CONGENITAL HEART DISEASE

Transoesophageal atrial pacing combined with transthoracic two dimensional echocardiography: experience in patients operated on with arterial switch operation for transposition of the great arteries

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Heart 2003;89:91-95

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Accepted
2 October 2002

Objective: To assess the feasibility, safety, and diagnostic accuracy of transoesophageal atrial pacing stress echocardiography (TAPSE) combined with two dimensional transthoracic echocardiography (TTE) for evaluation of coronary perfusion in patients undergoing arterial switch operation for transposition of the great arteries.

Design: TAPSE combined with TTE was performed at the end of cardiac catheterisation. An ischaemic response was defined as > 1.5 mm horizontal or downsloping ST segment depression or as a new or worsened wall motion abnormality. The results were compared with results of coronary angiography.

Setting: Tertiary referral centre for paediatric cardiology and cardiac surgery.

Patients: 25 patients, mean (SD) age 29.5 (19) months, mean (SD) weight 12.5 (3.4) kg.

Main outcome measures: Target heart rate (200 beats/min) was attained in 22 of 25 (88%) patients. Electrocardiographic ischaemic changes occurred in 4 of 25 (16%) and wall motion abnormalities in 3 of 25 (12%). Coronary obstructions were found in 2 of 25 (8%) patients.

Results: The test was feasible in all patients, without clinical complications requiring treatment. Compared with coronary angiography, the test had a sensitivity and a specificity of 100% and 95%, respectively, for the echocardiographic stress, and of 100% and 91%, respectively, for the electrocardiographic stress. The negative predictive value was 100% for both the echocardiographic and the electrocardiographic stress tests. The positive predictive value was 66% for the echocardiographic stress and 50% for the electrocardiographic stress tests.

Conclusions: In these patients TAPSE combined with TTE was feasible and safe and apparently an accurate diagnostic method for evaluation of coronary perfusion. Patients with a negative test may have a low likelihood of major coronary abnormalities and may not require coronary angiography.

Arterial switch operation (ASO) has been increasingly used to correct transposition of the great arteries (TGA) and is preferable to intra-atrial baffle repair. However, early and late deaths related to coronary artery complications have been reported, and the impact of coronary artery translocation on survival continues to raise concern. Up to now, the various invasive and non-invasive techniques used to investigate coronary perfusion after ASO have had some limitations. Although transoesophageal atrial pacing stress echocardiography (TAPSE) has been proved to be a safe and accurate diagnostic method for detection of coronary disease in adults, its usefulness in children has been evaluated in only limited cases. The purpose of this study was to determine the feasibility, safety, and diagnostic accuracy of TAPSE combined with transthoracic two dimensional echocardiography (TTE) in paediatric patients undergoing ASO.

METHODS

Study patients

The study group consisted of 25 patients undergoing ASO for d-TGA at our institute.

Fifteen patients were operated on for simple TGA, seven for d-TGA and ventricular septal defect, and three for TGA, ventricular septal defect, and aortic coarctation. In all patients the coronary anatomy was investigated before operation with catheterisation, during which balloon atrial septostomy was performed in all but one patient. The coronary anatomical pattern was classified as described by Planché and

colleagues.¹ All but one of the patients underwent a one-stage repair. One patient, affected by d-TGA, ventricular septal defect, and aortic coarctation, had previously undergone surgery for banding of the pulmonary artery and end to end aortoplasty. Mean age at ASO was 14 days (range 4–60 days). During surgery the mean (SD) cardiopulmonary bypass time was 197 (38) minutes and the mean aortic cross clamp time was 119 (22) minutes. No problems were encountered during surgery in any patients, and the postoperative period was uneventful for most of them. Two patients (patients 6 and 20) developed a low cardiac output syndrome in the first few days and another one (patient 12) suffered from a junctional ectopic tachycardia.

All the patients were asymptomatic, in good clinical condition, and normotensive on TAPSE. Exclusion criteria for participation in the study were pacemaker dependence and the presence of left bundle branch block or pre-excitation on the ECG. The mean (SD) age during the study was 29.5 (19.5) months (range 12–87 months) and the mean (SD) weight was 12.5 (3.4) kg (range 10–23 kg). No patient was taking drugs except for one (patient 20), who was being treated with

Abbreviations: ASO, arterial switch operation; DSE, dobutamine stress echocardiography; TAPSE, transoesophageal atrial pacing stress echocardiography; d-TGA, transposition of the great arteries (in which the aorta is positioned on the right); TTE, transthoracic echocardiography

vasodilators and diuretics. All the patients were in good clinical condition and normotensive, but one (patient 6) had borderline systolic pressures because of a mild aortic coarctation. Informed consent was obtained by the parents or the legal guardians of each patient. TAPSE was performed at the end of cardiac catheterisation and selective coronary angiography, with the patient still under general anaesthesia.

