




Pulmonary Hypertension and Cardiac Surgery: Perioperative Management in a Resource Limited Setting

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Abstract

Introduction: Pulmonary hypertension (PH) is a hemodynamic and pathophysiological condition characterized by abnormally elevated pressures in the pulmonary vasculature. It is defined by a mean pulmonary arterial pressure \geq 25 mmHg at rest by right heart catheterization. It is frequently associated with cardiovascular surgery and is a common complication that has been observed after surgery utilizing cardiopulmonary bypass (CPB). Preoperative PH has been significantly linked to morbidity and is a risk factor for poor outcome post-surgery. Some specific features in sub-Saharan Africa: given the lack of access to cardiac surgery, PAH occurs very frequently in cases of advanced heart disease in patients with congenital heart disease or rheumatic valve disease that has been treated late. **Objective:** The purpose of this study was to evaluate a protocol for managing PH during cardiac surgery under cardiopulmonary bypass in resource limited settings. **Patients and Methods:** This is a descriptive and analytical retrospective study that included all patients who

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underwent cardiopulmonary bypass surgery at the “Le Luxembourg” Mother and Child University Hospital between January 1, 2023, and June 30, 2024, and who had a preoperative systolic pulmonary artery pressure (SPAP) \geq 35 mmHg. Preoperatively, all patients included were given Furosemide: 1 mg/kg and Sildenafil 5 or 10 mg/8 hours in children and 20 mg/8 hours in adults. In the operating room, a nasogastric tube was inserted to administer sildenafil at the end of surgery, and weaning from CPB was performed using Milrinone at a syringe pump rate of 5 μ g/kg/min, combined with Norepinephrine as needed depending on hemodynamic status. We analyzed the mean changes in PAPS from the preoperative assessment to discharge from intensive care. **Results:** During the period, 292 patients underwent surgery, 142 of whom had PH, representing a prevalence of 48.63%. Our patients had an average age of 11.57 ± 11 . There was a female predominance of 51.4%. The average length of preoperative hospitalization was 5 days [3 - 8]. The time between diagnosis and surgical treatment was between 1 and 5 years in 62.8% of cases. It was \leq 1 year in 29.6% of cases. The clinical signs were dominated by dyspnea in 43.7% of cases. Pulmonary artery systolic pressure was between 51 - 100 mmHg in 29.58% and >100 mmHg in 19.72% of cases, with a mean preoperative sPAP of 59 mmHg [35 - 110]. Congenital heart disease accounted for 52.11% of surgical indications, and valvular heart disease for 47.89%. Surgical indications for mitral valve disease accounted for 35.92% of cases and those for congenital heart disease for 52.11%. The mean duration of CPB was $110 \text{ min} \pm 50$. There were no intraoperative episodes of pulmonary hypertension. At the end of surgery, the average time to postoperative extubation in intensive care was $3.53 \text{ hours} \pm 2.2$. There was a significant decrease in sPAP between the preoperative and postoperative periods. A comparison of pre- and post-operative sPAP averages using a t-test was significant with a P-value < 0.001 (t: 27.978). The main postoperative complications are: Overall cardiac failure: 4.2%; respiratory failure: 2.1%; hematological complications: 0.7%. We recorded a perioperative mortality rate of 5.6%. **Conclusion:** PH complicates rheumatic valve disease and certain congenital heart diseases. It is common in our resource-limited setting, where access to cardiac surgery is insufficient. It is associated with high perioperative morbidity and mortality. Management is well codified, but the therapeutic classes are sometimes unavailable in our countries. The postoperative protocol of furosemide + sildenafil and milrinone appears to give good results.

Keywords

Cardiac Surgery, Pulmonary Hypertension, Cardiopulmonary Bypass, Sildenafil, Milrinone

1. Introduction

Pulmonary hypertension (PH) is a hemodynamic and pathophysiological condition characterized by abnormally elevated pressures in the pulmonary vasculature. It is defined by a mean pulmonary arterial pressure \geq 25 mmHg at rest by right

heart catheterization [1]. PH can be caused by an increase in pulmonary blood flow, pulmonary vascular resistance, pulmonary venous pressure or a combination of these factors. Pulmonary hypertension is frequently associated with cardiovascular surgery and is a common complication that has been observed after surgery utilizing cardiopulmonary bypass (CPB). Preoperative PH has been significantly linked to morbidity and is a risk factor for poor outcome post-surgery [2]. Accurate preoperative assessment and diligent anesthetic management are crucial for the best outcome [3]. The anesthetic management of such patients requires a thorough understanding of the etiology, pathophysiology, type, and severity of PH along with the nature of the surgical procedure [4]. Some specific features in sub-Saharan Africa: given the lack of access to cardiac surgery, PAH occurs very frequently in cases of advanced heart disease in patients with congenital heart disease or rheumatic valve disease that has been treated late.

