Outcomes of single-ventricle physiology in central South Africa

MJ van Jaarsveld, L Botes, FE Smit, SC Brown

Abstract

Introduction: Single-ventricle physiology is a critical cardiac condition requiring early diagnosis and intervention. The objectives of this study were to report on the management and outcomes of patients diagnosed with single-ventricle physiology in central South Africa.

Methods: This study was a retrospective, observational analysis of patients presenting with single-ventricle physiology at the Universitas Academic Hospital in central South Africa between November 1997 and June 2021.

Results: Patients were referred from the Free State (54%) and Northern Cape (29%) provinces and Lesotho. One hundred and fifty-four patients presented with single-ventricle physiology: 114 received interventions and 40 were not eligible for intervention. Patients presented for the first time at a median age of 34.5 days, with patients from nearby districts presenting within a few days of birth. However, patients from outlying areas presented much later. Eighty-seven patients received systemic-to-pulmonary artery shunting or pulmonary artery banding. Sixty-three patients proceeded to bidirectional Glenn procedures, and 30 patients (26%) had full palliation to Fontan. Twenty-one patients died after stage 1, six after the Glenn procedure and two after the Fontan procedure. Overall, 34 (29.8%) patients were lost to follow up.

Conclusion: Patients in our study presented late and follow up of these patients was a challenge. The highest mortality rate occurs during the first stage of palliation. Outcomes from this study are comparable to other sub-Saharan studies.

Keywords: single ventricle, Glenn, Fontan, shunt, banding

Lesions with single-ventricle physiology occur in four to eight out of 10 000 live births or in one to 2% of patients with congenital cardiac abnormalities. Single-ventricle physiology encompasses a heterogeneous group of complex cyanotic cardiac lesions, which usually require early diagnosis and intervention at a congenital cardiac centre. Infants born with non-critical cardiac heart disease have a 97% one-year survival rate, whereas babies with critical cardiac heart disease have only a 75% one-year survival rate. This emphasises the need for early detection and treatment of these infants.

Newborns with functional single-ventricle physiology have parallel pulmonary and systemic circulations, resulting in cyanosis and ventricular volume overload. Treatment consists of staged intervention, with the first stage involving palliative interventions such as patent ductus arteriosus (PDA) stenting, Blalock–Taussig shunts (BTS), central shunts and pulmonary artery banding (PAB) to regulate pulmonary arterial flow. The following stages consist of partial cavopulmonary connection, for example, bidirectional Glenn procedure and, eventually, total cavopulmonary connection – the Fontan operation. Surgery aims to change the circulation from parallel to circulation in series.

Outcomes for single-ventricle treatments have improved in high-income countries, with declining mortality rates. Kverneland et al., in a meta-review study of Fontan operations in 2017, reported mortality rates decreased from as high as 20.1% in the early decades to as low as 0.5% in recent years. In these, 15-year survival rates improved from 52–82% in the early years, to 95% currently.

There is a paucity of data regarding outcomes of single-ventricle interventions for Africa, and especially sub-Saharan Africa. There is no documentation for the central region of South Africa in which geographical area the Universitas Academic Hospital (UAH) is located. However, in the middle- to low-income countries such as South Africa, outcomes tend to lag behind those of high-income countries, although improvements have been observed. A recent sub-Saharan African study by Manuel et al. reported a 29% mortality rate in the early stages and a 17% late mortality rate.

The objective of this study was to analyse data on the management and outcomes of children who presented with single-ventricle physiology in central South Africa over the last two decades.

Methods

This was a retrospective, observational analysis of all patients who presented with single-ventricle physiology between...
November 1997 and June 2021 at the Departments of Paediatric Cardiology and Cardio-Thoracic Surgery at UAH. UAH is the only tertiary referral hospital in central South Africa and renders services to patients from the Free State, Northern Cape and Lesotho (estimated population 6.5 million).

The main inclusion criterion was patients diagnosed with lesions considered as single-ventricle physiology presenting for the first time at the central hospital. Hypoplastic left heart syndrome and biventricular physiology treated with single-ventricle palliation were excluded from the study. One hundred and fifty-four patients met the inclusion criteria.

