Is a learning curve for arterial switch operation in small countries still acceptable? Model for cooperation in Europe

V. Hraska\textsuperscript{a,*}, T. Podnar\textsuperscript{b}, P. Kunovsky\textsuperscript{c}, L. Kovacikova\textsuperscript{c}, M. Kaldararova\textsuperscript{d}, E. Horvathova\textsuperscript{a}, J. Masura\textsuperscript{d}, J.E. Mayer Jr.\textsuperscript{e}

\textsuperscript{a}Department of Cardiac Surgery, Children’s Hospital, Bratislava, Slovakia
\textsuperscript{b}Department of Pediatric Cardiology, Children’s Hospital, Ljubljana, Slovenia
\textsuperscript{c}Cardiac Intensive Care Unit, Children’s Hospital, Bratislava, Slovakia
\textsuperscript{d}Department of Pediatric Cardiology, Children’s Hospital, Bratislava, Slovakia
\textsuperscript{e}Department of Cardiac Surgery, Boston Children’s Hospital, Boston, MA, USA

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Abstract

Objectives: To assess the results of a cooperative arrangement between Slovakia and Slovenia for neonatal cardiac surgery. The aim of the study was to analyze the performance of this approach for complete transposition of the great arteries (D-TGA).

Methods: Due to the overall small number of new patients with D-TGA in Slovenia a decision was made to avoid a prolonged learning curve by centralizing the experience of two countries at one center. Since 1995 the center in Slovakia has become the only referral center for Slovenia. Between February 1993 and June 2002 in this center, 147 patients with D-TGA underwent arterial switch operation (ASO). The median age at operation was 11 days, with 110 patients from Slovakia and 37 patients from Slovenia.

Results: Overall hospital mortality was 4.8% (seven patients). The 1, 2, 3, 4 and 5 year survival rate was 95% with the mean follow-up of 4 years. Operation before 1997 ($P = 0.0001$) was identified as a risk predictor for death by multivariate analysis. There are no deaths among the 90 patients operated on after 1996. All patients are without medication with normal left ventricular function. Stenosis (gradient $>30$ mmHg) was noted in the pulmonary artery reconstruction in seven patients (5%). More than mild aortic regurgitation was noted in five patients (4%). The incidence of redo or reintervention was 5% at 5 years of follow-up. Conclusions: In the current era a prolonged learning curve for ASO is not acceptable to most European countries and their patients. The risk of surgery can be minimized by concentrating surgical experience as part of the quality control of congenital heart programs. If the number of new patients is small due to the birth rate and size of the population, institutions should merge activity. Such centralization amplifies the experience to the benefit of the patient.

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Keywords: Congenital heart disease; Complete transposition of the great arteries; Learning curve; Centralization of care

1. Introduction

Adverse outcome in pediatric cardiac surgery is highly associated with low hospital and surgeon annual caseload. The hospital volume–mortality relationship persists for both high-complexity and low-complexity pediatric cardiac procedures [1–5]. According to the guidelines of European Association for Cardio-thoracic Surgery (EACTS) the optimal overall number of pediatric cardiac procedures should be over 250 per year per unit. This caseload will be generated from a country or region with four to six million inhabitants, depending on the birth rate. This volume threshold poses a problem especially in small countries with less than five million inhabitants. One potential solution, which could benefit patients, is to merge activity to reach on optimal number of operations and performance of program. This policy was adopted between Slovakia (SVK) and Slovenia (SLO), which merged their activity for complex congenital heart disease in 1995, in an attempt to develop a more effective congenital heart program in both countries based on mutual cooperation. The aim of the study
was to analyze the performance of this approach for complete transposition of the great arteries (D-TGA).

2. Materials and methods

2.1. Background

SVK (five million inhabitants with 51,000 live births per year) and SLO (two million inhabitants with 18,000 live births per year) are the smallest countries in the central Europe. In 1992 the Ministry of Health for Slovakia made a decision to establish only one pediatric cardiac center for the entire country. During 3 years this center was comprehensively retrained by a group of physicians and nurses from Boston Children’s Hospital supported by Project Hope, Millwood, Virginia. Currently this center performs more than 350 operations per year with an in-hospital mortality approaching 2%, covering the entire spectrum of congenital heart disease. In 1995 an agreement was reached between the Cardiac Center in Bratislava and Pediatric Cardiology Department in Ljubljana that SLO would direct its five to seven new patients annually with D-TGA to SVK in order to avoid a learning curve.

