Outcome of the Glenn procedure as definitive palliation in single ventricle patients

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A B S T R A C T

Objective: In selected single ventricle patients, a Glenn procedure (SV-Glenn) may be considered as definitive palliation. Either the patient is unsuited to progress to a Fontan circulation or a SV-Glenn circulation is preferred. This study aimed at describing the clinical course, and long-term mortality/morbidity of SV-Glenn patients.

Methods: All SV-Glenn patients followed at the University Hospitals Leuven before May 2018 were included. Patients who underwent, or were awaiting, TCPC completion and those who underwent a Glenn in the setting of a biventricular circulation one-and-a-half repair (OAHR), were excluded.

Results: Of 65 Glenn-only patients identified, 21 (32%) had OAHR, whereas 44 (68%) were SV-Glenn patients. Of SV-Glenn patients, 19 died within 6 months after the Glenn procedure. Over a median follow-up time of 11 (IQR 3–18) years after the Glenn procedure, 5 (20%) patients died. At latest follow-up 10 (40%) had heart failure, 5 (20%) had atrial and 16 (60%) ventricular arrhythmias, 2 (8%) a thromboembolic event, 7 (28%) required pacemaker implantation, and 2 (8%) had infective endocarditis but none developed cirrhosis or protein-losing enteropathy. Mean saturation at latest follow-up was 87 ± 7%.

Conclusion: SV-Glenn patients represent a unique and heterogeneous patient population. Outcome was reasonable, although comorbidities, such as heart failure and arrhythmias were not uncommon. In SV-Glenn patients, ‘classic’ complications related to Fontan physiology, such as cirrhosis and protein-losing enteropathy, were absent.

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1. Introduction

In daily clinical practice, adult congenital heart disease (ACHD) healthcare providers regularly encounter well-functioning patients who have a Glenn as their definitive cardiac palliation, either in the setting of a single ventricle circulation (SV-Glenn) or a biventricular circulation (one-and-half-repair - OAHR) [1,2]. Nevertheless, the positive impression towards SV-Glenn circulation could be biased since ACHD healthcare providers only have an incomplete view on the preceding clinical course or mortality rate during early childhood.

The Glenn, or cavopulmonary shunt, is a palliative surgery where an end-to-side anastomosis is created between the superior caval vein and the pulmonary arteries1 2. This procedure is mostly used to unload the systemic ventricle and simultaneously improve oxygenation of the systemic blood flow in congenital heart disease (CHD) patients with a functional or anatomical single ventricle. Most often, but not necessarily, the Glenn is an intermediary step towards completion of a total cavopulmonary connection (TCPC) or Fontan circulation [3,4]. However, the presence or occurrence of contra-indications renders some patients unsuitable for Fontan completion. In other patients, a SV-Glenn circulation may be preferred over a complex biventricular repair or a Fontan circulation since it may diminish some of the medium to long-term disadvantages associated with biventricular repair (e.g. need for

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reinterventions, risk of infective endocarditis) or Fontan circulation (e.g. chronic liver congestion with cirrhosis, protein-losing enteropathy) [5–7].

In this study, we aimed to define the characteristics of the SV-Glenn population, to describe their clinical course prior to their definitive palliation, and to describe long-term mortality/morbidity.

2. Methods

2.1. Patient selection

All patients from the database of Pediatric and Adult Congenital Heart Disease of the University Hospitals Leuven, who underwent Glenn palliation before May 2018, were included. Patients with missing files, patients who underwent Fontan completion, patients awaiting Fontan completion, and those who had a Glenn in the setting of a biventricular circulation (ODHR) were excluded from the study. Patients’ records were reviewed after pseudonymizing patient data conform the Global Data Protection Regulation (GDPR). The institutional ethics committee approved the study protocol and the study was conducted in compliance with the principles of the Declaration of Helsinki.

2.2. Data collection

Original anatomy, demographic data, medical and surgical history, clinical data, echocardiographic recordings, invasive hemodynamic data, and date of latest follow-up were reviewed. Around the time of the Glenn procedure, records were reviewed in detail for perioperative complications (bleeding, thrombotic complications), the need for reintervention or take down of the shunt, and the occurrence of heart failure. Early (within 6 months of the Glenn procedure) and late (>6 months after the Glenn procedure) mortality were recorded. At latest follow-up, the presence of heart failure, New York Heart Association class (NYHA), the occurrence of atrial and ventricular arrhythmias, thromboembolic events, infective endocarditis, need for pacemaker implantation, presence of cirrhosis and presence of protein-losing enteropathy were recorded. Heart failure was defined as signs and/or symptoms of heart failure requiring medical therapy [8].

