ARTYKUŁ ORYGINALNY / ORIGINAL ARTICLE

Pulmonary artery growth in univentricular physiology patients

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Abstract

Background: A Fontan-type operation, i.e. a connection of the systemic veins and pulmonary arteries without subpulmonary ventricle, with different surgical techniques, is nowadays the only treatment option for patients with a functionally univentricular heart (UVH). Understanding the development of pulmonary arteries in patients who are considered for the Fontan procedure is important clinically.

Aim: To evaluate the development of pulmonary arteries in patients with univentricular circulation.

Methods: Between 1995 and 2007, 111 patients underwent a bidirectional Glenn procedure. In all patients, preoperative catheterisation was performed to assess the anatomy and haemodynamics of UVH, especially the size of the pulmonary arteries. Ninety nine patients were included in the bidirectional Glenn group; 62 of these underwent repeat catheterisation before Fontan completion. The late results, after one stage extracardiac total cavopulmonary anastomosis performed in 24 patients between 1992 and 2002, were reinvestigated (one-stage Fontan group). We assessed the changes in the McGoon ratio and Nakata index for the whole cohort of patients. McGoon ratio is the sum of the diameter of pulmonary arteries divided by the diameter of the aorta. Nakata index is the sum of the cross-sectional area of the pulmonary arteries divided by the body surface area.

Results: During cardiac catheterisation prior to Glenn procedure, the mean Nakata index was 351.9 (range 131.2–886) mm²/m² and was higher in patients with increased pulmonary flow (p = 0.0135). Mean McGoon ratio was 2.5 (range 1.1–4.9). An average 40.3 months after Glenn procedure, the Nakata index and McGoon ratio decreased significantly to 226.4 ± 125 mm²/m² (p < 0.003), and to 2.14 ± 0.58 (p < 0.008) respectively. In the group of patients after one-stage Fontan in late follow-up, mean 7.4 years after procedure, the Nakata index decreased from 318.7 ± 159.1 mm²/m² to 120 ± 40 mm²/m² (p < 0.0001) and McGoon ratio from 2.4 ± 0.6 to 1.4 ± 0.27 (p < 0.0001). Only size of pulmonary arteries before Glenn procedure, in the bidirectional Glenn group, or before Fontan operation, in the one-stage Fontan group, were inversely correlated with the changes of size of pulmonary arteries (p = 0.0015 and p = 0.0012).

Conclusions: The relative decrease of the size of pulmonary arteries in the inter-stage period (between bidirectional Glenn anastomosis and Fontan completion) and after Fontan completion may indicate that pulmonary artery sizes should probably not be an absolute limiting factor in the decision on treatment of functionally UVH patients, especially at the stage of Fontan approach.

Key words: bidirectional Glenn, total cavo-pulmonary connection, Nakata index

INTRODUCTION

A Fontan-type operation, involving connection of the systemic veins and pulmonary arteries without subpulmonary ventricle, is nowadays the only treatment option for patients with a functionally univentricular heart (UVH). Since the first report in 1971 by Fontan and Baudet [1], the results of Fontan-type operations have improved significantly due to better understanding of the Fontan circulation, better patient selec-
tion, and appropriate, prior to Fontan completion, palliative procedures. The multi-stage approach most often performed by means of pulmonary arterial bloodflow control procedures (Blalock-Taussig shunt or pulmonary artery banding) followed by the bidirectional Glenn (BDG) (superior vena cava with pulmonary artery anastomosis) is considered one of the most important factors behind the good results of Fontan-type operations [2, 3]. Advantages of the staged approach include effective pulmonary bloodflow and stepwise adaptation of the single ventricle to the reduced volume load [4]. However, the BDG provides lower pulmonary bloodflow than in the normal or in the eventual Fontan circulation. This situation may lead to limited pulmonary artery growth before Fontan completion [5]. Adequate pulmonary artery size was one of the criteria in the selection of candidates for a Fontan operation as originally specified by Fontan and Choussat [6].

