Reliability of systolic time intervals in diagnosis of transposition of great arteries in newborn

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SUMMARY The diagnostic echocardiographic features of transposition of the great arteries have been described as (1) abnormal great vessel relations, (2) reversed systolic time intervals. The former has been shown to be unreliable and the systolic time intervals have not been critically evaluated in the neonate.

A cardiac opinion was sought in 17 cyanotic neonates, aged 7 to 80 hours in whom full clinical examinations, electrocardiogram, and chest x-ray could not distinguish between transposition of the great arteries and respiratory disease. Nine patients (group 1) had the former and eight (group 2) had the latter.

Standard echocardiograms were performed taking note of the great vessel relations, and systolic time intervals were measured. Reversed systolic time intervals were present (a) when the anterior root pre-ejection period was equal to or greater than the posterior root pre-ejection period, or (b) when the anterior root ejection time was equal to or shorter than the posterior root ejection time, or (c) when the anterior root electromechanical systole was equal to or shorter than the posterior root electromechanical systole, or (d) when the anterior root pre-ejection period/ejection time ratio was equal to or greater than the posterior pre-ejection period/ejection time ratio. When the great vessel relations were clearly reversed, that is the anterior root was medial, cephalad, and anterior to the posterior root, then the positions were diagnostic for transposition of the great arteries; other relations were either non-diagnostic or clearly normal.

The sensitivity, specificity, and predictive accuracy of these findings were calculated. The great vessel relations were determined with 78% sensitivity, 87.5% specificity, and 87.5% predictive accuracy. The systolic time intervals criteria were 44 to 89% sensitive, 0 to 50% specific, and had 50 to 66% predictive accuracy. Thus, taken alone, systolic time intervals are useless in excluding transposition.

By linear discriminant analysis using both the great vessel relation and systolic time intervals a formula was derived which would have predicted the diagnosis with 100% accuracy.

This requires a prospective study for proof of its validity. In the meantime, careful evaluation of all the clinical, laboratory, and echocardiographic data must be made in any cyanosed neonate and cardiac catheterisation must not be delayed if the diagnosis is in doubt.

Balloon atrial septostomy has dramatically changed the immediate prognosis for neonates with d-transposition of the great arteries but this procedure is not without significant risk.¹ The decision to undertake cardiac catheterisation and possible balloon atrial septostomy in a severely cyanosed neonate has been simplified by the introduction of echocardiography which can identify the cardiac structures and thus reduce the length of

catheterisation. The echocardiographic features of transposition of the great arteries are said to be (1) an abnormal relation of the great vessels,²⁻⁶ and (2) reversed systolic time intervals.⁵⁻⁹ While the former has been shown to be unreliable,¹⁰ the value of the latter has not been tested.

The purpose of this study was to determine the reliability of systolic time intervals in differentiating between transposition of the great arteries and non-cardiac causes of severe cyanosis in the newborn.

Table 1 Clinical details and systolic time intervals in patients

Case no.	Diagnosis	Wt (kg)	Age (h)	PO ₂ mm Torr	Anterior root (RV)				Posterior root (LV)			
					PEP	ET	QS ₂	PEP/ET	PEP	ET	QS ₂	PEP/ET
Group 1												
1	TGA	4.0	7	18	60	200	260	0.30	45	210	255	0.22
2	TGA	3.2	8	19	60	150	210	0.40	50	155	205	0.32
3	TGA	3.2	70	25	65	170	235	0.38	45	185	230	0.24
4	TGA	3.2	48	22	85	175	260	0.49	60	215	275	0.28
5	TGA+VSD	3.1	80	37	60	170	230	0.35	55	180	235	0.31
6	TGA+VSD	3.5	26	24	75	190	265	0.39	55	220	275	0.25
7	TGA+VSD+PS	2.4	48	51	80	170	260	0.47	65	205	270	0.32
8	TGA+VSD	2.7	34	29	55	140	195	0.39	60	135	195	0.44
9	TGA	3.3	8	36	130	140	270	0.93	60	180	240	0.33
	Mean	3.18	36.6	29	74	167	243	0.46	55	187	242	0.30
	SD±	45	27	11	23	21	27	0.19	7.1	29	29	0.07
Group 2												
10	Asphyxia, Down's	3.47	18	35	70	200	270	0.35	60	200	260	0.30
11	PFC	3.63	56	33	70	150	220	0.47	60	165	225	0.36
12	Meconium aspiration, PFC	3	18	22	65	185	250	0.35	65	185	245	0.35
13	PFC	1.67	36	22	65	180	245	0.36	50	185	235	0.27
14	Asphyxia, PFC	3.3	36	40	50	170	220	0.33	50	155	205	0.32
15	Asphyxia, PFC	3.8	50	45	65	150	215	0.43	60	145	205	0.41
16	PFC	3.4	17	77	60	170	230	0.35	50	190	240	0.26
17	PFC and omphalocele	1.9	18	28	95	200	295	0.32	70	205	290	0.34
	Mean	3.02	31.1	37.8	68	176	243	0.37	58	179	238	0.33
	SD	0.8	16	18	13	20	28	0.05	8	22	±30	0.05