TAPSE protocol

The test was performed with a commercially available transoesophageal cardiac stimulator (CB Bioelettronica, Firenze, Italy). After the pacing lead was positioned, an amplitude of 3–5 mA above the threshold was chosen for stable left atrium capture, with a pulse width of 10 ms. Pacing was initiated at 10 beats/min above the patient's spontaneously generated heart rate, and this rate was increased stepwise every two minutes by 10 beats/min until the target rate of 200 beats/min or another end point was reached. Atrioventricular Wenckebach block, ECG evidence of significant ischaemia (> 3 mm horizontal or downsloping ST segment depression at 80 ms after the J point), pronounced hypotension, and complex arrhythmias were the selected pacing end points. Throughout the study, ECG monitoring was continuous, and a 12 lead ECG was recorded every minute. The tracings were considered abnormal and suggestive of ischaemia if there was a > 1.5 mm ST segment depression compared with baseline that persisted at least one minute after pacing. Blood pressure was measured invasively at the end of each stage by use of a catheter left in the femoral artery at the end of the cardiac catheterisation. ECG and blood pressure were monitored until they returned to baseline values.

Echocardiographic protocol

TTE was performed with a Hewlett Packard multiphase probe connected to a Hewlett Packard Sonos 5500 ultrasounds scanner. With the patient in a slightly left lateral decubitus, parasternal short axis, apical four chamber, and apical two chamber views were obtained at rest, at the end of each stage, and until values returned to baseline. In the parasternal short axis view wall motion was evaluated at the mitral (basal segments), papillary muscle (midventricular segments), and apical levels, whereas only one plane was used in the apical four chamber view. We also used the subcostal four chamber and short axis views when it was not possible to obtain reliable echocardiographic images from the parasternal and apical planes.² Baseline segmental wall motion was graded as normal, hypokinetic, akinetic, or dyskinetic. Dyssinergy was defined as asynchrony in the contraction without wall motion abnormalities. A normal response to stress was defined as stability in myocardial thickening or wall motion, and an abnormal response was defined as a reduction in myocardial thickening or wall motion at any stage compared with the baseline. The end point was the development of an abnormal response accompanied by any of the pacing protocol end points.

The echocardiographer performing the test was blinded to the angiographic and ECG data.

Coronary artery angiography

Selective coronary angiography was obtained in all cases with 3 French right or left Judkins coronary catheters (Balt, Montmorency, France).

Statistical analysis

For comparison of data, a two tailed paired Student's *t* test was used. A probability value of $p < 0.05$ was considered significant.

RESULTS

Safety

No patient developed clinical complications throughout TAPSE study. Reasons for terminating the test were the

attainment of the target rate in 22 patients (88%), ECG evidence of ischaemia in two patients, and a major drop in systolic blood pressure in one. In the patients in whom the test was stopped prematurely both the ECG and the haemodynamic abnormalities disappeared promptly or within a few minutes after pacing was terminated and these patients did not require treatment. Blood pressure during the test decreased significantly ($p < 0.003$) and returned to rest values immediately after pacing was stopped. No patient developed significant arrhythmias. Rate pressure product increased from 11 856 (2388) (range 8200–17 850) at baseline to 16 507 (3915) (range 8000–28 600) at the end of the study ($p < 0.05$).

TAPSE

Baseline ECGs were normal in 19 patients. Six patients had either right ventricular conduction delay or complete right bundle branch block. Atrial capture was stable in all patients. The mean (SD) duration of pacing was 15.4 (2.9) minutes. The ECG during the test did not change significantly in 21 of 25 patients (84%), whereas 4 of 25 patients (16 %) met the criteria for ischaemia. In two patients the ECG abnormalities occurred quite early, were progressive, and lasted several minutes in the recovery period; in the other two they occurred during the last two stages of the test and disappeared in the first minutes of recovery. Of note, both coronary angiography and stress echocardiography were abnormal in the first two patients, while only abnormal stress echocardiography was present in one of the other two.

