Clinical Course and Outcome of Children with Single Ventricle Physiology at King Chulalongkorn Memorial Hospital

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Background: *Children with single ventricle physiology comprise 10% of all children with congenital heart disease (CHD) and one-third of children with cyanotic CHD seen at King Chulalongkorn Memorial Hospital. The prognosis of these children is generally thought to be poor, but no study of the outcome has previously been done in this hospital and in Thailand.*
Objectives: *To study the clinical course and outcome of children with single ventricle physiology at King Chulalongkorn Memorial Hospital during the current era.*
Material and Method: *One hundred and seventeen patients with single ventricle physiology were initially seen at this hospital during the year 1999-2001. Retrospective chart reviews were carried out in 90 children with available medical records. The status of the patients was determined in 2003 at clinic visits, by phone calls and mail.*
Results: *The main diagnoses were tricuspid atresia (TA, n = 10), pulmonary atresia with intact ventricular septum (PA/IVS, n = 16), single ventricle associated with cardiac malposition or heterotaxy syndrome (malposition, n = 35), hypoplastic left heart syndrome (HLHS, n = 11) and other complex single ventricle (others, n = 18). Most children did not have other major anomalies. Survival of patients with TA and PA/IVS was approximately 92 and 87% at 1 and 4 years, respectively. For patients in the other three groups, 1 and 4 year survival was 69 and 42%, respectively. Patients with HLHS had the worse survival, partly because of decisions not to pursue further treatments by the parents. Among HLHS patients who underwent Norwood procedure, the 1 and 4 year survival were 83% and 42%, respectively. Approximately 40 and 90% of all patients underwent heart surgery at 1 and 4 years follow-up, respectively.*
Conclusion: *Despite limited resource, the short-term outcome of Thai children with single morphologic left ventricle (TA and PA/IVS) is reasonably good. Timely evaluation and treatment of these children toward Fontan procedure should be ensured. After proper discussion with the parents, palliative care is still acceptable for patients with single morphologic right ventricle or other complex single ventricle due to poor survival in the current era. As access to health care improves, re-evaluation of these outcomes is necessary to find the best strategy for the management of these patients.*

Keywords: *Congenital heart disease, Outcome, Single ventricle*

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Congenital heart disease (CHD) is the most common form of symptomatic heart disease in children[1]. Among all varieties of CHD, children with cyanotic CHD require the highest resource for treatment[2]. Among cyanotic patients, children with functional single ventricle probably carry the worst prognosis, at the same time require the most resource for treatment. Because of limited resources for cardiac surgical care in Thailand[3], the outcome of Thai children with single ventricle may be different from those in developed countries and has not been previously studied. These data are important in determining the strategy for caring for these children and to direct improvement of care in public hospitals. The purpose of the present study was to determine the characteristic, clinical course and outcome of children with a single functional ventricle at King Chulalongkorn Memorial Hospital.

Material and Method

Clinical database of all patients with congenital heart disease who were first seen at the department of Pediatrics, King Chulalongkorn Memorial Hospital during the years 1999-2001 were reviewed. Patients who had the diagnosis, which entailed the final surgical treatment by Fontan procedure, were selected. These were patients who either had only 1 ventricle, 2 ventricles with one of them hypoplastic, or 2 good-sized ventricles in whom surgical correction to separate the systemic and pulmonary circulation was judged not to be possible (such as a patient with one of the atrioventricular valves being atretic or severely stenotic). The clinical outcome of these patients including mortality, complications and surgical treatments were surveyed during clinic visits in the year 2003. For patients who did not come to the scheduled follow-up, phone, or mail contacts were attempted twice at 3 months apart. The patients who could not be contacted were censored at the time of last clinic visit. Survival curves were constructed for actual survival, survival from complications, and survival from surgical treatment. Complications were defined as the illnesses occurring in association with the patients' heart conditions that required hospitalization. Four main complications were sought: cyanotic spell or increasing cyanosis, congestive heart failure, pneumonia and sepsis/meningitis. Differences between survival curves were evaluated by Logrank test. A p-value of < 0.05 was considered significant. Statistic analyses were done by SPSS version 13 program (SPSS, Inc., Chicago, IL, USA).

