Assessment of Myocardial Perfusion in Patients After the Arterial Switch Operation

Michael Vogel*, Jeffrey F. Smallhorn, David Gilday, Lee N. Benson, Judith Ash, William G. Williams, and Robert M. Freedom

Division of Cardiology, Nuclear Medicine and Cardiovascular Surgery, Departments of Pediatrics and Surgery, University of Toronto Faculty of Medicine, The Hospital for Sick Children, Toronto, Ontario, Canada

In 21 patients who had undergone the arterial switch operation, the adequacy of myocardial perfusion was evaluated by thallium-201 computed scintigraphy 2.6 ± 2 (0.3–7) yr after surgery. Fourteen patients had undergone the arterial switch procedure after pulmonary artery banding and seven as a primary repair. Isoproterenol stress increased the heart rate by at least 55%. Tomographic imaging was performed at peak stress and 3 hr later in the reperfusion phase. Nine patients had perfusion defects. The perfusion defects were located at the left ventricular apex in four (with extension to the inferolateral wall in one), left ventricular anterolateral wall in two, ventricular septum in one, left ventricular inferior wall in one, and right ventricular free wall in one. Some of these defects could be due to myocardial damage at the time of surgery, but these results also raise concern about long-term adequacy of myocardial perfusion following the arterial switch procedure.

J Nucl Med 1991; 32:237–241

One of the concerns about the long-term results of the arterial switch operation is the adequacy of coronary artery blood flow (*1*). This may be compromised by coronary artery kinking or failure of the coronary artery anastomosis to grow adequately after reimplantation (*2,3*). In patients with normal coronary blood flow at rest, exercise or pharmacologically-induced stress may precipitate changes, revealing inadequacy of perfusion (*4*). To address the problem of adequacy of coronary artery blood flow following the arterial switch procedure, we assessed myocardial perfusion at rest and after isoproterenol infusion by thallium 201 (^{201}Tl) computed tomographic scintigraphy.

Received Jun. 19, 1989; revision accepted Jul. 19, 1990.

For reprints contact: Jeffrey F. Smallhorn, MD, Division of Cardiology, The Hospital for Sick Children, 555 University Ave., Toronto, Canada M5G 1X8.

* Current address: Department of Pediatrics, Deutsches Herzzentrum, Lothstr. 11, D-8000 Munchen, West Germany.

PATIENTS AND METHODS

Patient Selection

Among 46 patients, who had survived an arterial switch operation at our institution, 23 were from or within a 100 km radius of the city. Of the 23, 21 agreed to participate in the study and gave informed consent. The study was approved by the hospital's human subjects committee. The male-to-female ratio was 1.8:1. The diagnosis, coronary artery anatomy, and timing of surgery and study in these patients are listed in Table 1.

We used the classification of coronary artery anatomy proposed by Yacoub and Radley Smith (*5*), with type A representing those where both right and left coronary arteries originate from different sinuses, type B the right and left originate from the same sinus, and type D the (left) circumflex arises from the right coronary artery.

Statistical Analyses

For comparison of data, a two-tailed paired Student's t-test was used. A p value of <0.05 was considered to present a significant difference between the two groups. Data are given as mean ± s.d. and range.

Surgical Procedures

Description of the Arterial Switch Procedure. The arterial switch operation is an anatomical correction of transposition of the great arteries. After both great arteries have been transsected a few millimeters above the aortic sinuses of Valsalva, the coronary ostia are excised with a rim of aortic wall. Most surgeons (*1,5–7*) also mobilize the first few proximal millimeters of each coronary artery to avoid tension or kinking of the main coronary arteries. The coronary artery transfer is completed by anastomosing the rim of aortic wall containing the coronary ostia to the pulmonary arterial wall. The defects in the aortic wall are closed by using autogenous pericardium. Following the transfer of the coronary arteries, the distal pulmonary artery is anastomosed with the proximal stump of aorta and the distal aorta with the proximal stump of the pulmonary artery, which now contains the coronary ostia. Thus, the aorta with its coronary arteries now arises from the left ventricle and the pulmonary artery from the right ventricle. The approach and optimal time for surgery has altered over the last few years, from that of pulmonary artery banding during the neonatal period, followed by repair at a later stage (*8,9*), to that of a primary repair during the first two weeks of life.

