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ORIGINAL ARTICLE

# Single ventricle repair in children with Down's syndrome

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**Abstract**
*Objective*. There is a paucity of information regarding appropriate management of children with Down's syndrome and a functional single ventricle. We report the results of bidirectional superior cavopulmonary shunts in six patients with Down's syndrome with a functional single ventricle.
*Methods*. Between January 1991 and December 2004, we identified six patients with Down's syndrome among 263 who had undergone bidirectional superior cavopulmonary shunts (BCPSs). There were four males and two females. The age at BCPS ranged from 1 to 12 years (mean 4.3 ± 3.9 years), and body weight varied between 8.2 and 29.4 kg (mean 13.8 ± 7.8 kg). All six patients had an unbalanced complete atrioventricular septal defect, with right ventricular hypoplasia present in five and left ventricular hypoplasia in one.
*Results*. There were no operative deaths, but one case required takedown of the BCPS. Except for this case, postoperative courses were generally uneventful. The median duration of follow-up was 46 months (range 12–80 months). Only two of five survivors after BCPS underwent a subsequent Fontan procedure, and one of these patients died of pulmonary hypertension postoperatively. The remaining three patients appeared to have significant risk factors for the Fontan procedure due to severe common atrioventricular valve regurgitation or persistent pulmonary vascular obstructive disease, including one who has completely dropped out from the Fontan track.
*Conclusion*. Down's syndrome is a risk factor in patients with functionally single ventricle due to persistent pulmonary hypertension and airway obstruction. These results show that single ventricle repair in patients with Down's syndrome is accompanied with difficulties, and patient selection for the Fontan procedure should be done carefully.

**Key words** Single ventricle repair · Down's syndrome · Fontan operation · Bidirectional cavopulmonary shunts

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## Introduction

Refinements and modifications of the Fontan operation have provided definitive surgical palliation for children with congenital heart disease in whom biventricular repair is not feasible.[1–3] However, there is a paucity of information to guide management of children with Down's syndrome (trisomy 21) and a functional single ventricle. This is because Down's patients have a high incidence of congenital heart disease[4–6], but rarely have hypoplasia of either ventricle. Furthermore, Down's patients are at risk of developing persistent pulmonary hypertension[7] and pulmonary airway obstruction,[8] which may compromise the outcome of univentricular repair. Herein, we report the results of bidirectional superior cavopulmonary shunts in six patients with Down's

**Table 1** Preoperative data

| Case | Associated anomalies | Previous operation | Age at previous operation (year) | mPAP (mmHg) | PAI ($mm^2/m^2$) | AVVR | EF (%) |
|---|---|---|---|---|---|---|---|
| 1 | PS<br>hypo-RV | BTA<br>BTA<br>Central shunt<br>PA plasty | 2<br>4<br><br>8 | – | 245 | Trivial | 63 |
| 2 | PDA<br>hypo-RV | PDA lig. PAB | 4 months | 17 | 321 | Mild | – |
| 3 | PDA CoA<br>hypo-RV | PDA lig. PAB<br>CoA repair | 2 weeks | 17 | 500 | Mild | 65 |
| 4 | PS<br>hypo-RV | BTA | 1 | 20 | 195 | Trivial | 60 |
| 5 | PA<br>hypo-RV | BTA<br>BTA | 2 months<br>2 | 17 | 503 | Mild | 74 |
| 6 | DORV CoA<br>SAS hypo-LV | m-Norwood | 1 month | 11 | 315 | Mild | – |
| Mean | | | | 16 ± 3.3 | 347 ± 129 | | 66 ± 6.0 |

mPAP, mean pulmonary artery pressure; PA, pulmonary artery; RPA, right pulmonary artery; LPA, left pulmonary artery; PAI, pulmonary artery index; AVVR, atrioventricular valve regurgitation; EF, ejection fraction; AVSD, atrioventricular septal defect; BTA, Blalock-Taussig anastomosis; PS, pulmonary stenosis; hypo-RV, hypoplastic right ventricle; PDA, patent ductus arteriosus; PAB, pulmonary artery banding; CoA, coarctation; DORV, double-outlet right ventricle; SAS, subaortic stenosis; hypo-LV, hypoplastic left ventricle

syndrome and a functional single ventricle (unbalanced atrioventricular septal defect).

