European Journal of Cardio-Thoracic Surgery 46 (2014) 14–19
doi:10.1093/ejcts/ezt604 Advance Access publication 12 January 2014

ORIGINAL ARTICLE

Hybrid approach for hypoplastic left heart syndrome and its variants: the fate of the pulmonary arteries

Hitendu Dave[a,b,†*], Barbara Rosser[a,b,†], Walter Knirsch[b,c], Michael Hübler[a,b], René Prêtre[d,†] and Oliver Kretschmar[b,c,†]

[a] Division of Congenital Cardiovascular Surgery, University Children's Hospital Zurich, Switzerland
[b] Children's Research Centre, University of Zurich, Switzerland
[c] Department of Pediatric Cardiology, University Children's Hospital Zurich, Switzerland
[d] Department of Cardiovascular Surgery, University Hospital Lausanne (CHUV), Lausanne, Switzerland

* Corresponding author. Division of Congenital Cardiovascular Surgery, University Children's Hospital, Steinwiesstrasse 75, 8032 Zurich, Switzerland. Tel: +41-44-2668020; fax: +41-44-2668021; e-mail: hitendu.dave@kispi.uzh.ch; hitendu@hotmail.com (H. Dave).

Received 18 October 2013; received in revised form 16 November 2013; accepted 18 November 2013

Abstract

OBJECTIVES: To analyse the results of hybrid palliation of hypoplastic left heart syndrome (HLHS) patients and its variants with an emphasis on the long-term fate of the pulmonary arteries.

METHODS: We analysed 28 neonates (2006–11) with HLHS and its variants, who underwent bilateral pulmonary artery banding, patent ductus arteriosus (PDA) stenting and balloon atrial septostomy using a true hybrid approach. Median age and weight were 4 (0–36) days and 3 (1.9–3.7) kg respectively. Diagnoses included 23 HLHS and 5 variants. The fate of all surviving branch pulmonary arteries (PA) after a hybrid approach were compared with their counterparts in 29 Norwood I survivors (2002–11).

RESULTS: Four of 28 hybrid procedures needed to be converted to a Norwood procedure. Mortality after stage I hybrid palliation was 3/24 (12.5%). All 21 acute survivors underwent a comprehensive stage II at a median age of 4 (2.3–5.7) months, without any mortality (0%). Eleven of 21 comprehensive stage II survivors have undergone extracardiac Fontan; including 1 who underwent a rescue Fontan at 7 months of age and died (1/11: 9%). While 18/21 (86%) needed branch PA intervention in the hybrid group during the median follow-up duration of 39 (10–81) months, 9/29 (31%) needed the same in the Norwood group during a median follow-up duration of 58 (16–128) months ($P < 0.001$). Eight of 21 (38%) needed stenting [all on the left pulmonary artery (LPA)] in the hybrid group vs 5/29 (17%) in the Norwood group ($P = 0.097$). Ten of 21 (48%) patients had surgical/catheter intervention on both branch PA in the hybrid group vs 2/29 (7%) in the Norwood group ($P = 0.001$). Pre-Fontan Nakata index was significantly better in the Norwood group 206 (118–406) compared with the hybrid group 153 (56–230) mm^2/m^2 ($P = 0.01$). The comparable lower lobe indices were 149 (103–333) and 137 (45–178) mm^2/m^2 ($P = 0.04$), respectively.

CONCLUSIONS: Hybrid approach can be pursued with a low mortality. However, the high frequency of catheter and/or surgical interventions, and the sluggish growth of the branch PA pre-Fontan need innovative solutions. A comparison of the neurodevelopmental outcome for the hybrid vs the Norwood cohort would define the role of the hybrid strategy in the treatment of HLHS and its variants.

Keywords: Hypoplastic left heart syndrome • Hybrid approach • Bilateral pulmonary artery banding • PDA stenting • Pulmonary artery

INTRODUCTION

When left untreated, 95% of the children with hypoplastic left heart syndrome (HLHS) die early. Since the 1980s, surgical options have become available. Multidisciplinary advancements have improved outcomes tending to a survival of ∼65% at 5 years and 55% at 10 years of age [1]. Till very recently, there were basically two main surgical approaches: (i) the staged univentricular pathway with a Norwood operation in the early neonatal period, followed by a bidirectional Glenn at 3–6 months of age and an extracardiac Fontan completion between 18 and 30 months of age. (ii) Primary cardiac transplantation.