In this patient population, pulmonary artery banding had

TABLE 1
Clinical Data in 21 Patients with Arterial Switch

Patient	Diagnosis	Coronary artery type	Age at surgery	Age at study	Pump time	X-Clamp time
1	TGA, VSD	A	1.6 yr	4.5 yr	182	88
2	TGA, VSD	D	1.5 yr	3 yr	190	84
3	TGA, VSD	B	1.7 yr	2.2 yr	194	72
4	TGA, IVS	A	1.2 yr	1.6 yr	231	91
5	TGA, VSD	B	2 yr	6.3 yr	226	98
6	TGA, VSD	A	1.3 yr	1.3 yr	197	82
7	TGA, VSD	A	7.9 yr	4.1 yr	281	120
8	TAUSSIG BING	D	2.2 yr	4.2 yr	267	108
9	TGA, VSD	A	1.1 yr	5.8 yr	244	132
10	TGA, VSD	A	1.6 yr	1.1 yr	212	81
11	TAUSSIG BING	3 Orifices	3.2 yr	7 yr	203	82
12	TAUSSIG BING	D	2.4 yr	2.2 yr	324	150
13	TGA, VSD	B	2.4 yr	2.1 yr	229	54
14	TGA, VSD, LVOTO	A	5.2 yr	4.2 yr	233	102
15	TGA, VSD	A	5 mo	6 mo	209	56
16	TGA, VSD, LVOTO	A	9 mo	4.2 yr	166	96
17	TGA, IVS	A	5 days	4 mo	144	73
18	TGA, IVS	A	10 days	3 mo	103	74
19	TGA, VSD	A	5 mo	6 mo	149	27
20	TGA, IVS	A	5 days	4 mo	87	63
21	TGA, VSD	A	2 mo	5 mo	186	108

TGA = Transposition of the great arteries; VSD = ventricular septal defect; IVS = intact ventricular septum; and LVOTO = left ventricular outflow tract obstruction.

been performed in patients 1–14 prior to corrective surgery, while seven patients had an arterial switch procedure as a primary operation (Patients 15–21). The mean age at arterial switch operation for the total group was 1.7 ± 1.8 yr (8 days–7.9 yr). For the 14 patients who had a two-stage repair, the mean age at surgery was 2.3 ± 4 (0.8–7.9) yr, while it was 3.1 ± 2 mo (10 days–9 mo) in the remaining 7 patients. The mean coronary nonperfusion time during surgery was 87.4 ± 11 (72–108) min and the mean cardiopulmonary bypass time 200 ± 33 (144–267) min in the first 14 patients, whereas it was 71 ± 22 (27–108) min and 149 ± 28 (87–209) min, respectively, in the 7 patients who underwent a one-stage repair. Table 1 lists the data for each individual patient. The same blood cardioplegia was used in all operations. Surgery was performed by three different surgeons in our institution, all of whom followed the same guidelines.

Thallium Perfusion Scintigraphy

The myocardial perfusion study was undertaken at a mean age of 4 ± 3 (4 mo–10.2) yr. The mean time after surgery was 2.6 ± (0.3–7) yr. Due to the young age of the patients, exercise studies could not be performed and, hence, stress was simulated with isoproterenol (*4*). Heart rate and blood pressure were continuously monitored throughout the study with a Dinamap oscillometric blood pressure recording device. One vial of isoproterenol was diluted in 500 cc of 5% dextrose solution and given intravenously through a drip. The rate of infusion was manually regulated and the dose of isoproterenol titrated such that the resting heart rate increased by at least 50% {from a mean of 89 ± 15, to 135 ± 22 ($p < 0.001$) bpm}. The blood pressure prior to isoproterenol infusion was 104 ± 12 (83–122) and 102 ± 10 (80–118) mm Hg at peak heart rate. Infants, who were restless prior to the study, were sedated with chloralhydrate. While lying supine ^{201}Tl was injected during maximal heart rate at a dose of 28 to 79 MBq, according to the patient's weight, yielding a dose of 1.5–4 MBq/kg body weight (*10*).