Results

One hundred and seventeen (117) new patients with a single functional ventricle were seen at this institution during the 3 years. The number of new patients

Table 1. Diagnosis and clinical data of the 90 patients

Diagnosis	n	%	Remark
A: Cardiac diagnosis			
- Cardiac malposition including heterotaxy syndrome	35	39	Known asplenia = 4, polysplenia = 2
- Hypoplastic left heart syndrome	11	12	
- Tricuspid atresia	10	11	
- Pulmonary atresia/intact ventricular septum	16	18	
- Other single ventricle	18	20	Other single ventricle without malposition of cardiac and/or visceral situs
Total	90	100%	
B: Non-cardiac diagnosis			
- Known genetic syndrome	4	4	Trisomy 18 (1), Dandy-Walker (1), Kabuki (1), 22q deletion (1)
- Renal anomaly	3	3	Hydronephrosis (1), VUR (1), double collecting system (1)
- Respiratory tract anomaly	2	2	Diaphragm eventration (1), tracheomalasia (1)
- Gastrointestinal tract anomaly	1	1	Hirschsprung (1)
Total	10	11%	

VUR = vesicoureteral reflux

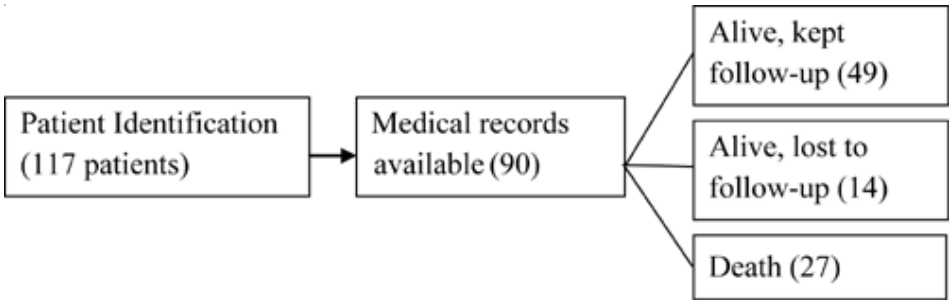


Fig. 1 Diagram showing the follow-up status of the 90 patients enrolled in this study

with CHD in these 3 years were 1187, thus these patients represented approximately 10% of all children with CHD during the same period and about one-third of all children with cyanotic CHD[1].

Of these 117 patients, medical records were available in 90 patients (76.9%) who comprised the subjects for the present study. There were 46 boys and 44 girls and the median age at first seen in these patients was 38 days (range 1-4,297 days). The diagnosis and clinical data in these 90 patients are summarized in Table 1. The status of follow-up visit in these 90 patients is shown in Fig. 1.

During follow-up (range 1-1471 days), 27 patients had died. The actuarial survival and causes of death in these patients are shown in Fig. 2 and Table 2, respectively. Mortality is dependent upon the diagnosis as shown in Fig. 3. Survival of patients with TA and PA/IVS was approximately 92 and 87% at 1 and 4 years, respectively. For patients in the other three groups, 1 and 4 year survival was 69 and 42%. Patients with HLHS had the worse prognosis, partly because of decisions not to pursue further treatments by the parents or perceived to be a poor surgical candidate at first presentation. Among patients who underwent Norwood procedure, the 1 and 4 year survival were 83% and 42%, respectively.

Table 2. The outcome and intervention in patients with single ventricle based on diagnostic category

Diagnosis	n	Interventions	Death	Causes of death (excluded unknown cause)	Complications Survival	4-year
Malposition	35	Surgery = 22 (63%) Cath = 25 (71%)	14 (50%)	Sepsis (21%), From intervention* (29%)	Pneumonia (29%) CHF (29%) Spell (7%)	43%
HLHS	11	Surgery = 5 (46%) Cath = 8 (73%)	7 (63%)	Sepsis (29%) Parents' choice (29%) Sudden death (14%)	Pneumonia (9%)	21%
TA	10	Surgary = 8 (80%) Cath = 9 (90%)	1 (10%)	Sepsis (100%)	Pneumonia (10%)	86%
PA/IVS	16	Surgary = 11 (69%) Cath = 11 (69%)	2 (12.5%)	Post surgery (50%) Pneumonia (12%)	Sepsis (6%) CHF (6%)	87%
Others Complex CHD	18	Surgery = 11 (61%) Cath = 12 (67%)	3 (16.7%)	Post surgery (33%) Pneumonia (11%)	Spell (17%) CHF (11%)	54%

