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A New Echocardiographic Approach in Assessing Pulmonary Vascular Bed in Patients with Congenital Heart Disease: Pulmonary Artery Stiffness

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Abstract
Objective: The state of pulmonary vascular bed in congenital heart disease is the predictor of the patients' clinical condition, prognosis and outcome of surgical intervention.This study aims to investigate the condition of pulmonary vascular bed analysing pulmonary artery stiffness by means of Doppler echocardiography.
Method: Thirty-three patients (16 females, mean age 26±15 years) with various congenital heart diseases such as atrial septal defect (20 patients), ventricular septal defect (10 patients), patent ductus arteriosus (2 patients), atrioventricular septal defect (1 patient) were enrolled in this study. Systemic flow (Qs), pulmonary flow (Qp), systemic vascular resistance, pulmonary vascular resistance were calculated according to Fick method by using data obtained during left and right heart catheterization. Echocardiographically, pulmonary artery stiffness (PAS) was calculated by using maximal frequency shift (MFS) and accelleration time (AcT) of the pulmonary artery flow trace. PAS (kHz/sec)= MFS/AcT.
Results: Invasively, the average Qp/Qs ratio, mean pulmonary artery pressure, and pulmonary vascular resistance were found as 2.58 ± 1.25, 25±20 mmHg, and 135±217 dyn.sec.cm-5, respectively. Echocardiographically, PAS was found to be 33±17 kHz/sec. Pulmonary artery stiffness was correlated with mean pulmonary artery pressure (r=0.63; p<0.001) and pulmonary vascular resistance (r=0.55, p<0.001), while no relation was found with Qp/Qs.
Conclusion: Estimation of pulmonary artery stiffness by using pulmonary flow maximal frequency shift and acceleration time obtained by means of Doppler echocardiography may give us an idea about the state of pulmonary vascular bed.
Key words: Pulmonary artery stiffness, pulmonary vascular bed *(Anadolu Kardiyol Derg, 2003; 3: 92-97)*

Introduction

In congenital left to right shunts, large pulmonary flow can produce a reactive hyperplasia in the arteriolar wall and anatomic reduction of the vascular bed (1). The state of pulmonary vascular bed in congenital heart disease is the predictor of the patients clinical condition, prognosis and outcome of surgical intervention (2). The reduction of pulmonary vascular bed ,which increases pulmonary vascular resistance (PVR), may result in progressive pulmonary hypertension (1). In other words, measuring PVR and pulmonary artery pressure (PAP) can give us an idea about the state of pulmonary vascular bed.

Although PVR can be assessed only invasively, it is possible to measure PAP both invasively and noninvasively. Doppler echocardiography allows estimation of PAP by measuring tricuspid regurgitation velocity (3), pulmonary regurgitation velocity (4) and

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right ventricular outflow tract flow acceleration time (5). Despite a good correlation between mean PAP and pulmonary artery acceleration (AcT), significant errors in noninvasive estimation of mean PAP using pulmonary AcT by Doppler echocardiography are still existed (6-8). Especially, these errors were evident in patients with mild pulmonary hypertension (8). Besides, all these methods depend on estimation and it may be impossible to measure PAP in patients without pulmonary or tricuspid regurgitation. Because of these obstacles, in order to understand the state of pulmonary vascular bed, it is necessary to develop new noninvasive methods.

Recent studies have indicated that systemic arterial pulse pressure, which is a parameter of aortic stiffness, is an important determinant of cardiovascular mortality and morbidity (9-11). In the same way, pulmonary artery stiffness (PAS) may be able to demonstrate the state of pulmonary vascular bed in patients with left to right shunt responsible for an increase in pulmonary artery flow. Several studies found a correlation between pulmonary artery elasticity and PAP, and indicated that PAS parameters can be used in determination of pulmonary hypertension (12, 13). Most of the studies concerning PAS have been performed invasively (12-15) and using invasive methods made it impossible to use this new parameter in clinical application. Studies using echocardiography to calculate PAS measured right pulmonary artery dimensions (16, 17). However, the change of the diameter of pulmonary artery during cardiac cycle may lead to an error of diameter measurement, (18) and this measurement is too cumbersome to justify its routine use for the evaluation of PAS. It may be impossible in some patients to visualize right pulmonary artery from the suprasternal window, and using transesophageal echocardiography is not convenient for clinical application. Decreased pulmonary artery distensibility abbreviates the duration of right ventricular-pulmonary artery systolic ejection time (19). In other words, an abbreviation in acceleration time of the pulmonary flow trace occurs. Taking into account this fact, it appears to be possible to apply a different method, which was used in determining aortic stiffness (20), in calculating PAS with a formulae associated with acceleration time.

