CASE REPORT

Improvements in exercise capacity following cardiac transplantation in a patient born with double inlet left ventricle

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SUMMARY
A 32-year-old man born with double inlet left ventricle (DILV) and other significant cardiac abnormalities underwent surgical palliation at 1 day, 2 years and 20 years, before receiving a donor heart at 29 years. To our knowledge, there are no case reports or cohort studies of the effect of exercise training on exercise capacity and peak oxygen uptake (VO2peak) following heart transplantation (HTx) for individuals born with DILV. The patient accessed our clinical exercise physiology service for assessment, advice and support for exercise training over a 7-year period spanning pre-HTx and post-HTx. An individualised exercise plan, together with careful assessment and monitoring, and the patient’s own motivation have contributed to him achieving an outstanding post-HTx doubling of VO2peak and exercise capacity.

BACKGROUND
Patients with congenital heart disease (CHD) comprise approximately 2% of all heart transplantation (HTx) recipients and 11% of HTx recipients aged 18–39 years, the age group of the case reported here.1 Double inlet left ventricle (DILV) describes a congenital syndrome of severe complex heart malformations that carries a high risk of mortality and often requires surgical palliation for symptom-atic relief and survival.2 Patients with DILV with significant haemodynamic compromise often progress to HTx.3 4 Peak oxygen uptake (VO2peak) and exercise capacity are strong predictors of survival in HTx recipients in general5 6 and provide a rationale for encouraging exercise training.7 8 Kaplan-Meier survival curves illustrate lower mortality outcomes for paediatric HTx recipients, compared with patients who receive their hearts as adults,9 but there has been a recent narrowing of this difference.10 Patients with CHD who undergo HTx have some of the best survival rates of all HTx patients.11

To our knowledge, there are no published data on the effects of exercise training on VO2peak and exercise capacity for patients with DILV before and after HTx. HTx in the absence of exercise rehabilitation only partially restores VO2peak, physical function and quality of life in patients with severe acquired adult heart failure.12 13 Although some improvement in VO2peak soon after HTx has been widely reported, VO2peak is typically lower in post-HTx patients who do not exercise, compared with those who do.14 15 Studies in paediatric16 and adult HTx17 cohorts have reported post-HTx gains in VO2peak to be modest in the absence of exercise, and appear to reverse somewhat in long-term follow-up. For these reasons, long-term exercise participation should be part of routine post-HTx management to try to improve and then preserve VO2peak.1 There are some data showing that younger HTx recipients achieve greater improvements in VO2peak with exercise training, compared with older recipients.18

Possible mechanisms limiting full restoration of physical function following HTx comprise central factors including chronotropic incompetence,9 diastolic dysfunction,10 coronary artery vasculopathies9 19 and peripheral factors including heart failure-related myopathies,10 microvasculature deficits9 18 and metabolic impairments that mimic the effects of severe detraining.18 Immunosuppressive drugs are also significant co-contributors to exercise limitations after HTx.9 10 There is evidence that endurance and resistance training programmes may reverse at least some of these deficits and should be part of overall management.7 12 13 16 20

The case described here is of an individual born with DILV and other cardiac abnormalities where a major focus was on trying to improve and then sustain exercise capacity following HTx. Prior to HTx, the patient had never been able to engage in sufficient health-promoting exercise. His exercise capacity was measured at regular intervals for several years both before and after HTx, with a total follow-up period of 7 years.

CASE PRESENTATION
We present a case of a 32-year-old man born with DILV, ventricular septal defect connecting LV to a rudimentary right ventricle, pulmonary atresia, global systolic dysfunction, aortic regurgitation, dextrocardia and situs inversus. At 1 day, he underwent a Blalock-Taussig shunt for cyanotic relief. At 2 years, he underwent an atrio pulmonary Fontan procedure where blood flow from his bulbous left-sided right atrium (RA) was shunted to the right pulmonary artery (PA) to improve pulmonary circulation (figure 1A). At 20 years, he underwent a Fontan revision which comprised a 24 mm Goretlex conduit connecting inferior vena cava to the right PA, a 17 mm bovine pericardium conduit from superior vena cava to the left PA and excision of...
Unexpected outcome (positive or negative) including adverse drug reactions

