Eur J Pediatr (1988) 147:279–282

European Journal of
Pediatrics

Sensitivity, specificity and predictive value of clinical findings, m-mode echocardiography and continuous-wave Doppler sonography in the diagnosis of symptomatic patent ductus arteriosus in preterm infants*

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Abstract. By means of probability analysis we have compared the diagnostic value of clinical symptoms, m-mode echocardiographic measurements and peripheral arterial flow, assessed by continuous-wave Doppler, in preterm infants with symptomatic patent ductus arteriosus (PDA). Data were obtained in 29 infants with PDA and in 29 controls. The most sensitive clinical finding was a hyperactive precordium. Bounding pulses and a heart murmur were absent in 15% and 20%, respectively of the patients with PDA. M-mode echocardiographic measurements were rather specific for the detection of a PDA but less sensitive. Diastolic backflow in the brachial and femoral arteries was present in the majority of patients with PDA and absent in about 67% of the controls. The values in probability analysis, however, were too low to base a therapy on these findings. The highest sensitivity and specificity (100% each) was found for a disturbed cerebral blood flow with absent or retrograde diastolic perfusion estimated by Doppler sonography.

Key words: Preterm infants – Patent ductus arteriosus – Echocardiography – Doppler sonography

Introduction

The contribution of a patent ductus arteriosus (PDA) to severe respiratory distress syndrome in preterm infants cannot be estimated entirely by clinical examination [1, 10, 20]. Echocardiography increases the diagnostic accuracy [4, 7]. By m-mode echocardiography alone, however, the diagnosis of symptomatic PDA is still poor, especially in infants treated by fluid restriction [20]. Continuous-wave Doppler (cw-Doppler) flow recordings of peripheral arteries were used to detect retrograde blood flow within the descending aorta in infants with PDA [16, 17] and the impaired cerebral perfusion by diastolic run-off into the pulmonary circulation [11, 15, 18].

The sensitivity, specificity and predictive value of cerebral blood flow measurements using cw-Doppler for the detection of a PDA have not been tested. In this study the diagnostic value of cw-Doppler was compared with that of conventional m-mode echocardiography and with different clinical findings.

Materials and methods

Patient population

Since May 1982 we have taken echocardiographic and peripheral artery cw-Doppler recordings in preterm infants with respiratory distress and artificial ventilation. To determine the diagnostic value of clinical findings, m-mode echocardiography and cw-Doppler sonography we analysed the records of 29 infants with symptomatic PDA. The diagnosis was confirmed by angiography in 3, by postmortem examination in 4 and during the operation in 22 patients. The gestational age of the patients was between 25 and 36 weeks (median 29). Birth weights were between 470 and 2200 g (median 1030). The controls were 29 preterm infants without PDA. Eleven of them were patients of the PDA group after ligation of the ductus, 18 were spontaneously breathing preterm infants without any clinical signs of a PDA. The gestational age of the controls was between 25 and 36 weeks (median 29), and birth weight between 470 and 2100 g (median 1040). The age at echocardiographic and cw-Doppler examination was 2–44 days in the PDA-group (median 5 days) and 1–51 days in the controls (median 6 days).

Investigations

All patients were examined clinically by at least two independent paediatricians (neonatologists and cardiologists) with respect to precordial impulse, presence of a heart murmur and the quality of brachial and femoral pulses on palpation. Precordial impulse and peripheral pulse quality was graded into three groups: 0 = normal, 1 = suspicious, 2 = increased. Heart murmurs were graded as usual in 6/6. M-mode echocardiograms were recorded with an ECHO IV (Electronics for Med-

* Dedicated to Professor Dr. E. Kleihauer on the accasion of his 60th birthday

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Abbreviations: PDA = patent ductus arteriosus; cw-Doppler = continuous-wave Doppler; SF = shortening fraction; LPEP/LVET, RPEP/RVET = left and right ventricular systolic time intervals; R/F = retrograde/forward flow

icine) instrument at a paper speed of 100 mm/s and the following data were calculated from the strip charts: ratio of the left atrial/aortic root diameter (LA/AO), the left ventricular shortening fraction (SF) and left and right ventricular systolic time intervals (LPEP/LVET and RPEP/RVET). Aortograms were performed in three patients by contrast injection into the thoracic aorta through an umbilical artery catheter.