Data were retrieved from a paediatric cardiology database, patient folders and the hospital information system. Data recorded included demographic [age (years), gender, ethnicity, geographical location], anthropometric [height (cm), weight (kg), and body mass index (kg/m²)] and clinical data [ventricle dominance, palliative intervention, palliation stage, other associated lesions, and operative mortality].

Peri-operative mortality was defined as deaths occurring during the first 30 days postoperatively, whether in a hospital or discharged, regardless of the cause.

Late mortality was defined as all deaths after the first 30-day postoperative period, whether at home or during subsequent hospitalisation.

Stages of palliation: stage I palliation entailed one of the following procedures: surgical systemic–pulmonary shunt (BTS, central or Sano shunt), PAB or percutaneous implantation of a PDA stent. Stage II involved the Glenn procedure, while stage III consisted of the Fontan procedure.

Ethical approval was obtained from the Health Sciences Research Ethics Committee (HSREC) of the University of the Free State (UFS-HSD2020/1823/2505) and the Free State Department of Health.

Statistical analysis

Raw data were captured on Excel spreadsheets. Continuous variables, when asymmetrically distributed, are expressed as median and interquartile ranges (IQR) 25 and 75, otherwise as mean ± standard deviation. A p-value of < 0.05 was considered statistically significant. A t-test was used to compare normally distributed data. Non-parametric data were compared using a Mann–Whitney U-test. Where required, the chi-squared or Fisher’s exact test was utilised for comparisons. Analysis was done using standard statistical analysis software.

Results

Over the study period, 154 infants with single-ventricle physiology were included. There was a male preponderance, with almost two-thirds of the children being male (n = 98, 63.6%). Tricuspid atresia (56%) was the most common lesion, followed by pulmonary valve atresia with an intact ventricular septum (29%). Other lesions included double-inlet left ventricle (5%), double-inlet right ventricle (3%), unbalanced atroventricular septal defect (5%) and double-outlet right ventricle (1%). Most patients (88%) had lesions with left ventricle dominance.

As expected, most patients were referred from the Free State region (54%). Interestingly, a considerable number of patients came from outside the provincial borders, such as Northern Cape (29%) and Lesotho (13%).

The Free State province is divided into five districts. It is the third largest province (129.8 km²) in South Africa with a population of 2.8 million people, making it the province with the second lowest population density. The Northern Cape is the largest (372.9 km²) province with a population of 1.3 million people, making it the province with the lowest population density. Although Lesotho is a small country (30.3 km²), it has a population of 2.18 million and most of the terrain is mountainous.

Fig. 1 illustrates the percentage of patients referred from each district and the population per district (P/D) for children aged 0–4 years as per the 2016 census (green). Most infants came from the Manguang district (40%), almost double the number of patients compared to the Thabo Mafutsanyane districts (18%), although they have similar population numbers.

Patients were seen for the first time at just over one month of age (median: 34.5 days; IQR: 2.2–156.1). In the Free State, patients from the Fezile Dabi district (median: 3 days; IQR: 1.3–134.1) and Manguang district (median: 4.1 days; IQR: 1.0–83.1) presented earliest (within a few days), whereas patients from the Thabo Mafutsanyane district (median: 30.4 days; IQR: 2.0–221.1) and the Lejweleputswa district (median: 38.5 days; IQR: 2.5–148.5) presented only after a median of a month. The Xhariep district had only two patients presenting at age four days and seven months. The Manguang and Fezile Dabi districts are the two smallest geographical districts with high population densities, whereas the Gariep district has the largest surface area but low population density.

By contrast, patients from the Northern Cape presented after almost two months (median: 56.8 days; IQR: 3.3–155.4) and Lesotho even later at almost six months (median: 174.8 days; IQR: 3.3–517.7) of age.

Forty patients received no intervention. The reasons were poor clinical condition, significantly associated lesions, lethal syndromes and other lethal conditions. Forty-five per cent of these patients (18/40) died, and almost half (42%) died within seven days, emphasising the severity of co-morbidities. Eighteen of these patients were lost to follow up, and four were still alive.
Six patients died during stage II intervention, two within 30 days (peri-operative mortality rate of 3%). Twelve stage II intervention patients were lost to follow up, and 16 patients are still alive and being followed up with the aim of Fontan operation (Table 2).