* = surgery and/or cardiac catheterization, Cath = cardiac catheterization procedure, CHD = congenital heart disease, CHF = congestive heart failure, HLHS = hypoplastic left heart syndrome, Malposition = single ventricle associated with cardiac malposition and/or heterotaxy syndrome, PA/IVS = pulmonary atresia with intact interventricular septum, S = surgery, Spell = hypercyanotic spell, TA = tricuspid atresia

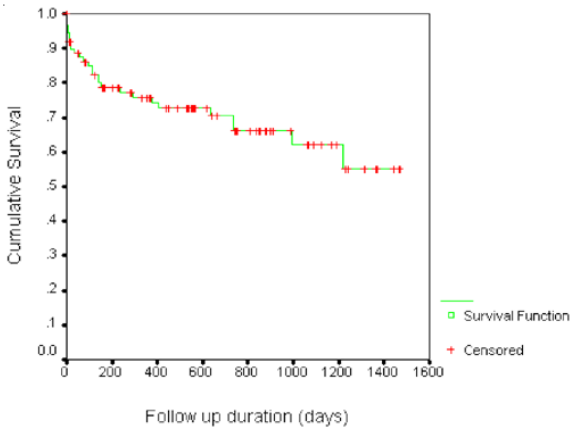
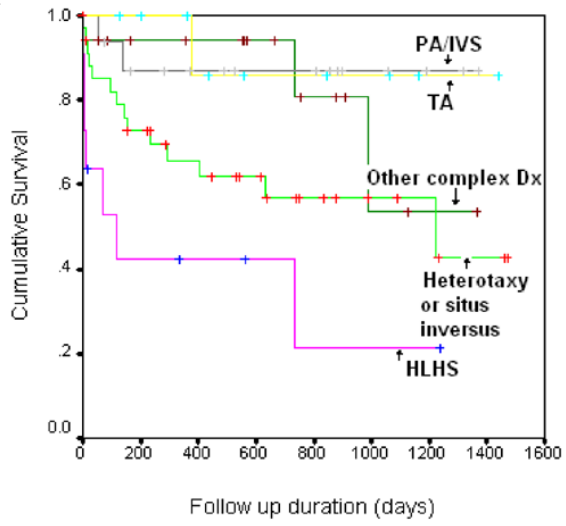
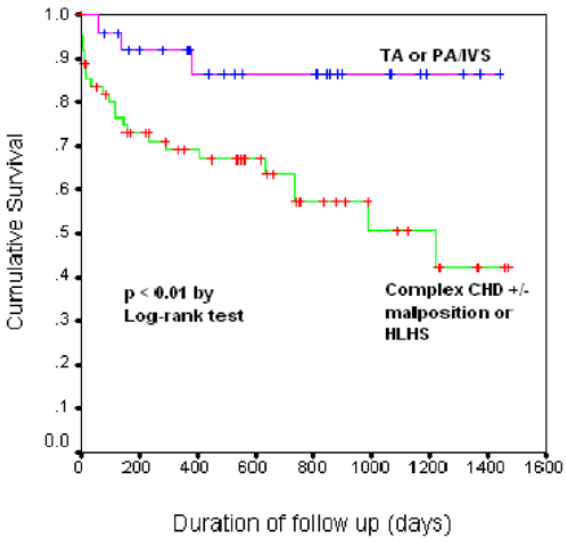


Fig. 2 Kaplan-Meier curve demonstrating survival of all patients from the time of first diagnosis at King Chulalongkorn Memorial Hospital

The morbidity (complication) associated with CHD in these patients can be grouped into two main categories; natural complications and those complications associated with surgical or cardiac catheterization procedures. Natural complications during follow up are summarized in Table 2. Freedom from natural complications and death in patients with TA or PA/IVS were 80 and 75% at 1 and 4 years, respectively. For all other diagnoses, freedom from natural complication and death were 56% and 36% at 1 and 4 years, respectively.

