CURRENT TOPIC

Diagnosis of patent ductus arteriosus in the preterm newborn

Nick Evans

Persisting patency of the ductus arteriosus (PDA) remains an important complication for the very preterm infant undergoing intensive care. There are two separate, but related, issues with respect to the diagnosis of PDA in the preterm, firstly there is the diagnosis of the physical patency of the duct and secondly, and much more controversially, there is the assessment of the haemodynamic and clinical significance of the shunt through that patent duct. Eighty per cent of preterm infants with hyaline membrane disease will have a duct that is physically patent during the first four postnatal days,¹ however only about a third of these infants will develop shunts large enough to cause symptoms. This article will consider these two issues, initially reviewing the current status of clinical and echocardiographic diagnosis of physical patency and then looking at the available non-invasive methods for assessing the size of the shunt through the duct.

Clinical diagnosis

A hyperdynamic precordial impulse, full pulses, widened pulse pressure, hepatomegaly, and a high parasternal systolic murmur have been described as the classical physical signs of the PDA. These signs usually appear from about day 5 onwards and, together with evidence of interrupted improvement of or worsening respiratory status, have been established as the clinical criteria of haemodynamic significance.² The accuracy of these signs in diagnosing a PDA is not high; Kupferschmid *et al* compared clinical and echocardiographic findings in infants with symptomatic PDA and found that bounding pulses and a murmur were absent in, respectively, 15% and 20% of the patients.³ These authors suggested that the most sensitive diagnostic sign was a hyperdynamic precordium, present in 95%. In the early postnatal period these signs are even less sensitive, with silent ductal shunting being the norm until the latter half of the first postnatal week.⁴ Wide pulse pressure has also not stood up to critical analysis as a physical sign. Two studies have now compared pulse pressure in preterm infants with and without PDA,^{5 6} in both studies no difference was found during the first postnatal week. A PDA seems to be associated with a similar reduction in both systolic and diastolic pressure that in the smallest infants may produce significant hypotension.⁵ False positive clinical findings

also occur, not all murmurs in preterm infants are due to PDA, pulmonary stenosis or pulmonary flow murmurs being common reasons for misdiagnosis.

The electrocardiogram (ECG) is usually normal, particularly early on, though the presence of abnormalities on the ECG may suggest that the condition is not simply a PDA and that further cardiac investigation is indicated. The chest radiograph may show some cardiomegaly and pulmonary plethora, however the presence of parenchymal lung disease often makes interpretation of both cardiac size and pulmonary vascularity difficult; 22% of infants with a symptomatic PDA in a study by Higgins *et al* showed no increase in radiological heart size.⁷

Echocardiographic diagnosis

M mode and more recently Doppler and two dimensional echocardiography have given us a window on the ductus arteriosus that has allowed for more accurate diagnosis^{8 9} and also more detailed study of the natural history of ductal shunting.^{1 10 11} There are basically three categories of ultrasound method for the diagnosis of PDA.

The first are the M mode methods for assessing the degree of left sided cardiac overload. The ratio of the diameter of the left atrium to that of the aortic root (the LA:Ao ratio) is probably the most widely used of these methods. This ratio depends on the fact that left to right ductal shunting increases the volume load on the left side of the heart so the left atrium will dilate relative to the aortic root which will be unaffected by the volume load (fig 1). Published mean normal ratios vary between 0.86:1 and 1.3:1,^{12 13} and the ratio that is said to indicate the presence of a PDA varies between 1.15:1 and 1.4:1.^{12 13} Certainly using a cut off towards the upper end of this range will increase the specificity of this technique. Used in isolation the LA:Ao is not very specific. False positives can result from left to right shunting through a ventricular septal defect, any cause of left ventricular dysfunction,¹⁴ and mitral valve abnormalities. If the M mode beam transverses the atrium at an oblique angle, this will also increase the ratio. On the other hand false negatives have been described in infants who had large ductal shunts on clinical grounds and a normal LA:Ao. One study hypothesised that the

Department of
Perinatal Medicine,
King George V
Hospital,
Missenden Road,
Camperdown,
Sydney, NSW 2050,
Australia

Correspondence to:
Dr Evans.