Despite encouraging surgical outcomes in pursuing the staged univentricular pathway, it was clear that the end result achieved remained at best a palliation with need for lifelong medical attention. Many of the survivors with optimal outcome had substantial developmental issues and health problems later in life—putting enormous strain on the family and the society at large.

Considering that in addition to pre-existing intranatal developmental anomalies of the brain, a complex intracardiac repair in the early neonatal period involving hypothermia, regional cerebral perfusion or even circulatory arrest may be harmful in the long run, a hybrid approach was developed. The goal of this approach was to postpone the complex correction to a later time. Although first described in the early 1990s by Gibbs *et al.* [2], it was reinvented by Akintuerk *et al.* [3] in 2002. This strategy

[†] The first two and the last two authors contributed equally to this paper.

involved interventional patent ductus arteriosus (PDA) stenting, followed by bilateral pulmonary artery banding (BPAB) through a sternotomy. This approach has since been adopted by various centres like Toronto [4], Delaware [5] and Ohio [6] and individualized. We introduced the hybrid approach for HLHS in 2006 [7]. This report analyses our experience with the hybrid approach in 28 HLHS patients or its variants (2006–11).

MATERIALS AND METHODS

We analysed 28 neonates (2006–11) who underwent BPB, PDA stenting and balloon atrial septostomy using a single stage true hybrid approach. Institutional review board permission was obtained to conduct this retrospective study. Median age and weight were 4 (0–36) days and 3 (1.9–3.7) kg, respectively. Diagnoses included 23 HLHS patients and 5 variants.

Contraindications

Since 2006, the hybrid approach has been our preferred approach. However, very small ascending aorta (≤2 mm) and stenosis of the arch anywhere upstream from the aortic isthmus were considered as relative contraindications for the hybrid approach. In one of the patients with arch obstruction detected after the hybrid procedure, a reverse modified Blalock–Taussig (BT) shunt from the main pulmonary artery to the truncus brachiocephalicus was performed, which served to reinforce the cerebral and coronary circulation (Fig. 1). Ventriculocoronary connection coexisting with aortic atresia and complete retrograde perfusion was considered a relative contraindication for a hybrid approach; however, we did subject one such patient to a hybrid procedure. As a rule, we would subject such a patient to a Norwood procedure with a right ventricle-pulmonary artery (RV-PA) shunt, thus improving diastolic blood pressure, making it possible to suture close the mitral valve thus reducing steal, and optimising post-capillary pulmonary venous flow.

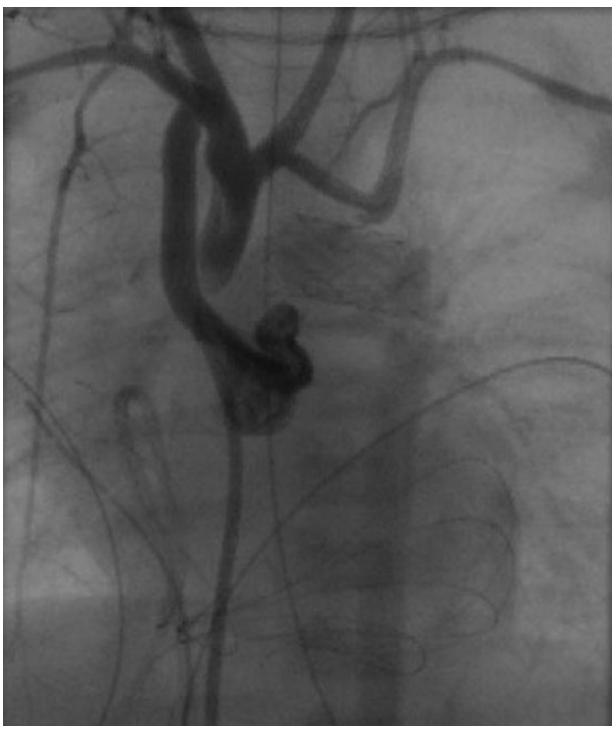

Figure 1: A reverse modified Blalock–Taussig shunt between main pulmonary artery and truncus brachiocephalicus demonstrating retrograde perfusion of the ascending aorta.