This study aims to investigate pulmonary artery stiffness by means of a new Doppler echocardiographic method which is introduced for the first time to calculate pulmonary artery distensibility and to correlate its results with the invasively measured PVR and mean PAP.

Material and Methods

Patients: Thirty-three patients (16 females, mean age 26±15 years) with various congenital heart diseases such as atrial septal defect (20 patients), ventricular septal defect (10 patients), patent ductus arteriosus (2 patients), atrioventricular septal defect (1 patient) were enrolled in this study. Conditions which could influence pulmonary artery Doppler flow like pulmonary stenosis, pulmonary artery aneurysm, poor echocardiographic visualisation, rhythm disturbances were the exclusion criteria of this study.

Echocardiographic Study: Transthoracic echocardiography was performed by one of the authors, who did not have any information on the patients' clinical data, using a Hewlett-Packard Sonos 1500 instrument (Hewlett-Packard, Andover, Mass.) with a 2.5 MHz phased-array transducer. Recordings were taken from patients positioned in the left lateral decubitus position. The M-mode traces were recorded at a speed of 50 mm/sec. Simultaneous electrocardiographic recordings were also taken. Measurements of the left and right ventricle diameters, left ventricular ejection fraction, left and right atrium systolic diameter and pulmonary artery diameter were obtained according to established standards (21).

Doppler Study: The echocardiographic device states were adjusted so that maximal frequency shift can be obtained, and all Doppler signals were recorded at a speed of 100 mm/sec. The Doppler frequency shift, acceleration time, maximal flow velocity, velocity time integral were measured from the Doppler flow trace obtained from the parasternal short axis view using pulsed Doppler ultrasound with the sample volume placed in the pulmonary artery just 1cm distal to the pulmonary valve annulus. To prevent possible influence of respiratory and cardiac cycle on measurements, the average of 7 consecutive Doppler flow traces was calculated for each parameter (22). The ratio of peak systolic frequency shift to acceleration time give us pulmonary artery stiffness (Figure 1).

Pulmonary artery stiffness (PAS) (kHz/sec)= maximal frequency shift of pulmonary flow (MFS)/acceleration time (AcT).

Catheterization: After echocardiography, pati-

ents were transferred to the angiography laboratory within 30 minutes, and right and left heart catheterization was performed. Echocardiography and catheterization procedures were performed, and interpreted by two different observers who had no information on other procedure results. Mean PAP was found using data obtained from right heart catheterization. Based on the Fick method, data obtained from right and left heart catheterization were used to calculate systemic flow (Qs), pulmonary flow (Qp), systemic vascular resistance (SVR) and pulmonary vascular resistance (PVR).

Statistical Analysis: Data values were expressed as mean ± SD. The relationship between pulmonary artery stiffness and other variables was assessed according to Pearson's linear regression analysis. The Bland-Altman and simple linear regression analyses were used for the assessment of interobserver reproducibility. All statistical analyses were performed using a computer software package with SSPS modality. A p value of less than 0.05 was considered as statistically significant.