Figure 1 This shows the M mode image from which the LA:Ao ratio is derived, the dotted line on the Duplex two dimensional image shows the position of the M mode beam through the aortic root. The Ao diameter is measured, at the end of diastole, between the anterior edges of the anterior and posterior aortic walls. The LA diameter is measured, at the end of systole, from the anterior edge of the posterior aortic wall to the endocardial surface of the posterior atrial wall. In this example the LA:Ao was 1.3:1 and the duct was closed.

atrium may be enlarging in a lateral rather than an anteroposterior direction,¹⁵ another that this may be a reflection of more severe fluid restriction.¹⁶ However the LA:Ao ratio remains a useful method because of its simplicity and it provides some index of the degree of left to right shunting, once the presence of the PDA has been confirmed by the other methods.

The second category of diagnostic method is the indirect use of pulsed Doppler. Pulsed Doppler analysis of flow in the main pulmonary artery allows demonstration of the characteristic diastolic turbulence associated with a PDA (fig 2). This method is both sensitive and quite specific.^{17 18} There are only two conditions that can mimic this flow pattern, aortopulmonary window and a coronary

artery fistula to the pulmonary artery, both are very rare. However, in isolation it does not give any assessment of the size of the duct or the shunt through it. Other authors have used Doppler assessment of descending aortic flow,¹⁹ looking for the reversed diastolic flow associated with a large ductal shunt. This method will pick up the largest and probably the clinically important ductal shunts, but it will not detect the small to moderate sized PDA which will not necessarily produce this pattern of flow.

The third and most accurate method of echocardiographic diagnosis is direct imaging of the duct with direct pulsed wave or colour flow Doppler analysis of the shunt.^{9 20} The duct can be imaged from the high left parasternal position with the beam cutting a true sagittal section through the body. If the operator angles the beam to the left through the long axis of the main pulmonary artery, the pulmonary end of the duct can be seen just superior to the root of the left pulmonary artery as it emerges posteroinferiorly (fig 3). If the pulsed Doppler sample is placed in the duct then the shunt pattern can be assessed. With colour Doppler, the flow through the PDA is seen as an orange jet streaming back up the anterior wall of the main pulmonary artery (fig 3). It is also possible to assess directly the ductal shunt with continuous wave Doppler, this allows analysis of a greater range of shunt velocities than pulsed wave Doppler. While assessment of the size of the lumen of the ductus arteriosus and the strength and direction of the Doppler signal from the shunt will give a qualitative measure of the size of the shunt, this method does not quantify the degree of shunting. This technique does require more echocardiographic expertise than the M mode or indirect Doppler methods. In the early postnatal days clear images of the whole length of the duct can be obtained, however towards the end of the first week imaging sometimes becomes more difficult, particularly when the infant is ventilated, as the left lung hyperinflates over the parasternal ultrasound windows.

A good approach to echocardiographic diagnosis is to start with direct imaging and Doppler, only if that is not possible then to use Doppler in the main pulmonary artery. Then, as an assessment of shunt size, to measure the LA:Ao ratio and the descending aortic flow pattern, with retrograde diastolic aortic flow and an LA:Ao >1.4 indicating a PDA likely to be of haemodynamic significance.

Diagnosis of the haemodynamically significant PDA

The fundamental problem that affects most studies of the PDA is how haemodynamic significance should be defined. Should it be defined by clinical criteria of when a PDA becomes symptomatic or should it be defined by echocardiographic criteria of the size of the shunt through the duct? Much of the work on this has involved applying echocardiography to infants who were felt to have symptomatic

Figure 2(A) Represents the normal pulsed Doppler flow pattern in the main pulmonary artery with minimal diastolic turbulence. (B) Shows the pattern of main pulmonary artery flow seen with a PDA with marked diastolic turbulence and a degree of systolic turbulence.