Procedure

The decision for a hybrid approach came during a combined cardiology–cardiac surgery consensus meeting. The procedure was performed in the catheter laboratory.

Through a sternotomy approach, BPAB was performed first. Depending on the size of the branch PA, a Gore-Tex graft (W. L. Gore & Associates, Inc., AZ, USA) 3–3.5 mm was ordered. A ∼3 mm long ring of the said graft was prepared. The Gore-Tex ring was split open at the blue dotted line and implanted at the origin of the branch pulmonary arteries (PA). The ring was closed using interrupted 7.0 polypropylene stitches. The ring was also fixed to the adventitia of the main pulmonary artery. Since the right pulmonary artery (RPA) was often bigger than the left pulmonary artery (LPA), the banding was titrated accordingly. The origin of the LPA was more difficult to circumvent, because of the dilated main pulmonary artery.

Banding both branch PA resulted in improvement of systemic blood pressure as well as a fall in arterial saturation. A saturation of ∼80% with an inspired oxygen concentration of 50% was aimed at. In some cases, an additional constriction of the Gore-Tex ring was effected, by placing a mattress absorbable suture; with the idea that the absorption of the suture could potentially compensate for the growth of the child. No pressure measurement across the banding site was performed. Median weight of patients receiving 3.5 mm Gore-Tex banding ring (n = 13) was 3.2 (2.6–3.8) kg; median weight of patients receiving 3.0 mm Gore-Tex banding ring (n = 5) was 3.1 (2.7–3.4) kg; in 6 patients the band size was not available.

Subsequently the interventional procedure was performed. A 4-French sheath was inserted across a purse-string placed on the body of the right atrium (Fig. 2). The sheath was marked at ∼1.5 cm from the tip (with a silk ligature) to guide the insertion (∼1 cm). The position of the purse-string was aimed in such a way that it provided a linear access to the tricuspid valve. The interventional cardiology team performed PDA stenting using balloon expandable stents. A balloon dilatation of the atrial septal defect (ASD) was also performed in the same setting. Following completion of the procedure, the sternum was closed. Figure 3 shows the PDA stents and the BPAB *in situ* at the end of the hybrid procedure. The patients were subjected to quick weaning and extubation was aimed at within 24 h.

Comprehensive stage II and extracardiac Fontan completion

The comprehensive stage II procedure was planned at ∼3 months of age. All intracardiac repairs were performed using cardiopulmonary bypass (CPB) and antegrade cerebral perfusion under moderate hypothermia. The duct was transacted from the pulmonary artery; the stent material lodged in the duct was removed *in toto*. The Damus-Kaye-Stansel anastomosis was performed and the aortic arch enlarged with Xeno-pericardium or a pulmonary

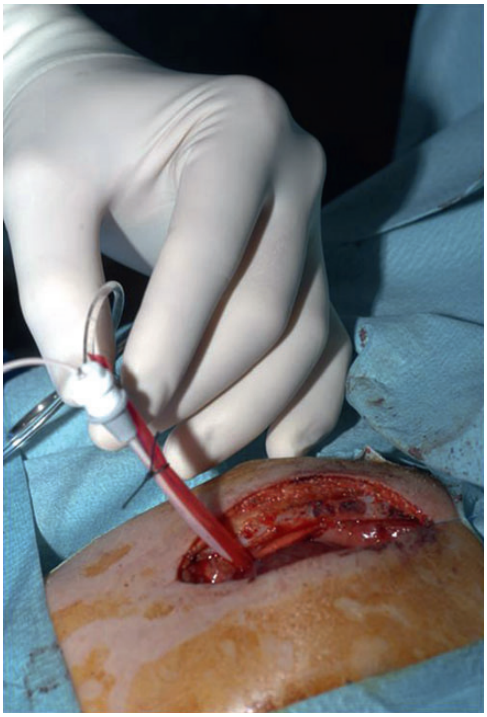

Figure 2: Intraoperative picture of the true hybrid procedure: transatrial sheath *in situ* for performing PDA stenting and balloon atrial septostomy.