A total of 62 operations and 65 cardiac catheterization procedures were done in 72 patients during follow-up. Freedom from heart operation in all patients is shown in Fig. 4. Approximately 40% and 90% of all patients had undergone heart surgery by 1 and 4 years after presentation with no difference between patients with single morphologic left ventricle (TA and PA/IVS) and patients with single morphologic right ventricle or complex diagnosis (HLHS, CHD associated with heterotaxy syndrome and/or cardiac malposition and other complex cyanotic CHD) (Logrank test p = 0.94).





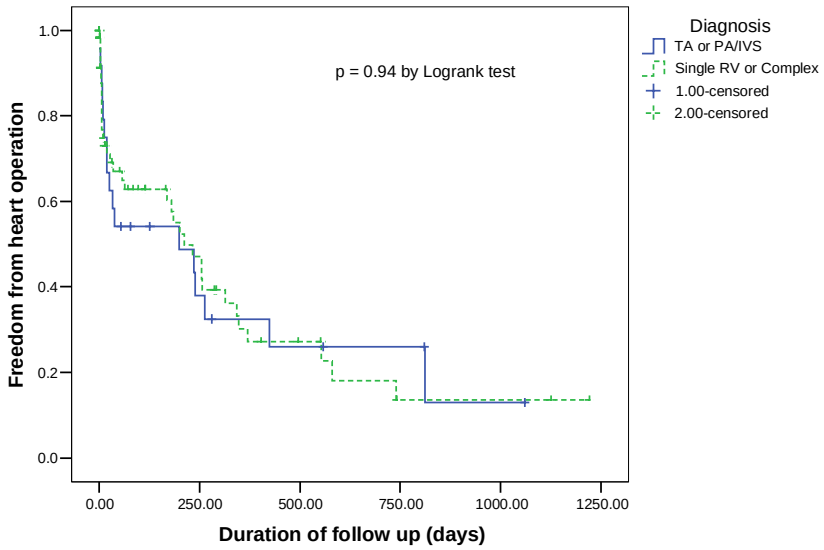
CHD = congenital heart disease, HLHS = hypoplastic left heart syndrome, Malposition = single ventricle associated with cardiac malposition and/or heterotaxy syndrome, PA/IVS = pulmonary atresia with intact interventricular septum, TA = tricuspid atresia

Fig. 3 Kaplan-Meier curve demonstrating survival (from the time of first diagnosis) based on the cardiac diagnosis

Discussion

Congenital heart disease (CHD) is the most important form of heart diseases in children. More than 80% of the new patients seen at this institution suffered from CHD[1]. While the outcome of patients with non-cyanotic CHD at this institution is generally good, the majority of mortality and morbidity occurred in patients with cyanotic CHD, which has not been systematically study previously.

Cyanotic CHD comprises about one-third of patients with CHD seen at this institution[1]. Based on surgical treatment options, two forms of cyanotic CHD are generally classified: 1) those in whom total correction to separate the systemic and pulmonary ventricles can be achieved and 2) those in whom only one functional ventricle are available (a single functional ventricle or univentricular heart). For the latter group, "total correction" to separate systemic and pulmonary circu-



Complex = complex congenital heart disease including those associated with cardiac malposition and/or heterotaxy syndrome, PA/IVS = pulmonary atresia with intact interventricular septum, single RV = single ventricle with right ventricular morphology, TA = tricuspid atresia

Fig. 4 Kaplan-Meier curve demonstrating freedom from cardiac operation in all 90 patients

lation with a ventricle for each circulation is not possible and the final palliation is generally the Fontan procedure[4]. Because of limited resources in developing countries, these patients were usually considered low in the priority for surgical treatment and the outcome is usually poor. As more resources and access to health care improve, more and more of these children will come to medical attention and get treatment. The purpose of the present study was to evaluate the outcomes of these children in the current era in order to find the appropriateness of the treatment strategies that the authors currently use and to use the data for further improvement of these outcomes. Comparisons of the outcomes will also be possible in the future as access to health care improves and/or new treatment strategies are implemented.