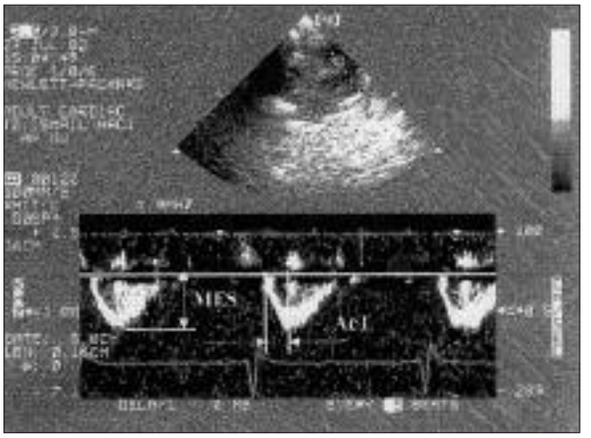

Figure 1: The ratio of maximal systolic frequency shift (MFS) to acceleration time (AcT) give us pulmonary artery stiffness (PAS).

Results

Each patients' diagnosis, Qp/Qs, PVR, mean PAP and PAS values are given in Table 1. The left ventricular diastolic diameter, right ventricular diastolic diameter, and pulmonary artery diameter were found as 41±9 mm, 42±12 mm, and 25±6 mm, respectively (Table 2). Echocardiographic PAS was calculated as 33±17 kHz/sec. There was no statistically significant difference between the heart rates during echocardiographic examination (86±16 beat/min) and during the catheterization procedure (90±17 beat/min) (p=0.15). Invasively measured mean Qp/Qs, mean PAP and PVR were as follows: 2.58±1.25, 25±20 mmHg, and 135±217 dyn.sec.cm-5, respectively. PAS was correlated with mean PAP (r=0.63, p<0.001; Fig. 2) and pulmonary vascular resistance (r=0.55, p<0.001; Fig. 3), while no relationship was found with Qp/Qs.

Reproducibility: Interobserver reproducibility was assessed on videotape recordings in 15 randomly selected patients. The Bland-Altman and simple linear regression analysis were used for the agreement. The agreement between two different observers was good for measuring of both maximal frequency shift (for correlation r=0.97, p<0.001; for comparing mean difference =-0.034±0.098 kHz, SEE=0.025 kHz, p=0.22) and acceleration time (for

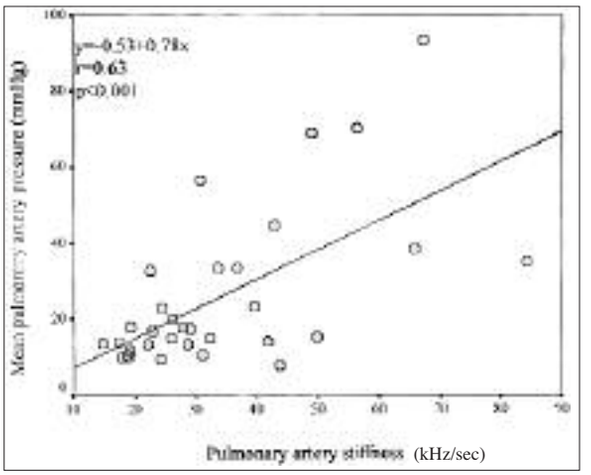

Figure 2: The relationship between pulmonary artery stiffness and mean pulmonary artery pressure.

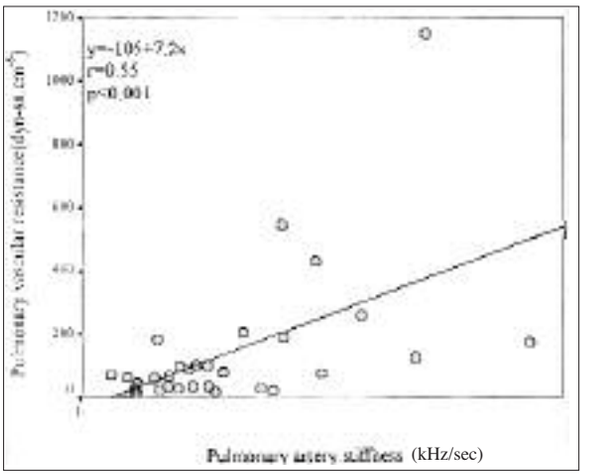

Figure 3: The relationship between pulmonary artery stiffness and pulmonary vascular resistance.

correlation r=0.97, p<0.001; for comparing mean difference =-4.1±8.3 msn, SEE=2.1 msn, p=0.08).