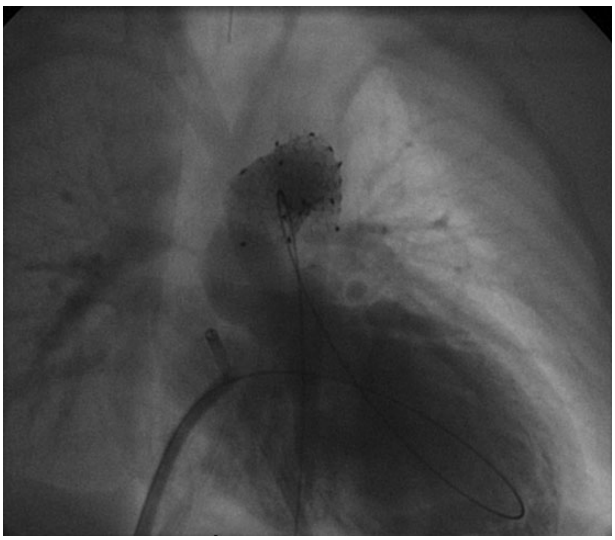

Figure 3: PDA stents and bilateral branch PA bands seen *in situ*.

homograft. The PA bands were removed. In general, while the LPA-banding site was only dilated using Hegar's dilator, the RPA-banding site was enlarged while performing the bidirectional Glenn anastomosis. Extracardiac Fontan completion was performed between 24 and 36 months of age.

Long-term fate of pulmonary arteries after hybrid approach

Long-term fate (pre-Glenn and pre-Fontan) of the surviving branch PAs after a hybrid procedure were compared with those after 29 Norwood I procedure survivors (2002–11). Nine non-survivors after the Norwood I procedure during this time frame were excluded from this comparison, since they did not provide a substrate for comparing the long-term fate of the branch PAs. The median follow-up observation period for the hybrid group was 39 (10–81) months as against 58 (16–128) months for the Norwood I survivors.

RESULTS

Conversion

In 4/28 (14.3%) patients, the hybrid approach was converted to a Norwood I procedure at day 0, 15, 42 and 85 due to ASD stent dislodgement, morphological factors (such as residual gradient across the isthmus) or haemodynamic factors.

Early events

In 2 patients with a restrictive foramen ovale and a thick atrial septum not yielding to balloon septostomy, an atrial septectomy using CPB and placement of BPAB was performed. In 1 patient the right atrial purse-string tore through, leading to dislodgement of the sheath and severe bleeding. The child could be resuscitated and stabilized and the intervention pursued to completion.

Late events

Stenosis of the aortic isthmus area necessitated balloon dilatation in 1 patient and stenting in 2 patients.

Other interventions performed include closure of left sided vertical vein (veno-venous collateral vein) and opening up of fenestration due to high Fontan pressure in 1 patient each.

Mortality

Overall mortality was 4/24 (17%), 3 after the hybrid stage I procedure (32, 12 and 43 days) and 1 after a rescue Fontan at 7 months of age. The cause of deaths included arrhythmias in 1 and occlusion of the LPA with a failing Fontan in 1; the cause remained unknown in 2 cases. The mortality reduced with experience and was 1/12 (8%) in the second half of the series. Kaplan–Meier survival at 60 months was 83 ± 8% for the hybrid group.

Revision of PA banding

Revision of banding was necessary in 5 of 25 cases; once to tighten it and four times to loosen it. Loosening was most often accomplished with a balloon dilatation while tightening was performed surgically.

Comprehensive stage II and stage III extracardiac Fontan completion

Twenty-one acute survivors underwent a comprehensive stage II without early mortality at a median of 4 (2.3–5.7) months of age.

Eleven of 21 survivors have undergone extracardiac Fontan completion; one of them being a rescue Fontan at 7 months of age, who eventually died (1/11: 9%). This child suffered occlusion of the LPA after comprehensive stage II, which was treated with a left-sided BT shunt and eventually with a rescue Fontan, of which she succumbed after a protracted course.

Duration of ventilation and hospital stay

The median duration of ventilation after hybrid stage I, comprehensive II and stage III extracardiac Fontan completion were 4, 3 and 1 days, respectively; the corresponding median hospital stay were 46, 43 and 25 days, respectively.

