

The pulse pressure in a premature infant less than 37 weeks gestational age with a patent ductus arteriosus

Cristina Vega-Barrera¹, Jonathan Muraskas¹, Rong Guo², Brooke Ray³

¹Neonatal Intensive Care Unit, Loyola University Medical Center, Maywood, USA

²Statistics Department, Loyola University Medical Center, Maywood, USA

³Illinois Mathematics and Science Academy, Aurora, USA

Email: cbaumker@lumc.edu, jmurask@lumc.edu

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ABSTRACT

A widened pulse pressure could be a sign of a patent ductus arteriosus in an infant. This is defined as a difference between systolic and diastolic blood pressure of greater than 15 to 25 mm Hg, in premature infants and greater than 25 mm Hg in term infants [1]. It is thought that diastolic runoff from blood flow shunting across the aorta to the pulmonary artery, through the patent ductus arteriosus, will produce a lower diastolic pressure and therefore widen the pulse pressure in the affected infant [1]. In our retrospective chart review, 116 premature infants were identified with a patent ductus arteriosus and compared to 42 premature infants without a patent ductus arteriosus. The blood pressures obtained were recorded for the first 7 days of life of the patients. Our studies revealed that premature infants with a patent ductus arteriosus had a mean pulse pressure of 19 mm Hg (p-value 0.129) when compared to infants without a patent ductus arteriosus, 16 mm Hg, on day 1 of life. The mean pulse pressures were ~20 mm Hg in both groups on days 2 - 3. On days 4 - 7 mean pulse pressures were greater than 20 mm Hg for both groups (p-values 0.35, 0.19, 0.74, 0.8). It was noticed that mean pulse pressures in the patent ductus arteriosus group were within 0 - 4 mm Hg when compared to the group without a patent ductus arteriosus and therefore not clinically relevant or statistically significant.

Keywords: Patent Ductus Arteriosus; Widened Pulse Pressure; Premature

1. INTRODUCTION

A premature infant with a patent ductus arteriosus (PDA)

is a common occurrence. Nearly 30% of premature infants with birth weight less than 1500 grams will have a PDA [2]. In a premature infant, the diagnosis of a hemodynamically significant ductus arteriosus in a timely manner would lead to early treatment of this condition and prevent complications such as pulmonary edema/overflow and respiratory failure [3]. A formal diagnosis of a PDA is typically made with a Doppler echocardiogram. The echocardiogram will identify the patent ductus arteriosus and allow the neonatologist to initiate treatment either through medical or surgical intervention. In a term neonate a patent ductus arteriosus is not a problem. The neonate will transit in the first few days of life and the PDA will constrict and functionally close. In the preterm infant, a PDA may not functionally close due to immaturity of the ductal chemical mediators and hypoxemia the infant undergoes from premature lung disease [2]. Thus having a PDA could lead to complications such as decreased lung compliance, pulmonary edema/overflow, respiratory failure [3] and heart failure from volume overload into the left side of the heart.

For the past 25 years of neonatal medicine, the goal has been to effectively diagnose a PDA in premature infants, through clinical and/or interventional techniques such as echocardiogram, treat the condition, reduce the duration of ventilator days, and therefore decrease the incidence of bronchopulmonary dysplasia [4]. The clinical diagnosis of a PDA has been historically taught in medical schools and residency programs to be a high para-sternal systolic murmur, hyperdynamic precordial impulse, bounding pulses, and a widened pulse pressure [5]. Evans *et al.* demonstrated that a widened pulse pressure is not seen in preterm infants with a PDA [6]. In this study by Evans, 41 subjects were evaluated in the first 7 days of life who were <1500 grams with serial echocardiograms and continuous intra-arterial blood pressure monitoring. It was noticed that infants whose birth

weights were between 1000 - 1500 grams with a hemodynamic significant PDA did not have a significant difference in mean systolic, diastolic or pulse pressures when compared to those without a PDA [6]. There was a significant difference in systolic, diastolic and mean blood pressures in 8 infants <1000 grams with a PDA, when compared to those without a PDA, but mean pulse pressures again were not different in both groups [6].