A number of studies have found pulmonary vascular anatomy and function to be an important risk factor of the Fontan procedure [7, 8]. Therefore it is important to understand the progression and management of specific pulmonary artery anomalies in patients who have or are considered for a Fontan procedure. In 1991, Kobayashi et al. [9] reported BDG with additional pulmonary bloodflow in children not suitable for the Fontan procedure. Advantages of this compared to BDG without additional pulmonary bloodflow include better growth of pulmonary arteries, higher oxygen saturation, lower mortality, favourable effects on cardiac function and prevention of arteriovenous fistulas [10–15]. The regression of the pulmonary arteries size (evaluated on the basis of Nakata index and McGoon ratio) after the Fontan procedure is likely to be related to low cardiac output and non-pulsatile flow within the pulmonary arteries due to the lack of a pumping chamber in the pulmonary circulation [16].

The aim of this study was to evaluate the development of pulmonary arteries in the univentricular physiology of patients with special attention to the inter-stage period (between Glenn procedure and Fontan completion) and in the late follow-up after Fontan operation.

### METHODS

The study was approved by the ethics committee of The Children’s Memorial Health Institute and was supported by an internal grant of The Children’s Memorial Health Institute, (number 135/06). Since individual patients were not identified, the need for parental consent was waived. Evaluation of the development of pulmonary arteries was based on retrospective analysis of preoperative, operative, postoperative and long-term follow-up data. Between 1995 and 2007, 111 patients with UVH anatomy or physiology underwent BDG at a single institution. In all the patients, preoperative cardiac catheterisation was performed to assess the preoperative anatomy and haemodynamics of UVH, especially the size of the pulmonary arteries. Twelve patients were excluded from the study. Five of them required isolation of the right pulmonary artery by closing its proximal part, due to elevated superior vena cava pressure after BDG procedure. All of these patients had originally increased pulmonary bloodflow controlled by pulmonary artery banding and well developed pulmonary arteries. The elevated pulmonary pressure after Glenn procedure could be associated with elevated resistance of pulmonary vasculature. In seven patients with interrupted inferior vena cava, the Kawashima procedure (BDG in the setting of azygos continuation of an interrupted inferior caval vein to superior caval vein) was performed. The remaining 99 patients were included in the BDG group.

In the BDG group, 76 of the 99 (76.8%) patients required initial procedures to optimise the pulmonary bloodflow. These included 54 Blalock-Taussig shunts and 22 main pulmonary artery bandings. In the remaining 23 (23.2%) patients, the pulmonary flow was balanced before BDG. Overall, the median weight at the time of BDG procedure was 9.8 (range 3.4–43.5) kg and median age was 17.9 (range 3.3–171.4) months (Table 1).

At the conclusion of the Glenn procedure, some degree of additional pulmonary bloodflow was present in 54 of the 99 (54.5%) patients. This additional pulmonary flow was limited by native pulmonary artery stenosis or restricted by

<table>
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<tr>
<th>Table 1. Summary of patient characteristics, bidirectional Glenn group</th>
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<tr>
<td><strong>Preoperative factors</strong></td>
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<tr>
<td>Weight at surgery [kg]</td>
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<tr>
<td>Age at surgery [months]</td>
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<tr>
<td>Saturation [%]</td>
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<tr>
<td>Single ventricle morphology:</td>
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<tr>
<td>Left</td>
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<tr>
<td>Right</td>
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<tr>
<td>Other</td>
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<tr>
<td>Presence of bilateral superior caval vein</td>
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<td>Previous operation</td>
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banding of the main pulmonary artery in 41 (41.4%) or provided by the Blalock-Taussig shunt in 13 (13.2%) patients. In 45 (45.5%) patients, the superior caval vein blood return was the only source of pulmonary flow.