The isoproterenol infusion was continued to maintain the heart rate close to the previously achieved peak for at least another 6 min. During this time, the tomographic camera was properly positioned. After data gathering had been started, the isoproterenol infusion was slowly reduced. A single-photon emission computed tomography (SPECT) study was performed, because of its advantages in terms of sensitivity and specificity in detecting perfusion defects (*11*). State-of-the-art equipment was used consisting of a General Electric 400 AC Starcam tomographic camera with a general-purpose low-energy collimator and a 64 × 64 byte matrix. The camera was rotated clockwise around the patient in a 180-degree arc in a circular orbit starting at a 45-degree right anterior oblique position. Sixty-four raw data images were acquired at 15 s a frame. Redistribution tomographic pictures were similarly obtained 2.50 hr postinjection and were considered to represent the resting phase. All tomographic images were flood corrected by a 30-million count flood. Images were spatially and temporally filtered using a Hanning filter with a 0.833 frequency cutoff. Reconstruction was done using an attenuation correction with an absorption coefficient of 0.12. Transaxial tomographic reconstruction was done at 1 pixel per slice. Vertical long-axis images were created from the transaxial images and subsequently short and horizontal axis images were obtained from the vertical long-axis data.

For the grading of the thallium scans, a semiquantitative approach was used. Thallium scans were graded as either normal, with homogenous uptake of thallium, partial defects, with a reduction in thallium uptake, or complete, with an absent area of thallium uptake.

Two experienced observers (*12,13*), independently reviewed the scans and graded them without prior knowledge of the second observer's opinion. Normal data on children and young adults are unavailable and unobtainable due to ethical reasons (*14*).

RESULTS

Perfusion Defects and Their Anatomic Location

Normal myocardial perfusion was found in 12 patients (57%). Nine patients had perfusion defects. The anatomic locations of the perfusion defects are listed in Table 2 (the patient number is as in Table 1). Figure 1 depicts an example of a reversible defect encountered in Patient 5 (Table 1). The mean coronary nonperfusion and cardiopulmonary bypass times for patients with or without a perfusion defect were not significantly different. There were significantly less defects in the patients who had the arterial switch operation as a primary procedure in infancy, compared to those patients with a two-stage repair at a later age.

Interobserver Variability

The interobserver data are listed in Table 3. There was no disagreement about the presence or absence of a perfusion defect. In one case, the severity of the defect was assessed differently by the two observers. In two cases, there was disagreement about the reversibility of the perfusion defects.

Surgical Complications in Patients with Perfusion Defects

Three patients with perfusion defects had complications at surgical repair, which might explain their defects. Patient 3 (Table 1) had kinking of the left coronary artery noted after reimplantation of this vessel with subsequent revision of the anastomosis. In Patient 4, the left anterior descending coronary artery was accidently lacerated and subsequently repaired, and in Patient 8 the right coronary artery had been compressed at pulmonary artery banding. In all other patients, the transfer of the coronary arteries was uncomplicated.

TABLE 2
Perfusion Defects in Nine Patients Following the Arterial Switch

Patient	Location of defect
3	LV anterolateral wall
4	LV inferolateral wall and apex
5	Apex
6	RV free wall
7	Apex
8	LV inferior wall
11	Apex
12	LV anterolateral wall
18	Basilar septum

LV = left ventricular and RV = right ventricular.

Correlation of Perfusion Defects with Other Investigations

On examining the electrocardiogram for evidence of ischemia, seven of nine patients with a perfusion defect were found to have a right bundle branch block; one had a pacemaker for complete heart block and one had abnormal ST segments with a biphasic T-wave in the right precordial leads and a 1-mm ST segment depression in the left leads. Cardiac catheterization and angiography had been performed on all patients except numbers 4, 18, 20, and 21. The details of these studies have been reported (*15*). In Patients 3 and 11, aortography demonstrated a narrowed origin of the left coronary artery, while in the remaining patients no obvious abnormalities of the coronary arteries could be detected. Selective coronary arteriography, however, was not performed.

