cardiac operations. The incidence of POAF in this study was similar to that in other surgical cardiac populations despite our patients being younger than most surgical cohorts. However, patients with POAF in this study did not seem to have more acute symptoms (need for inotropic support, need for reoperation, duration of intensive care unit stay) than patients remaining in sinus rhythm. This longer hospital stay was generally attributable to ensuring adequate heart rate control, restoring sinus rhythm, and administering anticoagulation therapy.

**The treatment of POAF depends in large part on the timing, duration, and hemodynamic milieu. This small study does not support a prophylactic strategy, because one third of patients developing POAF were receiving amiodarone before operation. Our results suggest that POAF occurs in approximately 30% of patients with obstructive HC after septal myectomy. AF was not associated with a more complicated postoperative period and is relatively easily controlled or converted.**


**1.** Ommen SR, Odell JA, Stanton MS. Atrial arrhythmias after cardiothoracic surgery. *N Engl J Med* 1997;336:1429–1434.
**2.** Fuller JA, Adams GG, Buston B. Atrial fibrillation after coronary artery bypass grafting. Is it a disorder of the elderly? *J Thorac Cardiovasc Surg* 1989;97:821–825.
**3.** Leitch JW, Thomson D, Baird DK, Harris PJ. The importance of age as a predictor of atrial fibrillation and flutter after coronary artery bypass grafting. *J Thorac Cardiovasc Surg* 1990;100:338–342.
**4.** Creswell LL, Schuessler RB, Rosenbloom M, Cox JL. Hazards of postoperative atrial arrhythmias. *Ann Thorac Surg* 1993;56:539–549.
**5.** Crosby LH, Pifalo WB, Woll KR, Burkholder JA. Risk factors for atrial fibrillation after coronary artery bypass grafting. *Am J Cardiol* 1990;66:1520–1522.
**6.** Hashimoto K, Ilstrup DM, Schaff HV. Influence of clinical and hemodynamic variables on risk of supraventricular tachycardia after coronary artery bypass. *J Thorac Cardiovasc Surg* 1991;101:56–65.
**7.** Mathew JP, Parks R, Savino JS, Friedman AS, Koch C, Mangano DT, Browner WS. Atrial fibrillation following coronary artery bypass graft surgery: predictors, outcomes, and resource utilization. MultiCenter Study of Perioperative Ischemia Research Group. *JAMA* 1996;276:300–306.
**8.** Aranki SF, Shaw DP, Adams DH, Rizzo RJ, Couper GS, VanderVliet M, Collins JJ Jr, Cohn LH, Burstin HR. Predictors of atrial fibrillation after coronary artery surgery. Current trends and impact on hospital resources. *Circulation* 1996;94:390–397.
**9.** Chung MK, Asher CR, Dykstra D, Dimengo J, Weber M, Whitman G, McCarthy PM, Nissen SE. Atrial fibrillation increases length of stay and cost after cardiac surgery in low risk patients targeted for early discharge (abstr). *J Am Coll Cardiol* 1996;27(suppl):309A.
**10.** Mohr R, Schaff HV, Danielson GK, Puga FJ, Pluth JR, Tajik AJ. The outcome of surgical treatment of hypertrophic obstructive cardiomyopathy. Experience over 15 years. *J Thorac Cardiovasc Surg* 1989;97:666–674.
**11.** McCully RB, Nishimura RA, Tajik AJ, Schaff HV, Danielson GK. Extent of clinical improvement after surgical treatment of hypertrophic obstructive cardiomyopathy. *Circulation* 1996;94:467–471.
**12.** Wigle ED, Rakowski H, Kimball BP, Williams WG. Hypertrophic cardiomyopathy. Clinical spectrum and treatment. *Circulation* 1995;92:1680–1692.
**13.** Vaziri SM, Larson MG, Benjamin EJ, Levy D. Echocardiographic predictors of nonrheumatic atrial fibrillation. The Framingham Heart Study. *Circulation* 1994;89:724–730.
**14.** Pozzoli M, Cioffi G, Traversi E, Pinna GD, Cobelli F, Tavazzi L. Predictors of primary atrial fibrillation and concomitant clinical and hemodynamic changes in patients with chronic heart failure: a prospective study in 344 patients with baseline sinus rhythm. *J Am Coll Cardiol* 1998;32:197–204.
**15.** Ommen SR, Tsang TSM, Ammash NM, Mahoney DW, Seward JB. Usefulness of serial echocardiographic parameters for predicting the subsequent occurrence of atrial fibrillation. *Am J Cardiol* 2001;87:1298–1301.


