Isolated Neonatal Ductus Arteriosus Aneurysm

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OBJECTIVES
A prospective study was performed to evaluate the incidence, clinical manifestations and outcome of ductus arteriosus aneurysm (DAA) in full-term neonates.

BACKGROUND
Ductus arteriosus aneurysm has been considered to be a rare congenital lesion and a potentially fatal abnormality.

METHODS
A total of 548 full-term neonates received echocardiographic screening.

RESULTS
There were 48 (8.8%) patients (28 boys and 20 girls) with DAA detected by echocardiography. The maximal diameter of the DAA ranged from 6.5 to 11.2 mm (8.2 ± 1.2 mm). All cases were asymptomatic. There were no significant differences in gender, gestational age, maternal age or Apgar score between the newborns with or without DAA. Newborns with DAA had a higher birth body weight, higher incidence of maternal gestational diabetes mellitus and more mothers with blood group A, compared with newborns without DAA (p < 0.05). Follow-up echocardiograms showed spontaneous closure of the ductus arteriosus in all patients except those without DAA. The DAA became progressively smaller after ductal closure in 33 patients (70.2%) and completely disappeared by 7 to 35 days of life. The other 14 patients (29.8%) with DAA had echocardiographic evidence of progressive formation of thrombi between the third and tenth day of life. The DAA and thrombi spontaneously disappeared in all patients by one month after birth.

CONCLUSIONS
There is a higher incidence of DAA with a good outcome in our series compared with previous reports. We speculate that the presence of DAA may be a normal variant of the ductal bump and part of a normal process of spontaneous ductal closure in full-term neonates. (J Am Coll Cardiol 2002;39:342–7) © 2002 by the American College of Cardiology

Aneurysmal dilatation of the ductus arteriosus has been considered a rare, but potentially fatal abnormality (1–4). It can be either congenital or acquired as a complication of surgical closure of patent ductus arteriosus (PDA) or after a ductal infection (5,6). Congenital ductus arteriosus aneurysm (DAA) was divided into two groups according to the age at diagnosis: infant and adult groups. The most common age at diagnosis was <2 months of age and were recognized incidentally (1–4,7–11). Although there was a reported incidence of 0.8% in neonatal autopsies (8), the true incidence of DAA is still unknown. More recently, some isolated cases of DAA were diagnosed by echocardiography of the fetus (1,2,9–11). These reports suggest that congenital DAA may be more common than those cases observed postnatally, with the majority of affected fetuses being asymptomatic at birth. From our observation, we believe that the incidence of congenital DAA may be higher than that reported previously. The purpose of this prospective study was to evaluate the incidence, clinical manifestations and outcome of congenital DAA in full-term neonates. In addition, to the best of our knowledge, this is the first report of DAA and its regression detected by three-dimensional surface-rendering magnetic resonance angiography (MRA).

METHODS
A total of 548 full-term neonates (gestational age ranging from 37 to 41 weeks and 6 days) received echocardiographic screening at Taichung Veterans General Hospital (Taichung, Taiwan), a tertiary referral center, during the year 2000, after written, informed consent was obtained from the parents. The demographic data, perinatal history, maternal history and clinical manifestations were recorded and analyzed. Small for gestational age was defined as the birth body weight (BBW) in the <10th percentile of the mean BBW for their gestational age, and large for gestational age (LGA) as BBW in the >90th percentile. Appropriately for gestational age (AGA) is BBW between the 10th and 90th percentile (12). Echocardiograms were obtained with a Sonos 5500 ultrasound system (Hewlett-Packard, Andover, Massachusetts), equipped with a 5- to 12-MHz multifrequency transducer for two-dimensional imaging and continuous, directional spectral and color flow Doppler mapping. All of the diagnoses of DAA were confirmed by at least two pediatric cardiologists. The diagnostic images of

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the neonatal DAA showed the following features: 1) an unusual ductal shunt jet: a horizontal or left-low quadrant ductal shunt, from the DAA to the main pulmonary artery, in the high parasternal short-axis view (Fig. 1A); 2) “triple star sign” (13): the composition of the ascending aorta, main pulmonary artery and DAA in the high parasternal short-axis view (Fig. 1A); 3) “rabbit ear sign”: the right-side ear is the transverse arch of the aorta and descending aorta, and the left-side ear is the elongated ductal bump, with terminal aneurysmal dilatation in the modified high parasternal short-axis view (Fig. 1B); 4) sacular dilatation of the ductus arteriosus with a maximal internal diameter must be equal to or larger than the adjacent transverse arch or descending aorta; and 5) false images, including a mirror image of the pulmonary artery, normal ductal bump, left superior vena cava, dilated atrial appendage and vertical ductus arteriosus should be excluded.