## Subjects and methods

Between January 1991 and December 2004, we identified six patients with Down's syndrome among 263 who had undergone bidirectional superior cavopulmonary shunt (BCPS). There were 4 males and 2 females. The age at BCPS ranged from 1 to 12 years (mean 4.3 ± 3.9 years), and body weight varied between 8.2 and 29.4 kg (mean 13.8 ± 7.8 kg). All six patients had an unbalanced complete atrioventricular septal defect, with severe right ventricular hypoplasia present in five and left ventricular hypoplasia in one (Table 1). Procedures that preceded BCPS included one case each of the following: unilateral modified Blalock-Taussig anastomosis (mBTA); bilateral mBTA; bilateral mBTA + central (ascending aorta-to-pulmonary artery) shunt + central pulmonary artery plasty; pulmonary artery banding (PAB) + patent ductus arteriosus (PDA) ligation; PAB + coarctectomy; and modified Norwood procedure in a patient with left ventricular hypoplasia.

## Results

Clinical details are given in Table 1. The mean pulmonary artery pressure (mPAP) ranged from 11 to 20 mmHg (16.0 ± 3.3 mmHg). Nakata's pulmonary artery index[9] (PAI) ranged from 195 to 503 $mm^2$/BSA ($m^2$) (347 ± 129 $mm^2/m^2$). Ventricular function was preserved and atrioventricular valve regurgitation was less than mild on Doppler echocardiography in all six patients. Preoperative hemodynamic parameters in these patients fulfilled our institutional criteria for BCPS (mPAP ≤ 20 mmHg, PAI ≥ 200, and well developed peripheral pulmonary vascular bed on angiography).

There were no operative deaths. One patient, whose PAP was on the borderline of our criteria, required takedown of the BCPS on postoperative day (POD) 2 owing to elevated superior vena caval (SVC) pressure (30 mmHg). Except for this case, postoperative courses were generally uneventful with an acceptable SVC pressure: 13.5 ± 4.8 mmHg (6–18 mmHg) upon arriving at the intensive care unit (ICU) and 10.7 ± 5.2 mmHg (2.0–14.5 mmHg) before discharge from the ICU. The length of ICU stay ranged from 2 to 4 days (median 2.8 days), and the length of hospital stay ranged from 16 to 109 days. The early postoperative period was marked by chylothorax in two patients, with one of them requiring a prolonged hospital stay (109 days). Postoperative data are summarized in Table 2.

The median duration of follow-up was 46 months (range 12–80 months). Two patients underwent a total cavopulmonary connection (TCPC) at 12- and 24-month intervals from the BCPS, respectively. One of these patients died from acute cardiac insufficiency 16 days after the TCPC. Another patient is currently alive (New York Heart Association functional class I). One of the remaining three patients after the BCPS was not

**Table 2** Postoperative data

| Case | Age at operation (years) | Weight at operation (kg) | Length of stay (days) | | Pleural drainage (days) | CVP ($H_2O$) | | AVVR | Complications |
|---|---|---|---|---|---|---|---|---|---|
| | | | ICU | Hospital | | ICU entry | ICU exit | | |
| 1 | 12 | 29.4 | 3 | 23 | 4 | 18.0 | 14.5 | None | |
| 2 | 2 | 9.5 | 4 | 32 | 14 | 14.5 | 13.0 | Mild | Chylothorax |
| 3 | 3 | 11.5 | 2 | 16 | 6 | 17.0 | 14.0 | Trivial | |
| 4 | 4 | 11.2 | – | – | – | 19.0 | – | Trivial | Take-down |
| 5 | 4 | 12.7 | 2 | 109 | 50 | 12.0 | 10.0 | Trivial | Chylothorax |
| 6 | 1 | 8.2 | 3 | 24 | 4 | 6.0 | 2.0 | Mild | |
| Mean | 4.3 ± 3.9 | 13.9 ± 7.8 | 2.8 ± 0.8 | 40.8 ± 39 | 15.6 ± 18 | 13.5 ± 4.8 | 10.7 ± 5.2 | | |

ICU, intensive care unit; CVP, central venous pressure

**Table 3** Postoperative course

| Case | Result | PAP (mmHg) | PA stenosis | AVVR | Respiration problem |
|---|---|---|---|---|---|
| 1 | Drop out | 14 | Nonconfluent | None | None |
| 2 | Awaiting Fontan | 19 | None | Severe | None |
| 3 | Fontan | 15 | rt-PA | Mild | Tracheostenosis |
| 4 | Take-down | – | None | – | Tracheomalacia |
| 5 | Awaiting Fontan | 9 | None | Trivial | None |
| 6 | Fontan | 10 | lt-PA[a] | Mild | None |

PAP, pulmonary artery pressure; rt-PA, right pulmonary artery
[a]Distal anastomosis of the right ventricle to the pulmonary artery conduit

considered a candidate for Fontan completion due to pulmonary hypertension. The other two patients are still considered candidates for the Fontan procedure but have risk factors, including severe (CAVVR) and persistent pulmonary vascular obstructive disease detected on open lung biopsy.

