FOLIA MEDICA CRACOVIENSIA
Vol. LVIII, 3, 2018: 11–21
PL ISSN 0015-5616
DOI: 10.24425/fmc.2018.125070

Risk factors for recoarctation of aorta after Norwood procedure in patients with hypoplastic left heart syndrome

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Abstract: Background: Recoarctation (reCoA) of the aorta is a common complication after the Norwood procedure. Untreated, it can lead to failure of the systemic ventricle and death. The main goal of the study is to define risk factors of reCoA after the Norwood procedure in hypoplastic left heart syndrome (HLHS).
Methods: We retrospectively analyzed the pre-, intra- and postoperative data of 96 successive patients who underwent the Norwood procedure between 2007 and 2011. In case of reCoA balloon angioplasty was performed. We analyzed and compared the data of the patients with reCoA and without reCoA using the StatSoft STATISTICA™ 10 software.
Results: ReCoA was noted in 23 patients (33.3%). This complication was diagnosed 95.1 days (49–156 days) on the average after the Norwood procedure. Balloon angioplasty successfully allowed for decreasing the mean gradient across the site of the narrowing from the average 27.5 mmHg to the average 9.7 mmHg ($p = 0.008$) and enlarged the neo-isthmus by the average of 2 mm ($p < 0.05$). The risks factors seemed to be the diameter of the ascending aorta OR = 7.82 ($p = 0.001$), atresia of the mitral valve OR = 7.00 ($p = 0.003$) and atresia of the aortic valve — OR = 6.22 ($p = 0.002$).
Conclusion: Balloon angioplasty seems to be an effective intervention in case of reCoA. A low diameter of the native ascending aorta (≤3mm) and the presence of atresia of the mitral and/or aortic valve should intensify the vigilance of a cardiologist in the search for signs of reCoA of the aorta.

Key words: hypoplastic left heart syndrom, coarctation, angioplasty, risk analysis.

Introduction

The Norwood procedure (NP) is the first stage of the surgical treatment of hypoplastic left heart syndrome (HLHS) [1]. The procedure is associated with numerous complications that may lead to death in the late postoperative period. One of the most common and most serious complications following the Norwood procedure is recoarctation of the aorta (reCoA), which occurs in 11 to 37% [2, 3] of children. The prolonged high pressure gradient across the region of the aortic isthmus may contribute to deterioration of the function of the right, single ventricle and to death [4] (Fig. 1). Risk factors of the neo-aorta recoarctation are not clearly defined. Such factors are suspected of affecting the phenomenon as the surgical technique, remnants of ductus arteriosus tissue and remnants of ductus tissue present in the pulmonary homograft employed in aorta reconstruction [4–7].

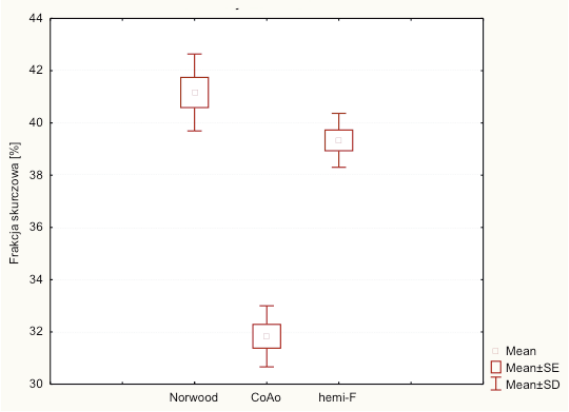

Fig. 1. The figure presents the mean heart function (systolic function in %) in patients after the Norwood procedure, in patients with recoarctation of the aorta (reCoA) and in patients after the hemi-Fontan operation (hemi-F) as seen in echocardiography.

The objective of the paper is the assessment of risk factors involved in reCoA after the Norwood procedure in children with HLHS. We hope the results will allow for defining a group with an increased risk of reCoA development.

