Myocardial perfusion defects and associated systemic ventricular dysfunction in congenitally corrected transposition of the great arteries

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Abstract

Background—Patients with systemic ventricles of right ventricular morphology are at high risk of contractile dysfunction, the cause of which has not been fully elucidated.

Objective—To assess whether ischaemia or infarction contributes to ventricular impairment in unoperated patients with uncomplicated congenitally corrected transposition of the great arteries (TGA) by studying myocardial perfusion and function.

Setting—Paediatric and adult congenital cardiac clinics of a tertiary referral centre.

Patients—Five patients with congenitally corrected TGA but without associated structural cardiac defects (aged 3.5 to 34 years).

Interventions—Maximal exercise stress testing using standard or modified Bruce protocols. Sestamibi (technetium-99m methoxy isobutylisonitrile) scanning after isotope injection at maximal exercise and rest.

Main outcome measures—Maximum exercise capacity; right ventricular myocardial perfusion, regional wall motion, and thickening; right ventricular ejection fraction.

Results—The two youngest patients (3.5 and 11 years) had normal exercise capacity for age, while the others had reduced exercise performance. Sestamibi scanning showed reversible myocardial ischaemia in four patients and fixed defects indicating infarction in five. Irreversible defects were mostly associated with impaired wall motion and thickening. The ejection fraction was normal (65%) in the youngest patient but < 55% in the others (mean (SD) 47 (11)%).

Conclusions—Patients with unoperated congenitally corrected TGA have a high prevalence of myocardial perfusion defects, with consequent abnormalities of regional wall motion and thickening, and impaired ventricular contractility. These data suggest that ischaemia and infarction are important in the pathogenesis of ventricular failure in this condition.

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Keywords: congenitally corrected transposition of the great arteries; ventricular dysfunction; myocardial perfusion; sestamibi scanning

Patients with congenitally corrected transposition of the great arteries (TGA) are at high risk of developing systemic ventricular dysfunction, independent of their commonly associated structural defects. The systemic ventricle is of right ventricular morphology and it is considered that long term exposure to systemic pressure may cause gradual failure of the myocardium. Patients with this condition have hypertrophy of the systemic ventricle persisting beyond the neonatal period, placing an increased demand on the coronary arterial supply, which mostly frequently is from a morphologic right coronary system. Research has shown that patients with a systemic right ventricle following atrial baffle repair for simple transposition of the great arteries (dTGA) have defects of right ventricular myocardial perfusion, which may contribute to right ventricular dysfunction in this group. In these patients, however, the effects of systemic arterial hypoxaemia for the first three to 12 months of life and of cardiopulmonary bypass (CPB) are not known and may contribute to the observed abnormalities on perfusion imaging.

Isolated case reports suggest that perfusion defects may also be present in patients with congenitally corrected TGA. The aim of this investigation was to assess the contribution of myocardial ischaemia or infarction to the aetiology of systemic ventricular dysfunction in a group of unoperated, fully saturated patients with congenitally corrected TGA, using advanced nuclear medicine techniques to evaluate right ventricular myocardial perfusion, wall motion, and wall thickening.

Patients and methods

Five patients (three male and two female aged from 3.5 to 34 years) with congenitally corrected TGA and without associated structural cardiac defects were studied (table 1). They were considered representative of all patients with uncomplicated, unoperated congenitally corrected TGA from the Sydney area attending our institution at the time of the study. One patient had a permanent transvenous pacemaker system (VVIR) implanted three years earlier, but the others had not undergone surgery. Significant Ebstein’s anomaly of the tricuspid valve was not present, but echocardiograms showed mild or moderate tricuspid regurgitation in each patient except the youngest. None had complained of chest pain suggestive of angina pectoris. Informed consent was given by all patients and/or parents. The study protocol
Table 1  Results of exercise testing and functional assessments

