Clinical-Statistical Analysis of the Determinant Factors in the Evolution, Closure, and Mortality of Patent Ductus Arteriosus in Neonates

Guadamud Intriago Ana Maria[1], *Maldonado Vivanco Sara*[2]

[1]Neonatology Resident, University Catolica Santiago de Guayaquil, Hospital Roberto Gilbert Elizalde, Ecuador

[2]Neonatologist, Hospital Roberto Gilbert Elizalde, University Catolica Santiago de Guayaquil, Ecuador

***Corresponding author:**

Ana María Guadamud Intriago

Neonatology Resident, University Catolica Santiago de Guayaquil, Hospital Roberto Gilbert Elizalde, 90504, Ecudaor, Phone: 0958613779,
E-mail: Ana.guadamud@cu.ucsg.edu.ec

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ABSTRACT

Introduction

Patent Ductus Arteriosus (PDA) is one of the most prevalent cardiovascular abnormalities during the neonatal period, significantly affecting morbidity, mortality, and respiratory stability in preterm patients admitted to intensive care units.

Objectives

To determine the clinical-statistical and demographic factors correlated with ductal diameter evolution, the effectiveness of conservative versus pharmacological management, the need for surgical ligation, and mortality rate in a sample of 247 neonatal patients.

Methodology

A quantitative, correlational, descriptive, and cross-sectional study was conducted based on the clinical records of 247 neonates diagnosed with PDA. Baseline variables (sex and gestational age), ductal morphometry (echocardiographic diameter in millimeters and grading classification), therapeutic management (conservative management and duration of pharmacological treatment), closure success rate, and final outcome (mortality) were evaluated. Descriptive analysis included means, standard deviations, kurtosis, variances, and relative/cumulative frequency analyses.

Results

Among the 247 neonates analyzed, 126 (51.01%) were male and 121 (48.99%) were female. The mean gestational age of the cohort was 32.68 weeks (SD = 2.66), with a marked predominance of moderate to very preterm infants (28–33 weeks). The mean ductal diameter was 1.69 mm (SD = 0.66; range 1–4 mm), with most patients classified as Grade 1 (n = 133; 53.85%), followed by Grade 2 (n = 64; 25.91%) and Grade 3

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(n = 50; 20.24%). Conservative treatment demonstrated a 100% closure success rate in the 186 cases in which it was indicated (75.30%). Pharmacological treatment was administered in 61 cases (24.70%), lasting 7 days in 73.77% and 5 days in 26.23% of these patients, achieving medical closure in 25 neonates. The remaining 36 patients (14.57% of the total cohort) experienced failure of medical closure and required surgical ligation, with 100% belonging to Grade 3 PDA. Overall mortality was 7.69% (19 neonates), strongly correlated with extreme prematurity and luminal diameters > 2 mm.

Conclusions

Initial ductal diameter and gestational age constitute the main predictive factors for failure of conservative/medical treatment and overall mortality. Sequential pharmacological management and selective surgical ligation are consolidated as effective strategies for advanced echocardiographic stages.

INTRODUCTION

Patent Ductus Arteriosus (PDA) represents one of the essential fetal vascular structures whose failure of physiological obliteration during the first hours after birth triggers significant hemodynamic alterations in the newborn. During intrauterine life, the ductus arteriosus connects the left pulmonary artery to the descending aorta, diverting right ventricular blood flow away from the collapsed and nonfunctional fetal lungs toward the placental systemic circulation. At birth, pulmonary expansion, the abrupt increase in systemic partial oxygen pressure (PaO2), and the drastic reduction in circulating prostaglandins (PGE2)—due to placental removal and pulmonary metabolism—induce coordinated vasoconstriction of the ductal smooth muscle, culminating in functional closure within the first 24–48 hours of life, followed by permanent anatomical fibrosis [1].

However, in preterm patients, this regulatory mechanism is critically compromised. The intrinsic immaturity of voltage-dependent calcium channels in ductal smooth muscle, combined with greater sensitivity to circulating prostaglandins and persistently elevated baseline plasma nitric oxide levels, leads to structural failure in vessel constriction. Persistence of the ductus generates a left-to-right shunt, redirecting blood flow from the high-pressure systemic circulation toward the low-resistance pulmonary vascular bed. This phenomenon produces a dual clinical scenario of pulmonary hyperflow concomitant with systemic hypoperfusion (ductal steal), overloading the left ventricle, increasing capillary hydrostatic pressure, and exacerbating the risk of pulmonary edema, pulmonary hemorrhage, necrotizing enterocolitis (NEC), intraventricular hemorrhage (IVH), and bronchopulmonary dysplasia (BPD) [2].

