Early results of bilateral pulmonary artery banding for hypoplastic left heart syndrome

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Abstract

Objective: To compare the haemodynamics and perioperative course of initial palliation with bilateral pulmonary artery banding (PAB) and the Norwood procedure. Methods: Between April 2004 and December 2007, 43 consecutive children with hypoplastic left heart syndrome (HLHS) or a variant underwent initial palliation (PAB, n = 18; Norwood, n = 25). Clinical perioperative data were analysed. In the PAB group, lipo-prostaglandin E1 administration was continued with hospitalisation until stage 2 palliation with a bi-directional Glenn shunt and the Norwood procedure. Results: There were no significant differences in the age and operative weight of patients who received stage 1 palliation (PAB, 12 ± 9 days, 2.7 ± 0.6 kg; Norwood, 12 ± 8 days, 2.8 ± 0.4 kg). The PAB group had more high-risk patients than the Norwood group (PAB, 83%; Norwood, 48%, p = 0.04). Increased early and inter-stage mortality were observed in patients who underwent the Norwood procedure (early mortality with PAB, 6% vs Norwood, 12%; inter-stage mortality, 6% vs 27%, respectively). Mortality between stages 1 and 2 was 11% for the PAB group and 36% for the Norwood group. The Kaplan—Meier survival estimate at 1 year did not differ between groups (77% for the PAB group, 64% for the Norwood group). Ductal stenosis was found in one patient in the PAB group during the follow-up period. Twenty-eight patients underwent stage 2 reconstruction, and the patients in the PAB group were younger at the time of surgery (PAB, 116 days; Norwood, 224 days). There were no significant differences between groups in pulmonary artery index regarding body surface area (BSA) (PAB, 179 mm² BSA⁻¹; Norwood, 194 mm² BSA⁻¹) and the incidence of ventricular dysfunction after stage 2 construction (PAB, 21%; Norwood, 21%). Conclusions: Bilateral PAB with continuous lipo-prostaglandin E1 administration may improve early and intermediate mortality in infants with HLHS. Intimate care with hospitalisation may contribute to the results.

Keywords: Hypoplastic left heart syndrome; Pulmonary artery banding; Hybrid; Surgery

1. Introduction

Although surgical outcomes with the Norwood stage 1 operation for hypoplastic left heart syndrome (HLHS) have improved dramatically over the past two decades [1—4], high-risk neonates undergoing this procedure still face a mortality rate of 20—50% [3,4]. Even after initial success with the Norwood procedure, inter-stage mortality remains suboptimal. A hybrid approach consisting of bilateral pulmonary artery banding (PAB) and ductal stenting has emerged as a new strategy for the initial palliation of HLHS [5,6]. Early successes with the hybrid approach have prompted the increasing use of this strategy for high-risk patients as a less-invasive initial procedure to improve outcomes [7,8]. At Fukuoka Children’s Hospital, we initiated a modified hybrid procedure consisting of bilateral PAB and lipo-prostaglandin E1 (PGE1) infusion with hospitalisation until stage 2 palliation to improve the outcome of high-risk patients and to reduce the inter-stage mortality with intimate hospitalisation care. This article reviews our experiences with bilateral PAB for stage 1 palliation and provides a comparison of the mid-term outcomes between PAB and the Norwood procedure.

2. Methods

2.1. Patient population

Between April 2004 and December 2007, 43 consecutive children with HLHS or a variant underwent initial palliation (PAB, n = 18; Norwood, n = 25) at Fukuoka Children’s Hospital. We excluded patients bridged to two-ventricle repair. During this period, two patients with complex HLHS underwent the Yasui procedure. According to the physician’s
recommendation and family preferences, patients underw ent a conventional stage 1 Norwood procedure or bilateral PAB. The two groups in this study were contemporary and non-randomised. A retrospective review of the departmental database was undertaken to identify these patients, and their hospital records were reviewed. Children with a history of closing duct or ascending aorta diameter less than 2 mm were not considered preferred candidates for PAB, because the patency of the ductus and the coronary flow are the main concerns of postoperative management in this strategy. We felt it was better to perform bilateral PAB without cardiopulmonary bypass (CBP) than to perform the Norwood procedure for patients with contraindications to CBP, even though we assumed that they were a high-risk group for bilateral PAB.