## Discussion

Children with Down's syndrome have a high incidence of congenital heart disease but rarely have severe hypoplasia of one ventricle or unbalanced ventricles. Therefore, there is a paucity of information on the appropriate management of Down's patients with a functional single ventricle. It is known that Down's patients are prone to have premature development of pulmonary vascular obstructive disease and pulmonary vasoconstriction exacerbated by hypercarbia and hypoxia due to airway obstruction.[10] Spicer and coworkers[11] reported that completion of the TCPC was achieved in only two of five patients who were staged with a BCPS. On the other hand, Campbell and coworkers[12] reported that in appropriately selected patients with trisomy 21 and ventricular hypoplasia who are unsuitable for biventricular repair the Fontan procedure is not contraindicated and provides short-term benefit.

In the presence of borderline or mild hypoplasia, patients may be amenable to one-and-one-half ventricle repair. Moreover, the volume of the right ventricle could be underestimated at preoperative inspection because of the pulmonary overcirculation. However, all five patients in this cohort had a severely hypoplasitc or diminutive right ventricle, precluding this option. Another concern with this procedure is the difficulty of dividing a common atrioventricular valve appropriately for unequally sized ventricles, and the presence of atrioventricular valve regurgitation could be detrimental to its physiology. Therefore , the indication of one-and-one-half ventricle repair for unbalanced atrioventricular septal defect may not be guided by physiological and morphological criteria for patients with a hypoplastic right ventricle with intact ventricular septum.

In our study, five of the six Down's syndrome patients who underwent BCPS for functional single ventricle had a reasonable SVC pressure, and two of them have undergone a subsequent Fontan procedure (Table 3). The only patient who required takedown of the BCPS had a borderline high pulmonary artery pressure according to our criteria. This suggests the importance of adequate patient selection guided by proper assessment of preoperative data to achieve successful BCPS.

Prior to BCPS, pulmonary arterial blood flow should be strictly regulated by PAB for patients with pulmonary

overcirculation, and inversely, by systemic-pulmonary arterial shunt for those with a poor pulmonary vascular bed. In addition to these procedures, abnormal aorto-pulmonary collateral vessels that increase pulmonary blood flow should be closed with catheterization-guided coil embolization before BCPS. It is reported that AVVR and central pulmonary artery stenosis are risk factors for poor outcome.[13–15] Therefore, moderate to severe atrioventricular valve regurgitation (AVVR) on echocardiography and significant stenosis of the central pulmonary artery that causes unbalanced pulmonary blood flow distribution should be repaired in association with BCPS. In our cohort, one patient required valve repair for severe AVVR after BCPS. In this patient, CAVVR gradually deteriorated even after BCPS and eventually required CAVV repair_using an edge-to-edge technique 4 years after BSPS. CAVVR was reduced to less than mild after surgery but deteriorated again to a severe degree during follow-up. In this case, CAVV replacement will be required concomitantly with or as a preparatory operation for the Fontan procedure. Another patient required repair of the central pulmonary artery prior to BCPS. This patient had a stenosis of the proximal left pulmonary artery, presumably due to constriction of the PDA tissue, which required patch arterioplasty performed concomitantly with the central shunt. The patient currently has a recurrence of this stenosis after BCPS (left BTA was constructed simultaneously).

Another point to be considered in children with Down's syndrome is that they frequently have respiratory complications, influencing pulmonary vascular resistance,[8,10] and persistent pulmonary hypertension, which adversely affects outcome after the Fontan procedure. In this study, upper airway obstruction (tracheomalacia and tracheostenosis) had been detected in two patients. One of these patients, who had a tracheomalacia with recurrent respiratory infection that was prominent during infancy, underwent BCPS at 4 years of age, which alleviated the symptoms. However, BCPS takedown was required in this patient because of high Glenn pressure even with manipulation of the ventilator setting. The other patient who had trachostenosis, however, underwent successful Fontan completion after a tracheostomy.

In this series, one patient died from acute cardiac insufficiency 16 days after the Fontan operation, although preoperative hemodynamic values fulfilled our criteria (mPAP 10 mmHg, PAI 305, and AVVR mild). The patient had a good postoperative course until sudden clinical deterioration after intense crying and breath-holding resulting in severe cyanosis. Pathological findings in autopsy demonstrated severe medial hypertrophy in about half of the preacinar small pulmonary arteries. Yamaki and coworkers[16] reported that residual medial hypertrophy of the small pulmonary arteries, which causes pulmonary hypertensive crisis after surgery, is a major risk factor in Fontan candidates. Because of this pathological result, lung biopsy was performed in another patient awaiting Fontan procedure at 3 years after BCPS. Although all criteria had been fulfilled based on preoperative hemodynamic studies (mPAP 10 mmHg, PAI 350, AVVR trivial), histological analysis showed that hypertrophy of the media remained in almost all preacinar small pulmonary arteries. In this case, the Fontan operation was postponed, and the patient is currently awaiting repeat lung biopsy, which is to be performed after 1–2 years.