Figure 3 (A) Is the direct view of the PDA obtained from the high right parasternal window. A small PDA is seen running between the main pulmonary artery (MPA) and the descending aorta just superior to the root of the left pulmonary artery (LPA). (B) Is the same image with the colour flow Doppler mapping superimposed. The orange/red flow through the PDA is seen streaming up the anterior wall of the MPA whose forward flow is represented by the blue.

ducts and then defining echocardiographic criteria for haemodynamic significance from this.^{2 12 13 15}

If clinical criteria are used, which one accurately reflects the haemodynamic status of the PDA?³ The important symptoms of the PDA are respiratory and, because these infants almost always have associated acute and often chronic respiratory disease, there is scope for misinterpreting the influence of the duct on the respiratory status. In the early acute phase the clinical signs and influence of the PDA are usually not seen until the hyaline membrane disease starts to improve. Traditionally this has been interpreted as reflecting the increased left to right shunt through the duct resulting from falling pulmonary vascular resistance at this time. While this is certainly true, echocardiographic studies of ductal shunting in hyaline membrane disease have shown that even in the first three postnatal days that the usual direction of shunting is left to right¹ and that shunts that are going to later cause clinical symptoms are usually significant, by echocardiographic criteria, by 48 hours after delivery.^{11 21} The later chronic respiratory phase, in affected infants, is characterised by fluctuations in respiratory status and oxygenation, these fluctuations are seen whether the duct is patent or not though often these changes are ascribed to the duct when it is patent.

Of the accepted physical signs of PDA, the lack of sensitivity of full pulses, wide pulse pressure, and the murmur have been mentioned above. And while an hyperdynamic precordium is a sensitive sign when symptoms develop³ it has not been assessed as a method for early recognition of PDA. Likewise hepatomegaly is often found in the chronic respiratory phase; this can be caused by hyperinflated lungs and or elevated pulmonary artery pressures as well as ductal shunts. Thus while clinical symptoms and signs are clearly

important in the assessment of ductal status, they are open to misinterpretation and it is difficult to argue that they should be the 'gold standard' of haemodynamic significance.

In physiological terms the measure of haemodynamic significance is the size of the shunt relative to the baseline cardiac output. Accurate measurement of this requires cardiac catheterisation and is clearly not practical or ethical in preterm infants. So which echocardiographic criteria have the best correlation with these invasive measures? The M mode measures of left sided volume overload, that is left atrial diameter (LAD) and left ventricular end diastolic diameter (LVEDD), were the first to be studied in this field. Left atrial volume and left ventricular end diastolic volume, measured by angiographic techniques, have been correlated with ventricular septal defect and PDA shunt size.²² Left atrial diameter, measured echocardiographically, has been shown to correlate well with left atrial volume²³ and also with shunt size through ventricular septal defects.²⁴ Because cardiac catheterisation is rarely indicated in the preterm newborn, the available data is derived from the study of older subjects. When applied to the study of the newborn, both LAD and LVEDD were related to aortic root diameter to control for the range of body size.¹² In the newborn these measures have been shown to be increased in infants with symptomatic PDA^{12 13} and to fall promptly after ductal ligation.¹³ Direct correlation with invasive measures of shunt size has not been performed in the preterm. There do seem to be good reasons for suggesting that the relationship described in older subjects²⁴ holds for the neonatal period and, allowing for specificity problems mentioned earlier, these methods remain the simplest means, if not necessarily the most accurate, of assessing the degree of shunt through a duct.

Two methods of assessing shunt size have evolved from Doppler studies of flow in the descending aorta. One method involved pulsed Doppler assessment of flow volume in the aortic arch before and after the ductal insertion.²⁵ This method has not been validated and because Doppler flow assessments depend on an accurate peak velocity, it depends on being able to insonate at an angle of less than 20°, not always easy in the descending aorta. Despite these limitations these authors derived estimates of shunt size which were in line with what has been described using other methods. A simpler method was described by Serwer *et al* who showed in infants outside the neonatal period that there was a close correlation between the ratio of the velocity time integrals (that is the area under Doppler frequency shift/time curve) of the retrograde diastolic and systolic antegrade flow and the size of the shunt through a PDA measured by a radioisotope method.¹⁹ This method has two advantages, firstly it does not depend on the angle of insonation and secondly it has been validated against invasive measures of shunt size. If

there is diastolic retrograde flow in the descending aorta then it is highly likely that the shunt through the PDA is significant.