Anatomical diagnoses were divided into (1) typical HLHS with mitral stenosis or atresia and aortic stenosis or atresia, (2) Shone syndrome, (3) unbalanced atroventricular septal defect, (3) double-outlet right ventricle with mitral stenosis or atresia, (4) tricuspid atresia with transposition of the great arteries and systemic outflow obstruction and (5) large ventricular septal defect (VSD) with aortic atresia. The distribution of cardiac anatomy among stage 1 palliation methods is shown in Table 1.

Risk factors included age, birth weight less than 2.5 kg, prematurity (gestational age <34 weeks), severe ventricular dysfunction, moderate-to-severe atroventricular insufficiency, intact or restrictive arterial septum requiring emergent intervention, additional cardiac anomalies and non-cardiac malformations or genetic syndrome. Additional cardiac risk factors in our population included coarctation of the aorta, total anomalous pulmonary venous drainage (TAPVD), and inferior vena cava (IVC) defect with bilateral superior vena cavae (SVCs). Patients with a preoperative pH <7.0, creatinine >2 mg dl⁻¹, and hepatic enzymes >500 U l⁻¹ were classified as having preoperative shock [1,3—5,7,8].

### 2.2. First-stage surgical procedure

PAB was performed in 18 patients (PAB group). After a median sternotomy and mobilisation of the pulmonary artery, bilateral branch PAB was performed with 3.5 mm Gore-Tex (W.L. Gore, Newark, DE, USA). Evaluation of PAB was made by epicardiac colour-flow Doppler echocardiography, and the tightness of the band was adjusted to achieve a peak flow velocity of 3.5 m s⁻¹ at both bilateral banding sites. A stage 1 Norwood procedure was performed in 25 patients (Norwood (NWD) group). As we reported previously [9], the descending aorta cannulation technique combined with innominate artery perfusion and bicaval cannulations was performed through a standard median sternotomy to avoid circulatory arrest. The neo-aorta reconstruction was performed by direct anastomosis of the pulmonary trunk to the combination of the transverse arch and the descending aorta. Pulmonary blood flow was supplied through a modified Blalock–Taussing shunt in 11 patients and a right ventricle to pulmonary artery conduit in 14 patients. The low-resistance strategy was carried out for perioperative management of patients who underwent the Norwood procedure [10].

### 2.3. Inter-stage follow-up

Patients in the PAB group continued hospitalisation with PGE1 administration through a peripherally inserted central catheter until stage 2. Echocardiography was performed weekly to monitor for patency of the ductus, obstruction at the atrial septum and evaluation of ventricular function. The patients were scheduled for stage 2 surgery 12 weeks later, and comprehensive catheterisation was performed beforehand. Patients in the NWD group were discharged from the hospital after adequate assessment, and outpatient follow-up, including echocardiography, was performed at 4-week intervals or earlier, depending on the clinical condition. Patients were referred for elective haemodynamic, angiographic and echocardiographic evaluation 16–20 weeks before the stage 2 procedure. We planned stage 2 surgery for the PAB group as early as possible, because coronary flow and patency of the ductus were the two main concerns for inter-stage follow-up in this group until the Norwood operation was performed, but we had to wait for the pulmonary vascular resistance to decline before we could carry out the bi-directional Glenn procedure safely. In contrast, after the stage 1 Norwood procedure, we could more safely wait for stage 2 surgery, because coronary flow and patency of ductus are not major postoperative issues after the Norwood procedure.

### 2.4. Stage 2 procedure

The stage 2 surgical reconstruction after PAB consisted of removal of the ductal tissue, direct aortic arch reconstruction, arterial septectomy, and removal of the pulmonary artery band and the connection between the pulmonary artery and the SVC. Pulmonary artery augmentation was not needed in any of the patients. Procedures were performed on CPB without circulatory arrest by the descending aorta cannulation technique, as with the first-stage Norwood procedure in our institution. Circulatory arrest was not required by any of the patients. A bi-directional cavopulmonary shunt was performed as the stage 2 procedure following the Norwood procedure on CPB.