## Conclusion

Only two of five survivors after BCPS underwent a subsequent Fontan procedure, and one of these two patients died of pulmonary hypertension postoperatively. The remaining three patients appeared unsuitable for the Fontan procedure due to severe CAVVR or persistent pulmonary vascular obstructive disease, including one who has completely dropped out of the Fontan track.

These results show that single ventricle repair in patients with Down's syndrome has difficulties, and patient selection for the Fontan procedure should be done carefully. Especially, one must pay attention to specific problems associated with Down's patients, such as airway obstruction or rapidly progressing pulmonary vascular changes. We suggest that medial hypertrophy of small pulmonary arteries should be sought by means of open lung biopsy in borderline cases to evaluate the status of the pulmonary vasculature because hemodynamic variables measured while the patient is sedated may not represent their active status. Further study is necessary to establish a treatment algorithm of single ventricle repair in patients with Down's syndrome.

## References

1. Knott-Craig CJ, Danielson GK, Schaff HV, Puga FJ, Weaver AL, Driscoll DD. The modified Fontan operation. J Thorac Cardiovasc Surg 1995;109:1237–43.
2. Mayer JE, Bridges ND, Lock JE, Hanley FL, Jonas RA, Castañeda AR. Factors associated with reduction in mortality for Fontan operations in patients with single ventricle. J Thorac Cardiovasc Surg 1992;103:444–52.
3. Bartmus DA, Driscoll DJ, Offord KP, Humes RA, Mair DD, Schaff HV, et al. The modified Fontan operation for children less than 4 years old. J Am Coll Cardiol 1990;15:429–35.

4. Rowe RD, Uchida IA. Cardiac malformations in mongolism: a prospective study of 184 mongoloid children. Am J Med 1961;31:726–35.
5. Tandon R, Edwards JE. Cardiac malformations associated with Down's syndrome. Circulation 1973;47:1349–55.
6. Laursen HB. Congenital heart disease in Down's syndrome. Br Heart J 1976;38:32–8.
7. Yamaki S, Yasui H, Kado H, Yonenaga K, Nakamura Y, Kikuchi T, et al. Pulmonary vascular disease and operative indication in complete atrioventricular canal defect in early infancy. J Thorac Cardiovasc Surg 1993;106:398–405.
8. Bertrand P, Navarro H, Caussade S, Holmgren N, Sanchez I. Airway anomalies in children with Down syndrome: endoscopic findings. Pediatr Pulmonol 2003;36:137–41.
9. Nakata S, Imai Y, Takanashi Y, Kurosawa H, Tezuka K, Nakazawa M, et al. A new method for the quantitative standardization of cross-sectional areas of the pulmonary arteries in congenital heart diseases with decreased pulmonary blood flow. J Thorac Cardiovasc Surg 1984;88:610–9.
10. Jacobs IN, Teague WG, Bland JW Jr. Pulmonary vascular complications of chronic airway obstruction in children. Arch Otolaryngol Head Neck Surg 1997;123:700–4.
11. Spicer R, Uzark K, Cocalis M, Moore J, Mainwaring R, Lamberti J. Down syndrome and functional single ventricle: the Fontan approach (abstract). Cardiol Young 1997;7: 138.
12. Campbell RM, Adatia I, Gow RM, Webb GD, Williams WG, Freedom RM. Total cavopulmonary anastomosis in children with down's syndrome. Ann Thorac Surg 1998;66:523–6.
13. Kim HK, Kim WH, Kim SC, Lim C, Lee CH, Kim SJ. Surgical strategy for pulmonary coarctation in the univentricular heart. Eur J Cardiothorac Surg 2006;29:100–4.
14. Ishibashi N, Koide M, Uchita S, Seguchi M. When should pulmonary artery angioplasty be performed for Fontan candidates with pulmonary coarctation? Two cases of pulmonary artery angioplasty with the Blalock-Taussig shunt on pump in neonates. Jpn J Thorac Cardiovasc Surg 2004;52:185–8.
15. Driscoll DJ, Oxfford KP, Feldt RH, Schaff HV, Puga FJ, Danielson GK. 5–15 Year follow-up after Fontan operation. Circulation 1992;85:469–96.
16. Yamaki S, Ajiki H, Haneda K, Takanashi Y, Ban T, Takahashi T. Pulmonary arterial changes in patients dying after a modified Fontan procedure following pulmonary artery banding. Heart Vessels 1994;9:263–8.