Given the phenotypic heterogeneity of PDA in intensive care units, the clinical decision between observation (conservative management), pharmacological intervention with cyclooxygenase inhibitors (such as ibuprofen or indomethacin) or paracetamol, and surgical closure by thoracotomy or interventional catheterization remains the subject of intense debate in contemporary neonatology. Variability in treatment response and associated morbidity and mortality require robust statistical analyses capable of accurately identifying which demographic and echocardiographic factors determine closure success and patient survival. This study presents a complete analytical breakdown of a cohort of 247 neonates, multivariately correlating ductal morphometry with therapeutic outcomes and vital prognosis [3-11].

METHODOLOGY

Study Design and Population

A quantitative, correlational-descriptive, cross-sectional, and retrospective study was conducted. The study population consisted of all newborns admitted to neonatal critical care units who received a formal echocardiographic diagnosis of Patent Ductus Arteriosus (PDA) within a defined clinical period. After applying inclusion criteria (confirmed echocardiographic diagnosis and complete data records in the hospital database) and exclusion criteria (associated complex cyanotic congenital heart diseases dependent on ductal patency), a final census sample of 247 neonatal patients was established.

Definition of Variables and Clinical Criteria

For data collection and structuring, the following essential operational variables were defined:

- **Sex:** Binary nominal categorical variable coded as Male (1) and Female (2).
- **Gestational Age (GA):** Continuous quantitative variable analyzed in gestational weeks at birth. It was additionally categorized according to biological maturity into: Term Newborn (1; ≥37 weeks), Late Preterm (2; 34–36 weeks), Moderate Preterm (3; 32–33 weeks), Very Preterm (4; 28–31 weeks), and Extremely Preterm (5; <28 weeks).

- **Ductus Size:** Echocardiographic measurement of the luminal ductal diameter expressed in millimeters (mm). It was operationalized into three clinical ranges: ≤1.5 mm (Grade 1), 1.5–2 mm (Grade 2), and >2 mm (Grade 3).
- **Therapeutic Management:** Evaluated through two independent and mutually exclusive initial approaches: Conservative Treatment (observation, fluid restriction, and optimized ventilatory support; Yes = 1, No = 2) and Pharmacological Treatment (cyclooxygenase inhibitors or intravenous paracetamol; Yes = 1, No = 2), recording the net number of days of medical treatment (scale from 0 to 7 days).
- **Closure and Surgical Approach:** Nominal variables evaluating vessel occlusion success (Closure: Yes = 1, No = 2) and the need for escalation to surgical ligation via thoracotomy (Surgical Treatment: Yes = 1, No = 2) after pharmacological failure [6].
- **Vital Outcome:** Nominal safety variable recording patient survival or in-hospital death (Deceased: Yes = 1, No = 2).

Statistical Analysis

Raw data were anonymized, validated, and processed using the Microsoft Excel complementary statistical analysis package and multivariate descriptive analysis scripts. Measures of central tendency (mean, median, mode), dispersion measures (standard deviation, sample variance, standard error, range, minimum and maximum values), and distribution statistics (kurtosis and skewness coefficient) were calculated for continuous quantitative variables (ductus size and GA). Contingency tables and cross-frequency tables were implemented to evaluate discrete correlations between ductus size, treatment type, closure success rate, and overall mortality, applying a 95.0% confidence interval ($p < 0.05$).

RESULTS AND STATISTICAL ANALYSIS

The following official statistical tables consolidate the descriptive and cross-sectional findings obtained from the analysis of the cohort of 247 neonatal patients (Table 1).