### 2.5. Data analysis

Surgical, haemodynamic and laboratory data for all of the patients who underwent first-stage palliation for HLHS or a variant were retrieved from the database of Fukuoka Children’s Hospital and reviewed retrospectively. The
diagnosis, operation and additional procedures, age and weight at the time of the staged operation, status of the patient, cause of late death, atrioventricular valve regurgitation (AVVR), pulmonary artery (Nakata) index (PAI), mean pulmonary artery pressure (MPAP), pulmonary resistance index (Rpi), single ventricular ejection fraction (SVEF), cardiac index (CI) and postoperative clinical parameters were analysed. Data were sampled at the examination immediately after stage 1 palliation, at the preoperative examination before stage 2, and at the latest catheterisation before the Fontan procedure. These are the regular diagnostic procedures in our hospital. Early death was defined as death within 30 days of surgery, and late death as death occurring more than 30 days after surgery. All data are expressed as mean ± SD. Two-group comparisons were performed with an unpaired, two-tailed t-test for means of normally distributed variables and with Wilcoxon rank-sum tests for skewed data. The χ² or Fisher exact test was used to analyse differences among the categorical data. A p value <0.05 was considered significant. Statistical analysis was performed with Statview version 5.0J software.

3. Results

3.1. Patient characteristics

Patient characteristics and risk factors are summarised in Table 2. No significant differences between groups were observed regarding age and weight at the time of surgery. The PAB group had more high-risk patients (PAB, 83%; Norwood, 48%, p = 0.04). Patients in the PAB group had a higher incidence of restrictive atrial septal defect (ASD) (PAB, 28%; Norwood, 4%). Additional cardiac factors in the PAB group included cor triatrium and IVC defect with bilateral SVC, whereas two cases of TAPVD were included in the NWD group. In the PAB group, one patient had anal atresia and a congenital right-hand defect, and one patient had duodenal atresia; in the Norwood group, one patient had Kabuki make-up syndrome, and one patient had duodenal atresia.

3.2. Outcomes

Table 3 lists the mortality of the two groups according to the surgical intervention. The PAB group had less early deaths (PAB, 6%; Norwood, 12%, p = 0.62) and inter-stage deaths (PAB, 6%; Norwood, 27%, p = 0.11), although statistical significance was not achieved. The mortality between stages 1 and 2 was 11% in the PAB group and 36% in the Norwood group (p = 0.09).

Table 4 shows the mortality of the high-risk patients. The high-risk patients in the PAB group had less early deaths (7%) and inter-stage deaths (7%), and the high-risk patients in the Norwood group had higher mortality (50%) between stages 1 and 2, although these differences did not reach statistical significance. Kaplan–Meier survival using both early and cumulative death end-points stratified by the type of initial palliation demonstrated no difference in survival along the staging process. The Kaplan–Meier 1-year survival estimate was 77% in the PAB group and 64% in the Norwood group (log rank p = 0.23, Fig. 1). In addition, Kaplan–Meier survival curves for high-risk patients are shown in Fig. 1 (log rank p = 0.12). High-risk patients in the Norwood group had more decline than high-risk patients in the PAB group.

3.3. Stage 1

There was one early death in the PAB group. The patient had preoperative shock due to pulmonary over circulation, and soon after the PAB procedure, he had sudden junctional bradycardia and circulatory collapse. Three patients died early after the Norwood procedure. One patient died of long QT block on the operative day, one patient died of sudden uncontrolled pulmonary over circulation on postoperative day (POD) 1, and another had necrotising enterocolitis on POD 23.

3.4. Inter-stage between stages 1 and 2

One patient in the PAB group experienced sudden death during the inter-stage period. Since autopsy consent was not gained, the cause of death was unknown. All patients except...
one who had severe ductal stenosis received lipo-PGE1 between 2 and 8 ng kg\(^{-1}\) h\(^{-1}\); the dose of lipo-PGE1 was altered weekly based on the echocardiographic findings. Ductal stenosis was found in one patient in the PAB group 2 months after PAB. He recovered after the dose of lipo-PGE1 was increased and he underwent intubation, and he reached stage 2 at 3 weeks after ductal stenosis. Two patients in the PAB group had sepsis associated with a peripherally inserted central catheter, but both recovered.