ET, ejection time; LV, left ventricle; PEP, pre-ejection period; PFC, persistent fetal circulation; PO₂, pressure of oxygen; PS, pulmonary stenosis; QS₂, electromechanical systole; RV, right ventricle; SD, standard deviation; TGA, transposition of the great arteries; VSD, ventricular septal defect.

Patients

All 17 patients in this study were cyanosed neonates referred for a cardiac opinion at the Vancouver General Hospital between August 1977 and May 1979, and all had had an adequate echocardiographic examination. Their ages ranged from 7 to 80 hours. There were nine with transposition of the great arteries (group 1), four with an additional ventricular septal defect, one of those with pulmonary stenosis. Patients with more complex forms of transposition of the great arteries or who presented after 1 week of age were not included in the study. The clinical details are shown in Table 1. Group 2 comprised eight cyanotic neonates suspected of having congenital heart disease initially but all subsequently considered to have persistent fetal circulation caused by perinatal asphyxia. One had Down's syndrome; another had omphalocele. All were ventilated with maximal pressures and an inspired oxygen of 90% or more.

Methods

Echocardiograms were performed with an S.K.I. Eckoline echocardiograph using a 5 MHz 6 mm

unfocused transducer. The tracings were made on ultra-violet sensitive paper at 100 mm/s, with a Honeywell recorder for systolic time intervals and at 50 mm/s for "sweeps" to determine the presence of structures and their relations. Systolic time intervals were calculated in the standard manner.⁹ The pre-ejection period was measured from the onset of the Q wave to semilunar valve opening and the ejection time from the opening to the closure of the semilunar valve. The total duration of electromechanical systole was measured from the onset of the Q wave to valve closure and was the sum of pre-ejection period and ejection time. Five cardiac cycles were used and the mean of each value was taken to the nearest 5 ms. The position of the great vessels was noted in each case. The systolic time intervals were measured independently. Statistical analysis was performed using Student's *t* test. The two groups were compared with each other and the results of the anterior and posterior root systolic time intervals compared. The following were calculated:

(1) Sensitivity—per cent of all patients with transposition of the great arteries who showed reversed systolic time intervals,

$$\text{that is } \frac{\text{True positive}}{\text{True positive} + \text{false negative}} \times 100$$

(2) Specificity—per cent of negative tests in patients without transposition of great arteries (group 2),

$$\text{that is } \frac{\text{True negative}}{\text{True negative} + \text{false positive}} \times 100$$

(3) Predictive accuracy—per cent of positive tests that are true positive,

$$\text{that is } \frac{\text{True positive}}{\text{True positive and false positive}} \times 100$$

For the calculation of sensitivity, that is true positive, the anterior had to exceed the posterior pre-ejection period, the anterior had to be shorter than the posterior ejection time and electromechanical systole, respectively, and the ratio of anterior had to be greater than that of posterior pre-ejection period/ejection time. When the values of any of the measured indices were equal, they were considered non-diagnostic and therefore "negative". This rule was also applied for specificity and predictive accuracy. For specificity, the reverse had to hold true, that is for a true negative, the anterior had to be shorter than the posterior pre-ejection period, the anterior had to exceed the posterior ejection time and electromechanical systole, respectively, and the ratio of anterior had to be less than that of posterior pre-ejection period/ejection time. The predictive accuracy was derived from a combination of true and false positives as defined.