Table 1: Descriptive Analysis of Continuous Variables: Ductus Size (mm) and Gestational Age (GA)

Statistical Parameter	Ductus Size (mm)	Gestational Age (Weeks)
Mean	1.6923	32.6801
Standard Error	0.0422	0.1695
Median	1.5000	32.0000
Mode	1.0000	30.0000
Standard Deviation	0.6644	2.6654
Sample Variance	0.4415	7.1046
Kurtosis	-0.5108	-0.7972
Skewness Coefficient	0.5860	0.1592
Range (Minimum/Maximum)	3.0000 (1.0000/4.0000)	13.0000 (26.0000/39.0000)
Confidence Level (95.0%)	0.0832	0.3340

Distribution Analysis

Descriptive analysis revealed that the mean luminal ductal diameter was 1.69 mm (standard error = 0.042), with a modal value of 1.00 mm and a maximum value of 4.00 mm. The negative kurtosis of -0.51 indicates a moderately platykurtic distribution with uniform dispersion around the mean, while the positive skewness coefficient (0.58) confirms a bias toward smaller diameters. Regarding gestational age, the mean was 32.68 weeks, reflecting the prematurity profile of the sample, with a biological mode concentrated at 30 weeks of gestation (Table 2).

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Table 2: Frequency and Grading of Patent Ductus Arteriosus by Clinical Stage

Clinical Stage	Absolute Frequency (n)	Relative Frequency (%)
Grade 1 (≤1.5 mm)	133	53.85%
Grade 2 (1.5–2.0 mm)	64	25.91%
Grade 3 (>2.0 mm)	50	20.24%
Total Sample	247	100.00%

Distribution Analysis by Grade

More than half of the cohort presented a Grade 1 ductus (53.85%), clinically correlated with hemodynamically restrictive shunts with lower initial systemic repercussion. Advanced and highly significant forms represented by Grade 3 affected one-fifth of the sample (20.24%) (Table 3).

Table 3: Cross-Contingency Table: Initial Management Strategy and Closure Success Rate

Initial Therapeutic Strategy	Successful Closure (Yes)	Medical Closure Failure (No)	Total Patients
Conservative Treatment	186 (100.0%)	0 (0.0%)	186 (75.30%)
Pharmacological Treatment	25 (40.98%)	36 (59.02%)	61 (24.70%)
Total Cohort	211	36	247

Therapeutic Analysis

A critical clinical-statistical finding was that 75.30% (n = 186) of neonates responded optimally to expectant or conservative management (spontaneous closure or closure guided by fluid restriction). Conversely, in the group requiring pharmacological treatment due to symptoms and hemodynamic instability (n = 61; 24.70%), medical closure failure reached 59.02% (36 of 61 patients), forcing the search for alternative management strategies (Table 4).

Table 4: Correlation Between Initial Ductus Size and Need for Surgical Treatment (Ligation)

Initial Ductus Grade	Surgical Ligation (Yes)	Sustained Medical Management (No)	Total Patients
Grade 1 (≤1.5 mm)	0 (0.0%)	133 (100.0%)	133
Grade 2 (1.5–2.0 mm)	0 (0.0%)	64 (100.0%)	64
Grade 3 (>2.0 mm)	36 (72.0%)	14 (28.0%)	50
Total Sample	36	211	247

Correlation of Surgical Intervention Scale

The data demonstrate a perfect and statistically significant correlation between severity grading and invasive intervention. One hundred percent of patients requiring surgical treatment (n = 36) belonged to the Grade 3 PDA group (>2 mm). In fact, if a neonate presented with a Grade 3 ductus, the mathematical probability of requiring surgical ligation was 72.0%, highlighting the refractory nature of large ducti to traditional therapeutic options (Table 5).

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Table 5: Analytical Distribution of Neonatal Mortality According to Clinical Variables

Clinical Stratification Variable	Deceased Patients (n)	Specific Mortality Rate (%)
Size Stratification: Grade 1 (≤1.5 mm)	5	3.75% (5/133)
Size Stratification: Grade 2 (1.5–2.0 mm)	2	3.12% (2/64)
Size Stratification: Grade 3 (>2.0 mm)	12	24.00% (12/50)
Maturity Stratification: Extremely Preterm (<28 GA)	1	50.00% (1/2)
Overall Cohort Mortality	19	7.69% (19/247)

Mortality Analysis

The overall mortality rate in the analyzed cohort was 7.69% (19 of 247 newborns). When this indicator was stratified, ductal diameter acted as a major vital risk marker: the group of patients with Grade 3 ductus accounted for most deaths (12 of 19 deceased patients), with a specific lethality rate of 24.00%, quintupling the risk observed in Grades 1 and 2. Likewise, extreme immaturity (<28 weeks of gestation) demonstrated a critical impact with a lethality rate of 50.00%.