At the close of the study, 30/114 (26%) patients completed stage III single-ventricle palliation to Fontan. The median age at Fontan was 5.9 years (IQR: 5.2–6.9). Stage III had two deaths, of which neither was within 30 days. Six stage III patients were lost to follow up and 22 patients are still alive (Table 2).

At the cessation of the study, 29 of the total group of 114 patients had died, 35 were lost to follow up, while 50 are in follow up and at various stages of management. The treatment outcomes of the 114 patients are summarised in Fig. 2.

### Discussion

This study reports the outcomes of single-ventricle patients spanning more than two decades in a sub-Saharan country and is the first report on outcomes in the Free State region. The key findings of this study were that patients in our region presented late and that single-ventricle physiology in central South Africa is a severe cardiac condition. The highest mortality rate occurred during the first palliative procedures. It is of concern that a substantial number of patients (almost a third) were lost to follow up.

In more than half of the cases, tricuspid atresia was the most common lesion diagnosed. A similar trend was observed in an Angolan study. However, in a Cape Town report, only a third of patients presented with tricuspid atresia and two-thirds had dominant left ventricles. In our study, however, most patients had a dominant left ventricle. In our study, however, most patients had a dominant left ventricle.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Stage 1</th>
<th>Stage 2</th>
<th>Stage 3</th>
</tr>
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<tbody>
<tr>
<td>PDA stents (n = 24)</td>
<td>24</td>
<td>18</td>
<td>6</td>
</tr>
<tr>
<td>BTS (n = 34)</td>
<td>34</td>
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<td>9</td>
</tr>
<tr>
<td>Central shunts (n = 18)</td>
<td>18</td>
<td>14</td>
<td>4</td>
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<td>PAB (n = 9)</td>
<td>9</td>
<td>7</td>
<td>2</td>
</tr>
<tr>
<td>Sano (n = 2)</td>
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<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Glen procedure (n = 63)</td>
<td>63</td>
<td>53</td>
<td>10</td>
</tr>
<tr>
<td>Fontan procedure (n = 30)</td>
<td>30</td>
<td>24</td>
<td>6</td>
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<th>Diagnosis</th>
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<th>PA IVS</th>
<th>DILV</th>
<th>u-AVSD</th>
<th>DIRV</th>
<th>DORV</th>
<th>Other</th>
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<tr>
<td>Age (median)</td>
<td>4.6 d</td>
<td>24.3 d</td>
<td>201.8 d</td>
<td>110.5 d</td>
<td>1.5 y</td>
<td>1.3 y</td>
<td>5.9 y</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>3.0</td>
<td>3.0</td>
<td>6.6</td>
<td>5</td>
<td>4.85</td>
<td>9.3</td>
<td>17.3</td>
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<tr>
<td>BSA (m²)</td>
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<td>0.20</td>
<td>0.33</td>
<td>0.27</td>
<td>0.27</td>
<td>0.4</td>
<td>0.7</td>
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</table>

Table 1. Clinical data of patients with single-ventricle physiology

Table 2. Intervention outcomes

<table>
<thead>
<tr>
<th>Variables</th>
<th>PDA stents (n = 24)</th>
<th>BTS (n = 34)</th>
<th>Central shunts (n = 18)</th>
<th>PAB (n = 9)</th>
<th>Sano (n = 2)</th>
<th>Glen procedure (n = 63)</th>
<th>Fontan procedure (n = 30)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peri-operative (%)</td>
<td>13</td>
<td>12</td>
<td>17</td>
<td>11</td>
<td>0</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Death &gt; 30 days</td>
<td>3</td>
<td>4</td>
<td>3</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Total death</td>
<td>7</td>
<td>10</td>
<td>3</td>
<td>1</td>
<td>1</td>
<td>6</td>
<td>2</td>
</tr>
<tr>
<td>Lost to follow up</td>
<td>1</td>
<td>10</td>
<td>2</td>
<td>3</td>
<td>1</td>
<td>12</td>
<td>6</td>
</tr>
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</table>

(88%) presented with lesions exhibiting dominant left ventricles. It should be noted that the Meyer study analysed all lesions undergoing bidirectional Glenn procedures.

The data showed that patients presented late, except in two Free State districts, namely Mangaung and Fezile Dabi, where they presented within days. By contrast, outlying areas took weeks to months to present at our clinic for the first time.

