Value of Systolic Time Intervals in the Diagnosis of Large Patent Ductus Arteriosus in Fluid-Restricted and Mechanically Ventilated Preterm Infants

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With statistical analysis by Louis Houde

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ABSTRACT. M-mode echocardiographic features suggesting a patent ductus arteriosus are based on two groups of indirect criteria: dilation of the left cardiac cavities and changes of systolic time intervals. The reliability of the first group of criteria has been questioned in fluid-limited, mechanically ventilated preterm infants. The sensitivity of the systolic time intervals in the same circumstances is investigated. Twenty-three patients with a large patent ductus arteriosus were selected. Review of their echocardiograms shows that the sensitivity of the various criteria (expressed as percentage of positivity) was as follows: inversion of the ratio of left ventricular preejection period to right ventricular preejection period, 91.3%; left ventricular preejection period to left ventricular ejection time <1, 83%; left atrium dilation, 74%; shortening of left ventricular pre-ejection period, 70%; dilation of left ventricular internal dimensions in diastole, 65%; increase in left atrium/aorta, 52%; and decrease of left ventricular preejection period to left ventricular ejection time, 48%. Three criteria involving time intervals (left ventricular preejection period to right ventricular preejection period, left ventricular pre-ejection period, and left ventricular preejection period to left ventricular ejection time) had 100% specificity. The lowest specificity was found with criteria involving the left atrium (left atrial to aortic root ratio 75% and left atrium 63%). It is concluded that study of systolic time intervals is a reliable means of detecting preterm infants with hemodynamically significant left-to-right shunt through a patent ductus arteriosus even if the infants are mechanically ventilated and fluid restricted. Pediatrics 1984;74:1069-1074; preterm infants, patent ductus arteriosus, systolic time intervals, mechanical ventilation, fluid restriction.

A frequent problem in the care of early preterm newborn infants is deciding whether their respiratory distress is mainly due to lung immaturity or to the presence of a significant left-to-right shunt through a large ductus arteriosus. Yet, the decision of closing the ductus whether by medical or surgical means, must be taken without delay in order to facilitate the weaning from the respirator and prevent serious damage to the lung. Recently, great hope has been put on echocardiography in the treatment of these infants. M-mode echocardiographic criteria of ductus patency have essentially been based on two hemodynamic consequences of this anomaly: the volume overload of the left cardiac cavities and the decrease in the systemic afterload which alters the systolic time intervals. However, the reliability of those criteria has been questioned in the presence of respiratory distress syndrome necessitating fluid restriction. Similarly, mechanical ventilation with positive expiratory pressure, frequently used in these cases, has been shown to decrease the left-to-right shunt and consequently lowers the sensitivity of the echocardiographic study.

In view of these uncertainties, systematic treat-
ment with indomethacin has been advocated for preterm infants in order to prevent potential problems caused by the patent ductus. \(^8\) In the past few years, we have adopted in Sainte-Justine Hospital a more selective attitude of reserving the use of indomethacin for patients with clinical signs of ductus arteriosus. Our clinical diagnostic criteria are similar to those described recently by Ellison and co-workers. \(^9\) The treatment of these infants also included standard medical therapy such as fluid restriction, or administering digoxin and/or diuretics. Surgical ligation of the ductus was contemplated after failure or counterindication of this regimen. An M-mode echocardiogram was performed on each patient mainly to rule out associated cardiac malformations.

This approach carried the risk of some delay in the diagnosis and decision-making process. In an attempt to shorten this time delay, especially in infants with a large ductus who are at a higher risk of lung \(^10,11\) and cerebral \(^12,13\) damage, we selected and reviewed, retrospectively, the preoperative echocardiograms of all infants in whom a large ductus was found at the time of surgery. The study was carried out on the assumption that the echocardiographic signs based on the decrease in the systemic afterload created by the ductus are less affected by mechanical ventilation and fluid restriction than the changes in the dimensions of the cardiac cavities.

**MATERIALS AND METHODS**

The echocardiograms of 23 preterm infants operated upon for a patent ductus arteriosus were evaluated. Only patients with a large ductus (external diameter of at least two thirds that of the descending aorta and a palpable thrill) were included in the study. Gestational age varied from 25 to 32 weeks (mean 28 weeks). Echocardiographic studies were performed at 8 to 36 days of age (mean 19 days). Eight infants were less than 10 days old. The patients weighed 0.78 to 1.82 kg (mean 1.20 kg) at the time of the study. They were all mechanically ventilated (intermittent mandatory ventilation with positive end-expiratory pressure). Fluid intake was limited to an average of 90 ml/kg/d. The echocardiographic studies evaluated were those done just before surgery. These were carried out at less than 24 hours in eight patients and between 24 and 72 hours in 15 patients. In eight patients the echocardiograms were repeated within 1 week after surgery.