Methods

The study is a retrospective analysis. All the data were obtained from medical records. HLHS was diagnosed based on echocardiography that evaluated the morphology of the mitral and aortic valves (obstruction or stenosis), diameter of the ascending aorta, diameter of the aortic arch and presence of atrial level restrictions. Intraoperative

data were also analyzed (the technique of aorta reconstruction, total time of cardiopulmonary bypass, time of circulatory arrest and age at the Norwood operation), as well as postoperative data (duration of ICU hospitalization, development of reCoA and early and late postoperative mortality).

ReCoA of the aorta was detected in diagnostic echocardiography performed when the condition of the child deteriorated or else while carrying out a routine cardiological follow-up. The suspicion of reCoA was invasively confirmed by heart catheterization.

The analysis included the parameters determined during the above procedure (the pressure gradient across the coarctation, diameter of the coarctation, systolic pressure in the ascending aorta, systolic and diastolic pressure in the descending aorta prior to and after balloon angioplasty). We took into consideration the age of the patients at the time of heart catheterization and the time lapse from the Norwood procedure.

Norwood procedure

The NP was performed using deep hypothermia and circulatory arrest. In patients with the ascending aorta above 3.5 mm, the aortic cannula was inserted close to the origin of the brachiocephalic trunk. In patients with smaller ascending aorta, the cannula was placed in the middle aspect of the ductus arteriosus and relocated to the ascending aorta after the reconstruction of the aorta. After initiating cardiopulmonary bypass, rapid cooling was started and maintained for at least 15 min, which usually led to establishing the temperatures as low as 14°C. During the cooling phase, the proximal aspect of the pulmonary trunk was transected and the distal part was fixed to Right Ventricle-Pulmonary Artery shunt (RVPAs). Myocardial protection was achieved with the single-dose crystalloid cardioplegia 15 ml/kg infused to ascendent aorta. The technique of reconstruction of the aorta consist to reconstruct the aorta with a pulmonary homograft patch in 91% of cases. The aortic arch was incised along its minor curvature, beginning at the open aortic isthmus and extending proximally down the ascending aorta. The residual ductal tissue was excised from the descending thoracic aorta. In the last 9% the pulmonary truck was connected directly to aortic arch. Atrial septectomy was performed through the cannulation site, the CPB was reinstituted. Proximal part of RVPAs was fixed to right ventricule about 1 cm under the pulmonary (neoaortic) valve.

Data analysis

To describe the investigated population, such mathematic calculations were employed as the percentage of occurrence of the phenomena that were important in the context of the study, arithmetic mean, median, range and standard deviation values.

The statistical analysis was based on the following tests: chi-square, T-student, Mann-Whitney, Fisher and logical regression test, with the significance level assumed to be $p < 0.05$. To meet the above objectives, the StatSoft STATISTICA™ 10 (Statsoft Inc., Tulsa, OK, USA) software was used.

Material

In the years 2008–2010, 96 children were subjected to the Norwood operation in the Krakow Department of Pediatric Cardiac Surgery as the first stage of the surgical treatment of hypoplastic left heart syndrome (Table 1 and 2).

Table 1. Characterization of the population qualified for the Norwood procedure.

Variable		N = 96 (100%)
Age at the Norwood procedure (days)	<7 days	3 (3%)
	7–14 days	49 (51%)
	>14 days	44 (46%)
Gender	boys	67 (70%)
	girls	29 (30%)
Diameter of ascending aorta (mm)	<2 mm	5
	2–3 mm	33
	>3 mm	50
HLHS morphology	AA/MA	18 (19%)
	AA/MS	34 (35%)
	AS/MA	2 (2%)
	AS/MS	37 (38%)
	undefined	5 (5%)

Table 2. General characterization of the Norwood population and operative data.

	Mean	Median
Birth body mass (g)	3340.00 ± 504.10	3300.0
Time of cardiopulmonary bypass (min)	141.56 ± 54.92	128.0
Time of circulatory arrest (min)	50.76 ± 24.38	46.5
Diameter of ascending aorta (mm)	3.76 ± 1.71	3.3
Diameter of aortic arch (mm)	5.06 ± 1.00	5.0

We excluded from the study group the children who died before the second stage of the treatment (the hemi-Fontan or Glenn procedure) in whom reCoA was not diagnosed in imaging studies or on autopsy (n = 20) and such patients whose further treatment was continued in other cardiac surgical centers (n = 7).

