Adenosine stress myocardial perfusion scintigraphy in pediatric patients after arterial switch operation

Arun Reddy, Akshay K Bisoi, Suhas Singla[1], Chetan D Patel[1], Sambhunath Das[2]

Departments of Cardiothoracic and Vascular Surgery, [1]Nuclear Medicine, and [2]Cardiac Anaesthesia, All India Institute of Medical Sciences, New Delhi, India

ABSTRACT

Context: Arterial switch operation (ASO) has become the established treatment for correction of transposition of great arteries (TGA). Despite the immediate correction of abnormal hemodynamics, acute and delayed complications related to the coronaries may cause morbidity and mortality. **Aims:** We evaluated the incidence of perfusion abnormalities and safety of adenosine by stress–rest myocardial perfusion single-photon emission computed tomography (SPECT) [myocardial perfusion scintigraphy (MPS)] using Tc-99m Sestamibi (MIBI) in asymptomatic children post-ASO. **Settings and Design:** Prospective study. **Materials and Methods:** We conducted a prospective, single-institutional study where stress–rest MPS was performed on 10 children of age between 1.25 and 6 years. Two of the patients had additional ventricular septal defect, one patient had left ventricular outflow tract obstruction, and another had Taussig–Bing anomaly. All the patients underwent corrective surgery as a single-stage procedure at the age of 176 ± 212 days (range 9-560 days). Adenosine was administered at a rate of 140 µg/kg/min intravenously as continuous infusion for duration of 6 min. **Statistical Analysis Used:** All the continuous variables were summarized as mean $\pm$ standard deviation, or range and median. Mann–Whitney test for unpaired data and Wilcoxon Rank test for paired samples were used. **Results:** The average increase in heart rate over the basal heart rate after adenosine stress was $59.7 \pm 17.0\%$. No acute or remote complications were observed in any case. None of the patients demonstrated myocardial perfusion defects, either at rest or after adenosine stress. **Conclusions:** MPS post-adenosine induced vasodilatation is safe and feasible in patients of ASO for transposition of great arteries. One-stage repair, implantation of excised coronary buttons within neo-aortic sinus, and minimal or no mobilization of proximal coronaries may eliminate the occurrence of perfusion defects in patients of corrected TGA.

Keywords: Adenosine, arterial switch, myocardial perfusion scintigraphy, pediatric

INTRODUCTION

Arterial Switch Operation (ASO) has become the procedure of choice for transposition of great arteries (TGA). Improvements in surgical techniques, myocardial protection, and postoperative management strategies have led to lowering of peri-operative mortality. But patients who have had an uncomplicated surgery and peri-operative period may still have coronary events. Therefore, patients who have undergone ASO need to be evaluated for the adequacy of coronary system. In this study, we evaluated the myocardial perfusion in post-ASO patients using stress adenosine Tc-99m Sestamibi single-photon emission computed tomography (SPECT) [myocardial perfusion scintigraphy (MPS)]. The secondary objective of this study was to assess the safety of adenosine stress in pediatric patients after ASO.

MATERIALS AND METHODS

Patients

We conducted a prospective, single-institutional study on asymptomatic group of children post-ASO and who were not on medical treatment. The postoperative cases of d-transposition of great arteries (d- TGA) with residual defects on echocardiography, abnormal electrocardiogram (bradycardia <50/min, conduction abnormality), hypersensitivity to adenosine, history of bronchial hyperreactivity, congestive cardiac failure or left ventricular dysfunction at rest were not considered for the study. Fourteen patients who underwent arterial switch for d-TGA and survived at least 6 months before initiation of the study were counseled for participation in the study. Of the 14 patients, 11 were

Address for correspondence:
Dr. Chetan D Patel, Room No. 36, Cardiothoracic and Neurosciences Center, All India Institute of Medical Sciences, Ansari Nagar, New Delhi - 110 029, India. E-mail: cdpatel09@gmail.com

recruited after written and informed consent was provided by the parents/guardians and 3 patients were not included as they refused to participate. The study protocol was approved by institutional ethics committee. The subjects fulfilling the inclusion criteria underwent resting and adenosine stress MPS with Tc-99m methoxyisobutylisonitrile (MIBI) (1-day protocol).

