Pulmonary Artery Size and Late Functional Outcome After Fontan Operation

Jae Suk Baek, MD, Eun Jung Bae, MD, PhD, Gi Beom Kim, MD, Woong-Han Kim, MD, PhD, Jeong Ryul Lee, MD, PhD, Yong Jin Kim, MD, PhD, Eun-Ah Park, MD, Whal Lee, MD, PhD, and Chung Il Noh, MD, PhD

Departments of Pediatrics, and Thoracic and Cardiovascular Surgery, Seoul National University Children's Hospital; and Department of Radiology, Seoul National University Hospital, Seoul, South Korea

Background. **Pulmonary artery (PA) growth after a Fontan procedure tends to be suboptimal to somatic growth. This study aimed to investigate whether the PA size affects the late outcomes of the Fontan procedure.**

Methods. **This study enrolled 120 Fontan patients. Their mean age was 19.3 ± 5.6 years. PA size was measured from computed tomographic images. Patients were divided into three groups according to the PA index (PAI) (Nakada index): PAI < 180 mm²/m² (group I: n = 37); 180 mm²/m² ≤ PAI < 250 mm²/m² (group II: n = 56); and PAI ≥ 250 mm²/m² (group III: n = 26). Data on hemodynamics, biochemical test, B-type natriuretic peptide, and cardiopulmonary exercise performance were analyzed.**

Results. **The three groups showed no differences in occurrence of adverse outcomes such as protein losing enteropathy, arrhythmia, and hepatic changes. No differences were observed after cardiac catheterization. Various parameters of exercise tolerance test were not different between the three groups. However, B-type natriuretic peptide level was significantly higher in group III than in the other groups ($p = 0.010$); there was no difference between groups I and II. Ventricular volume unloading in group III was later than that in group I (4.6 ± 3.7 vs 2.6 ± 2.7 years, respectively; $p < 0.05$).**

Conclusions. **PA size does not affect late outcomes or functional status in the survivors of the Fontan operation. Hence, a pre-Fontan palliative procedure to augment the PA size, at the expense of ventricular overload, is not recommended.**

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The first criteria for the Fontan operation by Choussat and colleagues [1] and Fontan and Baudet [2] have been modified during the past three decades, and the importance of a good pulmonary artery (PA) size has lessened in these modified criteria. A few studies showed that small PA affects the early outcomes after the Fontan operation [3–5]. On the other hand, Girod and colleagues [6] and Bridges and colleagues [7] reported no significant difference in mortality rate between patients with larger PA and those with smaller PA. Additionally, a recent report [8] showed that small PA before operation did not affect the midterm results after the Fontan operation. Although PA size itself may not influence the early or midterm outcomes after the Fontan operation, there is a concern related to the impaired PA growth after the Fontan operation. Some studies [9, 10] reported that the PA growth after a Fontan procedure fails to match the increase in body surface. This phenomenon may be more serious in patients with early bidirectional cavopulmonary shunt (BCPS) in the staged approach. Abnormal PA size may adversely affect late functional outcomes. However, we have found no studies about the influence of PA size on the late outcomes after Fontan operation. This study aimed to elucidate the correlation between the PA size and the late outcomes, including cardiopulmonary exercise capacity, in the Fontan population.

Patients and Methods

The study protocol was approved by the Institutional Review Board of Seoul National University College of Medicine, Seoul National University Hospital (H-0911-023-300). Individual parental consent for the study was waived.

Of the 204 late follow-up patients who had the Fontan operation in our institute between 1986 and 2003, 120 patients (59%) who underwent cardiac computed tomography (CT) were enrolled in this study (75 males). Their mean (SD) age was 19.3 ± 5.6 years (range, 9.2 to 37.2 years), and the mean (SD) age at their initial Fontan procedure was 3.9 ± 3.1 years (range, 0.8 to 17.6 years). The mean (SD) elapsed time since the initial Fontan operation was 12.8 ± 3.7 years (range, 5.1 to 20.4 years). The atriopulmonary connection was performed in 35 patients, lateral tunnel Fontan operation in 65 patients, and extracardiac Fontan operation in 20 patients.

The sizes of both left and right pulmonary arteries were assessed at the hilum by cardiac CT, and the PA index (PAI) was calculated as described by Nakata and

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Address correspondence to Dr Bae, Department of Pediatrics, Seoul National University Children's Hospital, 101 Daehag-Ro, Jongno-gu, Seoul 110-744, Korea; e-mail: eunjbaek@snu.ac.kr.