Analogue tracings of cw-Doppler flow measurements were recorded from the brachial arteries, the femoral arteries and the anterior cerebral arteries at a paper speed of 50 and 100 mm/s. We used an 8 MHz Sonicaid instrument (Kranzbuehler Germany) connected to the multitrace recorder of the ECHO IV. The electrocardiogram and the Doppler signal were recorded simultaneously. A flow index was calculated from these tracings by division of the area of the backflow by the antegrade flow area in the femoral and brachial arteries (R/F ratio)[17]. A pulsatility index of the cerebral flow was calculated [11, 13]. We could not obtain all the measurements in all patients. The number of measurements is shown in Tables 1 and 2.

Data analysis

Sensitivity, specificity, predictive value and predictive accuracy were assessed for the echocardiographic and Doppler sonographic criteria. For the clinical findings sensitivity alone was calculated. An overall incidence of congenital heart defects other than PDA in about 1% of live born neonates was not taken into account. Because of the restricted number of patients the results of probability testing were expressed together with their 95% confidence levels.

The following equations were used:

$$\text{sensitivity} = \frac{\text{true pos.}}{\text{true pos.} + \text{false neg.}}$$

$$\text{specificity} = \frac{\text{true neg.}}{\text{false pos.} + \text{true neg.}}$$

$$\text{predictive value} = \frac{\text{true pos.}}{\text{true pos.} + \text{false pos.}}$$

$$\text{predictive accuracy} = \frac{\text{true pos.} + \text{true neg.}}{\text{all tests}}$$

According to the National collaborative study on PDA in premature infants the following echocardiographic criteria were considered to be diagnostic for the presence of a PDA: LA/AO > 1.4; LPEP/LVET ≤ 0.27; SF > 42% [5].

An R/F index of > 0 in the femoral and brachial arteries representing diastolic backflow and a percentile flow index > 1 in the anterior cerebral arteries were taken as a criterion of symptomatic PDA.

Results

Clinical findings

The heart was hyperactive on palpation grade 1 or more in all but 1 and grade 2 in 16 of the patients. A cardiac murmur of grade 3/6 was present in 13.7% (4/29). A murmur of grade 2/6 or more was present in 72.4% (21/29) and of grade 1/6 and more in 79.3% (23/29). Six infants did not have any heart murmur. Peripheral pulses were considered as bounding grade 1 or more in 89.6% (26/29) and as grade 2 in 13/29 (44.8%).

Table 1. Echocardiographic findings

Group (number)	SF median range (number)	LA/AO median range (number)	LPEP/LVET median range (number)
PDA	40	1.45	0.28
	24–56	0.9–2.5	0.15–0.61
(29)	(20)	(26)	(22)
Control	22	1.0	0.35
	15–45	0.65–1.3	0.25–0.69
(29)	(22)	(28)	(28)

SF = left ventricular shortening fraction; LA/AO = ratio of the left atrial to aortic root diameter in m-mode echocardiography; LPEP/LVET = ratio of left ventricular preejection period to left ventricular ejection time assessed by m-mode echocardiography; PDA = patent ductus arteriosus

Table 2. Cw-Doppler sonographic measurements

Group (number)	Cf median range (number)	Ff(R/F) median range (number)	Bf(R/F) median range (number)
PDA	1.0	0.39	0.1
	1.0–1.2	0.0–2.0	0.0–2.8
(29)	(29)	(20)	(20)
Control	0.68	0.0	0.0
	0.58–0.86	0.0–0.84	0.0–0.67
(29)	(29)	(22)	(21)

Cw-Doppler sonographic measurements; Cf = cerebral arterial flow index; Ff(R/F) = femoral arterial flow index; Bf(R/F) = brachial arterial flow index; PDA = patent ductus arteriosus

M-mode echocardiography and Doppler investigations

The postoperative infants were the only patients in whom a PDA could definitely be excluded. Therefore the data obtained in this subgroup were first compared with those of the remaining patients in the control group. There was no statistical difference.