Surgical procedure

The ASO is an anatomical correction of TGA. After both great arteries had been transected a few millimeters above the aortic sinuses of Valsalva, the coronary buttons were excised. A conscious attempt was made to keep dissection to a minimum. Attempts were made to reimplant the coronary buttons into the neo-aortic sinus rather than above the sino-tubular junction. An attempt was always made to establish dual coronary system, even if both the coronary ostia lied within the same sinus initially. Neo-aortic anastomosis was completed after LeCompte maneuver in all cases. The defects in the aortic wall were closed by using autogenous pericardium and neo-pulmonary anastomosis was carried out.

Stress adenosine MPS

A mandatory fasting period of 6 h was ensured in all patients prior to the test. A dose of 140 μg/kg/min of adenosine was administered intravenously as continuous infusion using a peristaltic pump for duration of 6 min. Tc-99m MIBI was injected intravenously after 3 min of adenosine infusion [0.2 mCi/kg body weight (minimum 2 mCi/74 MBq)]. The infusion was continued for another 3 min post-injection of radiotracer. An increase in systolic blood pressure of 30% above baseline or a decrease of 20% below baseline, cardiac arrhythmias, and breathing discomfort were the indications for termination of adenosine infusion. Immobilization of patients during imaging was accomplished by sedation with low-dose midazolam (0.1-0.2 mg/kg) administered intravenously by the cardiac anesthesiologist accompanying the patient. The stress images were acquired about 30-45 min after adenosine stress on a dual-head SPECT system (Infinia, Hawkeye; General Electric Medical SystemUSA) equipped with a low-energy all-purpose collimator. Studies were performed in step-and-shoot mode with the heads at an angle of 90° (L-mode) to each other using a 15% window centered at 140 keV photopeak of Technitium-99m. Sixty projections of 15 sec per frame were acquired over 180°, with the arc spanning from 45° right anterior oblique to 135° left posterior oblique in a 64 × 64 matrix. Rest images were acquired after administration of 6-10 mCi (222-370 MBq) of Tc-99m MIBI, 3-4 h later with same acquisition parameters.

The studies were uniformly processed with commercially available Emory Cardiac Toolbox (ECTbox; Emory University, Atlanta, GA, USA) software on a Xeleris nuclear medicine workstation (GE Medical Systems, Milwaukee, USA). SPECT emission image data were processed by use of ordered-subsets expectation maximization reconstruction software with two iterations and 10 subsets. Reconstructed stress and rest images

were smoothed with a three-dimensional Butterworth low-pass filter with a critical frequency of 0.4 Nyquist with an order of 10 and a critical frequency of 0.52 Nyquist with an order of 5.0, respectively. Subsequently, the resulting transaxial image slices were then re-oriented to generate the conventional short axis, vertical long axis, and horizontal long axis images and analyzed using a 20-segment model. The study was considered as normal (no perfusion defects on stress and rest images) or abnormal [presence of perfusion defect on the stress which normalized on the rest images (reversible perfusion defect) or presence of perfusion defect on the stress which remain unchanged on the rest images (fixed perfusion defect)]. All SPECT images were analyzed according to the standard criteria and with the agreement of two independent observers. SPECT images of only 10 patients were analyzed as the myocardial perfusion SPECT of one patient showed severe motion artifacts and was excluded from the final analysis.

Statistical analysis

All the continuous variables were summarized as mean ± standard deviation, or range and median. Since the sample size was small, non-parametric tests were applied to deduce significance. Mann–Whitney test for unpaired data and Wilcoxon Rank test for paired samples were used. *P* value was considered significant when the value was <0.05. The statistical package used in the study was IBM SPSS Statistics 19.0.0.