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Abbreviations and Acronyms

ALT	= alanine aminotransferase
AST	= aspartate aminotransferase
AT	= anaerobic threshold
BCPS	= bidirectional cavopulmonary shunt
BNP	= brain natriuretic peptide
EDP	= end-diastolic pressure
FP	= Fontan pathway
GGT-γ	= glutamyl transpeptidase
HR	= heart rate
INR	= international normalized ratio
NYHA	= New York Heart Association
PA	= pulmonary artery
PAI	= pulmonary artery index
PLE	= protein losing enteropathy
Spo_2	= pulse oximeter oxygen saturation
VE/Vco_2	= ventilation/carbon dioxide production ratio
Vo_2	= oxygen consumption

colleagues [3]. We divided our patients into three groups according to the PAI: hypoplastic PA (group I, PAI < 180 mm^2/m^2), relatively small PA (group II, 180 $mm^2/m^2 \leq$ PAI < 250 mm^2/m^2), and good PA (group III, PAI ≥ 250 mm^2/m^2). We compared these groups on the basis of the parameters as follow. The CT images were obtained using the SOMATOM Definition (Siemens Medical Solutions, Forchheim, Germany) and SOMATOM Sensation (Siemens Medical Solutions) at the arterial phase and delayed phase. The CT scans were assessed by two consultant radiologists (E-A. P. and W.L.).

Clinical assessment included detailed history with functional class and the age of ventricular unloading surgery, exercise tolerance test (modified Bruce protocol), 12-lead electrocardiography, 24-hour Holter electrocardiogram recording, two-dimensional echocardiography, and cardiac catheterization. Ventricular unloading surgery was said to have occurred either at the time of the BCPS or at the time of Fontan, if no intermediate BCPS was performed.

At cardiac catheterization, we obtained pressure and oxygen saturation of the Fontan pathway, aortic pressure and oxygen saturation, and ventricular end-diastolic pressure. We also acquired the peak heart rate, peak oxygen consumption (Vo_2), Vo_2 at anaerobic threshold, ventilation/carbon dioxide production ratio (VE/Vco_2), systolic blood pressure, pulse oximeter oxygen saturation, and exercise duration by using a cardiopulmonary exercise test. We carried out detailed laboratory assessment, including the following: hemoglobin; white blood cell count; platelet count; alanine aminotransferase; aspartate aminotransferase; γ-glutamyl transpeptidase (GGT); total bilirubin; total protein; total albumin; prothrombin time; international normalized ratio; hepatitis A, B, and C serology; and brain natriuretic peptide (BNP).

We also investigated late Fontan complications: eg, protein losing enteropathy (PLE); arrhythmias such as atrial flutter, atrial fibrillation, and ventricular tachycardia; and sinus node dysfunction. We also investigated hepatic changes, including biochemical liver function test, thrombocytopenia, hepatic nodules and irregular hepatic surface on CT, and noninvasive hepatic fibrosis marker (Forns index), which is the best marker to predict the presence of Fontan hepatopathy [11]. Forns index combines platelet count, GGT, age, and cholesterol in the following formula: 7.811-3.131.ln(platelet count) + 0.781.ln(GGT) + 3.467.ln(age) - 0.014(cholesterol). As recommended by Forns and colleagues [12], values less than 4.21 were considered normal.

Statistical Analysis

The data were analyzed using the SPSS version 17.0 software (SPSS Inc, Chicago, IL). Quantitative variables were expressed as mean ± SD, while qualitative variables were expressed as percentages. Statistical analysis was performed by one-way analysis of variance and the Kruskal-Wallis test for quantitative variables and the χ^2 test for qualitative variables. A p value of less than 0.05 was considered significant.

Results

The mean absolute left PA diameter of enrolled patients was 13.9 ± 3.1 mm (range, 8.0 to 24.0) and mean right PA diameter was 13.8 ± 2.8 mm (range, 7.8 to 23). The mean PAI of the study population was 215.2 ± 65.8 mm^2/m^2 (range, 79.9 to 500.3). The PAI had no correlation with age and the elapsed time after Fontan operation.