2. SUBJECTS AND METHODS

We conducted a retrospective chart review of premature infants born at Loyola University Medical Center between August 15, 2006 and August 15, 2010. Infants included into the study were born premature, less than 37 weeks gestational age, had no congenital heart disease or major birth defects, and had medical charts in electronic version. There were 689 patients with complete medical charts identified beginning January 1, 2008 through December 15, 2010 in the EPIC computerized database. 419 patients did not have an echocardiograph performed. 7 patients were excluded due to congenital heart disease. The total patients reviewed were 263 (**Table 1**). Of the 263 patients reviewed, 158 patients had *invasive blood pressure* measurements available for analysis. 116 patients had a documented PDA and 42 did not have a PDA. We recorded the following data on infants who met the criteria (**Table 2**). The data included: identifying factors such as name, medical record number, DOB, gestational age, race, birth weight, mother's mode of delivery, gender, APGAR scores at 1 and 5 minutes, complications such as intraventricular hemorrhage (IVH), necrotizing enterocolitis (NEC), steroids prenatally given, and vital signs. The vital signs reviewed were systolic blood pressures (SBP), diastolic blood pressures (DBP), mean arterial blood pressures (MAP) from day of life 1 through 7. (**Table 3**) The pulse pressure was calculated using the recorded diastolic pressure and systolic blood pressures Eq.1.

$$PP = SBP - DPB . \quad (1)$$

We further subdivided the vital signs data into invasive blood pressures taken through a continuous monitoring arterial line versus a non-invasive blood pressure taken from a pressure cuff. The arterial lines were either peripherally inserted into an extremity or a UAC line; we did not distinguish between the two. We only used invasive blood pressures for the analysis. Our aim was to record 6 blood pressures per day of life for the first 7 days of life on each patient. However, some patients only had from 0 - 6 blood pressures recorded per patient per day for invasive blood pressure measurements. This was due to removal of the arterial line.

All patients in this study had an echocardiogram performed, and results documented into our database in-

Table 1. Total number of infants in study.

Year	Total	PDA by ECHO	No PDA by ECHO	ECHO not done
2008	278	56	36	186
2009	262	61	43	158
2010	149	43	31	75
(2008-2010)	689	160	110	419
excluded (did not meet criteria)		4	3	
Total (2008-2010)		156	107	
Total Reviewed-(2008-1010) with invasive BP		116	42	

Table 2. Characteristics of infants.

	No PDA	PDA
Gestational age (mean)	30.2 weeks	29.7 weeks
Birth weight (mean)	1551 grams	1273 grams
Gender male	64	97
Gender female	43	59
NEC all stages	13	14
IVH all grades	10	10

cluding the day of the infant's life it was performed; if an echocardiogram was not performed the patient was excluded from the study. We did not document the velocities of shunts, or direction of shunts.

Data Analysis

The blood pressure measurements were recorded in excel document and analysis through a two-sample t test was performed and results shown (**Table 3**). The infants were grouped into a PDA group vs. the no PDA group. There were 116 subjects in the PDA group and 42 subjects in the no PDA group. The blood pressures were statistically analyzed against the day the echocardiogram confirmed the presence of PDA or no PDA in the patient (**Figures 1-4**).

3. RESULTS

3.1. Systolic Blood Pressures (Figure 1)

Invasive systolic blood pressures were obtained for 116 patients with PDA and 42 without a PDA and plotted against days 1 through 7. There was no significant difference in systolic blood pressures between both groups. The mean systolic blood pressures were 50 mm Hg and 51 mm Hg in the PDA vs. no PDA group ($p = 0.865$) on day 1 and 48 mm Hg and 49 mm Hg on day 2 ($p = 0.92$). On day 3, the PDA group had a lower systolic pressure

Table 3. A comparison of blood pressures between PDA and no PDA by day.