The final analysis included data pertaining to 69 children. Seventy-four percent of them (n = 51) were boys, 26% (n = 18) — girls. The mean birth body mass was 3340 g (Me 3340 g, range: 2180–4450 g). The mean age at operation was 14.4 days (Me 14 days, range: 6–33 days). The most common HLHS morphology was aortic valve atresia with mitral valve stenosis (42.6%). On the other hand, the least frequent morphology was aortic valve stenosis with mitral valve atresia (3%). The perioperative mortality rate was 9.7% (n = 9), while mortality in the period between the first and second stage of HLHS correction was 21.8% (n = 19). ReCoA was detected in 23 children (33.3%).

The initial group was divided into two subgroups: Group A that included children with diagnosed reCoA in whom balloon angioplasty was performed, and Group B where reCoA did not occur.

Results

Comparison of Group A and B (Table 3).

Table 3. Comparison of group with reCoA (reCoA+) and without reCoA (reCoA–).

	All operated patient (n = 69)	Patient with ReCoA (n = 23)	Patient without ReCoA (n = 46)	p >0.05	OR (95% CI)
Age (days)	14.40 Me = 14	13.58 Me = 14	14.77 Me = 14	0.7	0.74
Body mass (g)	3340 Me = 3330	3360 Me = 3410	3320 Me = 3310	0.59	1.19
Gender (boys)	50.00	15 (68%)	35 (78%)	0.56	1.48
Ascending aorta (mm)	3.76 Me = 3.25	2.93 Me = 2.50	4.17 Me = 3.50	0.001	0.55
Aortic arch diameter (mm)	5.06 Me = 5.00	5.11 Me = 5.00	5.04 Me = 5.00	0.715	1.08
Atrial level restrictions	33	12 (55%)	21 (46%)	0.606	1.42
Type of surgery:					
Complete reconstruction	63	22 (91%)	41 (89%)	0.656	
Suturing to pulmonary trunk	6	1 (9%)	5 (11%)	0.656	
Aortic valve atresia	37	18 (78%)	19 (41%)	0.002	6.22
Mitral valve atresia	15	10 (43%)	5 (11%)	0.003	7.00

No significant difference was noted between Group A and Group B with respect to the birth body mass, age at the Norwood procedure, diameter of the native aortic arch (Group A — 5.11 mm, Group B — 5.04 mm), type of the performed procedure and time of circulatory arrest.

Significant differences were seen in the diameter of the native ascending aorta, which in Group A had the mean value of 2.93 ± 1.40 mm and in Group B — 4.17 ± 1.72 mm (p = 0.001). The ascending aorta diameter equal to or lower than 2.5 mm was seen in 50% of the reCoA group neonates and only in 17% newborns in the non-reCoA group. The highest probability of reCoA development was noted in case of the ascending aorta with the diameter between 2 and 3 mm (Fig. 2 and Table 4). In addition, we observed that in 72.7% of children diagnosed with reCoA, the diameter of the ascending aorta was below 3 mm (Table 4). Thus, the entire group of the patients was divided into two subgroups with respect to the length of the ascending aorta diameter: <3 mm and ≥3 mm. The analysis demonstrated that the chance of reCoA occurring in the group of patients with the ascending aorta diameter equal to or lower than 2.9 mm was almost eightfold higher — OR = 7.82 (95% CI 2.45–29.2) (p = 0.001).

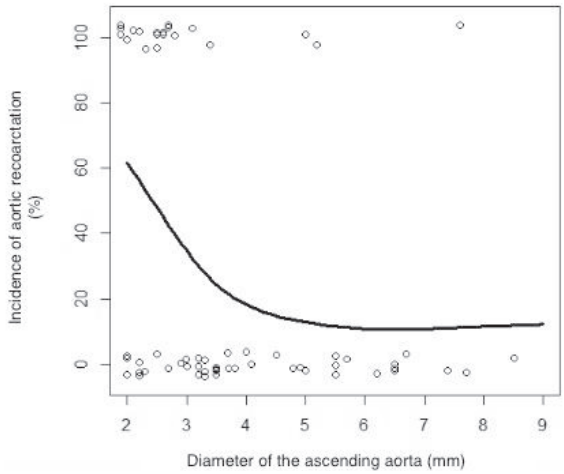

Fig. 2. The graph presents the incidence of reCoA depending on the ascending aorta diameter. At the top, marked with circles — patients with reCoA, at the bottom — patients without reCoA.