RESULTS

Of the 10 patients, 8 children were males and 2 were female children. None of them had any preoperative adverse events and/or hospitalization for any other indication. The mean age of children at the time of surgery was 176 ± 212 days (median 71 days, range 9-560 days). The median age at surgery for patients (*n* = 7) with a diagnosis of d-TGA and intact ventricular septum (IVS) was 45 days (range 9-550 days). All the surgeries were performed by a single experienced cardiac surgeon. The preoperative diagnosis and surgical procedure performed are presented in Table 1. Patients were operated under moderate hypothermia with aorto-bicaval canulation and cold blood cardioplegia [Table 2]. The average cardiopulmonary bypass time in the study population was 86 ± 10 min (range 67-99 min). The average cardiopulmonary bypass time in the dTGA-IVS subgroup was 85 ± 10 min and in the rest of the patients was 88 ± 9 min, the difference not being statistically significant (*P* = 0.358). There was no incidence of complete heart block in any of the patients. The average duration of hospital stay after surgery was 14 ± 8 days (range 7-34 days). No significant abnormalities were recorded in postoperative echocardiograms.

Adenosine stress and myocardial perfusion imaging

The mean follow-up duration was 2.7 ± 2.1 years (range 0.5-5.9 years) between surgery and MPS. The mean age of the patients at the time of MPS was 3.3 ± 1.9 years (range 1.3-6 years). The adenosine infusion was continued safely for 6 min in all patients with no serious adverse effects. No significant changes in 12-lead
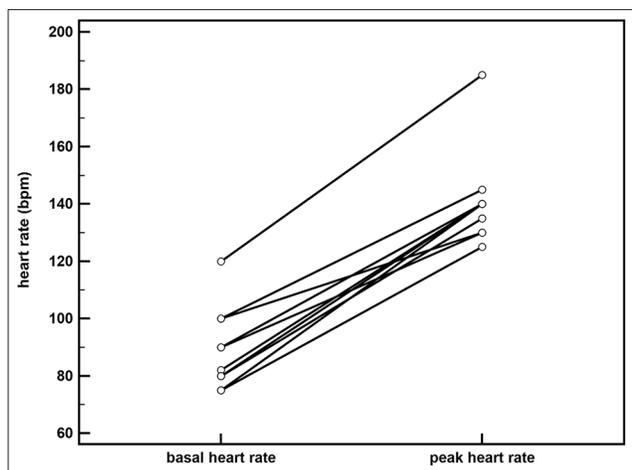
Figure 1: Dot and line diagram showing a change of heart rate during adenosine infusion. There was an increase in heart rate observed in all patients (*n* = 10) which was significant (*P* = 0.002)
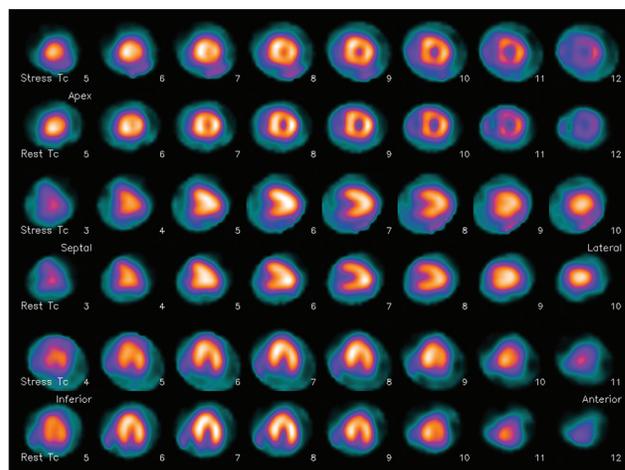
Figure 2: Stress–rest MPS images in a 4-year-old male patient (patient no. 9) showing normal perfusion in the left ventricular myocardium on both the stress and rest images

Table 1: Preoperative diagnosis, coronary anatomy, and surgical procedure performed in patients (*n*=10)