In the one-stage Fontan group of 24 patients, the late results after one-stage extracardiac total cavopulmonary connection performed between 1992 and 2002 and previously published [17] were reinvestigated. In this group, 18 of 24 patients required initial procedures to optimise the pulmonary bloodflow. These included 13 Blalock-Taussig shunts and five main pulmonary artery banding procedures. In the remaining six (25%) patients, the pulmonary artery flow was balanced before the Fontan procedure. The median weight at the time of Fontan procedure was 18.2 (range 12.5–37.5) kg and median age 77.3 (range 27.8–159.1) months. In nine patients, a direct extracardiac total cavopulmonary connection was performed, in ten others an aortic allograft, and in five PTFE grafts were used to connect the inferior caval vein to the pulmonary arteries (Table 2).

McGoon ratio and Nakata index were used to assess the development of pulmonary arteries. McGoon ratio is calculated as the sum of the diameters of the right and left pulmonary arteries at the prebranching point divided by the diameter of the aorta at the diaphragm level. The Nakata index is calculated as the sum of the cross-sectional area of the right and left pulmonary arteries divided by the body surface area.

For the statistical analysis the changes in the Nakata index were defined as the percentage change (% Nakata index change) and calculated according to the formula: (Nakata index before Fontan completion – Nakata index before Glenn procedure)/Nakata index before Glenn procedure × 100 for the BDG group and according to the formula: (Nakata index in late follow-up – Nakata index before Fontan procedure)/Nakata index before Fontan procedure × 100 for the one-stage Fontan group.

**Statistical analysis**

Statistical analysis was performed using Statistica for Windows v.8.0 (StatSoft, Poland). Continuous variables were reported as mean, 95% confidence interval (CI), ± standard deviation (SD) and were analysed using the unpaired t test, Mann-Whitney test. Linear regression analysis technique was used to evaluate correlation between variables. Kaplan-Meier analysis was used to assess actuarial survival. A p value of less than 0.05 was considered statistically significant.

**RESULTS**

**Bidirectional Glenn group**

*Preoperative cardiac catheterisation.* Mean age at catheterisation was 28.2 months (95% CI 21.5–34.8 [± 33.3]) and mean body weight 10.9 kg (95% CI 9.6–12.3 [± 6.6]). Mean McGoon ratio was 2.5 (range of 1.1–4.9). Mean Nakata index was 351.9 (range of 131.2–886 mm²/m²), and was significantly higher in patients after pulmonary artery banding compared to those after Blalock-Taussig shunt (p < 0.014). There were no differences in age, body weight, or mean pulmonary pressure between those patients. The distortion of pulmonary arteries occurred after Blalock-Taussig shunt in nine of 54 (16.6%) patients and in one of 22 (4.5%) patients after main pulmonary artery banding procedure.

**Glenn procedure.** The hospital mortality in the group of 99 patients was 5.05%. Actuarial survival after Glenn procedure was 93.7% ± 2.5%.

**Re-catheterisation before Fontan operation.** 62 (66%) patients underwent re-catheterisation before Fontan completion. The mean time between Glenn procedure and re-catheterisation was 40.3 months (95% CI 33.7–46.8 [± 25.7]) for the overall group, with 47 months (95% CI 37.9–56.3 [± 27.5]), and 30 months (95% CI 22.2–37.9 [± 19.1]) in patients with and without additional pulmonary bloodflow, respectively (p < 0.03). Table 3 illustrates the data from the pre-Glenn and pre-Fontan catheterisation in the BDG group.

During the follow-up period, arterial blood oxygen saturation increased and the mean pulmonary artery pressure decreased significantly. The Nakata index and McGoon ratio decreased in the inter-stage period to 226.4 mm²/m² (95% CI 235–298 [± 125]) and 2.14 (95% CI 2.0–2.03 [± 0.58]) respectively. The mean percentage change in Nakata index was –17 (95% CI –27.7 to –6.4 [± 42]). The regression of the size of pulmonary arteries was smaller after Glenn procedure in patients with additional pulmonary bloodflow compared to patients without additional pulmonary bloodflow, with percentage Nakata index changes of –10.3 ± 45 (95% CI –25 to –4.8) and –27 ± 35 (95% CI –42 to –12), respectively.