Fate of branch pulmonary arteries

A limited comparison of the post-Norwood branch PAs compared with post-hybrid branch PAs was made. Only 3 of 21 survivors remained free of any intervention on the branch PAs after the hybrid approach. Eighteen of 21 (86%) survivors needed branch PA reconstruction (6 patients) and/or catheter intervention (12 patients) in the hybrid group; 9/29 (31%) survivors in the Norwood group required the same; this was highly significant ($P < 0.001$) (Table 1). Need for branch PA stenting although showing a trend, was not significantly different between the hybrid group [8/21 (38%)] and the Norwood group [5/29 (17%)] ($P = 0.097$). All stenting were needed on the LPA. Ten of 21 (48%) patients needed bilateral PA (surgical or interventional) procedure in the hybrid group vs 2/29 (7%) patients in the Norwood group ($P = 0.001$) (Table 2).

Pulmonary artery indices

A comparison of the pulmonary artery indices for the hybrid as well as the Norwood group are given in Table 3.

DISCUSSION

After an initial learning curve [8], the overall results for the conventional Norwood – Fontan pathway strategy have continued to

Table 1: Branch pulmonary arteries surgical reconstruction and/or catheter intervention

	Any branch PA surgery/intervention (number of patients)		Total
	No	Yes	
Hybrid group			
n	3	18	21
% Within group	14%	86%	100%
Norwood group			
n	20	9	29
% Within group	69%	31%	100%
Total			
n	23	27	50
% Within group	46%	54%	100%

$P < 0.001$ (excludes early death patients).

Table 2: Bilateral branch pulmonary arteries surgical reconstruction and/or catheter intervention

	Bilateral branch PA surgery/intervention (number of patients)		Total
	No	Yes	
Hybrid group			
n	11	10	21
% Within Group	52%	48%	100%
Norwood group			
n	27	2	29
% Within group	93%	7%	100%
Total			
n	38	12	50
% Within group	76%	24%	100%

$P = 0.001$ (excludes early death patients).

Table 3: Comparison of branch pulmonary arteries indices

	Hybrid group mm^2/m^2	Norwood group mm^2/m^2	*P*-value
Pre-Glenn Nakata index	124 (46–236)	172 (94–437)	0.011
Pre-Glenn lower lobe index	103 (42–459)	169 (91–354)	0.003
Pre-Fontan Nakata index	153 (56–230)	206 (118–406)	0.014
Pre-Fontan lower lobe index	137 (45–178)	149 (103–333)	0.04

improve [9–10]. While the survival has improved to ∼74–93%, the inter-stage I–II mortality has continued to be a problem [11–14]. The use of RV–PA shunt [8] as well as introduction of home monitoring of transcutaneous oxygen saturation have somewhat alleviated this risk [15]. With the early survival improving, the impact of the complex neonatal operation and its consequences on the late neurodevelopmental outcome, have become the subject of increasing debate [9, 16].

It has been reported that patients with HLHS completing the staged Fontan pathway have significant neurocognitive difficulties [17]. A part of the neurocognitive deficiency is attributed to the structural abnormalities pre-existing in the brain of these patients [18]. Many studies have established a direct correlation between aortic atresia (complete retrograde perfusion of the arch) and poor late neurodevelopmental outcome [7, 19]. Magnetic resonance imaging studies have shown that neonates who undergo complex congenital heart surgery have a 34% increase in periventricular leukomalacia and non-specific signs of cerebral white matter injury [20]. It has thus been hypothesized that neonates with HLHS have a fragile central nervous system to begin with; and when subjected to an early neonatal repair under CPB (often with deep hypothermia and circulatory arrest) can lead to or aggravate neurological injury [21].

Operational issues

A hybrid approach has been pursued recently [3], with a view to postponing the complex intracardiac repair to a later age. Apart from the neurological advantage, it is argued that this strategy is useful for centres offering primary neonatal heart transplantation, where the potential recipient must wait long for getting a matching donor heart. This palliation can achieve stability and even allow discharge to home. This approach eliminates shunt-related complications. Additionally, in patients with borderline hypoplasia of left heart structures, this approach may buy time to see if the left heart structures grow big enough to allow a biventricular repair. Various groups described modified sequences and techniques of performing BPAB and PDA stenting [5, 6]. We have adopted a single stage true hybrid approach, with catheter intervention performed transatrially. This approach saves the femoroiliac venous system from potential postinterventional hazards. The BPAB are placed directly at the origin of the branch PA.