The echocardiographic tracings were obtained with an Ekoline model A ultrasonoscope coupled with a Honeywell Cambridge fiberoptics recorder. A 5-MHz unfocused transducer was always used.

An ECG with a well-defined Q wave was simultaneously recorded. The following left and right ventricular systolic time intervals were measured \(^14\): left and right pre-ejection time from the onset of the QRS complex to the opening of aortic (LPEP) and pulmonic (RPEP) valves; left and right ejection times from opening to closure of aortic (LET) and pulmonic (RET) valves. From these measurements, the ratios RPEP/RET and LPEP/LET were calculated. Left atrial (LA) and left ventricular internal dimensions in diastole (LVID\(_d\)) as well as that of the aortic root (Ao) were also measured according to the recommendations of the American Society of Echocardiography. \(^15\) Left atrial to aortic root ratio (LA/Ao) was calculated. All data represent an average of at least five separate complexes. Measurements were made to the nearest 5 ms at a paper speed of 100 mm/s.

**Statistical Analysis**

Difference from normal values was assessed for the mean data found in our group of patients. The normal regression equations for LA and LVID\(_d\) were taken from Lange and co-workers. \(^16\) The equation relating LVID to weight was 0.302 × weight + 0.89. For the left atrium this equation was 0.25 × weight + 0.34. Expected and observed values were compared using Student’s t test. Because LA/Ao is not influenced by weight, the mean ratio found in our group of patients was compared with the value found by Silverman and co-workers. \(^17\) The same procedure was carried out between the mean values observed for LPEP and LPEP/LET and those published by Halliday and co-workers \(^18\) for normal premature infants older than 5 days.

For all criteria, a normal range was found by constructing, from means and variances, an interval including 90% of the normal values. \(^16-18\) A given echocardiographic criterion was considered positive for ductus patency when found above or below this normal range. More specifically, positivity was defined as follows: LVID\(_d\), when greater than LVID\(_d\) expected + 2.9 mm; LA, when greater than LA expected + 2.5 mm; LA/Ao, when >1.15; LPEP, ≤40 ms; LPEP to LET ratio, when ≤0.22; LPEP to RPEP ratio, when ≤1 if LPEP is ≤40 ms (this last restriction aims at eliminating cases where equality between LPEP and RPEP would be caused exclusively by pulmonary hypertension); LPEP to LET ratio/RPEP to RET ratio when <1.

The results are expressed as percentage of positivity for a given criterion. In order to assess specificity, the same statistical treatment was applied to the eight echocardiograms taken after surgery, looking for false-positive signs of ductus patency.
RESULTS

The complete echocardiographic data for the 23 patients are shown in the Table. The average values observed for LVIDd, LA, LA/Ao, LPEP, and LPEP to LET differ significantly from normal ($P < .01$). In the group of infants with patent ductus, there was no difference between those less than 10 days of age and the others.

Sensitivity

The percentage of cases in which each individual criterion was found abnormal or “positive” for ductus is shown in Fig 1. The highest percentage of sensitivity (91.3%) is observed when the pre-ejection periods of the two ventricles are compared. This is due mainly to a shortening of LPEP as shown in Fig 2. The left ventricular and atrial cavities were enlarged in 65% and 74% of the cases, respectively.

Specificity

Specificity of individual criteria are shown in Fig 3. The only variables that were not associated with false-positive measurement (100% specificity) were those involving systolic time intervals. On the other hand, the highest percentage of false-positive findings (38%) was found when LA dimensions were taken as an isolated criterion.

### Table

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*Abbreviations used are: Ao, aorta; LA, left atrium; LET, left ventricular ejection time; LPEP, left ventricular pre-ejection period; LVIDd, left ventricular internal dimensions in diastole; RET, right ventricular ejection time; and RPEP, right ventricular pre-ejection period.
Fig 2. Echocardiogram of a preterm infant with large patent ductus arteriosus. Openings of aortic and pulmonary valves are well visualized. Left pre-ejection period is abnormally shorter than right.

Fig 3. Specificity for echocardiographic criteria expressed as percentage of cases in which no false-positive sign of ductus arteriosus was found after surgical closure of ductus. Abbreviations are defined in Fig 1 legend.

COMMENTS

In preterm infants with respiratory distress, a large ductus with a hemodynamically significant left-to-right shunt imposes a threat to survival. Detection of such patients must be prompt and, above all, with minimal stress to the patient. For these reasons, in the present study, attention has been exclusively focused on patients with a large ductus as actually measured at surgery. It can be argued that surgical manipulation and exposure to daylight could constrict the ductus. If so, this could lead to underestimation of ductus size at surgery without decreasing the value of the echocardiographic results.