Non-invasive Doppler methods of assessing cardiac output have been well studied and validated in the newborn.^{26 27} The product of the Doppler velocity time integral from either ventricular outflow tract and the area of that outflow tract gives a good estimate of stroke volume. The product of stroke volume and the heart rate gives the cardiac output. Left to right shunting at ductal level produces an increased volume load to the left side of the heart and the left ventricle has to increase output to cope. In theory the left ventricular output minus the right ventricular output should be equal to the ductal shunt, but in practice this may not be completely accurate in the newborn because there is always a degree of incompetence of the foramen ovale and so a left to right atrial shunt. While this shunt is often more obvious in infants with PDA because of the left atrial dilatation, it has not been thought to be of great haemodynamic significance.²⁸ While it has been shown that there is an increase in left ventricular output in association with PDA in the preterm newborn which falls after duct closure, the degree of this increase has not yet been directly correlated with shunt size.²¹

When considering the relative merits of clinical and echocardiographic criteria of ductal patency we have to consider not only accuracy, but also the method which allows the earliest definition of the duct which is causing or will cause problems. Echocardiography is better on both these counts but particularly on the latter. Using M mode criteria or increasing left ventricular output measured by Doppler, it is possible by day 3 of life to predict the patent ducts which will later become symptomatic.^{11 21} Mellander *et al* showed that using M mode and Doppler diagnosis on day 3 of life, one could predict with 100% sensitivity and 85% specificity those PDAs that would later become symptomatic.¹¹ Similarly, Walther *et al* showed that an increase of left ventricular output of more than 60 ml/kg/min consistently preceded the development of symptomatology by at least 24 hours.²¹ This is not dissimilar to another area of cardiology, that of valvular stenosis, where the aim of echocardiography is to define haemodynamic significance so that clinical symptoms can be predicted and so avoided. It seems rational that our approach to PDA in the preterm infant should be the same; by the time clinical symptoms appear it may well be too late. This is speculative, and whether treatment of the patent duct on echocardiographic rather than clinical criteria will improve the outlook for preterm infants remains an open question that needs to be answered by a randomised controlled trial.