Serial follow-up echocardiograms were obtained on the following schedule. Infants without DAA underwent echocardiography between 0 to 12 h after birth, 12 to 24 h after birth and then daily until the ductus arteriosus closed. If the ductus arteriosus remained open after hospital discharge, follow-up echocardiograms were obtained at 7 to 10 days of age and 1 month of age. Infants with DAA also underwent echocardiography between 0 to 12 h after birth, 12 to 24 h after birth and then daily until they were discharged. Follow-up echocardiograms were performed at 7 to 10 days, 1 month and 4 to 6 months of age. Aortography or three-dimensional MRA (Fig. 2A) was performed on the first five newborns with DAA between 3 and 5 days after birth, to confirm the echocardiographic diagnosis. None of our patients received indomethacin or anticoagulant drugs for persistent patency of ductus arteriosus or DAA.

Data are presented as the mean value ± SD, median (range) or percentages. Statistical analysis was performed with SPSS, version 8.0 for Windows (SPSS, Chicago, Illinois). Comparisons of data between newborns with

**Abbreviations and Acronyms**

AGA = appropriate for gestational age  
BBW = birth body weight  
DAA = ductus arteriosus aneurysm  
GDM = gestational diabetes mellitus  
LGA = large for gestational age  
MRA = magnetic resonance angiography  
PDA = patent ductus arteriosus

**Figure 1.** (A) Color Doppler mapping shows a ductal shunt jet (arrows) from the ductal aneurysm to the main pulmonary artery in a high parasternal short-axis view. The “triple star sign” consists of the ascending aorta, the main pulmonary artery and the ductal aneurysm. (B) The “rabbit ear sign” consists of the transverse arch and descending aorta as the right-side ear, and the elongated ductal bump, with terminal dilatation, as the left-side ear, in a modified high parasternal short-axis view. Arch = transverse arch of aorta; AsAO = ascending aorta; DAO = descending aorta; MPA = main pulmonary artery.

**Figure 2.** (A) The three-dimensional reconstructed magnetic resonance angiography shows a large ductal aneurysm three days after birth. (B) The follow-up three-dimensional reconstructed magnetic resonance angiography reveals a marked decrease in the size of the ductal aneurysm (arrow) at one month. DAA = ductus arteriosus aneurysm.
DAA and those without DAA were assessed by using the chi-square or Student t test, according to unequal or equal variance. The patent rate of ductus arteriosus was prepared by the Kaplan-Meier method, and the difference between newborns with DAA and those without DAA was evaluated using the log-rank test. A p value <0.05 was considered statistically significant.

RESULTS
A total of 48 patients (28 boys and 20 girls) with isolated neonatal DAA were identified during the study period, for an incidence of 8.8% in full-term neonates. Aneurysmal ductus arteriosus was diagnosed by echocardiography alone in 43 patients, echocardiography and three-dimensional MRA in 4 and echocardiography and aortography in 1. Chest radiographs were obtained in 12 patients, and a small, rounded mass could be visualized in the left upper mediastinum. Demographic information is summarized in Table 1. During the physical examinations, symptoms could not be identified or were found not related to cardiovascular conditions in all patients, with or without DAA. None of the newborns received cardiovascular-related treatment during the follow-up period. A nonspecific grade 1 to 2/6 systolic ejection murmur at the left upper sternal border was detected in 46 newborns without DAA (9.2%) and 6 newborns with DAA (12.5%), which was not a significant difference. Infants with DAA were predominantly males, with a male/female ratio of 1.4, but the difference was not statistically significant (p = 0.345). There were no significant differences in gestational age, para gravidity, Apgar scores or maternal age between the newborns with DAA and those without DAA. Neonates with DAA had a higher BBW, a higher incidence of maternal gestational diabetes mellitus (GDM) and more mothers with blood group A (p < 0.05). Five (31%) of 16 newborns with maternal GDM, 11 (24.4%) of 45 newborns with LGA and 4 (80%) of 5 newborns with both maternal GDM and LGA developed neonatal DAA (Table 1).