Patient	Sex	Pre-op diagnosis	Leiden classification[1]	Yacoub classification[2]	Procedure
1	M	dTGA, IVS	1L, 2RCX	Type D	ASO
2	M	dTGA, IVS	1LCX, 2R	Type A	ASO
3	M	dTGA, IVS	1LCX, 2R	Type A	ASO
4	M	dTGA, IVS	1LCX, 2R	Type A	ASO
5	M	dTGA, IVS	1LCX, 2R	Type A	ASO
6	M	dTGA, IVS	1LR, 2CX	Type E	ASO
7	F	dTGA, IVS	1LCX, 2R	Type A	ASO
8	M	dTGA, VSD	1LCX, 2R	Type A	ASO+VSD closure
9	M	dTGA, VSD, LVOTO	1LCX, 2R	Type A	ASO+VSD closure+ LVOTO resection
10	F	Taussig Bing	1LCX, 2R	Type A	ASO+VSD closure

dTGA: Transposition of great arteries, IVS: Intact ventricular septum, ASO: Arterial switch operation, LVOTO: Left ventricular outflow tract obstruction, VSD: Ventricular septal defect

ECG recording were observed during adenosine stress. The average increase in heart rate over the basal heart rate after adenosine stress was 60 ± 17% [Figure 1]. The mean basal heart rate was 89 ± 14 bpm and the mean peak heart rate during adenosine infusion was 141 ± 17 bpm. Myocardial perfusion SPECT was done, both after adenosine stress and at rest. None of the patients demonstrated myocardial perfusion defects, either on stress or on rest images [Figure 2].

DISCUSSION

There is adequate published evidence suggestive of grossly preserved myocardial function in children surviving ASO.[3] Neonatal ASO has become the surgical procedure of choice for correction of TGA with or without Ventricular Septal Defect (VSD), as demonstrated by encouraging early- and mid-term cardiac results.[4-7]

Studies have shown a bimodal incidence of coronary events after ASO. Coronary events most commonly occur in the first 3 months after surgery and are the main cause of death or morbidity, with a second peak after 6 years of age.[8]

Over the years, with accumulation of evidence, delayed coronary morbidity and mortality has decreased with a reported prevalence of approximately 2%.[9-13] The prevalence of coronary events has also declined over years with evolving surgical experience.[9,14-16] The surgical technique in the present study involved minimal mobilization of coronary buttons and proximal coronaries to translocate the coronary buttons into the sinuses of the neo-aorta. The coronary ostia always lie within the sinus ridge for optimal physiological function. Serious reduction in coronary flow has been observed when coronary ostia are present outside the sinuses on the aortic wall as a resultant loss of normal function of the sinus.[17] Similar findings were reported in another study where no perfusion deficits and preserved myocardial blood flow were observed in a group of patients in whom coronary artery ostia buttons were reimplanted into the sinus of the autograft valve.[18] It has been observed that late coronary events could occur in patients even with no intraoperative coronary issues and with a smooth postoperative course.[11,19] Progressive fibrocellular intimal thickening or stretching of the coronary artery with growth are the probable causes postulated to explain the same.[20] This subset could be the patients in whom the flow reserve could be compromised. Standard exercise testing can identify potential coronary lesions and ischemia, but is not sensitive enough to identify all cardiac lesions.[8] By means of adenosine-induced pharmacologic vasodilatation and rest imaging by myocardial perfusion imaging, the current study was

aimed to unmask lesions in patients who are susceptible to late coronary events.

The present study is the first in literature assessing the myocardial perfusion with Tc-99m Sestamibi SPECT in ASO patients post pharmacological stress, using adenosine. In our study, the age of the patients ranged from 1.3 to 6 years, and therefore, physical stress testing was not possible to perform in all cases. Standard stress electrocardiography has been found to be inadequate for detecting ischemia inpatients after ASO,[18] and non-specific ST–T changes due to hyperventilation may make the interpretation difficult.[21] Also, the exercise capacity in patients after ASO may be diminished, which may increase the false negatives on MPS.[22-24] Adenosine has been used safely in a number of studies involving patients of pediatric age group suffering from different corrected and uncorrected congenital cardiac anomalies including dTGA.[18,25-28] Adenosine has a half-life of 6 sec which makes it a very safe drug as any arrhythmias can be terminated by stopping the infusion.[29-31] In our study, an average of 60% increase in heart rate from baseline during adenosine infusion was observed. None of them had any arrhythmias or respiratory disturbance during adenosine infusion and did not warrant premature termination of the standard 6-min adenosine stress test.