Discussion

In the present study, based on our new parameter,which was used in determining aortic stiffness, we found that PAS was correlated with mean PAP and pulmonary vascular resistance, while no relationship was found with Qp/Qs ratio. As compared to invasive methods, this method (20) allows PAS to be determined by echocardiographic parameters and makes easier its clinical use. Moreover, pulmonary artery flow can be readily obtained by pulse wave Doppler in almost all patients.

Both invasive and noninvasive studies have reported an association among PAS, mean PAP and PVR (12-16). Furthermore, Zuckerman et al. (13) demonst-

Table1: Patients' Qp/Qs ratio, PVR, mean PAP and PAS values

No	Initials	Diagnosis	Qp/Qs	PVR	Mean PAP	PAS
1	YB	ASD	2.37	17,00	15.00	32.16
2	GA	ASD	3.66	183.00	32.67	22.50
3	ZK	ASD	1.16	98.00	20.00	26.17
4	EE	ASD	3.27	35.00	10.67	31.03
5	AE	VSD	4.81	259.00	70.00	56.43
6	FG	ASD	3.45	30.00	23.33	39.76
7	SB	ASD	3.00	71.00	23.00	24.46
8	BÇ	VSD	3.64	22.58	14.00	41.85
9	AK	AVSD	4.00	103.00	56.67	30.78
10	NA	ASD	2.90	21.00	12.00	18.95
11	EC	VSD	1.86	13.00	10.00	18.75
12	FK	ASD	1.30	80.00	33.33	33.55
13	AK	ASD	1.00	12.00	10.00	17.78
14	EG	ASD	2.00	124.00	38.33	65.60
15	OA	VSD	1.00	546.00	44.67	43.08
16	AC	PDA	3.20	74.00	13.67	14.79
17	Eİ	ASD	1.10	33.00	10.67	18.73
18	SK	ASD	3.70	30.00	15.00	25.88
19	ST	ASD	2.10	207.00	33.33	36.94
20	CT	VSD	1.20	49.00	11.33	19.21
21	KA	ASD	2.86	173.00	35.00	84.31
22	AE	ASD	2.70	36.00	13.33	28.55
23	HŞ	VSD	2.25	429.00	68.67	48.91
24	AT	VSD	1.53	62.00	13.33	22.00
25	OC	ASD	3.20	15.00	18.00	19.23
26	MTA	ASD	5.40	27.00	16.67	22.89
27	AK	PDA	2.90	65.00	14.00	17.33
28	EA	ASD	1.90	191.00	8.00	43.75
29	DK	VSD	5.50	78.00	15.33	49.89
30	AS	ASD	1.80	101.00	17.33	29.05
31	HC	VSD	0.9	1148.00	93.33	67.14
32	ZK	ASD	1.50	35.00	9.33	24.26
33	SH	VSD	2.00	90.00	17.67	27.78

Abbreviations; ASD; atrial septal defect, AVSD; atrioventricular septal defect, PAP; pulmonary artery pressure (mmHg), PAS; pulmonary artery stiffness (kHz/sec), PDA; patent ductus arteriosus, PVR; pulmonary vascular resistance (dyn.sec.cm-5), VSD; ventricular septal defect

Table 2: Demographic, echocardiographic and catheterization findings of the study patients.

Demographic Findings		**Echocardiographic Findings**	
Age (year)	26±15	Heart rate (beat/min)	86±16
Female (number)	16	LVDD (mm)	41±10
BSA (m2)	1.45±0.32	LVSD (mm)	26±8
Catheterization Findings		EF (%)	66±9
Heart rate (beat/min)	90±17	RVDD (mm)	42±12
Qp/Qs	2.58±1.25	PAD (mm)	25±60
Mean PAP (mmHg)	25±20	Pulmonary artery MFS (kHz)	3.27±0.75
PVR (dyn.sec.cm-5)	135±217	Pulmonary artery AcT (msn)	111±33
		PAS (kHz/sn)	33±17