2.2. Patient population

Between February 1993 and June 2002, 147 patients with D-TGA and associated anomalies have undergone arterial switch operation (ASO) at Children’s Hospital, Bratislava, SVK. Two patients did not reach the Children’s Hospital and they died in a local hospital and one patient died prior to ASO after admission at Children’s Hospital. One hundred and nine (74%) patients had simple D-TGA and the remaining 38 (26%) patients had D-TGA with ventricular septal defect. The median age at operation was 11 (from 3 to 181) days. According to the Leiden classification scheme the most prevalent coronary pattern was [1LAD,Cx; 2R] (76%) followed by [1LAD; 2R,Cx] (12%), [2R,LAD,Cx] (7%), [1R; 2LAD,Cx] (3%), [1R,LAD; 2Cx] (1%) and [1R,LAD,Cx] (1%) [6]. Intramural course of at least one coronary artery was found in three patients. Associated lesions were presented in 11% of all patients. Aortic coarctation or hypoplasia of aortic arch was noted in seven (6%) patients. Right ventricular outflow tract obstruction was found in four (4%) patients who had obstruction of aortic arch as well. Multiple ventricular septal defects were present in five (4%) patients. Cor triatriatum was noted in one patient.

Preoperatively 31 (22%) patients required inotropic support and 55 (40%) patients were mechanically ventilated. A prostaglandin E1 (PGE1) infusion was used in 121 (88%) patients. Balloon atrial septostomy was performed in 123 (88%) patients.

Before ASO three patients had been palliated. One needed retraining of the left ventricle; the other two underwent banding of the pulmonary artery and repair of coarctation, respectively.

2.3. Overall management strategy

2.3.1. Preoperative management

Long-distance transport from remote parts of SVK and transport from SLO were carried out by specialized teams using either helicopter or light plane [7]. Before transport, all patients were started on PGE1 and were intubated if needed. There were no adverse events during the transport. The diagnosis of D-TGA was established by two-dimensional echocardiography (ECHO). Cardiac catheterization was reserved for patients with complex anatomy found on ECHO. During the last 6 years a balloon atrial septostomy was performed in the Cardiac Intensive Care Unit (CICU) under ECHO guidance. Subsequently the PGE1 infusion was discontinued if arterial saturation remained > 70%.

2.3.2. Surgical and perfusion management

Initially the Boston Children’s Hospital surgical techniques and perfusion protocol were utilized [8]. Gradually this protocol was modified. At present, the operation is performed on continuous low flow (50–80 ml/kg/min) hypothermic (22–25 °C) bypass. Deep hypothermic circulatory arrest is used only if aortic arch reconstruction is needed. During perfusion the hematocrit is kept at 30%. Following heparinization, bypass is commenced and the ductus arteriosus is divided. During cooling the branch pulmonary arteries are thoroughly mobilized to the level of the first segmental branches. At a rectal temperature of 25 °C the ascending aorta is clamped and cardioplegia solution is delivered into the root of aorta. The ascending aorta is divided. The main pulmonary artery is divided just proximal

<table>
<thead>
<tr>
<th>Type</th>
<th>N</th>
<th>% of 147</th>
<th>Total deaths</th>
<th>N</th>
<th>%</th>
<th>CL (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TGA/IVS</td>
<td>109</td>
<td>74</td>
<td>6</td>
<td>6</td>
<td>6</td>
<td>4–8</td>
</tr>
<tr>
<td>TGA/VSD</td>
<td>38</td>
<td>26</td>
<td>2</td>
<td>5</td>
<td>5</td>
<td>3–10</td>
</tr>
<tr>
<td>[1LAD,Cx; 2R]</td>
<td>112</td>
<td>76</td>
<td>4</td>
<td>4</td>
<td>4</td>
<td>2–6</td>
</tr>
<tr>
<td>[1LAD; 2R,Cx]</td>
<td>17</td>
<td>12</td>
<td>1</td>
<td>6</td>
<td>6</td>
<td>2–14</td>
</tr>
<tr>
<td>[2R,LAD,Cx]</td>
<td>10</td>
<td>7</td>
<td>1</td>
<td>10</td>
<td>10</td>
<td>4–24</td>
</tr>
<tr>
<td>[1R; 2LAD,Cx]</td>
<td>4</td>
<td>3</td>
<td>1</td>
<td>25</td>
<td>25</td>
<td>10–51</td>
</tr>
<tr>
<td>[1R,LAD,Cx]</td>
<td>2</td>
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<td>0</td>
<td>0–35</td>
</tr>
<tr>
<td>[1LAD;2Cx]</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>50</td>
<td>50</td>
<td>20–80</td>
</tr>
</tbody>
</table>