In our study, MPS did not reveal any perfusion abnormality in our patient group. The incidence of abnormal MPS in studies compiled before 2002 has been reported to be between 11% and 100% [Table 3]. But in recent studies, the prevalence of coronary lesions and resultant perfusion abnormalities appears to have decreased to 3-5%, which is likely to be due to better surgical expertise and techniques being employed in current practice that are becoming more evident with recent studies having larger sample size.[22,37] Both fixed and reversible perfusion defects have been reported in literature.[18,22,33,36] Weindling *et al.*[34] found improvement in perfusion with exercise compared to rest images, presumably as a result of improved blood delivery through collateral vessels. The size of the defects reported is generally small and does not result in visually discernible changes in ventricular function or regional wall motion abnormalities which may reflect arteriolar or capillary processes.[18,34,36] In the study by Rickers *et al.,* coronary angiograms were normal in half of the patients with perfusion defects suggestive of non-coronary intraoperative insult. In a case-comparison study,

Table 2: Surgery-related variables (*n*=10)

Patient	Age at surgery (days)	Cross-clamp duration (min)	CPB duration (min)	Pre-op status	Days to discharge	Post-op events	Age at the time of study (years)
1	30	44	80	NPS	12	Nil	6
2	28	46	96	BAS	8	Nil	5
3	9	44	67	NPS	14	Nil	2.5
4	45	57	96	BAS	11	Nil	6
5	90	53	91	NPS	7	Nil	3
6	240	49	80	NPS	13	ECMO	1.75
7	550	56	82	NPS	11	Nil	2
8	153	55	84	BAS	34	Pneumonia	1.25
9	560	69	99	NPS	15	Nil	4
10	51	54	82	NPS	10	Nil	1.25

BAS: Balloon atrial septostomy, CPB: Cardiopulmonary bypass, ECMO: Extracorporeal membrane oxygenation, NPS: No prior surgery, Patient 6 was electively placed on extracorporeal membrane oxygenator (ECMO) support for 2 days in view of regressed ventricle. Patient was weaned off the ECMO support and decanulated on day 3 postoperatively and discharged 13 days after surgery. Patient 8 developed rash, thrombocytopenia, and lower respiratory tract infection for which he was medically managed and discharged 34 days postoperatively

Table 3: Comparison of incidence of fixed perfusion defects and associated variables in different studies

Reference	Radiotracer	Stress	Imaging	Age at surgery	Age at study (years)	Fixed perfusion defects (%)
Vogel *et al.*[32]	Tl-201	Isoproterenol	SPECT	1.7±1.8 years (8 days-7.9 years)	4±3 (0.3-10.2)	9/21 (43)
Hayes *et al.*[33]	99mTc-MIBI	Exercise	SPECT	7 days-18 months	7.5±1.77 years (5.25-9.83)	10/10 (100)
Weindling *et al.*[34]	99mTc-MIBI	Exercise	SPECT	2 days-2.4 years	5.9±1.1 (4.2-8.8)	22/23 (96)
Hauser *et al.*[18]	13N-NH3	Adenosine	PET	20 days-7.8 years	12.3 (8-16)	5/21 (24)
Oskarsson *et al.*[35]	99mTc-Tetrofosmin	None	SPECT	2 days-9 months	Median 6 (4-11)	2/11 (22)
Rickers *et al.*[36]	99mTc-MIBI	Bicycle exercise	SPECT	10 days-2 years	13.3±3.9 (6.5-16.6)	4/6 (66)
Rickers *et al.*[36]	18F-FDG	None	PET	10 days-2 years	13.3±3.9 (6.5-16.6)	3/6 (50); Non-transmural MI in 2/6 (33)
Raisky *et al.*[37]	Tl-201	Dipyridamole	SPECT	5.6±3.2 (0.3-10.5)	2.7±2.5 (follow-up after surgery)	2/18 (11)
Sterrett *et al.*[22]	99mTc-Tetrofosmin	Exercise	SPECT	Neonatal age in 39 cases (rest of the cases at 8 months-5 year)	11.7±3.1 (follow-up after surgery)	2/42 (5)
Reddy *et al.**	99mTc-MIBI	Adenosine	SPECT	176±212 days (9-560 days)	3.3±1.9 years (1.3-6 years)	0/10 (None)