2.3. Statistical analysis

Normal distribution for continuous variables was investigated and data reported as mean with standard deviation (±SD) or median with interquartile range (IQR) where appropriate. Descriptive data for discrete variables were reported as proportions with numbers and percentages (%). Kaplan-Meier survival curves of the SV-Glenn group was plotted to visualize outcome rates starting at birth. All analyses were performed using Statistical Package for the Social Sciences version 25 (SPSS, IBM headquarters, Armonk, New York, US).

3. Results

3.1. Patient characteristics

Sixty-five patients who underwent a Glenn procedure without creation of a TCPC, or who were not awaiting TCPC completion, were identified. Of those patients, 21 had a Glenn in the setting of a biventricular circulation (2 patients died within 6 months of the Glenn procedure, 1 underwent Glennakedown). Of 44 patients who had a Glenn in the setting of a single ventricle circulation, 19 died within 6 months of the Glenn procedure (Fig. 1).

3.2. Interventions prior to and early (<6 months) mortality after the Glenn

Of the SV-Glenn group, 17 patients underwent enlargement of the atrial septal defect (ASD), 10 had a ductal stent, 22 had a central, Sano or Blalock-Taussig–Thomas (BTT) shunt to the PAs (7 in the setting of a Norwood procedure), 11 underwent balloon dilation of the pulmonary valve and 19 patients had a pulmonary artery (PA) banding. Forty-three underwent a bidirectional Glenn and 1 a classic Glenn procedure. For the entire SV-Glenn group, median age at Glenn procedure was 11.9 months (IQR 6.5 months – 3.5 years). Nineteen patients died within 6 months of the Glenn procedure, of which 7 (37%) had hypoplastic left heart syndrome. Cause of death was cardiac in 15 (11 due to cardiogenic shock, 4 due to perioperative bleeding or thrombotic events), unknown in 3 and non-cardiac in 1 patient.

3.3. SV-Glenn survivors (>6 months)

Twenty-five patients had a Glenn in the setting of a single ventricle circulation (SV-Glenn). In this group, median age at Glenn was 6.3 (IQR 1.2–29.7) years. Eight SV-Glenn survivors were aimed for TCPC but had absolute/relative contraindications for TCPC completion, 3 due to small PAs, 2 due to severe ventricular dysfunction, 1 due to severe AV valve regurgitation, 1 due to significant comorbidities and 1 had a sudden death prior to TCPC. For the remaining 17 SV-Glenn survivors, TCPC completion was not considered an advantage for the functional outcome (Table 1).

Cardiac catheterization data was available in 19 before the Glenn procedure and in 17 after the Glenn procedure (median time after Glenn 4 (IQR 1–8) years; median time between cardiac catheterizations 5 (IQR 1–7) years). Before the Glenn, median mean PA pressure was 16 (IQR 11–21) mmHg, wedge pressure 9 (IQR 6–12) mmHg, and aortic saturation 86 (IQR 80–89) %. After the Glenn, median mean PA pressure was 19 (IQR 17–21) mmHg, wedge pressure 16 (IQR 13–18) mmHg, and aortic saturation 85 (IQR 80–89) %. After the Glenn, 15 (60%) had normal ventricular function, 6 (24%) mild ventricular dysfunction and 3 (12%) severe ventricular dysfunction. Atrioventricular valve regurgitation was absent in 5 (20%), mild in 9 (36%) and moderate to severe in 10 (40%).

During a median follow-up time of 11 (IQR 3–18) years, there were 5 late deaths in the SV-Glenn group (2 due to heart failure, 1 sudden cardiac death, 1 due to hemoptysis and 1 unknown). Fig. 2 plots the survival curve for the SV-Glenn survivors, with the dots indicating the timing of each Glenn procedure. Three of five late deaths occurred in patients unsuited for TCPC completion (median age of Glenn 0.6 (IQR 0.4–1.3) years, median follow-up after Glenn 3 (IQR 2–10) years, 38% mortality over a median follow-up of 4.5 years), whereas in the remainder of patients the Glenn served to improve oxygen saturation, unload the systemic ventricle (or a combination of both), but not necessarily as a next step towards TCPC (median age of Glenn 10 (IQR 6–38) years, median follow-up after Glenn 15 (IQR 8–19) years, 12% mortality over a median follow-up of 27 years) (Table 1).