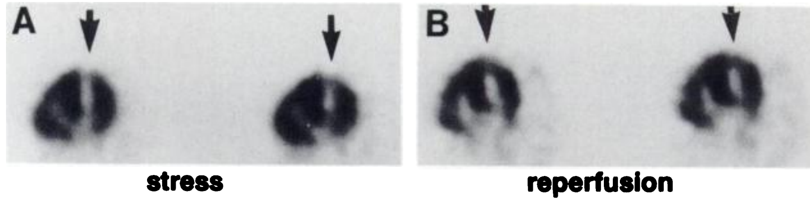
Left ventricular wall motion analysis by cross-sectional echocardiography using a floating model reference system was also performed (*16*). Standard echocardiographic views in the parasternal short-axis and apical position were employed. Regional wall motion was evaluated by digitizing the endocardium with an offline computer system at endsystole and enddiastole. After dividing the left ventricle into eight segments, regional area change was calculated and the results in the patient group compared with data obtained from echocardiographic studies in 40 age-matched children and 15 newborns all of whom had a normal heart. Except for Case 18, all patients with perfusion defects in the left ventricle had echocardiographic wall motion abnormalities in the corresponding anatomic segments (*17*). Thus far all patients are clinically well.

DISCUSSION

Myocardial Perfusion after the Arterial Switch Operation

The arterial switch operation for complete transposition of the great arteries, either in isolation or in association with other intracardiac defects, attempts to anatomically correct the cardiac abnormality (*1,2,6,12*). Evidence thus far points to grossly normal myocardial function in the majority of children surviving this procedure (*18*). Although animal experiments (*3*) and clinical studies (*19*) suggest growth of the coronary artery anastomosis and preservation of left ventricular function, recent reports of sudden unexpected death (*2,20*) raise some concern about the long-term patency of the coronary arteries, with potential problems being related to kinking of the vessel or ostial stenosis.

FIGURE 1
View of the left ventricle in the horizontal long axis. In panel A, a defect at the apex during isoproterenol-induced stress is demonstrated, which is partially reversible in the redistribution phase (B).



Detection of Myocardial Ischemia

Detection of coronary artery abnormalities may be possible through the application of the surface electrocardiogram, though a normal trace does not exclude ischemia (*21*). Likewise in the presence of complete bundle branch block ischemia may be masked. Coronary arteriography provides accurate data regarding vessel abnormalities in adults (*22*), but in young infants presents a greater challenge. It would therefore appear that a simple, reliable noninvasive assessment of myocardial perfusion would be ideal in this population to identify those patients who may be at greater risk for myocardial ischemia or potential sudden death.

Thallium Perfusion Scintigraphy

Thallium-201 SPECT is a well-accepted technique in the adult population (*22,23*) for the evaluation of coronary artery disease. This methodology appears to correlate well both with stenotic lesions detected at coronary angiography (*21,23*) and with the site of myocardial infarction detected at autopsy (*24*).

With angiographic methods being used as the "gold standard," the sensitivity and specificity of ^{201}Tl perfusion scans for detecting myocardial ischemia have been in the order of 80%, being higher for the anterior than the posterior segments of the left ventricle (*23*). The sensitivity and specificity of this methodology can be improved by applying tomographic instead of planar studies, with one study demonstrating a sensitivity as high as 94% and a specificity of 79% (*25*). The clinical usefulness of ^{201}Tl myocardial perfusion imaging has been further proven in one study with adults, in whom a voluntary control group could be gathered. Twenty-three of 25 volunteers with a structurally normal heart and absence of coronary artery disease had a normal thallium study (specificity 92%) with a low rate of false-positive studies (*26*). Although technical difficulties are encountered using a tomographic approach in infants less than 3 mo of age, our study demonstrates that this technique can be readily applied to children. It also emphasizes the importance of stressing the heart to detect more subtle reversible defects. While isoproterenol does not exactly simulate physiologic exercise, it increases myocardial oxygen demand (*4*) and may unmask reversible perfusion defects in this age group. We used isoproterenol instead of dipyridamole for the purpose of this study, because we had no prior experience with the latter drug in small children and it is unclear as to whether this is a safe drug to use in an infant with compromised coronary artery perfusion.