Table 2 Data used for discriminant analysis

Case no.	Diagnosis	Great vessel relation	Anterior—posterior root (ms)			
			PEP	ET	QS ₂	PEP/ET
1	Transposition	+1	+15	-10	+5	+0.08
2	Transposition	+1	+10	-5	+5	+0.08
3	Transposition	+1	+20	-15	+5	+0.14
4	Transposition	+1	+25	-40	-15	+0.21
5	Transposition	+1	+5	-10	-5	+0.04
6	Transposition	+1	+20	-30	-10	+0.14
7	Transposition	0	+15	-35	-10	+0.15
8	Transposition	+1	-5	+5	0	-0.05
9	Transposition	0	+70	-40	+30	+0.6
10	Pulmonary disease	-1	+10	0	+10	+0.05
11	Pulmonary disease	0	+10	-15	-15	+0.11
12	Pulmonary disease	-1	0	0	+5	0
13	Pulmonary disease	-1	+15	-5	+10	+0.09
14	Pulmonary disease	-1	0	+15	+15	+0.01
15	Pulmonary disease	-1	+5	+5	+10	+0.02
16	Pulmonary disease	-1	+10	-20	-10	+0.09
17	Pulmonary disease	-1	+25	-5	+5	-0.02

ET, ejection time; PEP, pre-ejection period; QS₂, electromechanical systole.

Code for great vessel relation: +1, diagnostic for transposition; 0, non-diagnostic; -1, diagnostic for normal.

These definitions were also applied to the position of the great vessels. There were basically three categories, (a) clearly normal, (b) clearly diagnostic for transposition of the great arteries, and (c) equivocal. The sensitivity, specificity, and predictive accuracy were calculated for each.

In an attempt to combine these two echo diagnostic criteria to improve their accuracy, linear discriminant analysis was used. The great vessel relation was coded for one of the above positions and the difference between the anterior and posterior root pre-ejection period, ejection time, electromechanical systole, and ratio of pre-ejection period/ejection time used to arrive at the most accurate discriminant combination of these (Table 2). For this, the magnitude of the difference in systolic time intervals was taken into account, unlike the simple derivation of sensitivity, specificity, and predictive accuracy.

Results

There was no difference in the mean birthweights, age, and PO₂ of the two groups. In case 15, the blood sample for the PO₂ of 77 torr was obtained just before cardiac assessment. Cases 8 and 9 were extremely acidotic with a pH of less than 7.0 and both received large doses of sodium bicarbonate.

The echo results for pre-ejection period, ejection time, electromechanical systole, and the ratio of pre-ejection period/ejection time are shown in Table 1. The mean results of the systolic time intervals for groups 1 and 2 were not different when the "anterior" root or "posterior" root were compared between the two groups.

RELATION OF GREAT VESSELS

In cases 7, 9, and 11 doubt was expressed about the great vessel relation and the position in these patients was therefore classed as "non-diagnostic". All three had systolic time intervals which were reversed, but at catheterisation case 11 was found to have persistent fetal circulation and not transposition of the great arteries. This was the only patient in group 2 who underwent diagnostic cardiac catheterisation. The sensitivity, specificity, and predictive accuracy were 78%, 87.5%, and 87.5%, respectively (Table 3).

SYSTOLIC TIME INTERVALS

Reversal of systolic time intervals was frequently found in group 1 and the sensitivity of this finding was high (89%). This is shown in Table 4. The only patient in whom reversal of systolic time intervals was not seen was a patient with transposition of the great arteries, ventricular septal defect, and severe acidosis. The left ventricular pressure was suprasystemic at the time of cardiac catheterisation and there was no pulmonary

Table 3 Great vessel relations

	Per cent
Sensitivity (Group 1)	78
Specificity (Group 2)	87.5
Predictive accuracy	87.5