Children with a single functional ventricle comprised approximately 10% of all children with CHD and one-third of cyanotic CHD seen at this institution. This number appeared to be high, probably reflecting referral bias as this institution is one of the major referral centers for surgical treatment of children with complex CHD in Thailand[3]. The proportion of children with a single ventricle and/or complex CHD in the authors' cohort is similar to the data form Siriraj Hospital[5], which is another major referral center for children with CHD in Thailand.

From the present data, the outcome of these children in the past 5 years was still poor although subgroup analysis demonstrated a reasonably good outcome in certain diagnostic groups. In general, patients with morphologic left ventricle (such as those with tricuspid atresia [TA] and pulmonary atresia/intact ventricular septum [PA/IVS]) did better than patients with morphologic right single ventricle or with a complex diagnosis (such as patients with heterotaxy syndrome or hypoplastic left heart syndrome [HLHS]). Patients with TA or PA/IVS had an initial mortality (< 1 years of first seen) of approximately 8%, half of which occurred because of complications associated with surgical or cardiac catheterization procedures. After proper treatment, these patients appeared to do well in the short term as no or minimal further mortality was observed up to 4 years of follow-up even with the long surgical waiting time at this hospital (median time of waiting list for surgical correction of CHD was longer than 6 months during these years)[3]. Improvement of care in these patients can be achieved by proper timing for evaluation and staged surgery toward separation of systemic and pulmonary circulation (Fontan-type procedure) to eliminate cyanosis, ventricular volume load and pulmonary vascular diseases. Access to surgical treatment for CHD is still a problem in Thailand[3] and improvement of the outcome in these patients is

still possible by improvement in this area. Further study is needed to confirm the good clinical outcome of these patients in the long-term.

In contrast to patients with TA or PA/IVS, patients with heterotaxy syndrome, HLHS or other complex single ventricle had a poorer outcome. The causes for the high mortality were probably multifactorial, including both their natural history and the selection bias for less aggressive treatment. Children with heterotaxy syndrome may have problems with immune function, which predispose these children for infections and septic complications, especially after invasive procedures. Reported 1 and 5 year survival of children with asplenia from a large cohort in Taiwan was 72 and 50%, which is close to the authors' figure[6]. The surgical repair for children with HLHS is usually difficult, rendering these children more susceptible for operative and postoperative complications[7]. Some of these children might have suffered shock and organ dysfunction prior to the admission that excluded them from surgery and some were excluded from surgical treatment because of parents' choice. The strategy for improving the outcome in these patients must consider these non-cardiac issues as well as cardiac issues. In contrast to patients with TA or PA/IVS, proper selection of these patients for surgical treatment could still have a role in the care of these children in Thailand in the current era, as some patients may not benefit from aggressive surgical treatments or invasive procedures because of poor long-term survival under the current medical system. To do so, the parents and/or family members must be included in the decision for the care of these children as well. For those patients who were selected for treatment, proper and timely evaluation, and staged surgery toward Fontan procedure are needed, similarly to patients with TA or PA/IVS. Although historically patients with single ventricle associated with heterotaxy syndrome or HLHS had a poor prognosis[7-9], advances in the surgical and medical care of CHD have improved the outcome of these children in developed countries remarkably[10-12]. Since the function of single right ventricle is likely to be inferior to the left ventricle, the long-term outcome after the Fontan procedure in these patients needs to be further assessed.

In conclusion, the outcome of children with a single functional ventricle at this institution in the current era is dependent upon the diagnosis. Children with tricuspid atresia or pulmonary atresia/intact ventricular septum had a reasonably good short-term survival and timely medical and surgical treatments toward completion of Fontan procedure should be offered to most, if not all patients. Patients with diagnosis that are more complex or with hypoplastic left heart syndrome had a poorer diagnosis due to the current limited resources. They could be selectively offered aggressive surgical treatment and/or other palliative treatment after proper discussion with the parents. In patients who are selected for aggressive treatments, proper and timely evaluation and treatment toward Fontan procedure will be needed to avoid further complications. The outcome of treatment of these children needs to be periodically assessed to find the most appropriate strategy(s) for the care of these patients in Thailand.