**Table 2. Summary of patient characteristics, one-stage Fontan group**

<table>
<thead>
<tr>
<th>Preoperative factors</th>
<th>No. of patients (%)</th>
<th>Mean ± SD</th>
<th>95% confidence interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight at surgery [kg]</td>
<td>19.8 ± 6.4</td>
<td>17.1–22.6</td>
<td></td>
</tr>
<tr>
<td>Age at surgery [months]</td>
<td>85.2 ± 40.7</td>
<td>68.1–102.5</td>
<td></td>
</tr>
<tr>
<td>Single ventricle morphology:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left</td>
<td>17 (70.8%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right</td>
<td>7 (29.2%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Previous operation</td>
<td>18 (75.0%)</td>
<td></td>
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</table>
but the difference was insignificant \((p = 0.07)\). We did not find any correlation between the percentage change in Nakata index and mean pulmonary artery pressure, oxygen saturation before Glenn procedure, age and body weight at Glenn procedure, and inter-stage period time. Only the size of pulmonary arteries (pre-Glenn Nakata index) before Glenn procedure was inversely correlated with % Nakata index change \((\beta = -0.39, \text{R}^2 = 0.14, p = 0.0015)\) (Fig. 1A).

Among 99 patients (the BDG group) included in the investigation, the extracardiac Fontan procedure was performed in 23 patients \((23/99 = 23.2\%)\) with hospital mortality of 4.3\% (one death). The mean follow-up time after Fontan procedure was 2.3 ± 2.1 years \((95\% \text{CI 1.3–3.2})\). The late mortality was 9.1\% (two deaths in 22 patients). Overall mortality in the investigated group of patients is 9.1\% (nine deaths among 99 patients included in the study). Overall actuarial survival at almost 12 years after Glenn procedure is 87.4\%.

### One stage Fontan group

In the one-stage Fontan group reinvestigated at follow-up, between 3.2 and 12.6 (mean 7.4) years, the Nakata index and McGoon ratio decreased significantly from 318.7 ± 159.1 mm²/m² to 120 ± 40 mm²/m² \((95\% \text{CI 101–139} \pm 40), p < 0.0001)\) and from 2.4 ± 0.6 to 1.4 ± 0.27 \((95\% \text{CI 1.3–1.6} \pm 0.27), p < 0.0001)\), respectively. The mean percentage change in Nakata index was −58 \((95\% \text{CI –67.6 to –48.6} \pm 18.5)\). We did not find any correlation between the percentage change in Nakata index and mean pulmonary artery pressure, oxygen saturation before Fontan procedure, age, and body weight at Fontan procedure. Only the size of pulmonary arteries (pre-Fontan Nakata index) before Fontan procedure was inversely correlated with the percentage change of Nakata index \((\beta = –0.72, \text{R}^2 = 0.51, p = 0.0012)\) (Fig. 1B).

Table 4 illustrates the comparison of the changes in the pulmonary arteries size between BDG group (inter-stage period), and one-stage Fontan group (pre-Fontan and post-Fontan late follow-up).