Mortality and morbidity

Kaplan–Meier survival at 5 years in our experience was 83 ± 8% for the hybrid group. Although not strictly comparable (cohorts), the 5-year survival in our Norwood group was 75.7 ± 7% ($P = 0.5$). In the Toronto experience, the corresponding survival at 3 years was 65.1% for the hybrid group and 58.9% for the Norwood group ($P = 0.7$) [4]. Akintuerk *et al.* [3] (Giessen, Germany) reported a transplant-free survival of 7/11 (64%) through to the comprehensive stage. Galantowicz *et al.* [6] (Ohio, USA) showed a transplant free survival of 32/40 (80%). Four of 32 survivors needed LPA stent and no patient needed PA augmentation during stage III, which are stand out results. This is in contrast with our findings and that of the Toronto group with increased incidence of banding-site interventions, most often on the LPA [4] as well as lower Nakata and lower lobe indices at the pre-Fontan stage.

Fate of the pulmonary arteries

The size and the quality of branch PAs and the arborization downstream is very important for the long-term outcome of the Fontan circulation. With our results echoing those from the Toronto group, we are worried at the frequency of interventions required on the branch PA.

We have observed that the banding site on the branch PA does not always recover spontaneously after debanding and simple dilatation with an olive tipped probe. It needs to be enlarged, occasionally even from one hilum to the other. How much does this extensive patching impinge on the long-term growth of the pulmonary arteries is open to debate.

The need for stenting (all on the LPA) in nearly 40% of our patients is a cause for additional concern, since the stent inserted in infancy cannot be dilated to adult size—meaning thereby that it needs to be cut through or replaced. Replacement even during a Fontan procedure is an invasive procedure ridden with risks. The stent fixes the branch PA to a static non-compliant state, which of course is advantageous when an external compression by a large neo-aorta is suspected. We wonder if the high incidence of banding site interventions that we have observed, could be related to tighter banding or reluctance to outright patch the pulmonary arteries during the comprehensive stage II.

In contrast, the lower rate of interventions on branch PA post-Norwood – Fontan pathway and better PA growth indices nearly 2 years after having corrected them (either with patches or stents) calls for technical modifications to ensure growth in the hybrid group patients.

Hospital resources

With the mortality rate after the hybrid approach being comparable with the Norwood approach, the hybrid approach may be

potentially advantageous in terms of reduced hospital resource utilization (duration of Intensive care unit and hospital stay) [6].

Neuroprotection

In spite of a few factors for and against the hybrid strategy, it is the much hypothesized neuroprotective advantage that will be the deciding factor regarding the long-term role of this approach.

A comprehensive study of neurodevelopment at 1 year comparing our hybrid and Norwood cohorts [7] has not shown statistically significant advantage for the hybrid group. In view of the wide variability of the CPB and hypothermia protocols used in centres around the world, results about the neurodevelopment outcome would have to be interpreted factoring in the influence of the bypass strategy used during the arch reconstruction operation.

LIMITATIONS

This report bears all the limitations inherent in a retrospective analysis. Moreover, the hybrid and Norwood groups are strictly not comparable since the more complex patients are likely to have been assigned to undergo the Norwood procedure.

CONCLUSION

Hybrid approach can be pursued with mortality comparable with the Norwood procedure. The need for interventions on the branch PAs as well as their reduced growth at the pre-Fontan time point, is a cause for concern, where technical improvements need to be evolved. However, it will be the long-term neurodevelopmental outcome results, which will determine the role of the hybrid approach in the treatment of HLHS and its variants.

Conflict of interest: none declared.