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การดำเนินโรคและอัตราการอยู่รอดของผู้ป่วยเด็กที่เป็นโรคหัวใจแต่กำเนิดชนิดที่มีหัวใจห้องล่างเพียงห้องเดียวที่โรงพยาบาลจุฬาลงกรณ์

อภิชัย คงพัฒนะโยธิน, กนกกร รัตนวิไลศักดิ์, วิชัย เบญจชลมาศ, จุล นำชัยศิริ, บุญชู ศิริจงกลทอง, ไพโรจน์ โชติวิทยธารากร, พรเทพ เลิศทรัพย์เจริญ

***ที่มา**: ผู้ป่วยเด็กที่เป็นโรคหัวใจชนิดที่มีหัวใจห้องล่างเพียงห้องเดียวพบได้ประมาณ 10% ของผู้ป่วยเด็กโรคหัวใจแต่กำเนิด และ ประมาณหนึ่งในสามของผู้ป่วยเด็กโรคหัวใจชนิดเขียวที่โรงพยาบาลจุฬาลงกรณ์ การพยากรณ์โรคของผู้ป่วยเหล่านี้มักจะไม่ดี แต่ยังไม่เคยมีการศึกษาในผู้ป่วยเด็กในประเทศไทย*

***วัสดุและวิธีการ**: ทำการศึกษาในผู้ป่วยโรคหัวใจชนิดที่มีหัวใจห้องล่างเพียงห้องเดียวที่ได้รับการตรวจที่โรงพยาบาลจุฬาลงกรณ์เป็นครั้งแรกในปี พ.ศ.2542- พ.ศ.2544 โดยการตรวจเวชระเบียน โทรถามอาการ และโดยจดหมายในปี พ.ศ.2546*

***ผลการศึกษา**: จำนวนผู้ป่วยทั้งหมด 117 คน, ค้นเวชระเบียนได้จำนวน 90 คน (คิดเป็น 77%) แบ่งเป็นผู้ป่วย Tricuspid atresia (TA, 10 คน), pulmonary atresia with intact ventricular septum (PA/IVS, 16 คน), single ventricle ที่พบร่วมกับความผิดปกติของตำแหน่งหัวใจ หรือ heterotaxy syndrome (malposition, 35 คน), hypoplastic left heart syndrome (HLHS, 11 คน) และอื่น ๆ (others, 18 คน) เด็กส่วนใหญ่ไม่มีความพิการอื่น ๆ ที่สำคัญ อัตราการอยู่รอดของผู้ป่วย TA และ PA/IVS = 92% และ 87% ที่ 1 และ 4 ปีตามลำดับ, อัตราการอยู่รอดในผู้ป่วยอื่น ๆ = 69% และ 42 % ที่ 1 และ 4 ปี ผู้ป่วย HLHS มีอัตราการอยู่รอดที่ต่ำสุด ส่วนหนึ่งเป็นเพราะพ่อแม่ตัดสินใจไม่ผ่าตัดผู้ป่วย HLHS ที่ได้รับการผ่าตัด Norwood procedure มีอัตราการอยู่รอด 83% และ 42% ที่ 1 และ 4 ปีตามลำดับ ผู้ป่วยจำนวน 40% และ 90% ได้รับการผ่าตัดภายใน 1 และ 4 ปีหลังจากวินิจฉัย*

***สรุป**: อัตราการอยู่รอดของเด็กไทยที่มีหัวใจห้องล่างห้องเดียวชนิด left ventricle อยู่ในเกณฑ์ที่ค่อนข้างดีในระยะสั้น ผู้ป่วยเหล่านี้ควรได้รับการรักษาที่ถูกต้องและไม่ช้าเกินไป ผู้ป่วยที่มีหัวใจห้องล่างห้องเดียวชนิด right ventricle หรือชนิดที่ซับซ้อน มีอัตราการอยู่รอดที่ต่ำในระหว่างปีที่ทำการศึกษา การให้การรักษาแบบประคับประคองในผู้ป่วยเหล่านี้ยังคงยอมรับได้ถ้าบิดามารดาเห็นด้วยและยินยอม การศึกษาอัตราการอยู่รอดของผู้ป่วยเหล่านี้เป็นสิ่งที่ควรทำอีกในอนาคต เมื่อประเทศไทยมีระบบสาธารณสุขที่ดีขึ้น*