Table 4 Systolic time interval criteria

	Systolic time interval criteria	Per cent
Sensitivity (Group 1)	Ant PEP>Post PEP	89
	Ant ET<Post ET	89
	Ant QS ₂ <Post QS ₂	44
	Ant PEP/ET>Post PEP/ET	89
Specificity (Group 2)	Ant PEP<Post PEP	0
	Ant ET>Post ET	25
	Ant QS ₂ >Post QS ₂	50
	Ant PEP/ET<Post PEP/ET	12.5
Predictive accuracy	Ant PEP>Post PEP	50
	Ant ET<Post ET	57
	Ant QS ₂ <Post QS ₂	66
	Ant PEP/ET>Post PEP/ET	53

Ant PEP, anterior pre-ejection period; ant PEP/ET, anterior pre-ejection period/ejection time; ant QS₂, anterior electromechanical systole; post PEP, posterior pre-ejection period; PEP/ET, posterior pre-ejection period/ejection time; post QS₂, posterior electromechanical systole.

stenosis. The great vessel orientation was typical for transposition of the great arteries.

Patients in group 2 also showed reversal of systolic time intervals. The "anterior root" pre-ejection period was equal to or greater than the posterior root pre-ejection period in all cases. Similarly, the relation of the anterior to the posterior root ejection time, electro-mechanical systole, and pre-ejection period/ejection time, respectively, would be compatible with the diagnosis of transposition of the great arteries in most cases, thus making the test non-specific. The predictive accuracy for these individual findings varied from 50 to 66% as shown in Table 4.

Using discriminant analysis, the following formula was obtained which would have correctly classified all of the patients.

$$+ [31.584 \times \text{Vessel}] - [1.609 \Delta \text{ET}] + [1.674 \Delta \text{QS}_2] \\ - [128.681 \Delta \text{PEP/ET}] - 7.921$$

If the result was greater than zero the diagnosis was transposition of the great arteries and if less than zero, the diagnosis was pulmonary disease.

Discussion

This study was designed to assess the reliability of systolic time intervals in the diagnosis of transposition of the great arteries in the newborn period, when the acutely ill cyanotic neonate is at the greatest risk. Previously published work has stressed the abnormal relation of the great vessels in transposition.²⁻⁶ The anterior root semi-lunar valve is found medially and superiorly while the posterior root semi-lunar valve is lateral and posterior. Unfortunately, there is normally some variation in the great vessel relations in transposition of the great arteries. In 33% of patients there is an anteroposterior relation of the great vessels, with the aorta higher and anterior to the pulmonary artery.¹¹ The normal newborn has a relatively larger and more medially placed pulmonary artery than an older child.¹² Thus, the great vessels are closer together and may be almost in an anteroposterior relation in the normal newborn. Therefore, it is not surprising that in a recent study of the contribution of echocardiographs in the diagnosis of transposition, the arterial root position was diagnostic in only 80% of cases, and inconclusive or misleading in 20%.¹⁰ Our findings were similar, with seven out of nine patients with abnormal great vessel relations in whom the diagnosis could be made with confidence and two in whom it could not.

Earlier reports of the use of echo in the cyanosed newborn have mentioned the use of systolic time intervals to add further diagnostic accuracy but have not systematically assessed this.^{5-7,10} The standard values for systolic time intervals in transposition of the great arteries were measured in children aged 1 month to 7 years.⁹ In that study, the systemic always exceeded the pulmonary ventricular pre-ejection period, the right ventricular was shorter than the left ventricular ejection time, and the left ventricular electromechanical systole generally, but not always, exceeded the right ventricular electromechanical systole. The ratio of ventricular pre-ejection period/ejection time was greater on the right than on the left and ratios of left ventricular/right ventricular ejection time (1.22) and left ventricular/right ventricular pre-ejection period (0.55) were characteristic for transposition of the great arteries. These results were consistent with the systolic time intervals normally observed in the systemic versus the pulmonary circulation in older children and adults with normal pulmonary vascular resistance and myocardial contractility.^{9,13-15} In the neonate, with transitional circulation, these factors are variable and the rate of fall of the pulmonary vascular resistance in the neonate with transposition may be delayed.^{16,17} A recent echocardiographic study of the systolic time intervals in neonates with respiratory disease or transposition confirmed the variability of systolic time intervals in the latter, which we have also found.¹⁸