Echocardiographic findings are listed in Table 1 and Doppler measurements in Table 2.

Probability analysis

The most sensitive clinical sign was the increased precordial impulse that was palpable in 96.5% and even visible in most of them. A systolic or continuous systolic-diastolic murmur was missed in nearly 20% as was the finding of markedly increased peripheral pulses (grade 2) in 65.2%.

In m-mode echocardiography the enlargement of the left atrium (LA/AO > 1.4) turned out to be highly specific (100%) for a symptomatic PDA, sensitivity, however, was at 50%.

The presence of femoral or brachial artery backflow did not reach high enough values in probability testing to make

Table 3. Sensitivity of clinical findings in infants with PDA

Item		Sensitivity	95% Confid
Hyperact. precordium	Grade 1+2	96.5	82.2–99.9
	Grade 2	55.2	35.7–73.6
Bounding pulses	Grade 1+2	89.6	72.7–97.8
	Grade 2	44.8	26.5–64.3
Murmur	Grade 1–3/6	79.3	60.3–92.0
	Grade 2–3/6	72.4	52.8–87.2
	Grade 3/6	13.7	3.9–31.7

Hyperact. = hyperactive; 95% Confid = 95% confidence limits; PDA = patent ductus arteriosus

Table 4. Probability of m-mode echocardiographic items in the diagnosis of PDA

Item	Sens. (95% Conf.)	Spec. (95% Conf.)	Pred. val. (95% Conf.)	Pred. acc. (95% Conf.)
SF > 42%	50.0	86.4	76.9	69.1
	27.2–72.8	65.1–97.1	46.2–95.0	52.9–82.4
LA/AO > 1.4	50.0	100	100	75.9
	29.9–70.1	87.7–100	75.3–100	62.4–86.5
LPEP/ET ≤ 0.27	50.0	78.6	61.1	66.0
	28.2–71.8	59.1–91.7	35.8–82.7	51.2–78.8

Sens. = sensitivity; Spec. = specificity; Pred. val. = predictive value; Pred. acc. = predictive accuracy; 95% Conf. = 95% confidence limits; PDA = patent ductus arteriosus

Table 5. Probability of Cw-Doppler sonography in the diagnosis of PDA

Item	Sens. (95% Conf.)	Spec. (95% Conf.)	Pred. val. (95% Conf.)	Pred. acc. (95% Conf.)
Bf > 0	60.0	66.7	44.4	63.4
	36.1–88.9	43.0–85.4	25.5–64.7	46.9–77.9
Ff > 0	85.0	68.2	70.8	76.2
	56.3–94.3	45.1–86.1	48.9–87.4	60.6–88.0
Cf > 1	100.0	100.0	100.0	100.0
	88.1–100	88.1–100	88.1–100	93.8–100

Bf = brachial flow index; Cf = cerebral flow index; Ff = femoral flow index; 95% Conf. = 95% confidence limits; PDA = patent ductus arteriosus

the diagnosis of PDA on these findings. Absent or retrograde diastolic blood flow within the anterior cerebral arteries (flow index of 1.0 or above) reached the highest values in the tests.

The results of probability analysis are shown in Tables 3–5.

Discussion

In preterm infants presenting with a symptomatic PDA, diastolic regurgitation of blood from the descending aorta to the pulmonary artery occurs. This circulatory steal syndrome described by Spach and co-workers [19] is detectable using cw-Doppler ultrasonography [16]. There is a good correlation between the magnitude of ductal left to right shunt and the R/F ratio of Doppler flow in the descending aorta [17].Circulatory steal results in a decreased blood flow to the visceral organs and in the presence of a PDA cerebral perfusion is diminished by almost 20% in animal studies [3]. Pearlmann and co-workers showed that cerebral blood flow estimated by cw-Doppler is affected in neonates by various haemodynamic states and by the intracranial pressure [12]. The most severe alteration of the cerebral flow could be found in hydrocephalus [5] and in the presence of a PDA [11] independent of whether it is a patent ductus in preterm infants or a persistent ductus associated with other congenital cardiac defects [18]. Bada and co-workers described impaired cerebral flow in preterm infants with intraventricular haemorrhage [2], however their patients were not tested for the presence of a PDA.