CL, 70% confidence limits; TGA, transposition of the great arteries; IVS, intact ventricular septum; VSD, ventricular septal defect; [], descriptive coronary nomenclature; 1/2, sinus number; LAD, left anterior descending coronary artery; R, right coronary artery; Cx, circumflex coronary artery.
to its bifurcation. Lecompte maneuver is performed. The coronary arteries are mobilized on buttons of aortic wall. Appropriate O-shaped areas of tissue are excised from the proximal neoaorta. The coronary arteries are sutured on the corresponding sinuses on the neoaorta. The aortic end-to-end anastomosis is fashioned. Closure of either the atrial septal defect, or ventricular septal defect is performed. The neopulmonary artery is reconstructed using a single pericardial patch. The aortic cross clamp is released. During re-warming, the pulmonary anastomosis is fashioned. After weaning from bypass modified ultrafiltration is used. If there is a hemodynamic instability, bleeding or overall oedema, delayed sternum closure is utilized.

2.3.3. Postoperative care

Monitoring includes a standard surface electrocardiogram (ECG), pulse oximetry, arterial line, central venous line and transhoracically placed left atrial line. Temporary atrial and ventricular pacing wires are placed in all patients. Paralysis and continuous narcotic sedation with fentanyl are continued for the first 6–12 h postoperatively depending on the hemodynamic status. Inotropic support is provided with dopamine, usually in combination with milrinone.

2.3.4. Functional outcome and follow-up

Regular clinical check-up was performed at 3-month intervals during the first postoperative year and at 12-month intervals thereafter. All patients underwent ECG, ECHO and Doppler assessment of the intracardiac repair. In the first 30 patients cardiac catheterization was electively undertaken between 3 and 4 years of life and thallium scintigraphy was undertaken between 4 and 5 years of life. Follow-up data were complete in all patients.

2.4. Statistical analysis

Data were analyzed using a statistical program (JMP Statistical Analysis, Cary, North Carolina). The primary outcome variable was survival after operation. Early failure was defined as death within 30 days of operation and late failure was defined as death beyond 30 days after operation. Multiple clinical parameters were analyzed for their possible impact on survival using univariate analysis with Fisher’s exact test for categorical variables and unpaired t-test for continuous variables. Variables that were significant at the 0.05 levels in univariate analysis were included in a multivariate Cox proportional hazards regression model. A significance level of 0.05 was required for retention in the multivariate model. The Kaplan–Meier method was used for survival analysis. Subgroups were compared with the use of the Wilcoxon test.

3. Results

3.1. Follow-up and survival

The median follow-up for the entire group is 4 years (range 2 weeks–9.4 years). Considering both early and late events the probability of survival for the entire group from the time of surgery was 95% (70% confidence limits [93, 97]) after 30 days and remained unchanged during the rest of follow-up (Fig. 1). In-hospital mortality was 4.8% (seven patients). One patient died during follow-up (Table 1). After overcoming the learning curve there were no deaths among the 90 patients operated on after 1996 (Fig. 2). There was no difference in survival among patients from SVK and SLO.

3.2. Univariate and multivariate analysis of preoperative and postoperative variables impact on survival

Univariate analysis demonstrated only two variables associated with early death for patients undergoing an arterial switch. These included aortic cross clamp time more than 120 min \((P = 0.026)\) and earlier date of operation (before 1997) \((P = 0.001)\). Only operation before 1997 was identified as a risk predictor for poor outcome \((P = 0.0001)\) by multivariate analysis. Before 1997 the aortic cross clamp time more than 120 min was noted in 28 patients (56%) with
five early deaths, after 1996 only one patient (1%) had aortic cross clamp time more than 120 min with no death. All other variables including weight, age, associated lesions, complex anatomy and coronary anatomy had no impact on survival.