As compared to Group B, the Group A children more often presented with aortic valve atresia — 78% and 41%, respectively (p = 0.002) and mitral valve atresia — 43% and 11%, respectively (p = 0.003). In case of HLHS with aortic valve atresia, the risk of reCoA development was more than six-fold higher — OR = 6.22 (95% CI 1.69–29.4) (p = 0.002). A similar situation was noted in case of mitral valve atresia, where the risk

Table 4. Number of patients with reCoA (reCoA+) and without reCoA (reCoA–) in particular ranges of ascending aorta diameter values.

Ascending aorta diameter (mm)	reCoA– (n)	reCoA+ (n)	Cumulated number of events of reCoA (%)
1.9–2.4	8	9	39.1
2.5–2.9	4	8	73.9
3.0–3.4	7	2	82.6
3.5–3.9	7	0	82.6
4.0–4.4	2	0	82.6
4.5–4.9	3	0	82.6
5.0–5.4	2	2	91.3
≥5.5	13	2	100.0

of reCoA was seven-fold higher as compared to children without mitral valve atresia — OR = 7.00 (95% CI 1.76–32.1) (p = 0.003).

Aortic recoarctation was detected in 23 patients (33.3%). In one patient, the diagnosis was established postmortem during autopsy. The complication was suspected as a result of echocardiography and physical examinations performed during scheduled follow-up visits (every 2 and subsequently every 4 weeks) or when the condition of the child worsened and the patient reported to the emergency department. The final diagnosis of reCoA was established at the mean time of 91.95 ± 30.14 days after the Norwood procedure (49–156 days). Based on echocardiography results and general condition of the children, all the patients were qualified for urgent or scheduled heart catheterization with a simultaneous attempt at dilating the stenotic site by balloon angioplasty. The procedure allowed for decreasing the mean pressure gradient across the stenotic site from the mean value of 31.6 ± 13.1 mmHg to the mean value amounting to 11.3 ± 9.6 mmHg (p = 0.008) and for dilating the neo-isthmus by the mean value of 1.93 ± 0.98 mm (p <0.05) (0.7–4.5 mm). One patient died on the third day after catheterization due to systemic ventricular insufficiency and heart rhythm abnormalities. In one patient, because of ineffective BAA, a stent was implanted in the aortic isthmus. The patient required repeated heart catheterization procedures in order to dilate the stent. In three patients (13%) after BAA, recoarctation of the aorta was diagnosed prior to the second stage of the treatment and they required another isthmus aortoplasty. In one patient after the second stage of the treatment, recoarctation of the aorta was diagnosed; BAA was employed in the child 112 days

after first intervention. None of the patients required surgical correction of the stenotic segment.

Discussion

Recoarctation of the aorta is a common complication after the Norwood operation. When undiagnosed and untreated appropriately early, it leads to impairment of the systemic function of the right ventricle and to death due to circulatory insufficiency.

Despite modifications of surgical techniques, modern equipment and increasing experience of centers providing surgical treatment of single ventricle hearts, reCoA continues to be a serious, life-threatening complication after the Norwood procedure. Based on postmortem examinations, Van Praagh determined the most common causes of death after the Norwood operation. Approximately 14% of children with HLHS die due to reCoA. This is the fourth cause of all deaths in children with the above condition [8].

In our center, the prevalence of the complication was 32.3%. However, the value is within the range of values published as a result of studies performed in other centers.

It seems that one of the significant reCoA risk factors are the remnants of the ductus arteriosus tissue in the aortic isthmus region. In postmortem examinations, residual ductal tissue in the aortic wall was noted in 4 out of 5 patients with reCoA [9].