<table>
<thead>
<tr>
<th>Factors</th>
<th>Pre-Glenn</th>
<th></th>
<th>Pre-Fontan</th>
<th></th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean ± SD</td>
<td>95% confidence interval</td>
<td></td>
<td>Mean ± SD</td>
<td>95% confidence interval</td>
<td></td>
</tr>
<tr>
<td>Age [years]</td>
<td>2.2 ± 2.5</td>
<td>1.5–2.8</td>
<td>5.9 ± 3.3</td>
<td>5–6.7</td>
<td></td>
</tr>
<tr>
<td>Weight [kg]</td>
<td>10.9 ± 6.6</td>
<td>9.6–12.3</td>
<td>20 ± 9.3</td>
<td>17.6–22.4</td>
<td></td>
</tr>
<tr>
<td>Saturation [%]</td>
<td>80.3 ± 9.6</td>
<td>77.9–82.8</td>
<td>83.4 ± 4.2</td>
<td>82.3–84.5</td>
<td>0.028</td>
</tr>
<tr>
<td>McGoon ratio</td>
<td>2.5 ± 0.7</td>
<td>2.3–2.6</td>
<td>2.1 ± 0.6</td>
<td>2–2.3</td>
<td>0.008</td>
</tr>
<tr>
<td>Nakata index</td>
<td>351.9 ± 166</td>
<td>308–393</td>
<td>266 ± 125</td>
<td>235–298</td>
<td>0.003</td>
</tr>
<tr>
<td>Pulmonary artery pressure [torr]</td>
<td>16.7 ± 6.4</td>
<td>14.7–18.7</td>
<td>12.7 ± 3</td>
<td>11.9–13.4</td>
<td>0.001</td>
</tr>
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Figure 1. Correlation of the pulmonary arteries sizes with the percentage Nakata index change; A. Bidirectional Glenn group; B. One stage Fontan group.
DISCUSSION

Since 1984, when Nakata et al. [18] described a standardised method for quantification of pulmonary artery size and concluded that the Fontan operation was ideally indicated with a pulmonary artery index greater than 250 mm²/m², and especially since 1989 when Fontan et al. [19] concluded that the dimensions of the right and left pulmonary arteries, expressed as the McGoon ratio, were one of the most powerful risk factors for death after Fontan operation, the size of the pulmonary arteries has been a limiting factor for completion of the Fontan circulation.

The period before a Glenn procedure is the time of most extensive growth of pulmonary arteries, especially in patients with balanced pulmonary flow, which was confirmed by our results. After a Glenn procedure, the pulmonary bloodflow decreases and may not be sufficient to maintain the expected McGoon ratio and Nakata index [20, 21]. Nevertheless, it is sufficient to allow suitable oxygen saturation and somatic growth [17]. It has been speculated that the additional pulmonary bloodflow could maintain the size of the pulmonary arteries by increasing pulmonary bloodflow [22], but this was not confirmed by us. In contrast to other studies [22, 23], we did not find significant differences in the growth of pulmonary arteries and arterial blood oxygen saturation between groups with or without additional pulmonary bloodflow after Fontan completion. Similarly to Yoshida et al. [22], we found a correlation between pre-Glenn Nakata index and percentage Nakata index change, which shows that underdeveloped pulmonary arteries may increase in diameter after the Glenn procedure. The reduction of the diameter of overdeveloped pulmonary arteries could mean that arteries of such diameter are not necessary to provide blood to the lungs after bidirectional cavopulmonary connection (Glenn anastomosis). This was the only significant correlation including the mean pulmonary artery pressure. The regression in the Nakata index after the Fontan procedure is likely to be related to low cardiac output and non-pulsatile flow within pulmonary arteries. Similarly to Adachi et al. [16], we found regression in the size of the pulmonary arteries after the Fontan procedure, which was significantly higher compared with this after a Glenn procedure. It could be in the process of natural pulmonary artery remodelling when those sizes adjust to the amount of blood passing through. Adachi et al. [16] claimed that low Nakata index is not an important risk factor for Fontan completion and that it could be performed in patients with a preoperative Nakata index smaller than 250 mm²/m². Also Itatani et al. [24] revealed the lower limit of pulmonary artery index (110 mm²/m²), considering the exercise tolerance. In our earlier study [17], we confirmed good clinical and haemodynamic status of the patients after Fontan operation in which the mean McGoon ratio in the late follow-up was 1.4 ± 0.3. It is questionable whether Nakata index truly represents the condition of the lung vascular bed or possibly the functional parameters of the pulmonary circulation and single ventricle function are more important in the decision-making process before the Fontan completion.

Obvious limitations of this study include its retrospective nature and the lack of long-term changes in pulmonary artery sizes after two-stage Fontan, as well as their comparison with the dimension of pulmonary arteries after one-stage Fontan.