Reversed systolic time intervals were seen in most of our patients with transposition. The majority showed a longer right ventricular/pre-ejection period (89%), a shorter right ventricular ejection time (89%), and the ratio of the right ventricular pre-ejection period/ejection time larger than the left ventricular one (89%). In case 8, however, this was not the case and though the patient was severely acidotic, circulatory collapse had not occurred. The systolic time intervals on the pulmonary side truly reflected the haemodynamics found at cardiac catheterisation with a suprasystemic left ventricular pressure. Thus, the pulmonary vascular resistance in transposition has the same capacity to remain high as in persistent fetal circulation and in fact many neonates with simple transposition have near systemic pulmonary artery pressures if catheterised in the first few days of life.^{19,20} The presence of a ventricular septal defect may also retard the fall in left ventricular pressure. In this study, the left ventricular pre-ejection period/ejection time was not necessarily below 0.30, as was suggested by Riggs *et al.*¹⁶

In the acidotic, asphyxiated, and cyanosed neonate with persistent fetal circulation raised pulmonary arterial pressures may be reflected by changes in the systolic time intervals similar to those found in this study.¹⁶ Riggs *et al.* studied neonates with persistent fetal circulation and showed a right ventricular pre-ejection period longer than the left and a right ventricular ejection time shorter than the left; the ratio of pre-ejection period/ejection time was 0.6 for the right ventricle and 0.48 for the left. These ratios were larger than we found but the direction of change was similar. Gutgesell *et al.*¹⁸ found similar values for transposition but also noted reversal of systolic time intervals in almost all the patients with respiratory disease, as we did. Thus, such reversal is not specific; the left ventricular pre-ejection period was greater in none of the cases, left ventricular ejection time was shorter in 25%, left ventricular electromechanical systole was shorter in 50%, and the ratio of the posterior pre-ejection period/ejection time was larger in 12.5%.

In the preceding discussion, the correctness of diagnosis between transposition of the great arteries and persistent fetal circulation has been assumed, but when the clinician is faced with the echocardiogram of an undiagnosed cyanotic newborn the great vessels may only be designated "anterior" or "posterior", as has been done in this study. Based on the position of the vessels, the assumption that an artery is pulmonary or systemic may be erroneous. In this situation, it is important to know the sensitivity, specificity, and predictive accuracy of the systolic time intervals, rather than the mean values for the two ventricles. Using the criteria, previously published, for transposition, the sensitivity of systolic time interval reversal at the

anterior root was very high (89%), but specificity ranged from 0 to 50% (Table 4). Thus, many patients who did not have transposition had systolic time intervals diagnostic for this condition, understandable in the light of the haemodynamic changes in persistent fetal circulation. The predictive accuracy of the systolic time intervals ranged from 50 to 60%.

Thus the use of systolic time intervals alone would by these criteria overdiagnose transposition. Few cases would be missed but many neonates with respiratory problems would be catheterised, and we do not advocate this. In our study, we catheterised only one patient with persistent fetal circulation because our echocardiographic criterion to proceed to catheterisation has been simply doubt about the relation of the two great vessels in the presence of cyanosis. The diagnosis of transposition requires both clinical and laboratory investigations, including echocardiography, at which time both the great vessel orientation and systolic time intervals must be taken into consideration. Though discriminant analysis produced a cumbersome formula, its use would have increased the diagnostic accuracy to 100% but the numbers of patients in the study were small and the formula was derived retrospectively. The logical step now would be to perform a prospective study to assess its reliability. Until this has been done, catheterisation must not be delayed in doubtful cases.

Of course, the use of contrast echocardiography may now enhance the diagnostic accuracy of M-mode echocardiography with the suprasternal approach.²¹ Two-dimensional echocardiography has also simplified the diagnosis of transposition.^{22,23}

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References

- 1 Rashkind WJ, Miller WW. Creation of an atrial septal defect without thoracotomy: a palliative approach to complete transposition of the great arteries. *JAMA* 1966; **196**: 991-2.
- 2 Gramiak R, Chung KJ, Nanda N, Manning J. Echocardiographic diagnosis of transposition of the great vessels. *Radiology* 1973; **106**: 187-9.
- 3 Dillon JC, Feigenbaum H, Konecke LL, *et al.* Echocardiographic manifestations of d-transposition of the great vessels. *Am J Cardiol* 1973; **32**: 74-8.
- 4 Godman MJ, Tham P, Kidd BSL. Echocardiography in the evaluation of the cyanotic newborn infant. *Br Heart J* 1974; **36**: 154-66.
- 5 Sahn DJ, Allen HD, Goldberg SJ, Solinger R, Meyer RA. Pediatric echocardiography: a review of its clinical utility. *J Pediatr* 1975; **87**: 335-52.