Burkhart *et al.* presented their therapeutic results achieved following the employment of a novel surgical technique consisting in total resection of the ductal tissue when reconstructing the aorta in the course of the Norwood procedure. The "alternating" method allowed for a significant reduction of reCoA occurrence from 46% to 0% [10].

Some authors suggest the effect of the type of material employed while reconstructing the aorta on the prevalence of neo-aorta coarctation. The theory has not been confirmed by the most recent studies [11]. The results of surgical treatment employing a femoral vein homograft published by Jonas point to a better survival rates in late follow-up as compared to standard materials and techniques. Nevertheless, the effect of the method on restricting the occurrence of reCoA has not been proven [12]. In our center, all the patients in whom material for aortic reconstruction was employed were operated on using a pulmonary artery homograft.

In 2013, Cleuziou *et al.* published a report where the percentage of reCoA in the study population amounted to 13.4% [13]. Nevertheless, no risk factor associated with the complication was determined. Our study demonstrated significant differences in the two groups with and without reCoA; the said differences included the ascending aorta diameter, mitral and aortic valve atresia. As it follows from the analysis, the chance of reCoA occurrence in the group of patients with the ascending aorta diameter below 4 mm is almost eight-fold higher as compared to the other patients.

In case of the HLHS variant with aortic valve atresia, the risk of the complication is more than six-fold higher. The same situation was noted in case of mitral valve atresia, where the risk of reCoA is seven-fold higher as compared to the HLHS variants without mitral valve atresia.

Under hemodynamic conditions of hypoplastic left heart syndrome after the Norwood procedure, the stricture of the outflow tract from the right ventricle may permanently impair its function [4]. For this reason, an early diagnosis and treatment of recoarctation of the neo-aorta is of an utmost importance for the future of the child. In all the patients we analyzed, the preliminary diagnosis of reCoA was established based on echocardiography. Our suspicion was triggered by dysfunction of the right ventricle, pressure gradient across the aorta in echocardiogrphy above 20 mmHg while the systemic ventricular function was good or by a visible narrowing of the neo-aorta. In each case, the diagnosis was confirmed by heart catheterization. According to the European Cardiology Society, the diagnosis of hemodynamically significant stenosis is warranted if the pressure gradient across the stenotic site measured in the course of heart catheterization is at least 20 mmHg [14]. However, an early diagnosis of the complication seems to be a challenge. As it follows from the preliminary observations in the present group, some patients developed signs of reCoA over several months, while in others significant recoarctation appeared suddenly, without any prior symptoms.

The standard in treating reCoA used by many center is balloon angioplasty performed during heart catheterization [15–18]. The procedure turned out to be effective in 74% of the patients who did not require repeated interventions.

Conclusions

1. In the postoperative course following the first stage of surgical treatment of hypoplastic left heart syndrome, the risk factors associated with recoarctation of the aorta include: ascending aorta diameter below 2.5 mm and aortic valve atresia and/or mitral valve atresia detected at echocardiography prior to qualification for the Norwood procedure.
2. Balloon angioplasty seems to be an effective mode of reCoA treatment that is associated with a low risk of complications and does not interfere with the strategy of routine three-stage treatment of hypoplastic left heart syndrome.

Based on the results of the present study, one may define a group with a high risk of reCoA occurrence after the first stage of HLHS treatment. Subjecting these patients to intensive care would allow for an early detection of recoarctation of the aorta and for preventing the development of life-threatening complications.

Limitations

Due to the low number of subjects in the investigated population, the results of the present study require confirming by other analyses based on more numerous databases.

Conflict of interest

None declared.