Table 1 shows demographic data of these three groups. The initial palliative procedure was for systemic-to-pulmonary shunt in 41 patients (16 in group I, 21 in group II, and 4 in group III), for banding of the pulmonary trunk in 12 patients (3 in group I, 5 in group II, and 4 in group III), for bilateral cavopulmonary shunt in 15 patients (9 in group I, 5 in group II, and 1 in group III), and for any open heart palliation (including the Norwood procedure, pulsatile BCPS, and Kawashima procedure) in 8 patients. Group III had the least number of patients who had a staged Fontan completion through the BCPS (15 in group I, 11 in group II, and 2 in group III) ($p = 0.007$).

The mean age of ventricular unloading was 3.4 ± 3.2 (range, 0.3 to 17.6) years. Groupwise mean age of ventricular unloading is described in Table 1. The age of ventricular unloading in the large PA group (group III) was higher than that of small PA group (group I) ($p = 0.044$) (Fig 1B).

Late Complication of the Fontan Operation

Of all the enrolled patients, seven were PLE patients. Intractable PLE was observed in four patients, medically controlled PLE in two patients, and transient PLE in one patient. Three of the seven PLE patients were from group I, two from group II and the rest from group III. There were no differences among the number of PLE patients among the three groups ($p = 0.574$).

Table 1. Baseline Characteristic of Patients

Characteristic	Total	Group I (PAI < 180 mm²/m²)	Group II (180 ≤ PAI < 250 mm²/m²)	Group III (≥ 250 mm²/m²)	p Value
Number of patients	120	37	57	26	
Age (years)	19.3 ± 5.6 (9.2–37.2)	15.9 ± 4.5 (9.7–30.6)	16.3 ± 4.8 (8.0–26.7)	18.3 ± 6.6 (7.6–32.4)	0.163
Time of the initial Fontan	3.9 ± 3.1 (0.8–17.6)	3.4 ± 2.5 (1.2–15.4)	3.8 ± 3.2 (0.8–17.6)	4.8 ± 3.6 (0.8–12.6)	0.234
Duration since the initial Fontan operation (years)	12.8 ± 3.7 (5.1–20.4)	12.6 ± 3.4 (6.9–18.6)	12.5 ± 3.6 (5.1–19.0)	13.5 ± 4.4 (5.7–20.4)	0.456
Age of ventricular unloading surgery (years)	3.4 ± 3.2 (0.3–17.6)	2.6 ± 2.7 (0.4–15.4)	3.3 ± 3.0 (0.3–17.6)	4.6 ± 3.7 (0.8–12.6)	0.044
Initial Fontan type (APC/LT/EC)	35/65/20	12/20/5	12/37/8	11/8/7	0.064
Dominant ventricle (RV/LV undetermined)	38/70/12	15/20/2	15/36/6	8/14/4	0.489
Pre-Fontan procedure					
No procedure	44	9	22	13	0.027
Norwood	1	0	0	1	0.162
BT shunt	33	12	17	4	0.432
BT shunt followed by BCPS	8	4	4	0	0.293
PA banding	7	1	3	3	0.238
PA banding followed by BCPS	5	2	2	1	0.934
Pulsatile BCPS with PA banding	1	0	0	1	0.162
Pulsatile BCPS	5	0	4	1	0.250
Kawashima operation	1	0	0	1	0.162
BCPS as 1st operation	15	9	5	1	0.049
Total number of BCPS patients	28	15	11	2	0.006
Mean age when BCPS was performed (years)	1.33 ± 1.38 (0.3–5.5)	1.2 ± 1.10 (0.4–4.4)	1.53 ± 1.84 (0.3–5.5)	1.2 ± 0.42 (0.9–1.5)	0.841
Initial fenestration	49	17	27	5	0.061
Remained fenestration	26	12	12	2	0.063
Branch pulmonary artery augmentation (surgery or intervention)	21	9	9	3	0.370

Number or mean ± SD (range).

APC = atriopulmonary connection; BCPS = bidirectional cavopulmonary shunt; BT = Blalock-Taussig; EC = extracardiac; LT = lateral tunnel; PA = pulmonary artery; PAI = pulmonary artery index; RV/LV = right ventricle to left ventricle.