Abbreviations; BSA; body surface area, LVDD; left ventricular diastolic diameter, LVDS; left ventricular systolic diameter, EF; ejection fraction, RVDD; right ventricular diastolic diameter, PAD; pulmonary artery diameter, PAP; pulmonary artery pressure, PVR; pulmonary vascular resistance, MFS; maximal frequency shift, AcT; acceleration time, PAS; pulmonary artery stiffness

rated that pulmonary artery elasticity was related mainly to mean PAP, and pulmonary artery wall thickening without PAP increase had no influence on PAS. Although Graettinger et al. (6) and Pasiersky et al. (17) failed to estimate mean PAP by using AcT as accurate as they measured invasively, they observed that the AcT/pulmonary ejection time ratio was correlated with invasively measured mean PAP and PVR. In regard to the fact that decreased pulmonary artery distensibility abbreviates the duration of right ventricular-pulmonary artery systolic ejection time (19) and the above mentioned relationships, we sought for the first time to calculate pulmonary artery distensibility by means of a method, which was used in determining of aortic stiffness (20) and to correlate its results with the invasively measured PVR and mean PAP. Our study showed that PAS was related to mean PAP and PVR, and these results were also in accordance with previosly reported (12-15). In other words, it seems to be posibble to evaluate the pulmonary vascular state using PAS obtained by Doppler echocardiography.

Chronic pulmonary hypertension is characterized by muscularization of pulmonary arterioles and deposition of excess matrix proteins in the walls of large pulmonary arteries (23). This thickening in pulmonary arterioles increases PVR and finally results in pulmonary artery hypertension. In addition, excess of collagen in hypertensive pulmonary artery may explain the reason for increased pulmonary artery stiffness in pulmonary hypertension (24). From a different point of view, all these mean that PAS may be related directly to the pulmonary vascular bed state as well as may show the reduction of pulmonary vascular bed via its association with PVR and mean PAP increase as it was demonstrated in our study.

Stiffening of large pulmonary arteries may be important in pulmonary hypertension because changes in pulmonary artery elasticity contribute to the increase in oscillatory load which increases right ventricular systolic pressure (13). In addition, pulmonary artery stiffening increases pulsatility in the pulmonary circulation (25) possibly contributing to vascular damage at more distal sites. As it was indicated in the present study, there is a need to apply PAS to clinical use, because its relation with PVR and mean PAP. By using the introduced stiffness parameter in clinical practice, it may be possible to have an idea about pulmonary vascular bed state. From this perspective, the stiffness parameter used in our study may be important for other prospective studies. More important, large scale studies using our method, which seems to be possible to use in clinical practice, are needed to obtain cut off points for echocardiographic PAS matching with invasively measured PVR and mean PAP.

In conclusion, calculation of pulmonary artery stiffness by using pulmonary flow maximal frequency shift and acceleration time obtained by means of Doppler echocardiography may give us an idea about the state of pulmonary vascular bed.

References

1. Mcgoonn MD, Fuster V, Freeman WK, Edwards WD, Scott JP. Pulmonary hypertension. In: Giulia ER, editor. Mayo Clinic Practice of Cardiology. St Louis; Mosby; 1996. p.1815.
2. Steele PM, Fuster V, Cohen M, et al. Isolated atrial septal defect with pulmonary vascular obstructive disease-long-term follow-up and prediction of outcome after surgical correction. Circulation 1987; 76:1037-42.