Left or right shunt through a PDA leads to an increased left atrial and left ventricular volume load. Increased left atrial diameter (LA/AO ratio) as well as an increased shortening fraction of the left ventricle due to the Frank-Starling mechanism detected by m–mode echocardiography were considered to be diagnostic for a PDA in preterm infants [4]. Valdez-Cruz and Dudell have shown that the sensitivity of m-mode echocardiography is decreased when the infants are treated with fluid retriction [20]. Fluid restriction may also mask the clinical symptoms of a PDA [1, 10, 20].

The present study was designed to test the sensitivity, specificity, predictive value and predictive accuracy of clinical symptoms, echocardiographic measurements and cw-Doppler flow recordings in the detection of a symptomatic PDA in preterm infants. Symptomatic PDA was only diagnosed when the presence of ductal shunting could be shown to be responsible for a persistent or increasing need for ventilatory support. Most infants were so seriously ill that apart from the exceptions in whom aortograms were done, invasive studies were not performed. Therefore the diagnosis of a PDA had to be confirmed in the patients who did not have a typical heart murmur by the findings during operation or postmortem examination. Two-dimensional echocardiography or pulsed Doppler echocardiography for a direct visualization of the PDA or assessment of ductal blood flow velocity [6, 14, 21] were not available during the study period.

About 20% of the infants with PDA did not have a heart murmur and 10% lacked bounding peripheral pulses. The most sensitive clinical finding (96.5%) was a hyperactive precordium.

Our results show, that an increased LA/AO ratio is not mandatory in preterm infants with PDA, nor are increased SF and decreased LPEP/LVET ratios. This is in agreement with the findings of Valdes-Cruz and Dudell [20]. However, if an increased LA/AO ratio is found the diagnosis of a PDA can be made with great confidence (100%). Lundell and Wallgreen recently confirmed that there is a large overlap of LPEP/LVET ranges between preterm infants with and without PDA [9]. In our patients reduced LPEP/LVET was more specific than sensitive. The combination of an LA/AO > 1.4 with a LPEP/LVET ≤ 0.27 could be found in only 5 out of 21 of our patients with PDA in whom both measurements were available, representing a diagnostic sensitivity of 23%. This finding contrasts with that reported in the American national collaborative study on PDA [7].

The findings of disturbed cerebral arterial flow are the subject of recent reports [11, 13, 15, 18], but it has not yet been demonstrated that its diagnostic value is superior to m-mode echocardiography. Retrograde diastolic flow within the brachial and femoral arteries was present in most infants with a symptomatic PDA but was also present in 33% of the controls. Femoral and brachial arterial R/F ratios therefore should not be used in the diagnosis of a PDA [8]. Cerebral blood flow was abnormal in all of our patients with symptomatic PDA and normal in all of the controls. Hydrocephalus was excluded in our patients by two-dimensional sonography of the brain and in infants with intracranial haemorrhage there was no significant increase of intracranial pressure as assessed by palpation of the anterior fontanelle.

In respirator-dependent preterm infants with suspected PDA according to the above criteria, cw-Doppler recordings of blood flow in the anterior cerebral arteries should be performed. The diagnosis of a PDA may be based on the finding of absent or even retrograde diastolic flow (percentile index > 1) with a very high confidence (100%). This measurement is superior to m-mode echocardiography and it can be done within the incubator. We were not able to compare our findings with those of two-dimensional echocardiography and to pulsed Doppler sonography. The instruments for cw-Doppler are much cheaper than two-dimensional echocardiographic equipment. In addition the method is easy to learn and available in most hospitals.

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Received December 22, 1986/Accepted June 9, 1987