DISCUSSION

The comprehensive statistical analysis of this cohort of 247 neonates provides highly valuable clinical data for the standardization of Patent Ductus Arteriosus (PDA) management. Sex distribution demonstrated near-perfect equality (51.01% male vs. 48.99% female), confirming that PDA does not present gender-linked predisposition in critically ill populations. However, gestational age distribution (mean of 32.68 weeks and modal value concentrated at 30 weeks) corroborates the solid epidemiological basis described in international literature: the lower the gestational age, the greater the incidence and persistence of the vessel due to structural immaturity of the elastic and muscular tissue of the ductal tunica media.

A central finding of our investigation is the high success rate of expectant or conservative management, which achieved functional closure in 100% of the 186 cases in which it was indicated (75.30% of the cohort). This finding challenges the aggressive systematic interventional approaches of previous decades and supports current neonatology trends promoting restrictive parenteral fluid management and optimization of positive end-expiratory pressure (PEEP) parameters in respiratory support to reduce pulmonary shunting, thereby allowing spontaneous physiological closure in small- and medium-caliber ducti (Grades 1 and 2).

Conversely, the group requiring specific pharmacological management (n = 61) represented the subgroup with the greatest hemodynamic complexity. Within this group, the 5- to 7-day therapeutic window (where 73.77% completed a full 7-day cycle and 26.23% a shorter 5-day cycle) demonstrated a medical failure rate of 59.02% (36 patients). Clinically, the relevant finding is that all pharmacological treatment failures strictly belonged to Grade 3 PDA (>2 mm), mandating escalation to surgical closure by thoracotomy ligation. Clinically, this indicates that ducti with diameters greater than 2 mm possess lower densities of functional receptors or intrinsic resistance to prostaglandin inhibitors, making a diameter ≥2 mm an independent predictive factor for pharmacological failure and surgical need.

Finally, the overall mortality of 7.69% (19 of 247 patients) is closely consistent with worldwide intensive care registries for preterm neonates complicated by cardiovascular disease. However, the critical finding is the isolated lethality rate of 24.00% observed in the Grade 3 ductus group, demonstrating that chronic massive pulmonary hyperflow and systemic steal perpetuated by large ducti undermine perfusion of target organs (mesenteric, renal, and cerebral ischemia), increasing patient vulnerability and doubling the risk of terminal multisystem failure [13-15].

CLINICAL RECOMMENDATIONS

1. **Early Echocardiographic Stratification as a Therapeutic Guide:** It is recommended to implement universal and standardized echocardiographic screening within the first 72 hours of life in all neonates under 34 weeks receiving respiratory support. Exact luminal diameter measurement should guide decision-making: ducti ≤1.5 mm (Grade 1) should prioritize exclusive conservative management,

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whereas diameters >2 mm (Grade 3) should be closely monitored due to their high probability of pharmacological failure.

2. **Optimization of Conservative Management in Early Grades:** Establish strict protocols for judicious fluid restriction (avoiding overloads >130–140 mL/kg/day during the first week) and optimal PEEP ventilatory support in patients with Grade 1 and Grade 2 ducti, maximizing spontaneous occlusion rates while reducing unnecessary exposure to renal and gastrointestinal toxicity associated with COX inhibitors [12].

3. **Protocolization of Sequential Pharmacological Treatment:** In neonates with advanced ducti and hemodynamic instability, it is suggested to standardize the duration of medical pharmacological cycles based on serial echocardiographic response. The finding that 73.77% of treated patients required complete 7-day regimens underscores the need for mature treatment cycles instead of shorter regimens when the vessel exceeds 1.5 mm.

4. **Timely and Selective Surgical Criteria:** Since 100% of newborns requiring surgical ligation presented Grade 3 ductus, unnecessary prolongation of multiple ineffective pharmacological cycles should be avoided in this specific group, planning timely surgical interruption to promptly halt pulmonary hyperflow and mitigate the documented specific lethality of 24%.

5. **Post-Closure Follow-Up and Surveillance of Sequelae:** All patients undergoing surgical ligation or prolonged pharmacological cycles should receive medium-term echocardiographic follow-up to rule out residual left pulmonary artery stenosis or iatrogenic aortic coarctation, as well as strict pediatric pulmonology monitoring due to the elevated underlying risk of developing chronic bronchopulmonary dysplasia.

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