# Incidence of Patent Ductus Arteriosus and Patent Foramen Ovale in Normal Infants


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As part of a study on the effects of in-utero cocaine exposure on the heart, a cohort of 104 full-term, healthy infants who did not have intrauterine drug exposure underwent extensive echocardiographic examination at birth and at 2 to 6 months of age. These studies were evaluated for the presence of a patent ductus arteriosus (PDA) and patent foramen ovale (PFO). Infants were eligible for the study if they were $<$72 hours old, weighed $>$1,500 g, and were between 33 and 42 weeks gestation. In all, 64 infants were excluded from the study because of various maternal and neonatal causes. We excluded infants born to mothers who used medications during pregnancy, such as bronchodilators, that may have affected the cardiovascular system. We also excluded infants of mothers with acute or chronic diseases such as systemic hypertension, hepatitis, diabetes mellitus, sepsis, and human immunodeficiency virus infection, symptomatic infants who required administration of oxygen beyond 5 minutes, ventilatory support, or admission to neonatal intensive care unit; and newborns with associated congenital anomalies including cardiac defects (except PDA, PFO, or physiologic mitral, tricuspid, or pulmonary regurgitation).

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Demographic and medical characteristics at the time of infant birth were abstracted from the hospital record. A pediatric cardiologist confirmed all physical examinations in infants with PDA. The study was approved by the institutional review board for human investigation at MetroHealth Medical Center and Case Western Reserve University. Informed written con-


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**TABLE 1** Demographic Data of Normal Newborns by PDA Status at Birth

| | PDA Absent (n = 56) | PDA Present* (n = 46) |
|---|---|---|
| Infants | | |
| Time evaluated (h) | 29 ± 11 (5–58) | 26 ± 10 (9–49) |
| Body surface area ($m^2$) | 0.21 ± 0.02 (0.18–0.27) | 0.21 ± 0.01 (0.18–0.25) |
| Boys | 27 (48%) | 25 (54%) |
| Birth weight (kgs) | 3.32 ± 0.44 (2.4–4.6) | 3.18 ± 0.38 (2.4–4.1) |
| Birth length (cm) | 50 ± 2 (47–57) | 50 ± 2 (45–55) |
| Gestational age (wks) | 40 ± 1 (36–42) | 39 ± 1 (36–42) |
| Head circumference (cm) | 34 ± 1 (31–40) | 34 ± 1 (31–37) |
| Apgar 1 min | 8.5 ± 0.7 (7–9) | 8.5 ± 1.2 (4–9) |
| Apgar 5 min | 9.0 ± 0 (9–9) | 8.9 ± 0.5 (6–9) |
| Mothers | | |
| Age (yrs) | 22 ± 4 (18–37) | 22 ± 3 (18–32) |
| Caucasian | 14 (25%) | 7 (15%) |
| African-American | 37 (66%) | 32 (70%) |
| Hispanic | 5 (9%) | 7 (15%) |
| Prenatal visits | 8.4 ± 3.4 (2–15) | 7.1 ± 3.5 (1–16) |
| Gravida | 2.7 ± 1.7 (1–10) | 2.9 ± 1.4 (1–8) |
| Employed | 14 (25%) | 19 (42%) |
| Parity | 2.2 ± 1.3 (1–8) | 2.2 ± 0.9 (1–5) |
| Education (yrs) | 11.6 ± 1.5 (8–16) | 11.8 ± 1.7 (7–15) |

*There were no statistically significant differences between groups for any of the demographic characteristics.