- 6 Hagler DJ. The utilization of echocardiography in the differential diagnosis of cyanosis in the neonate. *Mayo Clin Proc* 1976; **51**: 143–54.
- 7 Paquet M, Mullins CE. Echocardiogram in d-transposition of great vessels (letter). *Am J Cardiol* 1975; **36**: 121.
- 8 Laird WP, Shelton SL. Simultaneous echocardiographic recording of the semilunar valves in patients with normally related great arteries. *Radiology* 1976; **118**: 397–9.
- 9 Hirschfeld S, Meyer R, Schwartz DC, Korfhagen J, Kaplan S. Measurement of right and left ventricular systolic time intervals by echocardiography. *Circulation* 1975; **51**: 304–9.
- 10 Bass NM, Roche AHG, Brandt PWT, Neutze JM. Echocardiography in assessment of infants with complete d-transposition of great arteries. *Br Heart J* 1978; **40**: 1165–73.
- 11 Guerin R, Soto B, Karp RB, Kirklin JW, Barcia A. Transposition of the great arteries. Determination of the position of the great arteries in conventional chest roentgenograms. *AJR* 1970; **110**: 747–56.
- 12 Rudolph AM. *Congenital diseases of the heart*. Chicago: Year Book Medical Publishers, 1974: 95.
- 13 Weissler AM, Harris WS, Schoenfeld CD. Bedside techniques for the evaluation of ventricular function in man. *Am J Cardiol* 1969; **23**: 577–83.
- 14 Harris LC, Weissler AM, Manske AO, Danford BH, White GD, Hammill WA. Duration of the phases of mechanical systole in infants and children. *Am J Cardiol* 1964; **14**: 448–55.
- 15 Leighton RF, Weissler AM, Weinstein PB, Wooley CF. Right and left ventricular systolic time intervals. Effects of heart rate, respiration and atrial pacing. *Am J Cardiol* 1971; **27**: 66–72.
- 16 Riggs T, Hirschfeld S, Riggs T, Liebman J, Fanaroff A, et al. Persistence of fetal circulation syndrome: an echocardiographic study. *J Pediatr* 1977; **91**: 626–31.
- 17 Halliday H, Hirschfeld S, Riggs T, Liebman J, Fanaroff A, Bormuth C. Respiratory distress syndrome: echocardiographic assessment of cardiovascular function and pulmonary vascular resistance. *Pediatrics* 1977; **60**: 444–9.
- 18 Gutgesell HP, Pinsky WW, Duff DF, Adams J, McNamara DG. Left and right ventricular systolic time intervals in the newborn. Usefulness and limitation in distinguishing respiratory disease from transposition of the great arteries. *Br Heart J* 1979; **42**: 27–34.
- 19 Tynan M. Transposition of the great arteries. Changes in the circulation after birth. *Circulation* 1972; **46**: 809–15.
- 20 Rudolph AM. *Congenital diseases of the heart*. Chicago: Year Book Medical Publishers, 1974: 507–9.
- 21 Mortera C, Hunter S, Tynan M. Contrast echocardiography and the suprasternal approach in infants and children. *Eur J Cardiol* 1979; **9**: 437–54.
- 22 Lange LW, Sahn DJ, Allen HD, Goldberg SJ. Subxiphoid cross-sectional echocardiography in infants and children with congenital heart disease. *Circulation* 1979; **59**: 513–24.
- 23 Bierman FZ, Williams RG. Prospective diagnosis of d-transposition of the great arteries in neonates by subxiphoid, two-dimensional echocardiography. *Circulation* 1979; **60**: 1496–502.

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