There were six inter-stage deaths in the NWD group, including three sudden deaths with uneventful post-operative courses. One patient died of low output syndrome due to severe ventricular dysfunction, one died of necrotising enterocolitis, and another had postoperative liver dysfunction. Major cardiac events between stages 1 and 2 were balloon atrial septectomy in two patients in the PAB group and ducral stent and ASD stent in one patient in the PAB group because of severe ventricular dysfunction perioperatively. In this patient, it seemed to be very difficult to perform the scheduled stage 2 procedure, and we are currently waiting for improvement in the patient’s ventricular dysfunction. Two patients in the NWD group had balloon angioplasty for re-coarctation of the aortic arch, and one patient received a right modified Blalock-Taussing shunt because the pulmonary vascularity of his right lung was not sufficient to perform a bi-directional shunt, and he had progressive cyanosis.

3.5. Stage 2

A stage 2 procedure was performed in 14 patients in each group. At the time of the stage 2 procedure, the PAB group was younger and weighed less (PAB, 116 ± 24 days, 4.8 ± 0.9 kg; Norwood, 224 ± 134 days, 6.1 ± 1.8 kg). There was no early death in either group. Two patients in the PAB group died in the late follow-up period. One patient did not receive the bi-directional Glenn procedure due to high pulmonary resistance — this patient underwent only the Norwood procedure. He died at POD 32 because of respiratory failure. Another patient in the PAB group died of severe ventricular dysfunction. One patient in the Norwood group died of severe ventricular dysfunction 8 months after stage 2. The patient with an IVC defect in the

PAB group had the Norwood operation as a stage 2 procedure; she received a total cavopulmonary shunt at 1.5 years, and she is now waiting for a Fontan operation. Haemodynamic variables in cardiac catheterisation after the bi-directional Glenn shunt are shown in Table 5. Catheter evaluation was carried out in eight patients in the PAB group and 11 patients in the NWD group after stage 2. There were no significant differences between the PAB group and the Norwood group in MPAP, PAI, Rpi, Qp/Qs, CI and SVEF. At the time of stage 2, pulmonary augmentation for the banding site was not carried out in any patient. Debanding and Hagar dilation were sufficient for preparation of the pulmonary artery for the bi-directional Glenn operation. Long after main pulmonary artery banding, we usually observe dilation of the main pulmonary artery trunk. As for bilateral PAB, we did not see a significant change in the pulmonary artery trunk after the procedure. We assume the reason is that the waiting time was short, and there was run-off to the ductus. Three patients in each group had severe ventricular dysfunction after the stage 2 procedure. Overall, nine patients underwent a successful Fontan operation with no mortality. Four patients in the PAB group and five patients in the NWD group completed the protocol. Table 6 shows age, body weight and interval after stage 2 at the Fontan operation.

4. Discussion

Despite significant improvements in survival, the Norwood stage 1 operation for HLHS and variants remains a high-risk operation, and a neonatal Norwood operation requires complicated postoperative management, such as delayed sternal closure or prolonged mechanical ventilation. In addition, inter-stage death after a stage 1 Norwood procedure is still an issue. Recently, the hybrid strategy consisting of PAB and ductal stenting has emerged as a new
strategy for palliation for HLHS or associated anomalies, minimising the invasiveness and avoiding exposure to CPB [6—8,11]. Not only an option for transplantation, encouraged by the initial success of combined stage 2 surgical reconstruction, but the hybrid strategy has also been applied to a broad range of patients based on institutional experiences for standard and high-risk patients [8,12].