Stress echocardiography

Good quality echocardiograms were obtained in all patients. In the basal echocardiography 14 of 25 (56%) patients had normal regional wall motion of the left ventricle, 8 of 25 (32%) had dyssinergy of the basal septum, and 3 of 25 (12%) had hypokinesis of the basal, mid-, and apical septum. Stress echocardiography was abnormal in 3 patients (12%): in one patient (patient 13) there was a new wall motion abnormality, and in the others (patients 20 and 24) the baseline abnormality had worsened.

No patients with abnormalities at TAPSE had problems during surgery. One patient (patient 20) had a postoperative period complicated by a low output syndrome.

Coronary angiography

No abnormalities in the origin, course, and size of the coronary arteries were detected with coronary angiography in 23 of the 25 patients. Coronary abnormalities were seen in the other two patients (8%).

One of the two patients with coronary abnormalities (patient 20), who had undergone ASO, ventricular septal defect closure, and aortic arch enlargement, developed severe aortic insufficiency after the operation, and one year later he was reoperated on for aortic valve replacement. During the operation the left circumflex coronary artery was transected and a bypass was constructed with the left internal mammary artery. During the angiographic study the left subclavian artery was obstructed and the bypass was occluded. The other patient (patient 24) had simple TGA and type 2 coronary arterial anatomy. The two coronary arteries originated from the right posterior sinus and the left coronary artery had an intramural³ course between the aorta and the pulmonary trunk. For this reason a tunnel was made between the great vessels, instead of the coronary reimplantation. In this patient the coronary angiography showed occlusion of the left coronary artery. In both patients there were large collateral vessels arising from the right coronary artery.

During angiography complications occurred in only one patient (patient 9), in whom a ventricular tachycardia requiring direct current shock developed after the injection of

Table 1 Patient characteristics and test results

Patient	Age (months)	Weight (kg)	Coronary anatomy	Basal ECG	Pacing rate (beats/min)	TAPSE ECG	Basal WM	TAPSE WM	Basal BP (mm Hg)	Post-pacing BP (mm Hg)	Rate pressure product		Coronary stenosis
											Baseline	End of study	
1	20	10	3	N	200	N	ABN	N	99/53	91/52	13000	18200	No
2*	18	12	1	N	200	N	N	N	91/52	114/62	11800	22800	No
3	12	10	3	N	200	N	ABN	N	74/44	79/52	8880	15800	No
4	15	10	3	N	200	N	ABN	N	90/41	72/50	10800	14400	No
5*	18	13	1	N	200	N	N	N	119/61	83/50	17850	16600	No
6*†	36	15	1	RBBB	200	N	ABN	N	120/55	105/60	14400	21000	No
7	19	12	1	RVCD	200	N	N	N	85/45	95/60	10200	19000	No
8*	44	18	1	N	200	N	N	N	103/65	83/62	12360	16600	No
9*	62	12	3	RBBB	170	N	N	N	102/63	62/42	12240	10540	No
10	35	13	1	N	200	N	ABN	N	75/50	70/50	11250	14000	No
11	35	13	1	N	200	N	ABN	N	115/55	143/73	18400	28600	No
12	43	14	1	RVCD	200	N	N	N	83/49	65/49	9960	13000	No
13	17	12	3	N	200	ABN	N	ABN	86/47	40/16	9804	8000	No
14	18	13	1	N	200	N	N	N	100/50	85/58	10320	17000	No
15	20	12	1	N	200	N	N	N	92/53	73/58	13000	14600	No
16*	13	10	3	RBBB	200	N	N	N	97/43	90/44	11960	18000	No
17	18	9	3	N	200	N	N	N	87/44	76/50	11640	15200	No
18	47	14	1	N	170	ABN	ABN	N	94/54	92/57	10440	15640	No
19*†	87	23	1	N	200	N	ABN	N	100/46	85/54	8200	17000	No
20*†	13	5	3	N	200	ABN	ABN	ABN	86/45	83/56	11610	16600	Yes
21	12	10	3	N	200	N	N	N	100/60	90/50	13500	18000	N
22	19	12	1	N	200	N	ABN	N	95/51	68/53	12160	13600	N
23*	24	11	3	RBBB	200	N	N	N	105/45	85/50	12390	17000	N
24	63	20	2	N	170	ABN	ABN	ABN	105/50	90/61	10710	15300	Yes
25*	17	17	1	N	200	N	N	N	85/51	81/55	9520	16200	N

*Ventricular septal defect closure.