This study shows that criteria involving volume measurements are less sensitive in this group of infants. The LA/Ao ratio values were particularly disappointing despite the selection of 1.15 as the maximal limit of normality. Some authors would consider 1.25 as the minimal value above which a ductus can be suspected. On the other hand, Bhat et al. proposed that in preterm infants a ratio >1 is abnormal. The apparently normal dimensions of the left cardiac cavities despite the presence of a left-to-right ductal shunt have been explained either by fluid restriction, mechanical ventilation, or anteroposterior flattening of the cardiac cavities by severe sternal retraction.

Criteria based on systolic time intervals, especially decreased LPEP, are by far the most reliable. In the presence of a ductus, left ventricular isovolumic period, which is a part of the pre-ejection period, is significantly shorter than normal. This is due to the low aortic diastolic pressure and to an increase in left ventricular preload caused by the increase in the pulmonary venous return. In the majority of our patients, LPEP was shorter than RPEP thus reversing the normal relationship between left and right pre-ejection periods. Lengthen-
ing of the RPEP in the presence of pulmonary hypertension secondary to a large left-to-right shunt and to hyaline membrane disease could be an additional factor responsible for the abnormal relationship between left and right systolic time intervals. This combination of factors renders these sets of criteria very sensitive to a hemodynamically significant patent ductus even if the left-to-right shunt is partially decreased by mechanical ventilation. However, the association of cardiac failure by lengthening the isovolumic period could counteract the ducal effect and be responsible for an apparently normal pre-ejection period. This could explain the findings in the two cases in which the left cardiac cavities were dilated but the relationship between the left and right systolic time intervals remained normal. The postoperative study also showed that the changes in the systolic time intervals are more specific because, with these criteria, no false-positive results were noted after closure of the ductus.

It is unlikely that the changes in systolic time intervals noted in this study are due to positive pressure ventilation alone. Unfortunately, finding a specific morbidity group required for an adequate control group without the preterm infants having a patent ductus is very difficult. However, five of the infants included in this study had an echocardiogram after ductal ligation while still requiring positive pressure ventilation. All of these infants had a ratio of LPEP to RPEP < 1.

Other ultrasonic techniques have been advocated; all have drawbacks. No flow information can be obtained from two-dimensional echocardiography. Contrast echocardiography can be useful for detecting left-to-right shunt, but this technique is invasive and carries the risk of arterial catheter clotting and clot embolization. Pulsed Doppler flow evaluation permits detection of turbulent flow in the pulmonary arteries with patent ductus arteriosus. However, the relatively high incidence of false-positive findings and the technical problems related to pulsed Doppler study in patients with tracheal intubation and pulmonary hyperinflation prevent generalization of this technique. In general, the benefits obtained from these various techniques are frequently counterbalanced by the excessive manipulation they require. Undue manipulation of sick infants may lead to cold stress and accidental extubation. In view of our present findings, we suggest that study of systolic time intervals be regarded as a safe and reliable means of detecting preterm infants with a hemodynamically significant left-to-right shunt through a ductus arteriosus even for those who are fluid restricted and mechanically ventilated.

ACKNOWLEDGMENTS

This paper was supported by grants from Le fonds de la Recherche en Santé du Québec and by the Quebec Heart Foundation.

The authors acknowledge the technical assistance of Marguerite Poirier and Jean Boileau and thank Michele Raymond for typing the manuscript.

REFERENCES

THE INFLUENCE OF CULTURE

In the most simple societies, habits are developed for self-preservation and the preservation of the tribe. Thus various customs may accompany pregnancy, childbirth, and weaning, the aim being to ensure successful reproduction and to protect the life of mother and infant. Looked at from a modern, scientific point of view, however, not all of these customs will be considered helpful. Some of them, indeed, may be positively harmful. ...

The Hausa women living around Zaria in northern Nigeria traditionally eat rock salt (kanwa) during the puerperium in order to promote the flow of breast milk. They also consider themselves vulnerable to cold—which they regard as a factor in the genesis of disease—and so they heat their bodies for at least 40 days after childbirth. The excess dietary sodium and the heat, both from the fires they kindle and from the tropical climate, combine to cause heart failure. Culturally, the custom of eating salt and lighting fires is responsible; environmentally, the high ambient temperature provides a certain level of stress to begin with; biologically, childbirth enhances the susceptibility of some women to heart failure. Ultimately, it is the combination of these factors that may prove fatal.

Submitted by Student

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*Pediatrics* 1984;74;1069

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the development of an appropriate microprocessor assisted on-line system.

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REFERENCES


ERRATUM

In the article “Value of Systolic Time Intervals in the Diagnosis of Large Patent Ductus Arteriosus in Fluid-Restricted and Mechanically Ventilated Preterm Infants” by Heitz et al (Pediatrics 1984;74:1069–1074), there is an error in the text. The last sentence of the second paragraph on page 1073 should read: All of these infants had a ratio of LPEP to RPEP >1.
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Pediatrics 1984;74;1069

The online version of this article, along with updated information and services, is located on the World Wide Web at:
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An erratum has been published regarding this article. Please see the attached page for:
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