is relatively unimportant in determining pulmonary blood flow, particularly that relevant to cardiovascular col-

lapse on the operative day. At this point the size and the placement of systemic-pulmonary arterial shunt might be more important than perioperative ventilatory and pharmacologic management.^{2,7} Our previous study with a simplified rigid model of the Norwood procedure demonstrated that a central shunt constructed with a duct of 3.1 or 4.0 mm in inner diameter would supply an excessive pulmonary blood flow in neonates weighing 3.0 kg.¹⁴ Theoretically speaking, the difference of the location of a proximal anastomosis in a systemic-pulmonary arterial shunt among the ascending aorta, the innominate artery, the innominate artery bifurcation, and the subclavian artery would be significantly related to the prevalence of excessive pulmonary blood flow after a Norwood operation.¹⁹ We have therefore suggested that in the Norwood procedure in small infants a systemic-pulmonary arterial shunt should be constructed with a prosthesis of 3.0 to 3.5 mm diameter from the innominate artery.¹⁴ That recommendation is nearly compatible with these results.

Jonas and colleagues² reported in 1986 that a modified Blalock-Taussig shunt with 4-mm polytetrafluoroethylene graft would provide satisfactory flow so long as it was placed sufficiently distally on the subclavian artery. However, Forbess and colleagues¹² in the same institution reported in 1995 that the patients with a 3.5-mm modified Blalock-Taussig shunt were more likely to survive a first-stage Norwood operation to a stage II procedure. Bartram and associates²⁰ reviewed 122 patients from 1980 to 1995 who died after a first-stage Norwood procedure at the same hospital and reported that excessive pulmonary blood flow was the second most common cause of death and occurred significantly more often when the size of the modified Blalock-Taussig shunt was 4 mm or greater than when the size of shunt was 3.5 mm or less. Iannettoni,⁶ Mosca⁷ and their colleagues advocated the tactics for the optimal shunt size in a Norwood operation based on their experience. Although a classic shunt was preferentially used only for a too-small baby, a polytetrafluoroethylene conduit was usually anastomosed from the innominate artery to the central pulmonary artery. Shunt size was determined by a general rule that classic or 3.5-mm shunts were used in patients weighing less than 3.5 kg and a 4.0-mm shunt was used in those weighing more than 3.5 kg. Consequently, early mortality has significantly improved, in contrast with results obtained during the earlier years of their series in which 4.0-mm shunts had been commonly used.²¹ Bando and coworkers¹³ adopted another determination of the optimal shunt size, and most patients weighing less than 4 kg received a 3.5-mm conduit. As a result, operative survival in patients with a 3.5-mm conduit improved significantly, and larger shunt size (≥ 4 mm) was one of the significant risk factors for early death.

Thus, favored use of a smaller shunt, such as 3.0 or 3.5 mm in diameter, for a systemic–pulmonary arterial shunt in first-stage Norwood palliative surgery is the current trend in preventing excessive pulmonary blood flow. However, specific management guidelines for suitable shunt size have not yet been presented. This study demonstrated that the pulmonary blood flow was controllable within physiologically tolerable hemodynamic parameters by adjusting P_{aCO_2} or F_{IO_2} when the SS/BW ratio was 0.8 to 1.1; however, the pulmonary blood flow became uncontrollably excessive even with such adjustments when the SS/BW ratio was 1.1 to 1.4. Consequently, each of the animals with SS/BW ratios of 0.8 to 1.0 received adequate $\dot{Q}_s$; in contrast, SS/BW ratios of 1.0 to 1.4 resulted in inadequate $\dot{Q}_s$ and acidic status. If a patient 3.0 to 3.5 kg in body weight were to receive a 3.5-mm conduit shunt such as is commonly used, the SS/BW ratio would be 1.0 to 1.17, and if such a patient were to receive a 4.0-mm conduit shunt, the SS/BW ratio would be 1.14 to 1.33.

The factors that determine effective graft impedance are many. The type of synthetic material, its distensibility, the

graft length, the way that the graft is sewn into the vessels, and the exact takeoff point from the feeding vessel all contribute to the impedance calculation. In neonates, exact lie relative to the right pulmonary artery may be a factor; this was avoided by sewing into the main pulmonary artery in our model. The length of the shunt in this experimental model was enormously longer than that seen in clinical situation. According to our previous studies,¹⁴ changing the length of a graft from 20 to 40 mm made little contribution to the regulation of the pulmonary blood flow. A minute change in the inner diameter of the systemic–pulmonary arterial shunt, in contrast, exerted a great influence on the pulmonary blood flow. We therefore suppose that the SS/BW ratio of 1.1 provides an indication of whether pulmonary blood flow can be regulated by physiologic respiratory manipulation. To provide both $\dot{Q}_s$ and $\dot{Q}_p$ according to our results, we believe that the SS/BW ratio of an ideal shunt in the Norwood operation would 0.9 to 1.0. Because grafts only come in 0.5-mm increments, the surgeon should try to stay as close to this ratio as possible.

Three major limitations are present in this animal model: species, age of animals, and single left ventricle physiology. Dogs are different from human beings in terms of aortic arch anatomy; that is, only two head vessels originate from the dog's aortic arch and the right subclavian artery is the third branch of the first head vessel. Animals in this study were not neonates, and they might possibly have weaker pulmonary vascular responses than neonates to the changes in the physiologic factors manipulated in the study.²² Although the exclusion of the right ventricle from the circulation by closure of the tricuspid valve closely approximates the single ventricle physiology such as is seen after the Norwood procedure, the single ventricle performing stroke work is the left ventricle, not the right ventricle. This study model must work on an inferior single ventricle physiology, particularly with abruptly forced hypoxemic environment, immediately after myocardial ischemia.⁶ A variation on the model that would further increase statistical power would involve two grafts in each animal (3.5 and 4 mm, for example), alternating flow in each and making the series of measurements. Then the effect of graft diameter could be determined partially by using each animal as its own control. The interaction of these differences could lead to a slightly different result.

In conclusion, when the SS/BW ratio is 0.8 to 1.1, pulmonary blood flow after a Norwood operation is controllable by changing P_{aCO_2} and F_{IO_2} values. However, an unreasonably larger SS/BW ratio of 1.1 will produce excessive pulmonary blood flow, which is uncontrollable by physiologic respiratory manipulation. Although the site of shunt anastomosis and individual variations must be considered, we recommend that 0.9 to 1.0 is a useful index SS/BW value for suitable systemic–pulmonary arterial shunt in the Norwood operation.

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