1 Evans NJ, Archer LNJ. Doppler assessment of pulmonary artery pressure and extrapulmonary shunting in the acute

- phase of hyaline membrane disease. *Arch Dis Child* 1991;66:6-11.
- 2 Gersony W, Peckham GL, Lang P, *et al*. Effects of indomethacin in premature infants with patent ductus arteriosus: results of a collaborative study. *J Pediatr* 1983;102:895-906.
- 3 Kupferschmid Ch, Lang D, Pohlandt F. 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. *Eur J Pediatr* 1988;147:279-82.
- 4 Hammerman C, Strates E, Valaitis S. The silent ductus: Its precursors and aftermath. *Pediatr Cardiol* 1986;7:121-7.
- 5 Evans NJ, Moorcraft J. Effect of patency of the ductus arteriosus on blood pressure in very preterm infants. *Arch Dis Child* 1992;67:1169-73.
- 6 Ratner I, Perclmuter B, Toews W, Whitfield J. Association of low systolic and diastolic blood pressure with significant patent ductus arteriosus in the very low birth weight infant. *Crit Care Med* 1985;13:497-500.
- 7 Higgins CB, Rausch J, Friedman WF, *et al*. Patent ductus arteriosus in preterm infants with idiopathic respiratory distress syndrome. *Radiology* 1977;124:189-95.
- 8 Huhta JC, Cohen M, Gutgesell HP. Patency of the ductus arteriosus in normal neonates: two dimensional echocardiography versus Doppler assessment. *J Am Coll Cardiol* 1984;4:561-4.
- 9 Vick GW, Huta Gutgesell HP. Assessment of the ductus arteriosus in preterm infants utilising suprasternal two dimensional/Doppler echocardiography. *J Am Coll Cardiol* 1985;5:973-7.
- 10 Evans NJ, Archer LNJ. Postnatal circulatory adaptation in healthy term and preterm newborns. *Arch Dis Child* 1990;65:24-6.
- 11 Mellander M, Larsson LE, Ekstrom-Jodal B, Sabel KG. Prediction of symptomatic patent ductus arteriosus in preterm infants using Doppler and M-mode echocardiography. *Acta Paediatr Scand* 1987;76:553-9.
- 12 Silverman NH, Lewis AB, Heymann MA, Rudolph AM. Echocardiographic assessment of ductus arteriosus shunt in premature infants. *Circulation* 1974;50:821-5.
- 13 Johnson GL, Breart GL, Gewitz MH, *et al*. Echocardiographic characteristics of premature infants with patent ductus arteriosus. *Pediatrics* 1983;72:864-71.
- 14 Sahn DJ, Vaucher Y, Williams DE, *et al*. Echocardiographic detection of large left to right shunts and cardiomyopathies in infants and children. *Am J Cardiol* 1976;38:73-9.
- 15 Hirschlau MJ, Disessa TG, Higgins CB, Friedman WF. Echocardiographic diagnosis: pitfalls in the premature infant with a large patent ductus arteriosus. *J Pediatr* 1978;92:474-7.
- 16 Valdes-Cruz LM, Dudell GG. Specificity and accuracy of echocardiographic and clinical criteria for diagnosis of patent ductus arteriosus in fluid restricted infants. *J Pediatr* 1981;98:298-305.
- 17 Stevenson JG, Kawabori I, Guntheroth WG. Pulsed Doppler echocardiographic diagnosis of patent ductus arteriosus. sensitivity, specificity, limitations and technical features. *Cathet Cardiovasc Diagn* 1980;6:255-63.
- 18 Gentile R, Stevenson G, Dooley T, *et al*. Pulsed Doppler echocardiographic determination of the time of ductal closure in normal newborn infants. *J Pediatr* 1981;98:443-8.
- 19 Serwer GA, Armstrong BE, Anderson PAW. Continuous wave Doppler ultrasonographic quantitation of patent ductus arteriosus flow. *J Pediatr* 1982;100:297-9.
- 20 Reller MD, Ziegler ML, Rice MJ, Solin RC, McDonald RW. Duration of ductal shunting in healthy preterm infants: an echocardiographic color flow Doppler study. *J Pediatr* 1988;112:441-6.
- 21 Walther FJ, Kim DH, Ebrahimi M, Siassi B. Pulsed Doppler measurement of left ventricular output as an early predictor of symptomatic patent ductus arteriosus in very preterm infants. *Biol Neonate* 1989;56:121-8.
- 22 Jarmakani MM, Graham TP, Canent RV, Spach MS, Capp MP. Effect of site of shunt on left heart volume characteristics in children with ventricular septal defect and patent ductus arteriosus. *Circulation* 1969;40:411-8.
- 23 Hirata T, Wolfe SB, Popp RL, Helman CH, Feigenbaum H. Estimation of left atrial size using echocardiography. *Am Heart J* 1969;78:43-52.
- 24 Carter WH, Bowman CR. Estimation of shunt flow in isolated ventricular septal defect by echocardiogram. *Circulation* 1973;48(suppl IV):IV-64.
- 25 Drayton MR, Skidmore R. Ductus arteriosus blood flow during the first 48 hours of life. *Arch Dis Child* 1987;62:1030-4.
- 26 Mellander M, Sabel K, Caidal K, Solymar L, Eriksson B. Doppler determination of cardiac output in infants and children: comparison with simultaneous thermodilution. *Pediatr Cardiol* 1987;8:241-6.
- 27 Mandelbaum-Isken VH, Linderkamp O. Pulsed Doppler evaluation of cardiac output in neonates using an apical window. *Pediatr Cardiol* 1991;12:13-6.
- 28 Zhou TF, Guntheroth WG. Valve incompetent foramen ovale in premature infants with ductus arteriosus: a Doppler echocardiographic study. *J Am Coll Cardiol* 1987;10:193-9.