All of the newborns with DAA had echocardiographic images displaying the features described previously, and transthoracic echocardiography was always diagnostic for DAA. Ductal aneurysm was better visualized in the high parasternal short-axis view, with multiple angulations. In the first examination, within 12 h of birth, the DAA was always patent, with an unusual ductal jet from the ductal aneurysm to the main pulmonary artery. The maximal inner diameter of the DAA ranged from 6.5 to 11.2 mm (mean ± SD: 8.2 ± 1.2 mm). Follow-up echocardiograms detected spontaneous closure of the ductus arteriosus in all patients with DAA, except one patient in whom follow-up was lost. In 500 newborns without DAA, one patient (0.2%) retained patency of the ductus arteriosus detected by echocardiography at one month of age, and follow-up was lost in 61 patients. The ductus arteriosus closed, according to echocardiography, within 72 h of life in 86.1% of the newborns.

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<th>Table 1. Summary of Demographic Data, Perinatal History and Maternal History in Newborns With or Without Ductus Ateriosus Aneurysm</th>
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<td><strong>Birth History</strong></td>
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<td><strong>Gender</strong></td>
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<td><strong>With DAA (n=48)</strong></td>
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<td><strong>Without DAA (n=500)</strong></td>
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*Data are presented as the median value range and mean value ± SD or number (%) of patients.*

- **BBW** = birth body weight; **DAA** = ductus arteriosus aneurysm; **GA** = gestational age; **GDM** = gestational diabetes mellitus; **LGA** = large for gestational age; **SGA** = small for gestational age.
without DAA and in 70.2% of the newborns with DAA (Fig. 3). The closure time of the ductus arteriosus was delayed in newborns with DAA compared with those without DAA, but the difference was not statistically significant ($p = 0.094$). The DAA became progressively smaller in size, without thrombus formation in the aneurysm after ductal closure in 33 patients (70.2%), and it completely disappeared by 7 to 35 days of life. The other 14 patients (29.8%) with DAA had echocardiographic evidence of formation of thrombi between the 3rd and 10th day of life. The ductal aneurysm and thrombi spontaneously resolved and disappeared in all newborns with DAA after one month of life, according to the echocardiograms. Three-dimensional MRA confirmed the spontaneous regression in two infants with DAA after one month of life (Fig. 2B).

**DISCUSSION**

**Symptoms.** Although aneurysm of the ductus arteriosus may be associated with many complications, including spontaneous rupture, thromboembolism, erosion into airways, infection, compression of adjacent structures and even death (1–4,14–16), none of the newborns with DAA in our study had symptoms, or their symptoms were not related to DAA at presentation. All of them had a benign clinical course during the follow-up period. We believe that complications may occur but are very rare in newborns with DAA. Dyamenahalli et al. (1) reported a prenatal diagnosis of nine patients with DAA. All of them were asymptomatic, and three patients had thrombus formation within the aneurysm.

**Risk factors.** We found that the high risk factors associated with neonatal DAA include newborns with LGA, maternal GDM and mothers with blood group A. The higher incidence of DAA in infants of diabetic mothers was reported previously (7). Interestingly, newborns with both poorly controlled maternal GDM and LGA had a higher incidence of neonatal DAA than those born to mothers with well-controlled maternal GDM and AGA or those with LGA without maternal GDM (80% vs. 9% vs. 17.5%, respectively). These results have not been described previously. Whether or not poorly controlled maternal GDM and mothers with blood group A affect the formation of ductal aneurysm is unknown.

**Incidence.** Although the incidence of neonatal DAA was previously reported to be 0.8%, based on neonatal autopsies (8), and 1.5% by fetal ultrasound studies at fetal age >30 weeks (1), the incidence is still not clearly established. To our knowledge, this report may be the first study to describe the incidence of neonatal DAA detected by echocardiographic study in full-term neonates. Surprisingly, 8.8% of full-term neonates had an isolated DAA. This rate is much higher than the rates in previous reports. We suggest that the incidence of isolated neonatal DAA was previously underestimated due to the lack of symptoms and signs before complications occur, because most patients do not develop complications (1,7). One report indicated DAA-related symptoms in 16% of patients (1). No newborns with DAA in this series had either symptoms at presentation or complications during the follow-up period.