Values are expressed as mean ± SD (range).

**TABLE 2** Demographic Data of Normal Newborns by PFO Status at Birth

| | PFO Absent (n = 39) | PFO Present* (n = 63) |
|---|---|---|
| Infants | | |
| Time evaluated (h) | 25.8 ± 10.8 (5–46.3) | 28.9 ± 10.8 (6–57.6) |
| Body surface area ($m^2$) | 0.21 ± 0.02 (0.18–0.27) | 0.21 ± 0.01 (0.18–0.25) |
| Boys | 19 (49%) | 33 (52%) |
| Birth weight (kg) | 3.29 ± 0.47 (2.44–4.61) | 3.24 ± 0.38 (2.45–4.18) |
| Birth length (cm) | 49.8 ± 2.6 (45–56.5) | 49.8 ± 2.1 (45–55) |
| Gestational age (wks) | 39 ± 1 (36–42) | 39 ± 1 (36–42) |
| Head circumference (cm) | 34 ± 1 (32–40) | 34 ± 1 (31–37) |
| Apgar 1 min | 8.5 ± 0.9 (4–9) | 8.5 ± 0.9 (4–9) |
| Apgar 5 min | 8.9 ± 0.5 (6–9) | 8.9 ± 0.1 (8–9) |
| Mothers | | |
| Age (yrs) | 22 ± 4 (18–32) | 22 ± 4 (18–37) |
| Caucasian | 9 (23%) | 12 (19%) |
| African American | 27 (69%) | 42 (67%) |
| Hispanic | 3 (8%) | 9 (14%) |
| Prenatal visits | 8.4 ± 3.9 (1–16) | 7.5 ± 3.2 (2–15) |
| Gravida | 2.8 ± 1.8 (1–10) | 2.8 ± 1.5 (1–8) |
| Employed | 9 (24%) | 24 (38%) |
| Parity | 2.3 ± 1.4 (1–8) | 2.1 ± 0.9 (1–5) |
| Education (yrs) | 11.8 ± 1.6 (8–16) | 11.6 ± 1.5 (7–15) |

*There were no statistically significant differences between groups for any of the demographic characteristics.

Values are expressed as mean ± SD (range).

sent was obtained from the legal guardians/parents of all participants.

All infants underwent echocardiography including color flow Doppler with a 5-MHz transducer (SONOS 5500 Ultrasonograph, Hewlett-Packard Company, Andover, Massachusetts) by an experienced pediatric-trained sonographer. Echocardiographic tapes were reviewed by at least 1 cardiologist (JPS or DC). Presence of PFO and PDA were determined by color flow Doppler recordings of the subcostal and parasternal short-axis view, with confirmation by pulsed-wave Doppler. We defined a PFO as a left-to-right atrial shunt through the secundum atrial septum, with a diameter of $<3$ mm, and a flap derived from the septum primum.

Data were analyzed using SAS Version 8.0 (SAS Inc., Cary, North Carolina). To examine differences between infants with or without a PDA or PFO, the demographic data were analyzed using Pearson's chi-square and the Wilcoxon rank-sum test for categorical and continuous data, respectively. The proportion of PDA and PFO was analyzed, using the Cochran-Armitage trend test, to test for trend in binomial proportions across hours of life categories. In comparison of the overall proportion of PDA and PFO between birth and 2- to 6-month follow-up, the generalized estimating equations were used to account for the correlated data and the fact that some infants were lost to follow-up. Exact 95% confidence intervals are also reported. Statistical significance was defined as $p < 0.05$ (2-tail).

Although our inclusion criteria allowed infants in the age range of 33 to 42 weeks gestation, the youngest gestational age infant enrolled in this study was 36 weeks. Likewise, infants up to 72 hours of age were eligible for inclusion in this cohort, but the oldest infant in the cohort was 57 hours of age at the time of first echocardiographic study.