Hepatic complications were found in 15 patients (40.5%) in group I, 23 patients (40.3%) in group II, and 15 patients (57.7%) in group III. In detail, hepatic nodules were found in 2 patients within group I, 1 each within groups II and III. Irregular hepatic surface was observed in 13 patients in group I, 12 patients in group II, and 10 patients in group III. Thrombocytopenia and hyperbilirubinemia were observed in 7 and 2 patients in Group I, 13 and 4 in Group II, and 8 and 2 in Group III, respectively. There were no significant differences

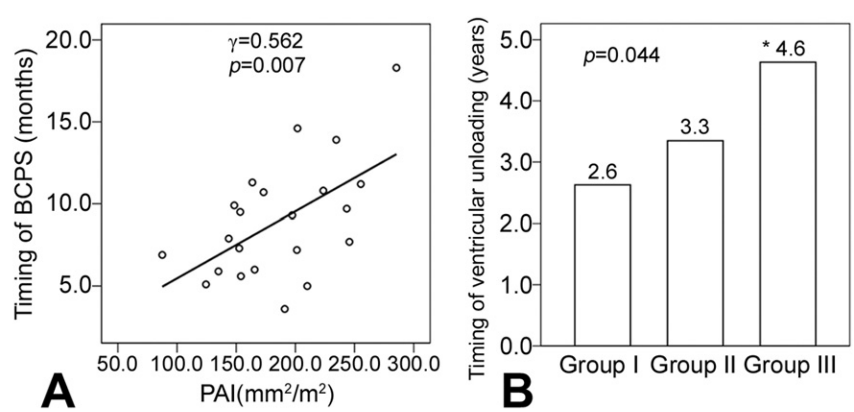

Fig 1. (A) The correlation between pulmonary artery index (PAI) and the timing of the bidirectional cavopulmonary shunt (BCPS) for the patients who went through BCPS before the age of 18 months. A positive correlation was observed. (B) The age of ventricular unloading of group III was older than that of group I.

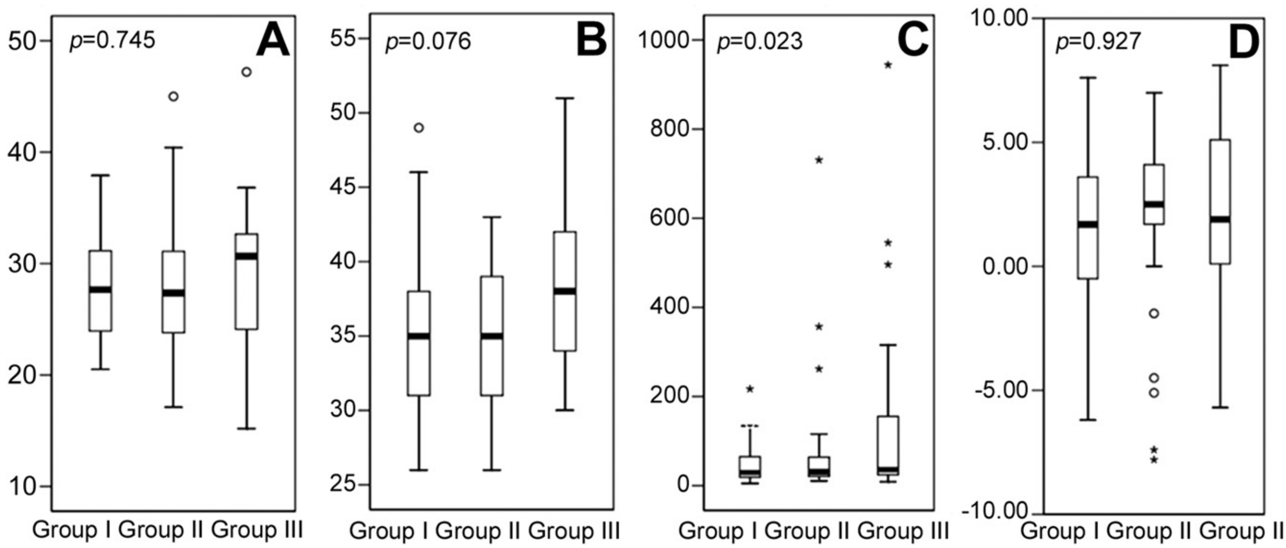

Fig 2. The comparison of peak VO_2 (A), peak VE/Vco_2 (B), BNP (C), and Forns index (D) between the three groups. Peak VO_2, peak VE/Vco_2, and Forns index were not significantly different between the three groups. The BNP was significantly higher in Group III. The top and bottom of each box are the 25th and the 75th percentiles. The line through the box is the median, and the error bars are the 5th and 95th percentiles. (BNP = brain natriuretic peptides; VE/Vco_2 = ventilation/carbon dioxide production ratio; VO_2 = oxygen consumption.)

in hepatic complication between three groups (p = 0.292). Forns index, a noninvasive hepatic fibrosis marker, was also not significantly different between the three groups ($p = 0.901$) (Table 2).