Figure 1  (A) Surgeon’s sketch and notes of the heart and great vessels prior to the Fontan revision surgery in 2005 when the patient was 20 years. The conduit between the right atrium (RA) and right pulmonary artery (RPA) was created during the atrio pulmonary Fontan procedure at 2 years in 1987. Numbers represent systolic/diastolic pressures (mm Hg). Numbers with bars represent mean pressures (mm Hg). (B) Surgeon’s sketch and notes of the heart and great vessels following the Fontan revision surgery at 20 years in 2005, consisting of a 24 mm Goretx conduit connecting inferior vena cava (IVC) to RA, a 17 mm bovine pericardium conduit from superior vena cava (SVC) to left pulmonary artery (LPA) and excision of most of RA except for the remnants of sinoatrial node. The hypoplastic tricuspid valve was closed which completed a series connection of pulmonary and systemic circulations. Excision of RA required the coronary sinus to drain into left atrium (LA). LV, left ventricle; RV, right ventricle; VSD, ventricular septal defect.

Figure 2  Heart rates (HRs) at rest and during incremental cycle ergometer protocols for 2009 and 2010 (pre-transplant) and 2015 and 2016 (post-transplant). His heart was paced a constant 80 beats per minute throughout 2009 and 2010 and did not respond to exercise. The HR data at rest and peak exercise were collected for the 2011 test (see table 1), but the incremental HRs were not archived.

most of RA except for the remnants of sinoatrial node (SAN) (figure 1B). The hypoplastic tricuspid valve was closed which completed a series connection of pulmonary and systemic circulations. Excision of RA required the coronary sinus to drain into left atrium (LA). A dual chamber pacemaker was fitted. The patient first accessed our exercise physiology service in 2009 (24 years) and presented with symptoms of exercise intolerance and severe shortness of breath on exertion (New York Heart Association class III; LV ejection fraction at this time was 15%) and occasional exercise-related presyncope. An incremental cycle ergometer test was performed and his peak power output and directly measured VO₂peak were 100 watts (W) and 16.9 mL/kg/min, respectively. We also estimated his VO₂peak to be 15.6 mL/kg/min using a validated predictive algorithm.21 His resting O₂ saturation was slightly low at 93% due to coronary sinus insertion in the LA. He desaturated a little further to 89% at peak exercise. There was no clinical evidence of impaired pulmonary diffusing capacity, nor evidence of ventilatory limitations based on spirometry at rest and during exercise. His pre-exercise, exercise and recovery blood pressures were moderately low, for which he was prescribed an inotrope, while his pacemaker did not respond to exercise, with heart rate (HR) fixed at 80 beats per minute throughout pre-exercise, exercise and recovery (figure 2). This, together with severe heart failure, indicates that he relied primarily on peripheral ‘non-cardiac’ factors (oxygen extraction), rather than inotropic and chronotropic activity as the main contributors to VO₂peak, consistent with a recent review on mechanisms of impaired pulmonary VO₂ in patients with heart failure and reduced ejection fraction.22

OUTCOME AND FOLLOW-UP

The main outcome measures for the series of exercise assessments before and after HTx (2009–2016) are summarised in table 1 and figure 2. At first, we recommended swimming (horizontal, weightless exercise) to promote venous return and pulmonary circulation, but he did not enjoy swimming due to very rapid fatigue. He preferred dancing and this was his main activity and follow-up.

Table 1  Main outcome measures for a series of exercise assessments for several years before and again after HTx

<table>
<thead>
<tr>
<th>Measure</th>
<th>Pretransplant</th>
<th>Transplant</th>
<th>Post-transplant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body mass kg</td>
<td>61</td>
<td>60</td>
<td>60</td>
</tr>
<tr>
<td>BP mm Hg at rest</td>
<td>90/60</td>
<td>124/74</td>
<td>126/74</td>
</tr>
<tr>
<td>HR at rest</td>
<td>80 P</td>
<td>80 P</td>
<td>80 P</td>
</tr>
<tr>
<td>VO₂peak mL/kg/min</td>
<td>15.6</td>
<td>14.1</td>
<td>14.1</td>
</tr>
<tr>
<td>Peak BP mm Hg</td>
<td>130/72</td>
<td>140/80</td>
<td>120/72</td>
</tr>
<tr>
<td>Peak power watts (W)</td>
<td>100 W</td>
<td>90 W</td>
<td>90 W</td>
</tr>
<tr>
<td>Peak RPE 6–20 point scale</td>
<td>18</td>
<td>17</td>
<td>16</td>
</tr>
<tr>
<td>RPE at 90 W</td>
<td>16</td>
<td>17</td>
<td>16</td>
</tr>
<tr>
<td>Peak HR</td>
<td>80 P</td>
<td>80 P</td>
<td>97 P</td>
</tr>
<tr>
<td>O₂sat%</td>
<td>93%</td>
<td>92%</td>
<td>93%</td>
</tr>
</tbody>
</table>

VO₂peak was predicted using a validated algorithm, based on the relationship between power and oxygen consumption for cycling exercise.21 BP, blood pressure; HR, heart rate; P, paced; RPE, ratings of perceived exertion26; SR, sinus rhythm.

active recreational pursuit, but he fatigued rapidly and needed to rest for long periods between short bursts of dancing.