One hundred four infants met criteria for inclusion in this cohort. Two infants did not have complete echocardiographic studies at birth, and were excluded from analysis. The average age of evaluation as a newborn was 28 ± 11 hours of age. The average age of evaluation for follow-up was 2.2 ± 1.0 months (range 1.7 to 6.8) of age. There was no significant difference in any of the demographic characteristics of infants with or without PDA or with or without PFO at birth (Tables 1 and 2). There was a predominance of African-Americans in this cohort. However, there was no difference between races in the incidence of PDA ($p = 0.35$) or PFO ($p = 0.58$).

Overall, 46 infants (45%) had presence of PDA at the time of initial study. Results of the Cochran-Armitage trend test concluded that there was no significant trend in the incidence of PDA over the first 60 hours of life ($p = 0.118$). In a logistic regression model, we controlled for the effect of gender on the linear trend across time. When controlling for gender,

**TABLE 3** Incidence of PDA and PFO in Newborns and at Two to Six Months of Age

| | Birth (n = 102) | 2–6 mo (n = 89) | p Value† |
|---|---|---|---|
| PDA present | 46 (45.1%, 95% CI 35.2, 55.3) | 4 (4.5%, 95% CI 1.2, 11.1) | <0.001 |
| PFO present | 63 (61.8%, 95% CI 51.6, 71.2) | 48 (54.5%, 95% CI 43.6, 65.2)* | 0.221 |

*PFO at follow-up is out of 88 infants.
†The p value from generalized estimation equation models testing the proportion of PDA and PFO presence, equal at birth and at 2 to 6 months.
CI = confidence interval.

male and female infants were similar ($p = 0.642$), and the linear trend in proportion across time was not significant ($p = 0.102$).

Eighty-nine of the 102 infants (87.2%) returned for the follow-up visit at 2 to 6 months of age. Four of the 89 infants (4.5%) had PDA. All the infants with PDA at follow-up also had a PDA noted during their initial examination. None of the 4 had an audible murmur at any examination during the study or at follow-up. At follow-up evaluation, the age of the infants with a PDA was $3.3 \pm 1.9$ months (range 1.8 to 6.1) versus $2.2 \pm 1.0$ months (range 1.7 to 6.8) for infants without a PDA. Two of the 4 infants with PDA were male. Two of the infants with PDA were lost to follow-up after the second visit (1 male and 1 female infant). Of the remaining 2 infants, 1 PDA spontaneously closed by 23 months of age (female) and the other still had a clinically undetectable PDA by echo at 9 months of age.

At the time of initial study, 63 infants (62%) had evidence of a PFO. Results of the Cochran-Armitage trend test concluded that there is no significant change in the proportion of infants with a PFO over the first 60 hours of life ($p = 0.287$). In a logistic regression model, we controlled for the effect of gender on the linear trend across time. There was no difference in the overall incidence of PFO between male and female infants ($p = 0.60$). The linear trend across time was different between male and female infants ($p = 0.033$). The proportion of female infants with a PFO increased over time, whereas male infants did not show evidence of a linear trend. Data were available for the detection of a PFO in 88 subjects at the follow-up visit. Forty-eight of 88 infants (55%) had a PFO. The age of the infants at the time of the follow-up visit was $2.2 \pm 0.8$ months (range 1.7 to 6.1) for those with versus $2.3 \pm 1.3$ months (range 1.7 to 6.8) for those without a PFO. There was no difference in the proportion of infants with a PFO at follow-up compared with the initial evaluation (Table 3), and there was no difference in the proportion of male to female infants with a PFO at follow-up.

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The key finding of our study is the presence of a "silent" PDA in 4.5% of normal infants at 2 to 6 months of age. This is higher than has previously been reported. Infants with a PDA were asymptomatic and had no clinical signs of PDA. Of the 2 subjects who were available for further follow-up, 1 had continued echocardiographic evidence of a PDA at 9 months of age, whereas the other had spontaneous closure of the PDA by 23 months of age. This provides evidence confirming that the silent PDA may close spontaneously up to 2 years of age, as has been reported.[1] This also supports the practice, as occurs in our institutions, of using endocarditis prophylaxis, but not intervening to close the silent PDA.