3.3. Morbidity

The median stay in CICU was 6 days (from 1 to 40) days. Since 1997 the median length of stay in CICU dropped from 8 to 5 days \( (P < 0.0230) \). The same trend was noticed in duration of ventilation. The median duration of ventilation was 111 h before 1997 and 44 h since 1997 \( (P = 0.0022) \).

Early postoperative complications included re-exploration for bleeding and tamponade in 16 (11%) patients, diaphragm paresis in 10 (7%) patients (one received diaphragm plication), chylothorax in seven (5%) patients, sepsis in 15 (11%) patients. The sternum was left open in 40 (27%) patients and delayed closure was performed at a median of 3 days postoperatively. Clinical seizures were detected in two (1.5%) patients. Supraventricular tachycardia was seen in three (2%) patients, junctional ectopic tachycardia was noted in three (2%) patients. After overcoming the "learning curve" there was a significant decline in morbidity (Table 2).

3.4. Functional outcome

All patients are in New York Heart Association class I with normal left ventricular function. All patients are in sinus rhythm with no cardiac medications. Pulmonary stenosis (gradient >30 mmHg) was noted in seven (5%) patients. Trivial and mild aortic regurgitation was detected by ECHO in 39 (27%) and five (4%) patients, respectively. At cardiac catheterization, two (1%) asymptomatic patients had a circumflex coronary artery occluded. Thallium scintigraphy showed no perfusion defect. Seven (5%) patients of 139 long-term survivals had either redo or reintervention. One patient with significant supravalvular aortic stenosis underwent surgical aortoplasty, six patients underwent balloon dilatation of pulmonary artery.

### Table 2

<table>
<thead>
<tr>
<th>Morbidity</th>
<th>&lt;1997 n [% of 57]</th>
<th>&gt;1997 n [% of 90]</th>
<th>Total n [% of 147]</th>
</tr>
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<tbody>
<tr>
<td>SVC thrombosis</td>
<td>1 [2]</td>
<td>0</td>
<td>1 [1]</td>
</tr>
</tbody>
</table>

SVC, superior vena cava.

4. Discussion

Complete transposition of the great arteries is the most common form of neonatal cyanotic heart disease. The surgical method of choice is ASO. Currently the low operative mortality (<5%), low incidence of reintervention (<10%) and promising functional long-term outcome have been well documented in institutions properly prepared for neonatal heart surgery \([9–16]\). However, the introduction of ASO, though currently associated with low operative risk, can be accompanied not only by a learning curve of an individual surgeon, but also the institutions that have to adapt to the demands of the new treatment \([17]\). In addition there is an association between hospital and surgeon volume and in-hospital mortality, with quality of outcomes clearly related to the caseload \([1,2]\). EACTS recommendation that, each pediatric cardiac surgical unit should perform more than 250 operations per year and should serve a population of four to six million inhabitants, is under discussion at this moment. These recommendations can create a problem in small regions or countries with or less than five million inhabitants, where five to 15 new patients with D-TGA are born each year. Any new treatment (for example ASO) is likely to be associated with ethical and logistical issues, but the benefit of the patient and his/her family is of paramount importance. In these days of globalization, any institution pioneering new treatment should provide the optimal training setting for other institutions. If the volume of patients is small due to a low birth rate, institutions should consider merging activity to have enough patients to enable rapid learning. Such centralization amplifies the experience to the benefit of the patient. The national governments and regional authorities can and should play an active role in centralization of pediatric cardiac units in accordance with the recommendations of EACTS \([4]\). Overall performance of the congenital heart program must be scrutinized by professional organizations as well as by governments or regional authorities. It is a responsibility of governments, insurance companies and physicians to find solutions which provide the optimal service for their patients. Currently in European countries there is little tolerance for results that are sub-optimal.