**Diagnostic images.** Plain chest radiography has proven helpful in the diagnosis of DAA before the application of
transthoracic echocardiography (17). The disadvantages of detecting ductal aneurysm by chest radiography include: 1) DAA presenting as a left, upper mediastinal mass was easily neglected if the mass lesion was not obvious; and 2) it could not be definitively diagnosed by the radiopaque shadow. Transthoracic echocardiography is still an important tool for the diagnosis and follow-up of DAA. Three important signs, including the unusual ductal shunt jet, “triple star sign” and “rabbit ear sign” (first described in this report), are diagnostic images. Careful manipulation of the transducer and analysis of the images are important when using echocardiography to diagnose DAA, because false images must be excluded by carefully tracing the aneurysm-like images from different angulations and views. We suggest that once the echocardiographer become familiar with the echocardiographic appearance of the ductal aneurysm, other imaging techniques are rarely necessary. If a thrombus extending into adjacent vascular structures cannot be ruled out, or if there was clinical evidence of compression of extravascular structures, alternative imaging technique, such as magnetic resonance imaging or computed tomographic scanning, should be considered.

Management and outcome. The use of oral or intravenous indomethacin has led to successful closure of PDA in premature infants (18), but it is ineffective in full-term infants. Although one case report demonstrated the regression of ductal aneurysm after indomethacin treatment (19), the definitive effect of indomethacin on the ductal aneurysm is uncertain. Surgical resection of the ductal aneurysm was suggested if any of the following conditions existed: 1) PDA and ductal aneurysm persisting beyond the neonatal period; 2) association with connective tissue disorder; 3) thrombus extension into adjacent vessels; 4) evidence of thromboembolism; and 5) functional compression of adjacent structures (1). Because we found that the ductal aneurysm with thrombus formation disappeared in all patients who had regular follow-up, it might be assumed that the DAA resolved spontaneously as a result of organization and fibrosis of the thrombus in the DAA (11,20). According to our clinical observations, the process of ductal aneurysm resolution may occur in two ways: 1) ductal aneurysms become progressively smaller with or without thrombus formation after ductal closure, as seen in two-thirds of our patients; and 2) progressive thrombus formation within the DAA becomes organized and fibrosed, as seen in one-third of our patients.

Pathogenesis. The mechanism of ductus aneurysmal formation remains uncertain, and there are several theories about its pathogenesis. First, delayed closure at the aortic end of the ductus arteriosus may expose the ductal wall to high systemic pressure (3). However, this mechanism is not likely to be a factor in fetal or early neonatal patients, when pressure in the pulmonary artery is higher or similar to that in the aorta, and the prenatal diagnosis has been established. Second, congenital wall weakness may result from necrosis and mucoid degeneration of the media in the ductal wall (3), but the same changes can be found in normal-closing ductal tissue (7,21). Third, increased flow through the ductus arteriosus in the uterus may lead to aneurysmal formation (2). Fourth, intruterine ductal constriction may cause post-stenotic dilatation of the ductus arteriosus (7). However, there was no evidence of ductal stenosis on the prenatal echocardiogram (1,2,9–11), and many patients had echocardiographic evidence of a large ductus arteriosus postnatally in our study. Finally, it may be the result of abnormal intimal cushion formation or defective elastin in the ductus arteriosus (1). None of these theories, however, can explain ductus aneurysmal formation in all patients. We consider that the presence of DAA may be a normal variant of an elongated ductal bump and part of a normal process of spontaneous ductal closure in full-term neonates. The definitive pathogenesis of DAA needs further investigation.

Conclusions. Newborns with LGA, poorly controlled maternal GDM and mothers with blood group A have a high risk of neonatal DAA. Echocardiography is a reliable and valuable method for diagnosing and monitoring newborns with DAA. An unusual ductal jet, as detected by color Doppler mapping, should prompt a careful evaluation of the peripulmonary artery area, to exclude ductal aneurysm. An unnecessary operation should be avoided if regression is confirmed. Surgical intervention may be delayed until the ductal aneurysm persists beyond the neonatal period or early complications develop. Continued echocardiographic follow-up of affected infants is suggested. We speculate that spontaneous closure of the ductal aneurysm may be a normal process in full-term neonates.

REFERENCES