2. Objective

The purpose of this study was to evaluate a protocol for managing PH during cardiac surgery under cardiopulmonary bypass in resource limited settings.

3. Patients and Methods

This is a descriptive and analytical retrospective study that included all patients who underwent cardiopulmonary bypass surgery at the “Le Luxembourg” Mother and Child University Hospital between January 1, 2023, and June 30, 2024, and who had a preoperative systolic pulmonary artery pressure (SPAP) ≥ 35 mmHg. Preoperatively, all patients included were given Furosemide: 1 mg/kg and Sildenafil 5 or 10 mg/8 hours in children and 20 mg/8 hours in adults. In the operating room, a nasogastric tube was inserted to administer sildenafil at the end of surgery, and weaning from CPB was performed using Milrinone at a syringe pump rate of 5 $\mu\text{g}/\text{kg}/\text{min}$, combined with Norepinephrine as needed depending on hemodynamic status. We analyzed the mean changes in PAPS from the preoperative assessment to discharge from intensive care using a T-test to compare averages.

4. Results

During the period, 292 patients underwent surgery, 142 of whom had PH, representing a prevalence of 48.63%. Our patients had an average age of 11.57 ± 11 . There was a female predominance of 51.4%. The average length of preoperative hospitalization was 5 days [3 - 8]. The time between diagnosis and surgical treatment was between 1 and 5 years in 62.8% of cases. It was ≤ 1 year in 29.6% of cases. The clinical signs were dominated by dyspnea in 43.7% of cases. SPO_2 was $< 80\%$ in 6.3% of patients and between 80% - 94% in 15.5% of cases. Pulmonary artery systolic pressure was between 51 - 100 mmHg in 29.58% and > 100 mmHg in 19.72% of cases, with a mean preoperative sPAP of 59 mmHg [35 - 110]. **Table 1** shows the preoperative epidemiological and clinical characteristics of our patients.

Congenital heart disease accounted for 52.11% of surgical indications, and val-

vular heart disease for 47.89%. Surgical indications for mitral valve disease accounted for 35.92% of cases and those for congenital heart disease for 52.11%.

Table 1. Epidemio-clinical characteristics.

Diagnosis delay	Frequency	Percentage
0 - 12 months	42	29.6
1 - 5 years	89	62.8
6 - 10 years	9	6.3
11 - 15 years	2	1.3
Total	142	100
Clinical signs	Frequency	Percentage
Dyspnea	62	43.7
Cough	16	11.3
Palpitations	9	6.3
Digital hippocratism	8	5.6
Hepatomegaly	2	1.4
Jaundice	2	1.4
Preoperative pulse oximetry (SPO2)	Frequency	Percentage
<80%	9	6.3
80% - 94%	22	15.5
>94%	111	78.2
TOTAL	142	100
Preoperative systolic pulmonary artery pressure (sPAP)	Frequency	Percentage
36 - 50 MMHG	72	50.70
51 - 100 mmHg	42	29.58
SUP A 100 MMHG	28	19.72
Total	142	100
Indication: Mitral valve disease	Frequency	Percentage
Mitral insufficiency	31	21.83
Mitral stenosis	20	14.08
Total	51	35.92
Indication: Aortic valve disease	Frequency	Percentage
Aortic insufficiency	13	9.15
Aortic stenosis	4	2.82
Total	17	11.97
Indication: Congenital heart disease	Frequency	Percentage
Ventricular septal defect	48	33.80
Atrial septal defect	23	16.20
Ventricular septal defect + Atrial septal defect	3	2.11
Total	74	52.11

The mean duration of CPB was 110 min \pm 50. There were no intraoperative episodes of pulmonary hypertension. At the end of surgery, the average time to postoperative extubation in intensive care was 3.53 hours \pm 2.2. **Table 2** and **Figure 1** show the different variations in sPAP on postoperative days 1, 2, and 3 compared to the preoperative period. A comparison of pre- and post-operative sPAP averages using a t-test was significant with a P-value $<$ 0.001 (t: 27.978). The main postoperative complications are reported in **Table 3**: Overall cardiac failure: 4.2%; respiratory failure: 2.1%; hematological complications: 0.7%. We recorded a perioperative mortality rate of 5.6%.