At latest follow-up, 10 (40%) had heart failure, 18 (72%) were in NYHA class II/III, 5 (20%) had atrial arrhythmias, 4 (16%) ventricular arrhythmias, 2 (8%) a stroke and 7 (28%) underwent pacemaker implantation. One (4%) patient had infective endocarditis. Mean oxygen saturation at latest follow-up was 87 ± 7 % (Table 1).

3.4. SV-Glenn during adulthood

Eight patients (age range 25–59 years) underwent a Glenn procedure in the setting of a single ventricle circulation (SV-Glenn) during adulthood with 1 perioperative death. Indication for a Glenn shunt was progressive desaturation causing functional impairment. Median mean PA pressure was 17 (IQR 4–22) mmHg and wedge pressure 12 (IQR 10–16) mmHg prior to the Glenn shunt. In all patients (except the perioperative death), clinical status and oxygen saturation improved, although all but one patient remained at least in NYHA class II, 1 to 14 years after the Glenn procedure.

4. Discussion

This study describes a heterogeneous group of patients with complex congenital heart disease who underwent a Glenn in the setting of a single ventricle circulation as definitive palliation. We described the underlying anatomy, the clinical course (including interventions prior to Glenn, complications and early and late outcome). SV-Glenn survivors, especially those who deliberately had a SV-Glenn circulation, have reasonable medium and long-term outcome although comorbidities, such as heart failure, arrhythmias, stroke and endocarditis are not uncommon. A Glenn shunt in adulthood is possible in selected patients.
4.1. Identifying the SV-Glenn patient

In cases of complex congenital heart defects, one always needs to decide whether biventricular repair is feasible or not. If biventricular repair is possible, even in ‘borderline’ patients, repair through complex surgeries may be attempted to avoid the hemodynamic disadvantages associated with a single ventricle circulation later in life [9]. If biventricular repair is not possible, a Glenn procedure as an intermediate step towards TCPC completion may be considered (with or without prior interventions). The 25 SV-Glenn survivors in our study who did not undergo TCPC completion did so for a variety of reasons. TCPC completion demands good ventricular function, low left atrial pressure, preserved pulmonary vasculature, an unobstructed flow without pulmonary vein stenosis or abnormal venous return, the absence of severe regurgitation or stenosis of the systemic atroventricular (AV) valve and the absence of aortic stenosis, systemic hypertension or coarctation of the aorta [3,10,11]. In our study, this was the case for 8 of 25 SV-Glenn survivors, whereas for the remaining 17 SV-Glenn survivors, TCPC completion was not considered an advantage for the functional outcome (also taking into consideration risk for long-term co-morbidities and need for (re-) interventions). In these patients, Glenn palliation mainly aimed at improving oxygenation and/or unloading the systemic ventricle. It is clear that those ‘deliberate’ SV-Glenn patients remain a small fraction of single ventricle patients followed at our institution. Since there are ≈220 TCPC patients in active follow-up at our center, we have an estimated completion rate from Glenn to Fontan of around 80%, which is similar to previously published studies [12].

4.2. Early mortality

In the SV-Glenn group, there was significant perioperative mortality. If we also consider those who successfully underwent TCPC completion at our institution (≈220), estimated overall mortality after the Glenn procedure is in line with previously published reports (estimated post-Glenn mortality ≈7%) [13,14]. Not unsurprisingly, a large proportion of early mortality can be attributed to a group of HLHS patients.

4.3. SV-Glenn survivors

The literature usually describes outcome for Glenn patients including those who underwent TCPC completion and reports survival rates around 90% [13]. Our study specifically aimed at evaluating outcome
of the SV-Glenn survivors. Among SV-Glenn survivors, we can distinguish a group of patients who were unsuited to progress to a Fontan circulation due to comorbidities and a group of patients in whom the Glenn mainly aimed at improving oxygenation and/or unloading the systemic ventricle with the latter having reasonable long-term outcome. The outcome of the former group, not unsurprisingly, is limited with only 1 patient who has reached adulthood. It’s the latter group of patients that also explains the ‘intuition’ of ACHD healthcare providers.

Table 1
Original anatomy, comorbidities and mortality of the 25 SV-Glen survivors.