3. Yock PG, Popp RL. Noninvasive estimation of right ventricular systolic pressure by Doppler ultrasound in patients with tricuspid regurgitation. Circulation 1984;70:657-62.
4. Masuyama T, Kodoma K, Kitabatake A, Sato H, Nanto S, Inoue M. Continuous-wave Doppler echocardiographic detection of pulmonary regurgitation and its application to noninvasive estimation of pulmonary artery pressure. Circulation 1986;74:484-92.
5. Mahan G, Dabestani A, Gardin J, Allfie A, Burn C, Henry W. Estimation of pulmonary artery pressure by pulsed Doppler echocardiography. Circulation 1983; 68(Suppl 3): 367.
6. Graettinger WF, Greene ER, Voyles WF. Doppler predictions of pulmonary artery pressure, flow and resistance in adults. Am Heart J 1987;113:1426-37.
7. Chan KL, Currie PJ, Seward JB, Hagler DJ, Mair DD, Tajik AJ. Comparison of three Doppler ultrasound methods in the prediction of pulmonary artery pressure. J Am Coll Cardiol 1987;9:549-55.
8. Torbicki A, Skwarski K, Hawrylkiewicz I, Pasierski T, Miskiewicz Z, Zielinsky J. Attempts at measuring pulmonary arterial pressure by means of Doppler echocardiography. Eur Respir J 1989;2:856-60.
9. Benetos A, Safar M, Rudnichi A et al. Pulse pressure: a predictor of long term cardiovascular mortality in a French male population. Hypertension 1997;30:1410-5.
10. Franklin S, Gustin W, Wong N et al. Hemodynamic patterns of age-related changes in blood pressure. The Framingham heart study. Circulation 1997;96:308-15.
11. Arnett DK, Evans GW, Riley WA. Arterial Stiffness a new cardiovascular risk factor. Am J Epidemiol 1994; 140: 669-82.
12. Jarmakani JMM, Graham TO, Benson DW, Canent RV, Greenfield JC. In vivo pressure radius relationship of the pulmonary artery in children with congenital disease. Circulation 1971:43:585-92.
13. Zuckerman BD, Orton EC, Stenman KR, et al. Alterations of the pulsatile load in the high-altitude calf model of pulmonary hypertension. J Appl Physiol 1991;70:859-68.
14. Slife DM, Latham RD, Sıpkema P, Westerhoff N. Pulmonary arterial compliance at rest and exercise in normal humans. Am J Physiol 1990;258:H1823-8.
15. Segers P, Brimioulle S, Stergiopulos N et al. Pulmonary arterial compliance in dogs and pigs: the three-element windkessel model revisited. Am J Physiol 1999;277:H 725-31.
16. Hopkins WE, Feinberg MS, Barzilai B. Automated determination of pulmonary artery pulsatility during transesophageal echocardiography. Am J Cardiol 1995;76:411-4.
17. Pasiersky TJ, Starling RC, Binkley PF, Pearson AC. Echocardiographic evaluation of pulmonary artery distensibility. Chest 1993;103:1080-3.
18. Harris P, Heath D, Apostolopoulos A. Extensibility of the pulmonary trunk in heart disease. Br Heart J 1965;27:660-6.
19. Murgo JP, Altobelli SA, Dorethy JF, Logsdon JF, McGranahan GM. Normal ventricular ejection dynamics in man during rest and exercise. Am Heart Assoc Monogr 1975;46:92-101.
20. Schieken RM, Moskowitz WB, Bodurtha J, Mosteller M, Eaves L, Nance W. Aortic stiffness: a new Doppler echocardiographic measure predictive of systolic blood pressure in children. J Am Coll Cardiol 1988;11:1297-300.
21. Sahn D, DeMaria A, Kisslo J, Weyman A. Recommendations regarding quantification in M-mode echocardiography: results of a survey of echocardiographic measurements. Circulation 1978; 58:1072-83.
22. Zoghbi WA, Habib GB, Quinones MA. Doppler assessment of right ventricular filling in a normal population. Comparison with left ventricular filling dynamics. Circulation 1990;82:1316-24.
23. Riley DJ. Vascular remodeling. In: Crystal RG, West JB, editors. The Lung: Scientific Foundations. New York: Raven Press; 1991. p. 1189-98.
24. Tozzi CA, Christiansen DL, Poiani GJ, Riley DJ. Excess collagen in hypertensive pulmonary arteries decreases vascular distensibility. Am J Respir Crit Care Med 1994; 149: 1317-26.
25. Milnor WR. Properties of the vascular wall. In: Milnor WR, editor. Hemodynamics. 2nd ed. Baltimore: Williams and Wilkins; 1989. p. 58-101.