†Aortoplasty for coarctation.

ABN, abnormal; BP, blood pressure; N, normal; RBBB, right bundle branch block; RVCD, right ventricular conduction delay; TAPSE, transoesophageal atrial pacing stress echocardiography; WM, wall motion.

contrast medium into the right coronary artery. Angiographic study showed normal coronary arteries and mild hypoplasia of the transverse aortic arch.

Diagnostic accuracy and predictive value

Compared with coronary angiography, the sensitivity and specificity were 100% and 95%, respectively, for the echocardiographic stress test, and 100% and 91%, respectively, for the electrocardiographic stress test. The negative predictive value was 100% for both the echocardiographic and the electrocardiographic stress tests. The positive predictive value was 66% for the echocardiographic stress test and 50% for the electrocardiographic stress test.

Table 1 summarises the clinical data. Tables 2 and 3 summarise the diagnostic accuracy and predictive value of TAPSE.

Table 2 Negative and positive results in the three diagnostic procedures

	Negative	Positive
TAPSE ECG	21	4
TAPSE WM	22	3
Coronary angiography	23	2

Table 3 Sensitivity, specificity, and negative and positive predictive values of the TAPSE procedures

	Sensitivity (%)	Specificity (%)	Negative predictive value (%)	Positive predictive value (%)
TAPSE ECG	100	91	100	50
TAPSE WM	100	95	100	66

DISCUSSION

Although ASO has become the treatment of choice for neonates with TGA, concerns remain about the fate of the coronary arteries. Coronary artery anomalies occur in 3–18% of patients and are the most important cause of morbidity and mortality after ASO.^{4,5} Although almost all of the deaths occur during the first year after ASO, the risk remains up to several years after the operation^{4,6} and may even increase with age because of atherosclerotic changes of the coronary arteries. Hence, the adequacy of the coronary circulation after ASO needs to be evaluated early and serially. For this purpose, the techniques currently used have some drawbacks.

Coronary angiography is invasive and has risks of vascular injury and bleeding, especially in very young children.⁷ Moreover, previous studies have shown that aortic root angiograms may ignore some peculiar coronary obstructions and that a detailed coronary anatomy can be obtained only by selective injections. However, sometimes one or both coronary ostia cannot be cannulated for selective coronary angiography.^{5,8} Indeed, anatomical disease does not necessarily mean functional disease, considering the potential supplying role of the collateral vessels. Thus, coronary angiography alone cannot allow an exhaustive evaluation of the coronary perfusion. In paediatric patients nuclear myocardial scintigraphy is of limited usefulness because of its applicability to the patient and radiation exposure. Furthermore, myocardial perfusion scan abnormalities at rest or with exercise or pharmacological stress have been commonly found after ASO. Most of these defects do not appear to be associated with symptoms, rest, or exercise electrocardiographic or echocardiographic signs of ischaemia, and they tend to be stable or improve with exercise. Their clinical significance is questionable and it was thought that they may be related to small myocardial infarctions, perhaps due to microemboli during the cardiopulmonary bypass procedure rather than to areas at ongoing risk for myocardial ischaemia. Whatever their origin, it is well established that in patients undergoing ASO myocardial scintigraphy may be biased by these features.^{2,8–10} Recently, promising results have been reported with the use of positron

emission tomography; however, this technique needs to be further evaluated and in any case appears to be of even more limited applicability in routine use than myocardial scintigraphy.^{11–13}

Exercise stress testing is another non-invasive technique used to evaluate coronary perfusion in patients undergoing ASO. However, ECG evidence of ischaemia has been reported in patients with normal coronary artery angiography, and in this group of patients the significance of the exercise ECG anomalies is still not clear.⁸ Furthermore, it is known that the diagnostic accuracy of the exercise stress test is greatly diminished in patients who achieve only submaximal exercise. Although in the study reported by Massin and colleagues¹⁴ all the patients reached heart rates > 180 beats/min, Mahle and associates¹⁵ found significant chronotropic impairment in 32% of their patients, and Bonnet and colleagues⁸ judged that more than 10% of their tests were not suitable for interpretation because of a poor increase in heart rate. Nevertheless, as stated above, almost all of the deaths related to coronary complications occur in the first year after ASO; hence, exercise stress testing appears to be ruled out for early risk stratification. Pharmacological stress echocardiography is a valuable alternative to exercise stress testing. Dobutamine is the pharmacological agent most used in paediatric patients. Dobutamine stress echocardiography (DSE) has been shown to be clinically useful in children with suspected myocardial ischaemia. Compared with coronary angiography, DSE sensitivity and specificity range from 72–90% and from 80–100%, respectively. No deaths have been reported but side effects, mostly hypertension, headache, and arrhythmias, occur in 11–20% of patients, sometimes requiring test termination or drug administration. Furthermore, the target heart rate is not always attained in 50–89% of cases, with or without atropine addition, and the optimal dose of dobutamine infusion is uncertain.^{16–19}