REFERENCES

[1] Barron DJ, Kilby MD, Davies B, Wright JG, Jones TJ, Brawn WJ. Hypoplastic left heart syndrome. Lancet 2009;374:551–64.
[2] Gibbs JL, Wren C, Watterson KG, Hunter S, Hamilton JR. Stenting of the arterial duct combined with banding of the pulmonary arteries and atrial septectomy or septostomy: a new approach to palliation for the hypoplastic left heart syndrome. Br Heart J 1993;69:551–5.
[3] Akintuerk H, Michel-Behnke I, Valeske K, Mueller M, Thul J, Bauer J *et al.* Stenting of the arterial duct and banding of the pulmonary arteries: basis for combined Norwood stage I and II repair in hypoplastic left heart. Circulation 2002;105:1099–103.
[4] Baba K, Kotani Y, Chetan D, Chaturvedi RR, Lee KJ, Benson LN *et al.* Hybrid versus Norwood strategies for single-ventricle palliation. Circulation 2012; 126:S123–131.
[5] Pizarro C, Derby CD, Baffa JM, Murdison KA, Radtke WA. Improving the outcome of high-risk neonates with hypoplastic left heart syndrome: hybrid procedure or conventional surgical palliation?. Eur J Cardiothorac Surg 2008;33:613–8.
[6] Galantowicz M, Cheatham JP, Phillips A, Cua CL, Hoffman TM, Hill SL *et al.* Hybrid approach for hypoplastic left heart syndrome: intermediate results after the learning curve. Ann Thorac Surg 2008;85:2063–70; discussion 2070–2061.
[7] Knirsch W, Liamlahi R, Hug MI, Hoop R, von Rhein M, Pretre R *et al.* Mortality and neurodevelopmental outcome at 1 year of age comparing hybrid and Norwood procedures. Eur J Cardiothorac Surg 2012;42:33–9.
[8] McGuirk SP, Stickley J, Griselli M, Stumper OF, Laker SJ, Barron DJ *et al.* Risk assessment and early outcome following the Norwood procedure for hypoplastic left heart syndrome. Eur J Cardiothorac Surg 2006;29:675–81.
[9] Mahle WT, Spray TL, Wernovsky G, Gaynor JW, Clark BJ III. Survival after reconstructive surgery for hypoplastic left heart syndrome: a 15-year experience from a single institution. Circulation 2000;102:III136–41.
[10] Sano S, Huang SC, Kasahara S, Yoshizumi K, Kotani Y, Ishino K. Risk factors for mortality after the Norwood procedure using right ventricle to pulmonary artery shunt. Ann Thorac Surg 2009;87:178–85; discussion 185–176.
[11] Mahle WT, Clancy RR, McGaurn SP, Goin JE, Clark BJ. Impact of prenatal diagnosis on survival and early neurologic morbidity in neonates with the hypoplastic left heart syndrome. Pediatrics 2001;107:1277–82.
[12] Stasik CN, Gelehrter S, Goldberg CS, Bove EL, Devaney EJ, Ohye RG. Current outcomes and risk factors for the Norwood procedure. J Thorac Cardiovasc Surg 2006;131:412–7.
[13] Tweddell JS, Hoffman GM, Mussatto KA, Fedderly RT, Berger S, Jaquiss RD *et al.* Improved survival of patients undergoing palliation of hypoplastic left heart syndrome: lessons learned from 115 consecutive patients. Circulation 2002;106:182–89.
[14] Gaynor JW, Mahle WT, Cohen MI, Ittenbach RF, DeCampli WM, Steven JM *et al.* Risk factors for mortality after the Norwood procedure. Eur J Cardiothorac Surg 2002;22:82–9.
[15] Ghanayem NS, Hoffman GM, Mussatto KA, Cava JR, Frommelt PC, Rudd NA *et al.* Home surveillance program prevents interstage mortality after the Norwood procedure. J Thorac Cardiovasc Surg 2003;126:1367–77.
[16] Mahle WT, Wernovsky G. Neurodevelopmental outcomes in hypoplastic left heart syndrome. Semin Thorac Cardiovasc Surg Pediatr Card Surg Annu 2004;7:39–47.
[17] Wernovsky G, Shillingford AJ, Gaynor JW. Central nervous system outcomes in children with complex congenital heart disease. Curr Opin Cardiol 2005;20:94–9.
[18] Glauser TA, Rorke LB, Weinberg PM, Clancy RR. Congenital brain anomalies associated with the hypoplastic left heart syndrome. Pediatrics 1990; 85:984–90.
[19] Mahle WT, Visconti KJ, Freier MC, Kanne SM, Hamilton WG, Sharkey AM *et al.* Relationship of surgical approach to neurodevelopmental outcomes in hypoplastic left heart syndrome. Pediatrics 2006;117:e90–97.
[20] Mahle WT, Tavani F, Zimmerman RA, Nicolson SC, Galli KK, Gaynor JW *et al.* An MRI study of neurological injury before and after congenital heart surgery. Circulation 2002;106:1109–114.
[21] Rychik J. Hypoplastic left heart syndrome: from in-utero diagnosis to school age. Semin Fetal Neonatal Med 2005;10:553–66.