Some of the perfusion defects may have been due to transmural infarction (*25*) sustained during surgical repair. These infarcts were encountered in those patients, who underwent the arterial switch operation at an early time of the learning curve. The fact that the newborns, in whom the arterial switch operation has been applied routinely since 1986, had no irreversible defects, is encouraging. Reversible perfusion defects, which were found in four patients in this study, have been reported by other authors (*27*) following the arterial switch operation, albeit with a much higher incidence. These authors used dipyridamole to simulate exercise and found ST segment depression in 17 of the 19 patients studied, as well as areas with decreased thallium uptake but normal redistribution in the same patients. Both isoproterenol as well as dipyridamole have been shown to increase the oxygen demand and thus coronary blood flow by about 2–4 times (*28*). An abnormal thallium uptake with normal redistribution in this situation points to a coronary flow reserve problem (*29*). To date we are not sure what these coronary flow reserve disturbances may mean for individual patients in the future. Perhaps selective coronary arteriography will clarify the issue in some. It is, however, encouraging to note that so far no patient from this group has suffered a sudden cardiac death.

TABLE 3
Interobserver Variability in Assessing Perfusion Defects in Nine Patients Following the Arterial Switch

	Observer A		Observer B	
Patient	Stress	Reperfusion	Stress	Reperfusion
4	Partial	Partial	Partial	Partial
5	Complete	Partial	Complete	Partial
7	Complete	Complete	Complete	Complete
11	Complete	Partial	Partial	Normal
12	Partial	Normal	Partial	Partial
3	Partial	Normal	Partial	Normal
6	Complete	Normal	Complete	Normal
8	Partial	Normal	Partial	Normal
18	Partial	Normal	Partial	Normal

CONCLUSIONS

Thallium-201 myocardial perfusion scan is a useful adjunct to a complete postoperative assessment following the arterial switch procedure. In experienced hands, it provides reliable reproducible data. The potential for a perfusion defect under stress in a patient with a normal resting scan, emphasizes the importance of stressing the myocardium. It may point to a potential coronary flow reserve problem in patients having undergone the arterial switch operation, although further studies perhaps with the use of selective coronary arteriography have to be undertaken to further define the future fate of these patients.