Day	Measurement	Group	N	Mean	Std Deviation	Minimum	Maximum	p value
1	DBP	No PDA	2	35.8350	13.6684	26.1700	45.5000	0.5055
		PDA	12	31.2500	8.1525	21.8300	50.0000	
	MAP	No PDA	2	41.1650	12.4946	32.3300	50.0000	0.7670
		PDA	12	39.0142	8.9433	30.0000	60.5000	
	SBP	No PDA	2	51.7500	13.5482	42.1700	61.3300	0.8652
		PDA	12	50.2908	10.7525	35.6700	71.3300	
	PP	No PDA	2	15.9150	0.1202	15.8300	16.0000	0.1291
		PDA	12	19.0417	6.5966	8.5000	30.5000	
2	DBP	No PDA	5	28.5660	3.3443	26.0000	33.0000	0.8263
		PDA	16	27.7869	7.4945	15.1700	43.1700	
	MAP	No PDA	5	37.5680	5.1796	33.1700	45.0000	0.6983
		PDA	16	36.0350	8.1271	26.1700	53.5000	
	SBP	No PDA	5	48.8340	7.0468	43.5000	59.6700	0.9218
		PDA	16	48.3438	10.1913	32.1700	68.0000	
	PP	No PDA	5	20.2680	3.8317	17.5000	26.6700	0.9245
		PDA	16	20.5569	6.3073	7.3300	32.1700	
3	DBP	No PDA	7	36.7857	12.8450	28.6700	64.8300	0.0671
		PDA	17	25.8829	4.9734	20.0000	39.6700	
	MAP	No PDA	7	44.5229	12.9709	37.3300	73.3300	0.1013
		PDA	17	34.9012	5.9291	25.6700	50.8300	
	SBP	No PDA	7	56.5700	13.4987	44.8300	85.8300	0.0428
		PDA	17	46.9024	8.3379	33.5000	65.6700	
	PP	No PDA	7	19.7843	3.3331	12.8300	22.8300	0.5330
		PDA	17	21.0206	4.6697	13.1700	29.1700	
4	DBP	No PDA	10	31.5830	10.8293	18.3300	54.8300	0.1007
		PDA	22	25.4318	8.9047	14.8300	57.5000	
	MAP	No PDA	10	40.8840	11.0071	28.1700	65.6700	0.1405
		PDA	22	35.1664	9.3905	25.5000	70.0000	
	SBP	No PDA	10	53.5010	12.1030	39.6700	80.1700	0.3146
		PDA	22	49.1518	10.7157	38.3300	87.0000	
	PP	No PDA	10	21.9170	5.6873	9.0000	28.8300	0.3538
		PDA	22	23.7191	4.7003	9.8300	29.5000	

Continued

5	DBP	No PDA	5	29.7660	5.8407	20.5000	36.3300	0.1246
		PDA	21	25.6395	5.0752	17.5000	35.0000	
	MAP	No PDA	6	39.1383	7.4982	25.8300	48.6700	0.3034
		PDA	21	35.9448	6.3112	26.8300	49.0000	
	SBP	No PDA	5	52.2000	11.1272	32.8300	60.0000	0.8810
		PDA	21	51.5324	8.3428	33.1700	67.0000	
PP	No PDA	5	22.4340	5.9712	12.3300	27.6700	0.1929	
	PDA	21	25.8919	5.0154	11.3300	34.5000		
6	DBP	No PDA	4	30.5850	4.0664	26.1700	35.6700	0.5743
		PDA	18	27.3433	11.0049	17.0000	66.5000	
	MAP	No PDA	4	39.9600	5.4421	34.1700	47.1700	0.6630
		PDA	18	37.2411	11.8438	27.0000	79.0000	
	SBP	No PDA	4	52.2925	7.0487	46.6700	62.5000	0.9470
		PDA	18	51.7867	14.4535	38.8300	101.3	
PP	No PDA	4	21.7075	3.4393	19.5000	26.8300	0.7410	
	PDA	19	23.1574	8.3812	0	36.0000		
7	DBP	No PDA	9	26.0189	4.3962	19.1700	32.0000	0.4354
		PDA	10	24.3330	4.7615	16.3300	31.1700	
	MAP	No PDA	9	35.9622	4.7073	29.3300	42.0000	0.3603
		PDA	10	33.4840	6.5161	22.5000	43.1700	
	SBP	No PDA	9	50.8511	6.5490	38.5000	58.0000	0.5758
		PDA	10	48.5990	10.0655	33.1700	64.8300	
PP	No PDA	9	24.8333	2.5053	19.3300	28.1700	0.8093	
	PDA	10	24.2670	6.7579	15.3300	36.6700		

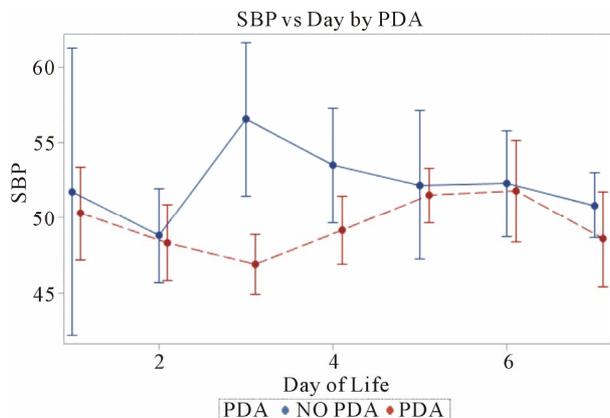


Figure 1. Systolic blood pressures plotted against day of life in the neonate. All patients reviewed were included.