CONCLUSIONS

The relative decrease of the size of pulmonary arteries, to values previously unacceptable at the time of qualification for Fontan operation, in the inter-stage period (between BDG anastomosis and Fontan completion) and after Fontan completion may indicate that pulmonary arteries sizes should perhaps not be an absolute limiting factor in the decision on treatment of functionally UVH patients, especially at the stage of Fontan approach.

This study was supported by an internal grant of The Children’s Memorial Health Institute, (number 135/06).

Conflict of interest: none declared

References


Rozwój tętnic płucnych u dzieci z czynnościowo pojedynczą komorą

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Streszczenie
Wstęp: Od pierwszej publikacji Fontana i Baudeta z 1971 r. wyniki operacji typu Fontana znacząco się poprawiły, głównie dzięki lepszemu zrozumieniu krążenia typu Fontana, odpowiedniemu doborowi pacjentów do operacji i poprzedzającym zabiegom operacyjnym, w tym zespoleniu Glenna. Rozwój tętnic płucnych jest jednym z podstawowych elementów umożliwiających leczenie dzieci z czynnościowo pojedynczą komorą. Zrozumienie dynamiki rozwoju tętnic płucnych pozwala na zaplanowanie wieloetapowego procesu terapeutycznego, którego ostatecznym elementem jest operacja Fontana.

Cel: Celem pracy była ocena rozwoju tętnic płucnych u dzieci z czynnościowo pojedynczą komorą.


Wyniki: W angiografii przed operacją Glenna średnia wartość wskaźnika Nakata wynosiła 351,9 (131,2–886) mm²/m² i była wyższa u pacjentów ze zwiększonym przepływem płucnym (p = 0,0135). Średni współczynnik McGoona wynosił 2,5 (1,1–4,9). Wskaźnik Nakata zmniejszył się istotnie (p < 0,003) w średnim okresie 40,3 miesięcy po operacji Glenna do wartości 226,4 ± 125 mm²/m². Średni współczynnik McGoona obniżył się do 2,14 ± 0,58 (p < 0,008). Średnia procentowa zmiana wskaźnika Nakata wynosiła –17. Wskaźnik Nakata zmniejszył się w średnim okresie 37,4 roku po operacji Fontana — znacznie toższy niż przed operacją (p = 0,07). W grupie osób po jednoetapowej operacji Fontana (zewnętrznaczærne połączenie żylno-płucne) w późnym okresie po operacji, średnio 7,4 roku, wskaźnik Nakata obniżył się z 318,7 ± 159,1 do 120 ± 40 mm²/m² (p < 0,0001), a współczynnik McGoona z 2,4 ± 0,6 do 1,4 ± 0,27 (p < 0,0001). Średnia procentowa zmiana wskaźnika Nakata wynosiła –58 (95% CI od –67,6 do –48,6 (± 18,5)). Wskaźnik Nakata zmniejszył się w średnim okresie 11,4 roku po jednoetapowej operacji Fontana — znacznie toższy niż przed operacją (p = 0,01). Wskaźnik Nakata zmniejszył się w średnim okresie 5,3 roku po jednoetapowej operacji Fontana — znacznie toższy niż przed operacją (p = 0,0015 i p = 0,0012). Im większe były tętnice płucne przed operacją, tym większe nasileństwo zmniejszenia się tętnic płucnych w okresie obserwacji.

Wnioski: Względne zmniejszenie się wielkości tętnic płucnych w okresie między operacją Glenna a operacją Fontana, jak również w okresie między etapami leczenia, jest jednym z podstawowych elementów umożliwiających leczenie dzieci z czynnościowo pojedynczą komorą. Wskaźnik Nakata może być wykorzystywany do oceny dynamicznych zmian tętnic płucnych w okresie obserwacji.

Słowa kluczowe: dwukierunkowe zespolenie Glenna, całkowite połączenie żylno-płucne, wskaźnik Nakata

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