Tl-201: 201-Thallium, 99mTc-MIBI: 99mTc-Sestamibi, SPECT: Single-photon emission computed tomography, PET: Positron emission tomography, *Present study in discussion, 18F-FDG: Fluorine 18-fluorodeoxyglucose

the frequency of perfusion defects was comparable in patients after ASO to those in a group of patients evaluated after bypass surgery.[33] The perfusion deficits have been assumed to be either due to difficulties during translocation of coronaries,[19,32] coronary anatomy variants,[8] intramural left coronaries,[22,37] inhomogeneous myocardial protection, two-stage repair,[33,35] or insult of open heart surgery itself.[18,32,33,38] In the present study, all the patients were operated upon by a single experienced surgeon as one-stage repair and 80% of the subjects underwent corrective surgery in infancy.

The notable limitations of the present study are small sample size and non-availability of coronary angiography. While coronary angiography is considered the gold standard for detection of lesions necessitating possible interventions, it is quite an invasive procedure to be carried out in asymptomatic children on a regular basis as part of a follow-up protocol.

The possible explanations for absence of perfusion defects in our study are one-stage repair, implantation of excised coronary buttons within neo-aortic sinus, and minimal or no mobilization of proximal coronaries, thus preserving vasa vasorum and dilator reserve. To conclude, MPS post-adenosine induced vasodilatation is safe and feasible in patients of ASO for TGA.