We observed the presence of a PDA in 45% of normal infants. There are at least 4 studies in which newborns were sequentially evaluated for PDA over the first 4 to 6 days of life.[2–5] Our data for the first 60 hours of life are similar to the first 60 hours of data in these studies. We observed that 1 infant had persistence of ductal flow at 57 hours, which is consistent with data from these 4 studies—that persistence of ductal patency occurs at this age. Each of the aforementioned studies shows a trend toward ductal closure with time. Two studies concluded that all PDAs were closed based on 2-dimensional and pulsed or continuous-wave Doppler examinations without the use of color flow Doppler.[1,3] This may have resulted in missing very small ductal shunts. In each of the 4 studies, follow-up ended with the closure of the ductus. Because there is a high rate of reopening of the ductus after initial closure (6 of 20 infants on postnatal days 4, 5, and 6 in 1 report),[6] the use of the criterion of ductal closure may cause an underestimation of the incidence of PDA after the early newborn period. Our data show no difference in the presence of PDA in the early newborn period between male and female infants or based on other demographic parameters.

We observed a PFO in 62% of infants in the first 60 hours of life and in 54% at 2 to 6 months of age. Despite knowing the possibility of a PFO at 2 to 6 months of age from catheterization and echocardiographic experience, the high incidence noted in our follow-up examination has not been reported. The high incidence is most likely a result of the sensitivity of color flow Doppler. We also noted an increased presence of flow through a PFO in newborn female infants over the first 60 hours of life, which was not present in male infants, or in the group taken as a whole. This gender difference has also not previously been reported. It is possible that this is a statistical difference due to decreased sample size when dividing our cohort into 2 groups. However, it could be a hemodynamic marker for factors that result in better survival of preterm female than preterm male infants.[7]

**In summary, our findings suggest that 45% and 62% of full-term, healthy, newborn infants have a PDA and/or PFO, respectively, during the first 60 hours of life. The incidences of silent PDA (4.5%) and PFO (54.5%) at 2 to 6 months of age, as observed by color flow Doppler, have not been previously reported. A larger, long-term prospective study is**

**needed to study the natural history and the long-term clinical implications of these lesions.**


**1.** Glickstein J, Friedman D, Langsner A, Rutkowski M. Doppler ultrasound and the silent ductus arteriosus. *Br Heart J* 1993;69:193.

**2.** Gentile R, Stevenson G, Dooley T, Franklin D, Kawabori I, Pearlman A. Pulsed Doppler echocardiographic determination of time of ductal closure in normal newborn infants. *J Pediatr* 1981;98:443–448.

**3.** Reller MD, Ziegler ML, Rice MJ, Solin RC, MacDonald RW. Duration of ductal shunting in healthy preterm infants: an echocardiographic color flow Doppler study. *J Pediatr* 1988;112:441–446.

**4.** Mandorla S. The ductus arteriosus in healthy newborn infants studied by continuous Doppler guided by two-dimensional Doppler color echocardiography. *G Ital Cardiol* 1990;20:705–712.

**5.** Hiraishi S, Misawa H, Oguchi K, Kadoi N, Saito K, Fujino N, Hojo M, Horiguchi Y, Yashro K. Two-dimensional echocardiographic assessment of closure of the ductus arteriosus in normal newborn infants. *J Pediatr* 1987;111:755–760.

**6.** Lim MK, Hanretty K, Houston AB, Lilley S, Murtagh EP. Intermittent ductal patency in healthy newborn infants: demonstration by colour Doppler flow mapping. *Arch Dis Child* 1992;67:1217–1218.

**7.** Cartlidge PH, Stewart JH. Survival of very low birthweight and very preterm infants in a geographically defined population. *Acta Paediatr* 1997; 86:105–110.