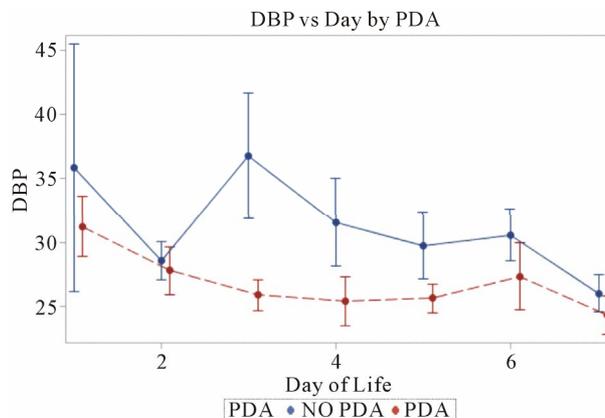


Figure 2. Diastolic blood pressures plotted against day of life in the neonate. All patients reviewed were included.

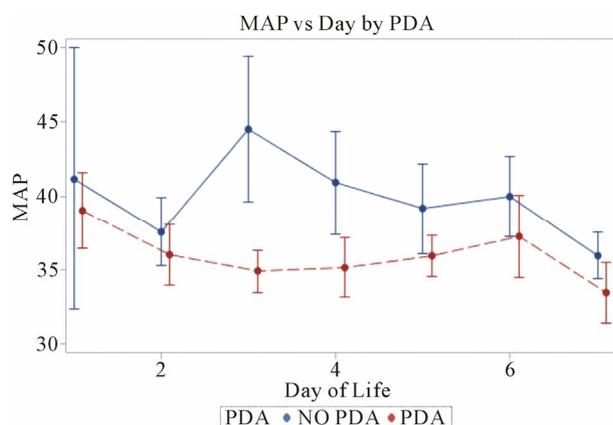


Figure 3. Mean arterial blood pressures plotted against day of life in the neonate. All patients reviewed were included.

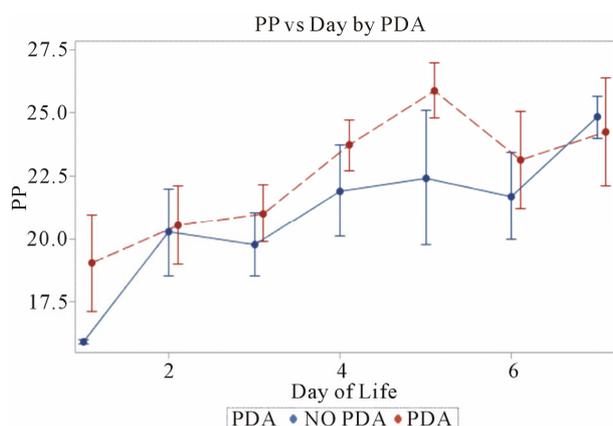


Figure 4. Pulse pressures plotted against day of life in the neonate. All patients reviewed were included.

47 mm Hg vs. 57 mm Hg ($p = 0.0425$) when compared to the no PDA group. On days 4 through 7, both groups had systolic blood pressures within 1 - 4 mm Hg difference and no clinical significance. Overall, the mean systolic blood pressures were the same in both groups, but there was a significant difference of ~10 mm Hg only on day 3.

3.2. Diastolic Blood Pressures (Figure 2)

Invasive diastolic blood pressures were obtained for 116 patients with PDA and 42 without a PDA on days 1 through 7. The mean diastolic blood pressures were 31 mm Hg and 36 mm Hg in the PDA vs. no PDA group ($p = 0.5$) on day 1 and 28 mm Hg and 29 mm Hg on day 2 ($p = 0.8$). On day 3, the PDA group had lower diastolic blood pressures when compared to the no PDA group; mean diastolic blood pressure of 25 mm Hg vs. 37 mm Hg respectively ($p = 0.07$). This was not clinically significant. The diastolic blood pressures in the PDA group continued to be lower than the no PDA group on day 4 and 5, 25 mm Hg vs. 32 mm Hg ($p = 0.1$) and 26 mm Hg

vs. 30 mm Hg ($p = 0.12$). Again, the difference was not clinically significant. Between days 6 - 7, the mean diastolic blood pressures in the PDA vs. no PDA were 2 - 3 mm Hg difference and not significant.