References

1. *Norwood W.I., Lang P., Casteneda A.R., Campbell D.N.*: Experience with operations for hypoplastic left heart syndrome. J Thorac Cardiovasc Surg. 1981; 82 (4): 511–519.
2. *Hornik Ch.P., et al.*: Complications after the Norwood Operation: An Analysis of the STS Congenital Heart Surgery Database. Ann Thorac Surg. 2011; 92 (5): 1734–1740.
3. *Ashcraft T.M., Jones K., Border W.L., Eghtesady P.*: Factors affecting long-term risk of aortic arch recoarctation after the Norwood procedure. Ann Thorac Surg. 2008; 85 (4): 1397–1401.
4. *Larrazabal L.A., Selamet Tierney E.S., Brown D.W., et al.*: Ventricular function deteriorates with recurrent coarctation in hypoplastic left heart syndrome. Ann Thorac Surg. 2008; 86 (3): 869–874.
5. *Hill K.D., Rhodes J.F., Aiyagari R., Baker G.H.*: Intervention for recoarctation in the single ventricle reconstruction trial: incidence, risk, and outcomes. Circulation. 2013; 27; 128 (9): 954–961.
6. *Sakurai T., Rogers V., Stickley J., Khan N.*: Single-center experience of arch reconstruction in the setting of Norwood operation. Ann Thorac Surg. 2012; 94 (5): 1534–1539.
7. *Bautista-Hernandez V., Marx G.R., Gauvreau K., Pigula F.*: Coarctectomy reduces neoaortic arch obstruction in hypoplastic left heart syndrome. J Thorac Cardiovasc Surg. 2007; 133 (6): 1540–1546.
8. *Bartram U., Grunenfelder J., Van Praagh R.*: Causes of death after the modified Norwood procedure: a study of 122 postmortem cases. Ann Thorac Surg. 1997; 64: 1795–1802.
9. *Machii M., Becker A.E.*: Nature of coarctation in hypoplastic left heart syndrome. Ann Thorac Surg. 1995; 59 (6): 1491–1494.
10. *Burkhart H.M., Ashburn D.A., Konstantinov I.E., De Oliveira N.C.*: Interdigitating arch reconstruction eliminates recurrent coarctation after the Norwood procedure. J Thorac Cardiovasc Surg. 2005; 130 (1): 61–65.
11. *Griselli M., McGuirk S.P., Stümper O., Clarke A.J.*: Influence of surgical strategies on outcome after the Norwood procedure. J Thorac Cardiovasc Surg. 2006; 131 (2): 418–426.
12. *Seery T.J., Sinha P., Zurakowski D., Jonas R.A.*: Femoral vein homograft for neoaortic reconstruction in the Norwood stage 1 operation: a follow-up study. J Thorac Cardiovasc Surg. 2013; 146 (3): 550–556.
13. *Cleuziou J., Kasnar-Samprec J., Hörer J., Eicken A.*: Recoarctation after the Norwood I procedure for hypoplastic left heart syndrome: incidence, risk factors, and treatment options. Ann Thorac Surg. 2013; 95 (3): 935–940.
14. *Baumgartner H., Bonhoeffer P., De Groot N.M., de Haan F.*: Task Force on the Management of Grown-up Congenital Heart Disease of the European Society of Cardiology (ESC); Association for European Paediatric Cardiology (AEPC); ESC Committee for Practice Guidelines (CPG). ESC Guidelines for the management of grown-up congenital heart disease (new version 2010). Eur Heart J. 2010; 31 (23): 2915–2957.

15. *Zellers T.M.*: Balloon angioplasty for recurrent coarctation of the aorta in patients following staged palliation for hypoplastic left heart syndrome. Am J Cardiol. 1999; 84 (2): 231–233, A9.
16. *Chessa M., Dindar A., Vettukattil J.J., Stumper O., Wright J.G., Silove E.D., De Giovanni J.*: Balloon angioplasty in infants with aortic obstruction after the modified stage I Norwood procedure. Am Heart J. 2000 Aug; 140 (2): 227–231.
17. *Tworetzky W., McElhinney D.B., Burch G.H., Teitel D.F., Moore P.*: Balloon arterioplasty of recurrent coarctation after the modified Norwood procedure in infants. Catheter Cardiovasc Interv. 2000 May; 50 (1): 54–58.
18. *Zeltser I., Menteer J., Gaynor J.W., Spray T.L., Clark B.J., Kreutzer J., Rome J.J.*: Impact of re-coarctation following the Norwood operation on survival in the balloon angioplasty era. J Am Coll Cardiol. 2005 Jun 7; 45 (11): 1844–1848.