Sinus node dysfunction was found in 7 patients (18.9%) in group I, 10 patients (17.5%) in group II, and 3 patients (11.5%) in group III. There were no significant differences between the three groups ($p = 0.719$). The frequency of arrhythmia was also not different between the three groups ($p = 0.480$) (10 patients in group I; 10 in group II; 7 in group III).

Functional Class and Exercise Tolerance Test

Following the NYHA (New York Heart Association) functional classification 18 patients were class II, three patients were class III, and all others were class I patients. There were no differences with NYHA functional class between the three groups. Various parameters of an exercise tolerance test, including peak Vo_2 and peak VE/Vco_2, were not different between the three groups (Table 2) (Fig 2A, B). However the bigger PA group had a tendency of higher VE/Vco_2, indicating poorer exercise tolerance ($p = 0.126$).

Cardiac Catheterization

Data from postoperative catheterization in the three groups are shown in Table 2. Cardiac catheterization at 8.0 ± 5.7 years postoperatively showed no difference in hemodynamics; the pressure of Fontan pathway, ventricular end-diastolic pressure, and arteriovenous oxygen difference.

Neurohormonal Activity

The BNP levels were significantly higher in group III (146.0 ± 230.6 pg/mL) as compared with the other two groups ($p = 0.023$), whereas there was no difference between groups I (50.0 ± 8.0 pg/mL) and II (63.8 ± 111.4 pg/mL) (Fig 2C).

Comment

Our study is a relatively large cross-sectional study of Fontan patients that correlates the late PA size and late functional outcome. There have been several controversial data related to the PA size and the outcome of the Fontan operation. The outcome of the Fontan operation largely depends on the selection of patients as this is not an anatomic procedure but a functional repair in which both the pulmonary and the systemic circulation must be maintained, fundamentally, by a single pump. Among the various selection criteria for the Fontan operation, the size of the PA has been considered as one of the most important factors that influence the results of the Fontan operation. However, the actual studies showed that the PA size itself was not as important as the pulmonary vascular resistance [5–7].

Furthermore, there are a few conflicting studies related to the midterm outcomes. One study [8] reported that a small pulmonary artery at the preoperative stage did not affect the outcomes after the Fontan completion, including functional outcomes in the intermediate term (mean follow-up duration: 2.8 ± 2.7years). On the other hand, another study [9] reported a conflicting result; small PAs and low PAI (less than 150 mm^2/m^2) correlated significantly with unfavorable Fontan outcome. The latter study had a smaller number of enrolled patients compared with our study and they did not show any objective indicators related to late functional outcomes after the Fontan operation.

According to our observation (follow-up duration:

Table 2. Comparison of Late Functional Outcome Between Groups by Pulmonary Artery Size