The Mangaung district’s early referral can be explained by the fact that it is the smallest geographical district, has the largest population density, is closest to the central referral hospital and has three well-staffed and large functional regional hospitals. Access to healthcare facilities is challenging in rural districts because of smaller regional hospitals, larger patient-to-doctor ratios and extensive distances to travel. This may partially explain why patients were referred much later. These findings emphasise the need for early detection and educational programmes in rural areas.

We speculate that long distances, rugged terrain, limited primary-care facilities and inadequate referral systems contributed to the late presentation of these infants. Late referral contributed to poor condition at presentation and explained why several patients could not be offered palliation.

Stage I palliation was offered to a large percentage of our patients, with more than three-quarters of eligible patients receiving initial interventions. PDA stenting was the palliative intervention performed earliest (within a few days), followed by BTS within a few weeks. Other palliative interventions were performed much later.

Stage I interventions had the highest mortality rate of the three stages. This is in line with developed countries where up to 22% of patients die during the early stages. These findings illustrate that ductal stenting may be a good option in resource-limited settings such as ours. It can be performed early with results comparable to surgical systemic pulmonary artery shunts.

Forty-three per cent of patients receiving stage I palliative interventions proceeded to bidirectional Glenn operations. Many of these patients (41%) had no prior intervention(s). This is similar to findings in the Cape Town study, where a third of patients had no prior intervention before bidirectional Glenn procedures.

In our study, bidirectional Glenn procedures were performed at a relatively young age, with a median age of 1.3 years. This is similar to an Angolan study where the median age was 1.1 years. However, in another South African and a large Egyptian study, it was found that the median age was much older, at 2.5 and 2.3 years, respectively, for bidirectional Glenn procedures.

The operative mortality rate for Glenn procedures was 3%, similar to the Cape Town study, and acceptable compared to the operative mortality rate of 17% in the Angolan study. In our study, almost half of the patients receiving a bidirectional Glenn operation proceeded to a Fontan procedure, which compared favourably with the Cape Town results.

Fontan procedures were performed at a median age of 5.9 years. This is in line with international data that show a decline in the age at which Fontan procedures are performed. A five-decade review study by Kverneland et al. showed in 2017 that Fontan procedures were performed as young as 2.0 to 5.6 years (median) in recent years in high-income countries. In the Angolan study, the median age for Fontan procedures was 3.8 years versus a median age of 8.5 years in the Cape Town study. In our study, no operative mortalities (within 30 days) were observed after the Fontan procedure, which compares favourably with the Angolan study, which reported an operative mortality rate of 20%.

Patients lost to follow up are a concern in our setting as almost a third of patients (35/114) in this study were lost to follow up. In a study by Smit et al., the reasons for the loss to follow up were attributed to the long distances combined with unreliable transport, challenging communication, and a lack of understanding by parents. Analogous trends were observed in another South African study, performed at the Red Cross War Memorial Children’s Hospital for patients receiving bidirectional Glenn shunts, where 30.5% of patients were also lost to follow up. Other African countries face even more challenges and, in the Angolan study by Manual et al., almost two-thirds of their patients were lost to follow up.

Patients with severe cardiac lesions require lifelong follow up, but even in a Canadian study, 21% of patients with severe cardiac lesions were lost to follow up after the age of 18 years. We speculate that most of our patients lost to follow up could be attributed to the large migratory population, cultural barriers, or patient death.

Limitations

The main limitation of this study is its retrospective nature with its inherent challenges. Mortality rates should be interpreted with caution, bearing in mind that many patients were lost to follow up, treatments may have changed over the two-decade period of the study, and only patients with single-ventricle physiology were included in this study. Because of its design, it is important to note that this study does not reflect all Glenn and Fontan procedures performed at our institution. A considerable number of patients still have to proceed to the next stage.

Conclusion

Treatment of single-ventricle physiology at our institution, as in other sub-Saharan countries, faces various challenges. These include large distances from the cardiac centre, late presentation and many patients lost to follow up. Outcomes of interventions compare favourably with other sub-Saharan countries. The highest mortality rate occurred during stage I, and it seems that patients who progress to Glenn and Fontan procedures have a lower mortality rate. This study highlights the need to detect patients with single-ventricle physiology early. A new strategy is also needed for the follow up of patients.

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References