REFERENCES

1. Gittenberger-de Groot AC, Sauer U, Oppenheimer-Dekker A, Quaegebeur J. Coronary arterial anatomy in transposition of the great arteries: A morphologic study. Pediatr Cardiol 1983;4 Suppl 1:15-24.
2. 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;33:418-24.
3. Castaneda AR, Norwood WI, Jonas RA, Colon SD, Sanders SP, Lang P. Transposition of the great arteries and intact ventricular septum. Anatomical repair in the neonate. Ann Thorac Surg 1984;38:438-43.
4. Wernovsky G, Mayer JE Jr, Jonas RA, Hanley FL, Blackstone EH, Kirklin JW, *et al.* Factors influencing early and late outcome of the arterial switch operation for transposition of the great arteries. J Thorac Cardiovasc Surg 1995;109:289-301.
5. Rhodes LA, Wernovsky G, Keane JF, Mayer JE Jr, Shuren A, Dindy C, *et al.* Arrhythmias and intracardiac conduction after the arterial switch operation. J Thorac Cardiovasc Surg 1995;109:303-10.
6. Colan SD, Boutin C, Castañeda AR, Wernovsky G. Status of the left ventricle after arterial switch operation for transposition of the great arteries. Hemodynamic and echocardiographic evaluation. J Thorac Cardiovasc Surg 1995;109:311-21.
7. Hövels-Gürich HH, Seghaye MC, Däbritz S, Messmer BJ, von Bernuth G. Cardiological and general health status in preschool- and school-age children after neonatal arterial switch operation. Eur J Cardiothorac Surg 1997;12:593-601.
8. Legendre A, Losay J, Touchot-Koné A, Serraf A, Belli E, Piot JD, *et al.* Coronary events after arterial switch operation for transposition of the great arteries. Circulation 2003;108 Suppl 1:II186-90.
9. Brown JW, Park HJ, Turrentine MW. Arterial switch operation: Factors impacting survival in the current era. Ann Thorac Surg 2001;71:1978-84.
10. Tsuda E, Imakita M, Yagihara T, Ono Y, Echigo S, Takahashi O, *et al.* Late death after arterial switch operation for transposition of the great arteries. Am Heart J 1992;124:1551-7.
11. Tanel RE, Wernovsky G, Landzberg MJ, Perry SB, Burke RP. Coronary artery abnormalities detected at cardiac catheterization following the arterial switch operation for transposition of the great arteries. Am J Cardiol 1995;76:153-7.
12. Yamaguchi M, Hosokawa Y, Imai Y, Kurosawa H, Yasui H, Yagihara T, *et al.* Early and midterm results of the arterial switch operation for transposition of the great arteries in Japan. J Thorac Cardiovasc Surg 1990;100:261-9.
13. Lupinetti FM, Bove EL, Minich LL, Snider AR, Callow LB, Meliones JN, *et al.* Intermediate-term survival and functional results after arterial repair for transposition of the great arteries. J Thorac Cardiovasc Surg 1992;103:421-7.
14. Prêtre R, Tamisier D, Bonhoeffer P, Mauriat P, Pouard P, Sidi D, *et al.* Results of the arterial switch operation in neonates with transposed great arteries. Lancet 2001;357:1826-30.
15. Mayer JE Jr, Sanders SP, Jonas RA, Castañeda AR, Wernovsky G. Coronary artery pattern and outcome of arterial switch operation for transposition of the great arteries. Circulation 1990;82 Suppl 5:IV139-45.
16. Blume ED, Altmann K, Mayer JE, Colan SD, Gauvreau K, Geva T. Evolution of risk factors influencing early mortality of the arterial switch operation. J Am Coll Cardiol 1999;33:1702-9.
17. Bellhouse BJ, Bellhouse FH, Reid KG. Fluid mechanics of the aortic root with application to coronary flow. Nature 1968;219:1059-61.
18. Hauser M, Bengel FM, Kühn A, Sauer U, Zylla S, Braun SL, *et al.* Myocardial blood flow and flow reserve after coronary reimplantation in patients after arterial switch and ross operation. Circulation 2001;103:1875-80.
19. Bonhoeffer P, Bonnet D, Piéchaud JF, Stümper O, Aggoun Y, Villain E, *et al.* Coronary artery obstruction after the arterial switch operation for transposition of the great arteries in newborns. J Am Coll Cardiol 1997;29:202-6.
20. Bonnet D, Bonhoeffer P, Piéchaud JF, Aggoun Y, Sidi D, Planché C, *et al.* Long-term fate of the coronary arteries after the arterial switch operation in newborns with transposition of the great arteries. Heart 1996;76:274-9.
21. Nechaev DD, Zhorova II, Levina GA, Tarichko IuV. Diagnosis of hyperventilation for elimination of false-positive results of physical exercise test. [Article in Russian]. Kardiologiia 1977;17:83-6.
22. Sterrett LE, Schamberger MS, Ebenroth ES, Siddiqui AR, Hurwitz RA. Myocardial perfusion and exercise capacity 12 years after arterial switch surgery for D-transposition of the great arteries. Pediatr Cardiol 2011;32:785-91.
23. Pasquali SK, Marino BS, McBride MG, Wernovsky G, Paridon SM. Coronary artery pattern and age impact exercise performance late after the arterial switch operation. J Thorac Cardiovasc Surg 2007;134:1207-12.
24. Giardini A, Khambadkone S, Rizzo N, Riley G, Pace Napoleone C, Muthialu N, *et al.* Determinants of exercise capacity after arterial switch operation for transposition of the great arteries. Am J Cardiol 2009;104:1007-12.
25. Bengel FM, Hauser M, Duvernoy CS, Kuehn A, Ziegler SI, Stollfuss JC, *et al.* Myocardial blood flow and coronary flow reserve late after anatomical correction of transposition of the great arteries. J Am Coll Cardiol 1998;32:1955-61.
26. Singh TP, Di Carli MF, Sullivan NM, Leonen MF, Morrow WR. Myocardial flow reserve in long-term survivors of repair of anomalous left coronary artery from pulmonary artery. J Am Coll Cardiol 1998;31:437-43.
27. Singh TP, Humes RA, Muzik O, Kottamasu S, Karpawich PP, Di Carli MF. Myocardial flow reserve in patients with a systemic right ventricle after atrial switch repair. J Am Coll Cardiol 2001;37:2120-5.
28. Muzik O, Paridon SM, Singh TP, Morrow WR, Dayanikli F, Di Carli MF. Quantification of myocardial blood flow and flow reserve in children with a history of Kawasaki disease and normal coronary arteries using positron emission tomography. J Am Coll Cardiol 1996;28:757-62.
29. Cerqueira MD, Verani MS, Schwaiger M, Heo J, Iskandrian AS. Safety profile of adenosine stress perfusion imaging: Results from the Adenoscan Multicenter Trial Registry. J Am Coll Cardiol 1994;23:384-9.
30. Wilson RF, Wyche K, Christensen BV, Zimmer S, Laxson DD. Effects of adenosine on human coronary arterial circulation. Circulation 1990;82:1595-606.
31. Bokhari S, Ficaro EP, McCallister BD Jr. Adenosine stress protocols for myocardial perfusion imaging. J Nucl Cardiol 2007;14:415-6.
32. Vogel M, Smallhorn JF, Gilday D, Benson LN, Ash J, Williams WG, *et al.* Assessment of myocardial perfusion in patients after the arterial switch operation. J Nucl Med 1991;32:237-41.
33. Hayes AM, Baker EJ, Kakadeker A, Parsons JM, Martin RP, Radley-Smith R, *et al.* Influence of anatomic correction for transposition of the great arteries on myocardial perfusion: Radionuclide imaging with technetium-99m 2-methoxy isobutyl isonitrile. J Am Coll Cardiol 1994;24:769-77.
34. Weindling SN, Wernovsky G, Colan SD, Parker JA, Boutin C, Mone SM,