Variable	Total	Group I (PAI < 180 mm²/m²)	Group II (180 ≤ PAI < 250 mm²/m²)	Group III (≥ 250 mm²/m²)	*p* Value
NYHA class (grade 1/2/3/4)	99/18/3/0	31/6/0/0	48/8/1/0	20/4/2/0	0.413
2D-echocardiography					
Visual ventricular function good/fair/decreased/poor	56/48/15/1	14/18/5/0	28/22/6/1	14/8/4/0	0.737
AV valve regurgitation (≥ moderate)	14	2	9	3	0.603
Aortic regurgitation (≥ moderate)	0	0	0	0	0.931
Laboratory test					
Hemoglobin (g/dL)	15.1 ± 2.1 (8.0–24.2)	15.2 ± 1.6 (11.5–18.5)	15.2 ± 2.4 (8.0–24.2)	15.1 ± 2.1 (9.9–18.4)	0.660
WBC ($10^3/\mu L$)	7.4 ± 4.7 (1.1–38.2)	7.7 ± 7.1 (4.4–38.2)	7.7 ± 3.7 (1.1–21.0)	6.4 ± 2.3 (2.4–11.4)	0.630
Platelet count ($10^3/\mu L$)	208.7 ± 86.7 (39.0–567.0)	207.8 ± 82.1 (49–382)	209.2 ± 80.8 (49–411)	208.7 ± 86.7 (39–567)	0.997
Total bilirubin (mg/dL)	1.6 ± 1.6 (0.2–16.0)	1.8 ± 2.5 (0.2–16.0)	1.5 ± 0.9 (0.4–4.2)	1.6 ± .8 (0.4–3.3)	0.511
AST (IU/L)	39.5 ± 102.8 (0.0–1,148.0)	31.2 ± 12.0 (17.0–80.0)	28.7 ± 13.5 (1.0–102.0)	74.7 ± 219.3 (11.0–1148.0)	0.141
ALT (IU/L)	24.6 ± 16.1 (1.0–135.0)	24.4 ± 13.7 (1.0–76.0)	22.9 ± 10.4 (2.0–54.0)	28.9 ± 26.3 (8.0–135.0)	0.277
GGT (IU/L)	53.9 ± 30.6 (16.0–129.0)	51.4 ± 25.3 (18.0–120.0)	51.4 ± 31.4 (16.0–122.0)	53.4 ± 30.6 (16.0–129.0)	0.508
Total protein (g/dL)	7.2 ± 0.92 (3.0–8.9)	7.3 ± 1.0 (3.0–8.9)	7.2 ± 0.86 (3.6–8.6)	7.0 ± 1.0 (3.0–8.9)	0.497
Total albumin (g/dL)	4.2 ± 0.57 (1.6–5.2)	5.3 ± 5.7 (1.6–5.0)	4.3 ± 0.6 (2.4–5.2)	4.1 ± 0.5 (2.8–4.9)	0.165
BUN (mg/dL)	14.1 ± 4.3 (6.0–40.0)	12.5 ± 3.0 (6.0–18.0)	13.9 ± 3.4 (8.0–23.0)	16.4 ± 6.4 (8.0–40.0)	0.002
Creatinine (mg/dL)	0.8 ± 0.4 (0.4–3.2)	0.7 ± 0.2 (0.4–1.2)	0.8 ± 0.2 (0.4–1.7)	0.9 ± 0.6 (0.5–3.2)	0.179
PT INR (n = 113)	1.7 ± 0.7 (1.0–3.6)	1.6 ± 0.4 (1.0–2.9)	1.6 ± 0.7 (1.0–3.2)	1.7 ± 0.7 (1.0–3.6)	0.468
With warfarin	1.2 ± 0.2 (1.0–2.0)	1.1 ± 0.1 (1.0–1.4)	1.2 ± 0.2 (1.0–1.8)	1.3 ± 0.3 (1.0–2.0)	0.208
Without warfarin					
BNP	77.8 ± 138.2 (5.0–944.0)	50.0 ± 8.0 (5–217)	63.8 ± 111.4 (11–731)	146.0 ± 230.6 (9–944)	0.023
Forns index	1.8 ± 3.6 (–7.8–8.1)	1.5 ± 3.3 (–6.2–7.6)	1.9 ± 3.7 (–7.8–7.0)	1.8 ± 4.0 (–5.7–8.1)	0.901
Hemodynamic data	61	10	38	13	
Aorta saturation (%)	91.2 ± 4.7 (77.0–99.0)	91.8 ± 4.5 (83–98)	90.3 ± 4.8 (77–99)	91.2 ± 0.6 (77–99)	0.488
Fontan saturation (%)	66.8 ± 8.8 (48.0–82.0)	66.8 ± 8.2 (48–82)	67.6 ± 9.3 (50–82)	64.5 ± 9.7 (51–82)	0.711
Fontan pressure (mm Hg)	13.6 ± 3.0 (9.0–24.0)	13.9 ± 2.1 (10–18)	13.5 ± 4.0 (9–24)	13.0 ± 2.6 (9–19)	0.694
Ventricular EDP (mm Hg)	8.9 ± 4.1 (0.0–20.0)	9.0 ± 3.4 (4–20)	9.0 ± 5.3 (0–20)	8.8 ± 4.1 (4–13)	0.992
$AVDo_2$ (%)	24.4 ± 8.8 (9.0–43.0)	24.9 ± 8.4 (13–43)	22.5 ± 8.7 (9–39)	27.1 ± 9.8 (15–41)	0.334
Fontan pressure–VEDP (mm Hg)	4.7 ± 3.8 (–6.0–14.0)	5.0 ± 4.1 (–5–13)	5.0 ± 4.5 (–6–14)	3.7 ± 1.8 (1–7)	0.58
Exercise test	83	31	35	17	
Peak HR	151.1 ± 25.0 (80.0–203.0)	151.4 ± 25.4 (80–193)	150.6 ± 22.5 (93–187)	152.5 ± 25.1 (99–203)	0.970
Peak HR/predicted HR (%)	78.7 ± 12.8 (42.0–103.0)	78.5 ± 13.9 (42–101)	78.8 ± 11.8 (50–102)	79.0 ± 15.3 (50–103)	0.989
Peak Vo_2 (mL/kg/min)	28.4 ± 5.9 (15.2–47.2)	28.4 ± 4.9 (20.5–37.9)	27.8 ± 5.9 (17.1–45)	29.4 ± 7.6 (15.2–47.2)	0.689
Peak Vo_2/predictedVo_2 (mL/kg/min)	59.3 ± 10.8 (34.0–88.0)	58.1 ± 10.0 (37–76)	58.7 ± 9.4 (34–76)	62.4 ± 10.9 (34–88)	0.388