In adults TAPSE has been shown to be a well established method of passive stress testing. The diagnostic accuracy of ECG changes during atrial pacing is quite good and it compares favourably with that of exercise testing, with reported values of sensitivity and specificity of 94% and 83%, respectively.^{20–21} The accuracy of TAPSE rises significantly when it is combined with TTE. Reported sensitivities and specificities for the detection of ischaemia induced wall motion abnormalities of TAPSE range from 87–91% and 84–100%, respectively.²² Side effects occur rarely and usually are of no clinical relevance—the most frequently reported is chest discomfort related to muscular stimulation. The major limitations to this technique occurring in adults are a low Wenckebach rate, poor acoustic window, and oesophageal disease, but they are rarely encountered in children. Despite these good clinical results TAPSE has been evaluated in only limited cases in paediatric patients.²³

Present study

In the present study TAPSE was feasible and safe in all patients. Since we routinely perform all our cardiac catheterisations under general anaesthesia, all our patients were intubated and ventilated at the time of TAPSE. However, TAPSE alone can be performed under light sedation, like the vast majority of transoesophageal electrophysiological studies in paediatric patients.

The echocardiographic images were of good quality in all the patients, the target heart rate was attained in most of them, and no children developed side effects of clinical relevance or required drugs to be administered. Although TAPSE has the disadvantage of increasing myocardial oxygen demand by increasing only the heart rate, the diagnostic accuracy was good, with similar sensitivity, specificity, and negative predictive value for the stress ECG and for the stress echocardiography. These values were higher than those of DSE

in children. This is quite surprising, considering that during DSE both heart rate and cardiac output increase. A possible explanation is that in the studies reported on DSE the target heart rate chosen was lower than the one we chose (75–85% of the maximal heart rate versus 200 beats/min) and that it was attained in fewer cases. Recently, a study comparing TAPSE with DSE in adults obtained good agreement of the two techniques in their assessment of wall motion abnormalities and showed that target heart rate was more frequently achieved with TAPSE.²⁴ The most relevant results of our study were the high sensitivity and negative predictive value of TAPSE. Patients undergoing ASO with normal TAPSE seem to have a low likelihood of coronary abnormalities and, as a practical implication, we believe that they may not require coronary angiography. Otherwise, patients with an abnormal TAPSE should undergo an invasive study.

Study limitations

One limitation of the study was the use of coronary angiography as the reference standard for comparison of the TAPSE results. As shown by Hauser and colleagues,¹³ in patients undergoing ASO coronary perfusion can be reduced, despite normal coronary angiograms. It has been hypothesised that altered endothelial function or coronary vasoreactivity and failure of the coronary arteries to grow affect coronary perfusion in patients with normal coronary angiograms. Whatever the mechanism, the true accuracy of a non-invasive test such as TAPSE as a marker of reduced coronary perfusion using coronary arteriography as the yardstick remains to be established in these patients.

Another limitation is the lack of a normal control group. However, in our mind, the necessity for a control group was questionable since the technique has already been validated in adult patients. Furthermore, in our opinion, in normal children it would be very difficult to justify use of TAPSE and a coronary angiography in those with a positive test.

Conclusions

Our study showed that TAPSE is safe and feasible in children. In patients undergoing ASO it appears to be a valuable non-invasive means of evaluating coronary perfusion. Therefore, it can be regarded as an alternative screening method for follow up of these patients. Patients with a normal test may have a low likelihood of major coronary artery complications and may not need an invasive evaluation, while patients with an abnormal test should undergo coronary angiography or nuclear tomography. Because of the small number of patients investigated in the present study and the limited experience with TAPSE in children, further research will be necessary to confirm our data.

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