<table>
<thead>
<tr>
<th>Patient ID</th>
<th>Original anatomy</th>
<th>Age at Glenn (years)</th>
<th>FU post Glenn (years)</th>
<th>Reason for SV-Glenn</th>
<th>Saturation</th>
<th>NYHA Heart failure</th>
<th>Arrhythmia</th>
<th>Pacemaker</th>
<th>TE event</th>
<th>IE</th>
<th>Death</th>
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<tbody>
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<td>DORV TGA PS</td>
<td>47</td>
<td>1</td>
<td>Functional impairment</td>
<td>94%</td>
<td>2</td>
<td>No</td>
<td>~/--</td>
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<td>No</td>
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<tr>
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<td>94%</td>
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<td>3</td>
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<tr>
<td>4</td>
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<td>2</td>
<td>3</td>
<td>Fontan not possible, ventricular dysfunction</td>
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<td>+/-</td>
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<td>94%</td>
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<tr>
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<td>38</td>
<td>13</td>
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<td>2</td>
<td>Yes</td>
<td>+/-</td>
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<td>No</td>
<td>No</td>
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<td>59</td>
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<td>Desaturation</td>
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<td>~/--</td>
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<td>+/-</td>
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<td>+/-</td>
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<td>2</td>
<td>Sudden death before Fontan</td>
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Marked in red: patients unsuited to undergo TCPC completion due to absolute/relative contraindications. Marked in black: patients in whom a SV-Glenn circulation was considered satisfactory/preferable.

that Glenn-only patients are doing rather well and should comfort pediatric cardiologists who often have to make this decision early in the life of their patients. These favorable longer-term outcomes are in line with a previous report, which evaluated sustained palliation with cavopulmonary, or aortapulmonary shunts for adults with single ventricle physiology [15]. Cohorts differ, however, as all but one of our patients underwent a bidirectional Glenn in our study (in contrast to a majority of classic Glenn in the Toronto cohort), but confirm a somewhat forgotten notion that the survival benefit of conversion of a Glenn to a Fontan circulation has long been controversial [16].

Despite reasonable medium- to long-term mortality, there remain significant comorbidities. It is our experience that heart failure symptoms may occur/persist in SV-Glenn patients. Systemic oxygen saturation at latest follow-up was acceptable and somewhat higher than reported in the study by Gatzoulis et al. [15]. Nevertheless, 2 patients had a stroke during follow-up. Arrhythmic arrhythmias, again due to volume load, atrioventricular valve regurgitation and progressive arterial dilatation, often complicated the clinical course of our patients [15]. Although this is not a randomized trial, we still believe that for certain selected patients this “balanced circulation”, capable of achieving a satisfying long-term outcome, may be preferable to a sub-optimal TCPC with low output and venous congestion (and subsequent complications such as cirrhosis and protein-losing enteropathy).

4.4. Glenn in adulthood

Our experience with functional outcome, survival and complication rate on short and long-term of patients who underwent a Glenn during adulthood was also rather favorable (8 patients, 1 perioperative death, 1 death after 19 years of follow-up at the age of 54). Consistent with other studies, our clinical experience warrants that the indication should be made carefully later in life when patients have less compliant and impaired pulmonary and cardiovascular systems [17]. Our data confirms that the Glenn is a valid treatment strategy in the course of the patient with complex congenital heart disease. On the other hand, we have no information on sensitization and the presence of a Glenn most likely increases risk if a transplant would be needed [18,19,20].

5. Limitations

Our study is limited by its retrospective study design, which is prone to bias and administration errors. Patients included in the study represent a heterogeneous cohort of patients with rare complex heart defects, who did not proceed to TCPC completion or complete biventricular repair. Despite being a sizeable cohort, the scarcity of patients makes subgroup analysis difficult. Combining databases for a multi-center study might be a goal in the future. Hence, results need to be interpreted cautiously, keeping in mind selection bias due to selecting Glenn-only patients as also outlined in the discussion above.

6. Conclusion

SV-Glenn patients represent a unique and heterogeneous patient population. Outcome was reasonable, although comorbidities, such as heart failure and arrhythmias were not uncommon. In SV-Glenn patients, ‘classic’ complications related to Fontan physiology, such as cirrhosis and protein-losing enteropathy, were absent.

Financial disclosures

None.

Declaration of competing interest

The authors report no relationship that could be construed as a conflict of interest.

References


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Fig. 2. Survival curve plotting the mortality rate in SV-Glenn survivors (≥6 months after Glenn procedure). Mortality over time is presented by the full line. Dots on the lower half of the graph indicate time when the Glenn was initially placed.


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