Continued

Table 2. Continued

Variable	Total	Group I (PAI < 180 mm^2/m^2)	Group II (180 ≤ PAI < 250 mm^2/m^2)	Group III (≥ 250 mm^2/m^2)	*p* Value
Vo_2 at AT (mL/kg/min)	21.3 ± 5.6 (11.3–43.2)	21.6 ± 5.6 (11.9–34.1)	20.8 ± 4.7 (12.3–31.5)	22.0 ± 7.5 (11.3–43.2)	0.763
VE/Vco_2 (base)	43.4 ± 7.7 (26.0–72.0)	42.7 ± 7.7 (26.0–60.0)	43.3 ± 6.8 (29.0–60.0)	44.7 ± 9.6 (29.0–72.0)	0.695
VE/Vco_2 (peak)	36.0 ± 5.6 (26.0–51.0)	35.8 ± 5.7 (26.0–49.0)	34.9 ± 5.0 (26.0–43.0)	38.2 ± 6.3 (30.0–51.0)	0.126
Exercise duration (min)	8.8 ± 2.7 (1.0–14.0)	8.6 ± 2.6 (1.0–14.0)	9.3 ± 2.2 (3.2–13.6)	8.3 ± 3.7 (1.0–113.6)	0.347
SBP (base) (mm Hg)	113.8 ± 14.6 (89.0–164.0)	112.6 ± 12.8 (89.0–138.0)	115.3 ± 13.6 (94.0–164.0)	112.6 ± 19.7 (89.0–164.0)	0.753
SBP (peak) (mm Hg)	144.9 ± 25.7 (92.0–205.0)	140.4 ± 24.8 (92.0–176.0)	145.0 ± 22.6 (108.0–194.0)	152.5 ± 35.4 (99.0–205.0)	0.583
Spo_2 (base) (%)	88.9 ± 6.2 (63.0–98.0)	88.1 ± 6.9 (63.0–97.0)	89.5 ± 5.9 (73.0–98.0)	88.9 ± 6.2 (72.0–96.0)	0.659
Spo_2 (peak) (%)	85.8 ± 6.9 (64.0–98.0)	86.0 ± 7.3 (69.0–97.0)	86.4 ± 5.9 (75.0–98.0)	85.0 ± 8.2 (64–95.0)	0.774

Number or mean ± SD (range).

2D = two dimensional; ALT = alanine aminotransferase; AST = aspartate aminotransferase; AT = anaerobic threshold; AV = arterioventricular; $AVDo_2$ = arterio&-venous differences of oxygen; BNP= brain natriuretic peptide; BUN = blood urea nitrogen; EDP = end-diastolic pressure; GGT = glutamyl transpeptidase; HR = heart rate; NYHA = New York Heart Association; PAI = pulmonary artery index; PT INR = prothrombin time international normalized ratio; SBP = systolic blood pressure; Spo_2 = pulse oximeter oxygen saturation; VEDP = ventricular end-diastolic pressure; VE/Vco_2 = ventilation/carbon dioxide production ratio; Vo_2 = oxygen consumption; WBC = white blood count.

12.8 ± 3.7 years), the late functional outcomes of the survivors of the Fontan operation were not influenced by the postoperative PA size. A study by Senzaki and colleagues [5] reported that PAI had a significant correlation with pulmonary vascular compliance. The pulmonary vascular compliance influenced postoperative hemodynamics of the Fontan operation by affecting the peak central venous pressure and total impedance, which was the afterload to the ventricle. However, in this study by Senzaki and colleagues a noteworthy finding was that impedance increased abruptly only when PAI was less than or equal to 100 mm^2/m^2. In other words, if the PA size is larger than a certain threshold (eg, PAI > 100 mm^2/m^2), it may not influence the Fontan circulation. This observation supports our data.