A strategy of collaboration was embraced between SVK and SLO by merging their activity for complex congenital heart disease, to create a more effective congenital heart program in both countries based on mutual cooperation. Initially the government of SVK made an important decision to centralize all pediatric cardiac care to one center. Subsequently cooperation between SVK and SLO was implemented in two steps. The first step included a comprehensive and long lasting training of the SVK institution by a highly experienced center for pediatric cardiac surgery, the Boston Children's Hospital. By adopting the Boston protocols the learning curve of individual surgeons and the institution itself was minimized. In addition to this, cooperation between SVK and SLO
cardiology departments was established. This cooperation included training of SLO cardiologist in SVK and adopting a single preoperative protocol. Since 1995, most of critical newborns, including D-TGA have been referred to SVK center.

The achievements of this cooperation are very promising. Overall in-hospital mortality was 4.8% (seven patients). The 1, 5 and 9 year survival rate was 95% with the median follow-up of 4 years. The increased risk resulting from the earlier date of operation was neutralized by the end of 1996. After experiencing a relatively brief “learning curve” there were no deaths among the 90 patients operated on after 1996. All patients are without medication with normal left ventricular function. Pulmonary stenosis (gradient > 30 mmHg) was noted in seven patients (5%). Mild aortic regurgitation was noted in five patients (4%). The rate of redo or reintervention was 5%. The relatively short period of follow-up precludes any firm conclusions.

5. Conclusions

In the current era with increasing scrutiny of results by government and patients it is increasingly difficult for any institution to experience a “learning curve” in the management of D-TGA or other forms of complex congenital heart disease. The risk of surgery can be minimized by referral patterns as part of the quality surveillance of overall performance of the congenital heart program. The performance of the congenital heart program is clearly related to the overall caseload and to flexibility of the program to be effectively and comprehensively trained at the very beginning. If the volume of patients is small due to the low birth rate, institutions should consider merging activity to have enough patients to enable rapid learning. Such centralization amplifies the experience to the benefit of the patients.

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References

Appendix A. Conference discussion

Mr J. Monro (Southampton UK): You mentioned a learning curve. If I understood correctly, you had seven patients who died, and they were all in the first year, but if there were, maybe you didn’t tell us, but perhaps 10 or 15 patients in that year, that represents a very high mortality in the first year. Some units might have been put off going on if they had a high mortality. You then proved that you could do it and had such excellent results. Do you know what the mortality was in that first year?

Dr Hraska: In fact, the learning curve was overcome in 1996. The seven patients died between 1993 and 1996. So the learning curve covers more than three and a half years of experience.

Mr Monro: So had you a pretty good learning curve anyway?

Dr Hraska: Yes. We were able to minimize this painful effect of learning curve because we were comprehensively trained by the group of physicians and nurses from Boston Children’s Hospital. That was the key to be successful, I guess.

Dr A. Corno (Lausanne, Switzerland): You evidently have good results and I fully agree with your conclusions, but I respectfully disagree with the method you used to reach the conclusions. If you want to demonstrate that merging two smaller units is giving better results than leaving them separate, you should compare the results of the two units before merging and the combined results afterwards.

Second, you should give more importance to the major variable that you included, which is the retraining in Boston, if you want, for the whole team, and this could give much more impact to the improvement or the results than a single merging per se.

Then I have another question. Do you have patients in the smaller unit, if you want, that died before referral to your unit after the diagnosis because they didn’t have any more closer units available for referral even if it was a smaller unit?

Dr Hraska: Yes, of course.

Dr T. Aberg (Umeå, Sweden): I would just like to clarify the position of the EACTS at the moment. We are preparing a document on the structure of congenital heart surgery. It is now in a fairly final stage of the manuscript. The manuscript will be put up on the Web. It will be open for discussion for anybody who wants to comment on it, and then we will take a formal vote in the February Council meeting, and then it will be published and distributed.

Dr E. Bacha (Chicago, IL, USA): I have a practical question. How would you manage a baby born in Slovenia with D-transposition and a restrictive atrial septum who needs an urgent atrial septostomy, for example? I would assume you don’t have time to transport him to your center, but you don’t have the interventional cardiology experience in Slovenia to deal with it, presumably.

Dr Hraska: Like I mentioned during my presentation, a single preoperative protocol was adopted for both institutions, so the cardiologists in Slovenia are fully trained to do the balloon atrial septostomy. So there is no problem at all to manage babies preoperatively.