et al. Myocardial perfusion, function and exercise tolerance after the arterial switch operation. J Am Coll Cardiol 1994;23:424-33.

35. Oskarsson G, Pesonen E, Munkhammar P, Sandström S, Jögi P. Normal coronary flow reserve after arterial switch operation for transposition of the great arteries: An intracoronary doppler guidewire study. Circulation 2002;106:1696-702.

36. Rickers C, Sasse K, Buchert R, Stern H, van den Hoff J, Lübeck M, *et al.* Myocardial viability assessed by positron emission tomography in infants and children after the arterial switch operation and suspected infarction. J Am Coll Cardiol 2000;36:1676-83.

37. Raisky O, Bergoend E, Agnoletti G, Ou P, Bonnet D, Sidi D, *et al.* Late coronary artery lesions after neonatal arterial switch operation:

38. Results of surgical coronary revascularization. Eur J Cardiothorac Surg 2007;31:894-8.

38. Lalezari S, Bruggemans EF, Blom NA, Hazekamp MG. Thirty-year experience with the arterial switch operation. Ann Thorac Surg 2011;92:973-9.

Author Help: Reference checking facility

The manuscript system (www.journalonweb.com) allows the authors to check and verify the accuracy and style of references. The tool checks the references with PubMed as per a predefined style. Authors are encouraged to use this facility, before submitting articles to the journal.

- The style as well as bibliographic elements should be 100% accurate, to help get the references verified from the system. Even a single spelling error or addition of issue number/month of publication will lead to an error when verifying the reference.
- Example of a correct style
  Sheahan P, O'leary G, Lee G, Fitzgibbon J. Cystic cervical metastases: Incidence and diagnosis using fine needle aspiration biopsy. Otolaryngol Head Neck Surg 2002;127:294-8.
- Only the references from journals indexed in PubMed will be checked.
- Enter each reference in new line, without a serial number.
- Add up to a maximum of 15 references at a time.
- If the reference is correct for its bibliographic elements and punctuations, it will be shown as CORRECT and a link to the correct article in PubMed will be given.
- If any of the bibliographic elements are missing, incorrect or extra (such as issue number), it will be shown as INCORRECT and link to possible articles in PubMed will be given.