Our report showed the result of bilateral PAB with continuous lipo-PGE1 administration by maintaining hospitalisation. The advantage of PGE1 infusion to ductal stenting is easier arch reconstruction at the stage 2 procedure without stent removal, and we expect better retrograde arch flow for cerebral and coronary perfusion, because continuous PGE1 administration may prevent stenosis of the isthmus, which often has an extension of ductal tissue [13,14]. The ductal stent itself, by necessity, covers the isthmus opening into the transverse arch, because it must cover the entire duct to prevent ductal constriction. Arch reconstruction may become easier if the pulmonary trunk is dilated after PAB, but in our series, we did not see a significant change in the pulmonary trunk. We assume that the reasons for this were that the waiting time was short, and there was runoff to the ductus. Stable coronary perfusion and patency of the ductus is important to safely achieve stage 2 for the PAB group with this strategy, and we carefully monitored patients in the hospital for these two concerns. PGE1 has known adverse effects, such as vasodilatation and apnoea, but we did not observe these adverse effects in this series. We did not observe obvious haemodynamic changes during the follow-up period, likely because we used a relatively low dose. It is also problematic to maintain a catheter line for a long time; two patients in the PAB group developed sepsis, but both recovered.

We do not recommend the use of a prophylactic reverse shunt [18]. These types of shunts create the potential of a coronary seal and have a more complicated postoperative course [19]. Prolonged hospitalisation and its associated costs are the disadvantages of this strategy. Nevertheless, patients with risk factors often require longer hospitalisation, and the inter-stage mortality was high in some reports of the hybrid strategy [8]; therefore, it is reasonable to keep the patients in the hospital until the stage 2 procedure [17].

The inter-stage mortality of the hybrid strategy in the previous report ranged from 5% for patients with typical risk to 21% for high-risk patients [5,8]. Our data showed an overall inter-stage mortality of 6% in the PAB group and 7% in the high-risk PAB group. The hybrid procedure and our strategy establish a connection between the systemic and the pulmonary circulations at the arterial level, allowing for diastolic run-off away from the systemic and coronary bed, much like a systemic to pulmonary artery shunt. Even with careful observation along with hospitalisation, one patient had a sudden death during the inter-stage period in this study. But without hospitalisation, such as after the Norwood procedure, our inter-stage mortality was suboptimal, especially in high-risk patients. Careful monitoring with hospitalisation until stage 2 is one option, even in patients with the Norwood operation as a first palliation to prevent sudden cardiac events during the inter-stage period.

Mortality associated with stage 2 reconstruction was similar between groups, although the PAB group required extensive surgical procedures. This is probably because the resultant circulation with a cavopulmonary shunt is more stable than a circulation in parallel, such as with the Norwood procedure, and ventricular function has been shown to be better after a volume unloading procedure [15,16]. Although the PAB group also had more high-risk patients at the stage 2 procedure, haemodynamic values were similar in both groups. The pulmonary artery is a major concern after PAB, but by debanding the pulmonary artery within 3–4 months, further complex manoeuvres were not required for preparation of the pulmonary artery for the bi-directional Glenn operation.

Our contraindications for PAB were history of closing duct and ascending aorta diameter less than 2 mm. Patency of the ductus is a key to this strategy, and the Norwood procedure was chosen for the patients with a small ascending aorta or obstructed anomalous pulmonary venous drainage in our series. Some patients had a contraindication to CPB, such as disseminated intravascular coagulation or severe ventricular dysfunction; in that case, PAB may be a suitable option. We believe that PAB and the Norwood procedure have their own indications to contribute to better survival for HLHS or variants.

While the patient data were collected prospectively, a small, non-randomised patient population and an institutional bias, for this approach, limit this review. To judge PAB for HLHS, we need to know the number of patients who survive to undergo the Fontan operation and to analyse the quality of their condition after the Fontan operation. To date, many patients have not completed the Fontan operation; therefore, more time and more patients are required to evaluate this technique precisely.

In conclusion, our study supports the use of PAB with PGE1 for the management of HLHS. Bilateral PAB with continuous PGE1 administration may improve early and intermediate mortality, especially in high-risk patients. Intimate care with hospitalisation may contribute to the results.

References

Third, the integrity of the venous system. Anytime your cardiologist uses a femoral vein as access to insert a stent, results in the destruction — thrombosis — of the femoral and iliac veins, probably an unfavourable situation in a Fontan setting.