<table>
<thead>
<tr>
<th>Case</th>
<th>Age (years)</th>
<th>Max HR</th>
<th>Stage (Bruce)</th>
<th>Total time (mins)</th>
<th>METS Equ.</th>
<th>Rhythm</th>
<th>NYHA</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>3½*</td>
<td>167</td>
<td>3*</td>
<td>18:49</td>
<td>9.4</td>
<td>Sinus</td>
<td>I</td>
</tr>
<tr>
<td>2</td>
<td>11</td>
<td>181</td>
<td>5</td>
<td>12:22</td>
<td>17.2</td>
<td>Sinus</td>
<td>I</td>
</tr>
<tr>
<td>3</td>
<td>18</td>
<td>161</td>
<td>4</td>
<td>10:51</td>
<td>13.2</td>
<td>VVIR</td>
<td>I</td>
</tr>
<tr>
<td>4</td>
<td>33</td>
<td>98</td>
<td>3</td>
<td>9:50</td>
<td>9.9</td>
<td>AF/AVD</td>
<td>II</td>
</tr>
<tr>
<td>5</td>
<td>34</td>
<td>198</td>
<td>4</td>
<td>10:32</td>
<td>13.2</td>
<td>Sinus</td>
<td>II</td>
</tr>
</tbody>
</table>

*The 3½ year old was exercised to a maximum treadmill velocity of 3.4 km/h and a gradient of 21°.

AF, atrial fibrillation; AVD, atrioventricular dissociation; HR, heart rate; NYHA, New York Heart Association.

Table 2  Location and severity of perfusion defects

<table>
<thead>
<tr>
<th>Fixed defects</th>
<th>Reversible defects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Site</td>
<td>Grade</td>
</tr>
<tr>
<td>----------------</td>
<td>-------</td>
</tr>
<tr>
<td>1</td>
<td>Inferior wall</td>
</tr>
<tr>
<td>2</td>
<td>Anterior wall</td>
</tr>
<tr>
<td>3</td>
<td>Inferior wall</td>
</tr>
<tr>
<td>4</td>
<td>Inferior wall</td>
</tr>
<tr>
<td>5</td>
<td>Anterior wall</td>
</tr>
</tbody>
</table>

RVEF, right ventricular ejection fraction.
dissociation, had reduced exercise tolerance, and in NYHA class II at the time of the study. Perfusion scanning showed moderate fixed defects in the anterior wall and basal septum indicating infarction, with a moderate reversible defect in the apical and mid-septum (fig 2). Wall thickening and motion of the septum and anterior wall were reduced, with an RVEF of 52%.

PATIENT 5
A 34 year old woman, was diagnosed at the age of three years, having presented with a murmur. She was mildly symptomatic (NYHA class II) at the time of the study. Perfusion scanning showed moderate fixed defects in the anterior wall and basal septum indicating infarction, with a moderate reversible defect in the apical and mid-septum (fig 2). Wall thickening and motion of the septum and anterior wall were reduced, with an RVEF of 38%.

Discussion
Although some patients with congenitally corrected TGA may lead normal lives without evidence of cardiac decompensation,27 many develop right ventricular failure.3-7 This may result in symptoms of congestive cardiac failure, decreased functional capacity, and early death. Most previous studies have suggested that dysfunction of the right ventricle is gradual in onset and may not be manifest until the third or fourth decade of life. The mechanism of failure is unclear but inability to tolerate long term functioning at systemic pressure may result from the macroscopic and microscopic structure of the right ventricular myocardium.17 18 This problem may be exacerbated by the common finding of insufficiency of the tricuspid valve. The contribution of inadequate right ventricular myocardial perfusion in this setting has not been assessed.