The cycle ergometer assessment was repeated in 2010 and 2011 (table 1) before he deteriorated to the extent of not being able to attend the exercise physiology service (2012–2014). He underwent HTx at the age of 29 years in 2014. HTx is relatively common in DILV patients with poor haemodynamics. Following HTx and several months of cardiac rehabilitation, we designed a multimodal exercise plan of aerobic exercise on most days of the week (mainly cycling on both a cycle ergometer and a road bike) and 2–3 sessions per week of resistance exercise training using large muscle groups and increasingly complex movement patterns.

Since transplant, he has made remarkable progress with VO2peak estimated21 to be 23.4 mL/kg/min (150 W peak power) in 2015 and 29.7 mL/kg/min (190 W) in 2016 (table 1). Notably, his improvement in VO2peak (15.6 mL/kg/min representing 97% improvement) is much higher in both actual and percentage...
terms than some exercise intervention cohort data following HTX, although one factor contributing to this could be his relative youthful age. On the other hand, his VO2peak 2 years after HTX reached only about 69% of age-related American College of Sports Medicine (ACSM) norms, and this is similar to HTx populations in general. It is possible that his very low VO2peak before HTx and inability to exercise sufficiently for the first 30 years of his life contributed to him not being able to fully restore his VO2peak after HTX to match his age peers. Since HTx, he has gained 4kg in body mass and he reports significant muscle development especially in the lower limbs. He no longer desaturates and is experiencing a gradual improvement in chronotropic competence, as evidenced by lower resting HRs, and lower HRs at the same submaximal work rates in 2016 compared with 2015, while peak HR was higher (figure 2). This is consistent with criteria for functional reinnervation defined by significant increases in HR during exercise of at least 36 beats per minute and rapid falls in HR during recovery. The mechanisms for the improvement in chronotropic competence may be associated with partial, progressive cardiac allograft sympathetic reinnervation and he is now unrestricted in exercise participation.

**DISCUSSION**

To our knowledge, this is the first case report documenting the effects of exercise training on exercise capacity before and after HTx in a patient with DILV. Peak oxygen uptake (VO2peak) and exercise capacity are strong predictors of survival in HTx recipients in general, and this patient was able to double both his peak exercise power and VO2peak at 2 years post-HTX. The improvement in VO2peak was 26% higher than the average improvement reported for 1700 adult heart transplant recipients leading to a recommendation that exercise should be part of routine management post-HTX in DILV patients.

**Learning points**

- The patient was born with disabling congenital heart failure that required palliative surgeries for survival. Since his heart transplantation (HTx) at 29 years, he has been able to very significantly improve his peak oxygen uptake (VO2peak), exercise capacity and quality of life. The evidence suggests that this will confer long-term clinical benefits.
- An individualised exercise plan was designed and administered by an accredited exercise physiologist and enthusiastically embraced by the patient. His exceptional improvements in VO2peak and exercise capacity following HTx are well in excess of mostly modest or absent rises described in the literature.
- Exercise training will continue to be important to limit the impact of immunosuppressive therapy on exercise capacity and quality of life.
- Heart rate at rest and responses to exercise indicate that chronotropic competence has continued to develop over the first 2 years following HTx.

**Contributors** Roles of the authors in this case report. SS: clinical cardiovascular exercise physiologist who provided the exercise physiology services for the patient from 2009 to 2016 inclusive, and was responsible for obtaining the patient’s permission and the patient’s perspective. He also led the preparation of the first, subsequent and final drafts of the manuscript. He is the corresponding author. SF: clinical exercise physiologist who assisted with the exercise physiology services for the patient from 2015 to 2016, and contributed to all drafts of the manuscript. MJFH: clinical cardiovascular exercise physiologist and researcher who made significant contributions to formulating the main directions of the manuscript and reviewing and editing all drafts.

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**REFERENCES**

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