I have one question to you. You said that, during the second stage, you simply remove the Gore-Tex band, perform a local dilatation and do a cavopulmonary anastomosis. When we did that, because we tried it too, the dilatation of the banded part of the artery with Hegar dilators resulted in the tearing out of the arterial wall. We had to patch the banded parts of the pulmonary arteries to have an unrestricted flow to the lungs, at least on the left pulmonary artery. I understand you have never had to patch the pulmonary arteries.

Dr Sakurai: I have some case to patch, to make the pulmonary augmentation, but within 3 to 4 months basically we can do without the patch. What’s the date you operate the patient.

Dr Prêtre: Two months.

Dr Sakurai: Two months. And do you use the same.

Dr Prêtre: Between 2 and 3 months, it is our rule for the Norwood patients.

Dr Sakurai: Do you use the same material as we do? Do you use the same material, I mean the Gore-Tex?

Dr Prêtre: We use the Gore-Tex just as it was described by the group of Giessen in Germany.

Dr Sakurai: And I showed this, it doesn’t make a difference between Nakata index, but actually Nakata index has a smaller pulmonary artery after PA banding. That doesn’t have a significant difference. But the PA banding group had a smaller pulmonary artery, that’s right. But until so far we think 3 to 4 months just dilatation was enough to make the pulmonary artery.

Dr Prêtre: Have you seen the problem of this pulmonary root, which can become extremely dilated, may be not extremely, but which is definitively dilated?

Dr Sakurai: Maybe it’s larger than neonatal Norwood, but it’s also better to perform our direct anastomosis to make arch reconstruction I think.

Dr J. Fragata (Lisbon, Portugal): We have sort of palliated a few patients in which you would consider they were very risky for a typical stage 1 Norwood.

I would like to ask you a question on management of this patient. Because we’re doing the same that you’re doing, pulmonary banding and putting in a stent in the ductus. How can you keep these patients on prostaglandins for so long? Because the times we have attempted that, they either have respiratory depression or necrotising enterocolitis. Is it easy for you to keep these patients on prostaglandins?

Dr Sakurai: Well, as I show in this slide, we do the peripheral inserted central catheter. But usually we have to change the catheter 2 or 3 times during the 2 or 3 months. And we have only 1 patient who had the line trouble and who had the closing of ductus, but we find very early, so we just dose up the prostaglandin and that was enough.

Dr Fragata: It is well tolerated.

Dr Sakurai: Yes. Careful monitoring is a very important component I think.

Dr C. Pizarro (Wilmingtion, Delaware, USA): Last year we had the opportunity to present some of our data, with the hybrid management among low-risk patients. We have shown that there is no difference between the overall outcome when we looked at survival after the second stage as the end point. This observation illustrates the idea that we may transfer the risk from the initial neonatal period to later date, without significantly improving the outcomes. I think that you pointed out very well that the reconstruction of the arch is a lot simpler if you don’t actually put a stent in there. I don’t know if you found out that this was particularly useful in patients who were not true hypoplasias, but rather variants, where the ductus has a little bit of a tortuous course.

My question is, first, did you see an increased number of overall episodes of bacteremia or sepsis related to the line that you keep in place for such a long period of time?

And secondly, I saw in your slide that you have 28% of patients with a restrictive atrial septal communication. How did you define that? Because I was surprised to see in your pre-second-stage haemodynamic data that those patients had normal PVR and similar Qp/Qs.

Dr Sakurai: The first question. We had 2 patients who had bacteremia, but all the 2 patients came out well during that time.

And the next question, could you explain the next question again?

Dr Pizarro: It’s about how did you define a restrictive atrial septal defect, because you said you had 28% of those. That did not seem to have an impact on the haemodynamics.

Dr Sakurai: I defined the restrictive ASD as one that needed emergency intervention.
Dr M. Masuda (Yokohama, Japan): I have only one question. Concerning to the contraindication for pulmonary artery banding, you mentioned the diameter of the ascending aorta less than 2 mm is contraindication for the banding. Could you explain the reason for that.

Dr Sakurai: As I mentioned, retrograde arch flow is very important and less than 2 mm usually doesn’t have the antegrade flow. And the retrograde flow is only flow to the cerebral or coronary perfusion. So basically if we have the patient with less than 2 mm, I think the Norwood procedure is better.