REFERENCES

1. Jatene AD, Fontes VG, Paulista PP, et al. Anatomic correction for transposition of the great vessels. *J Thorac Cardiovasc Surg* 1976;72:364–370.
2. Sidi D, Planche C, Kachaner J, et al. Anatomic correction of simple transposition of the great arteries in 50 neonates. *Circulation* 1987;75:429–435.
3. de la Riviere Brutel A, Quagebeur JM, Hinnis PJ, et al. Growth of an aortocoronary anastomosis. An experimental study in pigs. *J Thorac Cardiovasc Surg* 1983;86:393–399.
4. Combs D, Martin C. Evaluation of isoproterenol as a method of stress testing. *Am Heart J* 1974;87:711–715.
5. Yacoub MH, Radley-Smith R. Anatomy of the coronary arteries in transposition of the great arteries and methods of their transfer in anatomical correction. *Thorax* 1978;33:418–427.
6. Williams WG, Freedom RM, Culham G, et al. Early experience with arterial repair of transposition. *Ann Thorac Surg* 1981;32:8–15.
7. Major WK, Matsuda H, Subramanian G. Failure of the Jatene operation in a patient with d-transposition and intact ventricular septum. *Ann Thorac Surg* 1976;22:386–388.
8. Huhta JC, Edwards WD, Feldt RH, Puga FJ. Left ventricular wall thickness in complete transposition of the great arteries. *J Thorac Cardiovasc Surg* 1982;84:97–101.
9. Lange PE, Onnasch DGW, Stephan E, et al. Two-stage anatomic correction of complete transposition of the great arteries: ventricular volumes and muscle mass. *Herz* 1981;6:336–343.
10. Gilday DL. Special considerations for children. In: Maisey MN, Britton KE, Gilday DL, eds. *Clinical nuclear medicine.* London: Chapman and Hall; 1983:333.
11. Maublant J, Cassagnes J, Le Jeune JJ, et al. A comparison between conventional scintigraphy and emission tomography with thallium-201 in the detection of myocardial infarction: concise communication. *J Nucl Med* 1982;23:204–208.
12. Finley JP, Howman-Giles RB, Gilday DL, Olley PM, Rowe RD. Thallium-201 imaging in anomalous left coronary artery arising from the pulmonary artery. *Am J Cardiol* 1978; 42:675–680.
13. Finley JP, Howman-Giles RB, Gilday DL, Bloom KR, Rowe RD. Transient myocardial ischemia of the newborn infant demonstrated by thallium myocardial imaging. *J Pediatr* 1979;94:263–269.
14. Garcia EV, van Train K, Maddahi J, et al. Quantification of rotational thallium-201 myocardial tomography. *J Nucl Med* 1985;26:17–26.
15. Vogel M, Benson LN, Smallhorn JF, Trusler GA, Freedom RM. Catheter assessment of left ventricular function after arterial switch operation at rest and afterload stress [Abstract]. *J Am Coll Cardiol* 1988;11:29A.
16. Moynihan DE, Parisi AE, Feldman CM. Quantitative detection of regional left ventricular contraction abnormalities by two-dimensional echocardiography. I. Analysis of methods. *Circulation* 1981;63:752–760.
17. Vogel M, Smallhorn JF, Trusler CA, Freedom RM. Echocardiographic analysis of left ventricular wall motion in children after the arterial switch operation. *J Am Coll Cardiol* 1990;15:1417–1423.
18. Castaneda AR, Norwood WI, Jonas RA, Colan SD, Sanders SP, Lang P. Transposition of the great arteries and intact ventricular septum. Anatomical repair in the neonate. *Ann Thorac Surg* 1984;38:438–443.
19. Borow KM, Arensman FW, Webb C, Radley-Smith R, Yacoub MH. Assessment of left ventricular contractile state after anatomic correction of transposition of the great arteries. *Circulation* 1984;69:106–11.
20. Arensman FW, Sievers HH, Lange P, et al. Assessment of coronary and aortic anastomosis after anatomic correction of transposition of the great arteries. *J Thorac Cardiovasc Surg* 1985;90:597–603.
21. Quagebeur JM, Rohmer J, Ottenkamp J, Buis T, Blackstone E, Brom AG. The arterial switch operation. An eight-year experience. *J Thorac Cardiovasc Surg* 1986;92:361–384.
22. Ritchie JL, Trobaugh GB, Hamilton GW, et al. Myocardial imaging with thallium-201 at rest and during exercise. Comparison with coronary arteriography and resting and stress electrocardiography. *Circulation* 1977;56:66–73.
23. Kirsch CM, Doliwa R, Buell U, Roedler D. Detection of severe coronary heart disease with Tl-201. Comparison of resting single-photon emission tomography with invasive arteriography. *J Nucl Med* 1983;24:761–766.
24. Fletcher JW, Walter KE, Witzlum KF, et al. Diagnosis of coronary artery disease with ^{201}Tl. *Nucl Med* 1978;128:423–427.
25. Wackers FJT, Becker AE, Smanson G, et al. Location and size of acute transmural myocardial infarction estimated from thallium-201 scintiscans. *Circulation* 1977;56:72–78.
26. Taylor DN, Choraria SK, Maughan J, Mills J, Pilcher J. Diagnosis of coronary artery disease using thallium imaging. Tomographic versus planar imaging. *Nucl Med Comm* 1989;10:401–407.
27. Lösse B, Mecklenbeck W, Kramer HH, Krian A. Thallium myocardial imaging after anatomical correction of d-transposition of the great arteries [Abstract] *Circulation* 1988;(supp II)78:II-293.
28. Gould K. Noninvasive assessment of coronary stenosis by myocardial perfusion imaging during pharmacologic coronary vasodilatation. I. Physiologic basis and experimental validation. *Am J Cardiol* 1978;41:267–276.
29. Legrand V, Mancini J, Bates ER, Hodgson JM, Gross MD, Vogel RA. Comparative study of coronary flow reserve, coronary anatomy and results of radionuclide exercise tests in patients with coronary artery disease. *J Am Coll Cardiol* 1986;8:1022–1032.