3.3. Mean Arterial Blood Pressures (Figure 3)

Invasive average mean arterial blood pressures were obtained for 116 patients with PDA and 42 without a PDA, between days 1 through 7. The mean mean arterial blood pressures were lower in the PDA group than in the no PDA group on days 3 - 4, 35 mm Hg vs. 45 mm Hg ($p = 0.1$) and 35 mm Hg vs. 41 mm Hg ($p = 0.1$) respectively. The mean systolic blood pressures were not significantly different in both groups in days 1 - 7.

3.4. Pulse Pressures (Figure 4)

Pulse pressures were calculated from the invasive blood pressure measurements from both groups. On day 1, the mean pulse pressure in the patent ductus arteriosus group was 19 mm Hg vs. 16 mm Hg in the group without a patent ductus arteriosus ($p = 0.12$). The mean pulse pressures were greater than or equal to 20 mm Hg after day of life 2 reaching a maximum pulse pressure on day of life 5 in both groups. The mean pulse pressure at DOL 5 was 26 mm Hg vs. 22 mm Hg, in the PDA group and no PDA group respectively ($p = 0.19$). After DOL 5, mean pulse pressures became similar in the two groups. The mean pulse pressures in the PDA group were 0.3 - 4 mm Hg higher on days 1 through 7, when compared to the group without a PDA. Both groups had widened pulse pressures but not statistically significant.

4. DISCUSSION

Overall, the analysis revealed that the means of the systolic, diastolic, and mean arterial blood pressures to be higher in the group without a patent ductus arteriosus when compared to the group with a patent ductus arteriosus. This finding was not proved to be statistically significant. Both groups had a difference of only 0 - 5 mm Hg in all parameters of blood pressures. In theory, the patient with a patent ductus arteriosus would demonstrate a lower blood pressure due to failed compensatory mechanisms. In the first 2 days of life, the infant without a patent ductus would drop their systolic blood pressures secondary to a decrease in total body volume. Thus the infant will compensate through the baroreceptor reflex. This reflex would increase their cardiac output and stroke volume. The increase in stroke volume and cardiac output has a direct increase systolic blood pressures, diastolic blood pressures and mean arterial blood pressures [7]. In the patient with a patent ductus arteriosus, the cardiovascular system is not a completely closed cir-

cuit. The PDA allows a shunt to exist from the arterial system to the pulmonary vascular system. The arterial system has an overall higher vascular tone when compared to the low vascular tone of the pulmonary bed. The shunting from the arterial bed to the pulmonary bed will lead to an overall decrease in vascular tone and lower blood pressures. Also, the patient with a patent ductus will have increased pulmonary overflow, left atrial overload and ventricular overload, which may lead to some heart failure [6]. This heart failure could lead to lower blood pressures from the decreased cardiac output and stroke volume [6,8]. The aim of this study was to prove that there existed a statistically significant difference in blood pressures between both groups since in clinical practice the observed differences are seen.

In this study it was observed, in both groups, that the mean pulse pressures were widened. According to the definition, a widened pulse pressure exists when the difference of systolic and diastolic blood pressure is greater than 15 to 25 mm Hg, in a premature infant (1). The group with a patent ductus had widened mean pulse pressures between 19 - 26 mm Hg while the group without a patent ductus also had widened mean pulse pressures between 16 - 24 mm Hg. Although the analysis revealed it not to be statistically significant, this finding is still intriguing. In clinical practice, the patient with a widened pulse pressure is automatically thought to have a patent ductus arteriosus. The finding that both groups had similar widened pulse pressures would not support this thought. Although the theory of diastolic run-off from a patent ductus is currently taught to residents in hospital programs, it does not hold true according to this study. The large shunting of blood flow from the aorta to the pulmonary arterial bed [6] during diastole would cause this diastolic run off. This effect, of the diastolic run off, will decrease the peripheral vascular resistance and lead to a reduced diastolic blood pressure and thus a widening of the pulse pressures.

Identifying a ductus arteriosus in a preterm infant through clinical signs is still a challenge. One cannot rely only on clinical assessments of blood pressures for a definite sign of a patent ductus arteriosus in the pre-

term infant. Many studies have been performed to correlate widened pulse pressures with patent ductus arteriosus however none have proven so. The study may have been limited due to the small group sizes and/or the few blood pressure samples that were collected in the patients. This was a retrospective chart review and the data obtained was limited to what was documented in the electronic file. In the future, a study may be created to account for the power size and the data amount needed for each group.

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