MYOCARDIAL ISCHAEMIA AND CORONARY SUPPLY
We now report significant ischaemia and infarction in patients with unoperated congenitally corrected TGA, with consequent contractile dysfunction. These findings may result from an inadequate coronary arterial supply, the usual coronary arrangement in patients with congenitally corrected TGA being coro-
ary inversion\textsuperscript{17}; therefore, although the morphologic right ventricle is on the left side of the heart, it is supplied by a morphologic right coronary artery system (fig 3A). This system may provide inadequate flow in the presence of considerable myocardial hyperplasia and hypertrophy seen when the right ventricle functions at systemic pressures for long periods.\textsuperscript{17} \textsuperscript{19} \textsuperscript{20} Examination of the right ventricle subjected to systemic pressure shows gross hypertrophy compared with the thin wall of the right ventricle subjected to normal pressure, the discrepancy being especially conspicuous towards the apex (fig 3B). Hypertrophy places substantial extra demand on the right coronary arterial supply, which, as seen in fig 3A is less extensive than from a left coronary system. Progressive ischaemia will probably develop in this condition.

PERFUSION DEFECTS AND VENTRICULAR DYSFUNCTION
The data from this small group of patients suggest that substantial reversible and fixed right ventricular myocardial perfusion defects are common in patients with congenitally corrected TGA. Defects were most frequently found in the anterior and inferior walls and septum. The lateral wall of the ventricle was not involved. Perfusion defects at rest were frequently associated with reduced regional wall thickening and wall motion and reduced right ventricular systolic function. This finding suggests a causal relation between fixed myocardial perfusion defects and ventricular dysfunction. Interestingly, the only patient with normal systemic ventricular function was 3.5 years of age, suggesting possible progression of ischaemia related myocardial dysfunction with increasing age.

SESTAMIBI SCANNING OF THE RIGHT VENTRICLE
Assessment of myocardial perfusion, wall motion, and ejection fraction using the radioisotopes thallium-201 or sestamibi is well established in adults and children.\textsuperscript{21} \textsuperscript{22} While assessment of right ventricular perfusion is less well described, the technique should not be any less applicable to the right than the left ventricle. Recent studies have reported significant right ventricular perfusion defects associated with wall motion abnormalities in patients with dTGA who underwent atrial baffle repair (Mustard or Senning).\textsuperscript{9} \textsuperscript{10} The heart after a Mustard or Senning procedure is analogous to the congenitally corrected TGA heart in terms of long term functioning of the morphological right ventricle as a systemic ventricle. These groups, however, had a variable period of arterial hypoxaemia and a lengthy cardiopulmonary bypass procedure, often without modern techniques of myocardial protection: both factors may have contributed to the observed perfusion defects. Perfusion defects have been reported previously in other groups of patients who had surgery involving CPB.\textsuperscript{23} \textsuperscript{24} Hayes et al compared patients after both arterial switch and CPB surgery not involving the coronary arteries\textsuperscript{10}; each group had a high incidence of perfusion defects, suggesting that CPB may be responsible.

In contrast, our patients have a systemic right ventricle but have not undergone CPB surgery. They therefore serve as a model for anatomical situations in which the systemic ventricle is of right ventricular morphology. We considered that myocardial perfusion data from this group would help to clarify the aetiology of right ventricular dysfunction commonly seen in patients with congenitally corrected TGA and to validate data concerning impaired right ventricular perfusion in patients with dTGA after atrial baffle repair.

STUDY LIMITATIONS
This study examined only a relatively small number of unoperated patients, as congenitally corrected TGA is a rare condition often associated with intracardiac abnormalities requiring open heart surgery.\textsuperscript{1} The five patients with uncomplicated congenitally corrected TGA, who currently live in the Sydney area, were studied at our institute. In addition, data presented here are from single measurements in each patient and therefore only presumptive conclusions can be made regarding the progression of perfusion defects with increasing age. This question may be more clearly addressed by prospective serial studies.

CONCLUSIONS
In summary, we found evidence of impaired myocardial perfusion associated with regional cardiac dysfunction in the systemic ventricle of patients with unoperated, uncomplicated congenitally corrected TGA. These data suggest that the right ventricular coronary arterial supply may be inadequate for long term ventricular function at systemic pressures and that silent progressive irreversible ischaemia of the right ventricular myocardium may make an important contribution to the development of right ventricular dysfunction.