Some recent studies [8–10] reported that the PA growth after a Fontan procedure may be impaired despite somatic growth. However, they did not elucidate how impaired PA growth would affect late functional outcomes after the Fontan operation. Our study investigated the impact of the late abnormal PA size on the late functional outcome after the Fontan operation.

We observed that the BNP levels were higher in group III with the largest PAI. This cannot be simply explained by the expectation that small PA size would lead to lower cardiac output and ventricular dysfunction ultimately. The BNP is secreted mainly in the ventricles in response to volume expansion and pressure load. Although there are various factors contributing to ventricular loading condition, one possible explanation is that the late timing of the volume unloading procedure of group III may result in late ventricular dysfunction with a higher BNP. This may be an indirect neurohumoral evidence that prolonged ventricular volume overload in a functional single ventricle may affect late ventricular dysfunction in Fontan patients.

In our patients, the BNP levels were higher than those reported previously, where only small groups of Glenn and Fontan patients were studied. It was previously reported that the BNP level in Fontan patients had a median from 7.64 pg/mL to 13 pg/mL [13–15]. One study [15] showed that the BNP level was normal in 81% of patients. However, our data show that the BNP level was normal in only 43.3% of patients and the median value was 31.5 pg/mL. On the basis of this result, Fontan patients may have a clinical or subclinical ventricular dysfunction.

Second, the good PA group had a tendency of higher VE/Vco_2 despite statistical insignificance. The VE/Vco_2 increases in the condition of cardiopulmonary functional impairment, especially in cyanotic congenital heart disease [16, 17]. This finding may indicate a subtle disadvantage, in the group with good PA size, on the cardiopulmonary exercise function; although other parameters of the exercise tolerance test including peak Vo_2 were not different in the three groups.

Finally, our results also showed that BCPS, as a pre-Fontan procedure, was more frequently identified in small and intermediate PAI groups. In addition, as illustrated in Figure 1, there was also a positive correlation between PAI and the timing of BCPS for the patients who went through BCPS before the age of 18 months. These findings are predictable and they corroborate previous studies [18, 19]. The chance of PA growth after BCPS decreases to some degree, compared with normal individuals. However, despite the adverse effect of BCPS on PA growth, from the findings of this study it is evident that the current policy of the staged Fontan operation is highly recommended. Moreover, the patient group with a small PA size did not have a disadvantage on the late functional outcome, and a higher BNP level was found in a larger PA size group. Therefore the pre-Fontan palliative procedure to augment the PA size, at the expense of ventricular overload, may not be recommended.

Our study had the following limitations: (1) It was a cross-sectional study and as a result we did not compare the postoperative PA size with the preoperative PA size, and therefore the longitudinal change in the PA size after a Fontan operation could not be determined; (2) the study population did not include nonsurvivors or patients who underwent transplants after a failed Fontan operation, and thus the effect of the PA size on these subgroups was not considered in our study; (3) only one hypoplastic left heart syndrome-Norwood patient appeared in the study population. Thus our results may not be generally applicable to these types of patients.

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INVITED COMMENTARY

Concerning the issue of ideal pulmonary artery size in Fontan patients, it is well established that "too small" pulmonary arteries (eg, those with a pulmonary artery index [PAI] 100 mm^2/m^2 or less, may restrict transpulmonary blood flow hence affecting the early outcome, or even the feasibility, of a Fontan operation. Extrapolating from this unequivocal piece of evidence, a logical assumption would be that larger pulmonary arteries assure a smoother blood flow across the cavopulmonary system. Baek and colleagues [1] assessed a selected population of Fontan survivors with a pulmonary artery size, by default, at least compatible with this peculiar circulatory setup. They divided the patients into 3 groups according to PAI. The three groups showed no differences in the occurrence of adverse outcomes, postoperative heart catheterization data, and exercise tolerance. However, brain natriuretic peptide level, an index of ventricular performance, was significantly higher in the group with the greatest PAI; ie, the same group in which palliative procedures were deliberately left in place for longer time with the intent to promote pulmonary artery growth. Based on these data, the authors endorse early ventricular volume unloading in single ventricle patients by timely Glenn and Fontan procedures at the likely expense of a reduced pulmonary artery growth.

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