Table 2. Perioperative variations in pulmonary artery systolic pressure (sPAP).

sPAP interval	Percentage Preoperative	Percentage J1 Postoperative	Percentage J2 Postoperative	Percentage J3 Postoperative
20 - 35 mmHg		18	42	56
36 - 50 mmHg	50.70	32	30	25
51 - 100 mmHg	29.58	11	12	7
SUP A 100 mmHg	19.72	2	0	0
Total	100.00	63	84	88

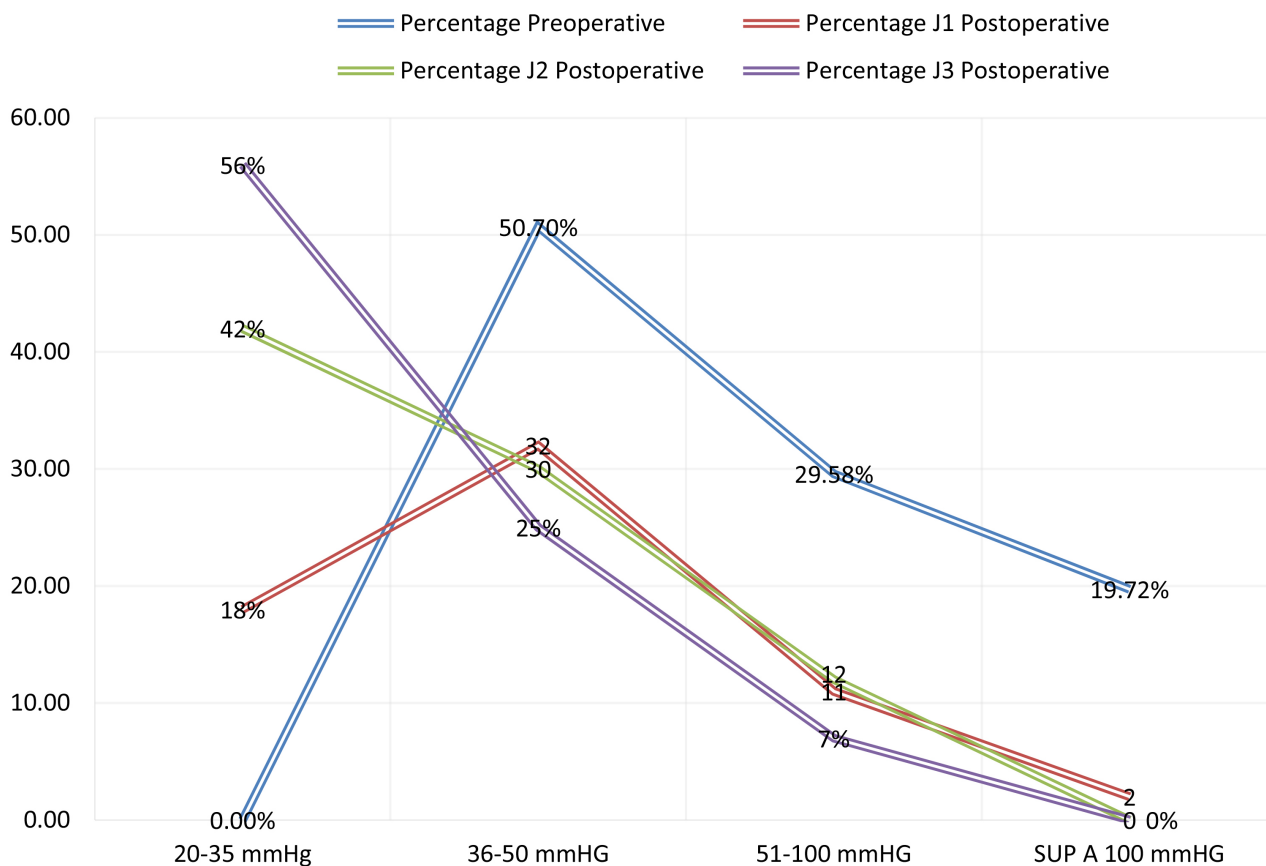


Figure 1. Perioperative variations in pulmonary artery systolic pressure (sPAP).

Table 3. Main complications.

Complications	Frequence	Percentage
Global heart failure	6	4.2
Respiratory complications	3	2.1
Hemorrhagic complications	1	0.7
Death	8	5.6

5. Discussion

Pulmonary hypertension (PH) is frequently associated with cardiovascular surgery and is a common complication that has been observed after surgery utilizing cardiopulmonary bypass (CPB). Preoperative PH has been significantly linked to morbidity and is a risk factor for poor outcome post surgery [2]. This effect is mediated via two pathways deleterious right ventricular remodeling, and exacerbation of perioperative stress placed on the Right Ventricle (RV) both of which predispose these patients to postoperative RV failure [5]. The prevalence of PH may vary widely across specific populations: from 7.4% in patients with systemic sclerosis to 68.7% in patients with cardiac surgery [1]. PH is common in low-income countries, unlike in other parts of the world. The REMEDY study found a prevalence of 29.9% and 19% in low-income countries and upper-middle-income countries, respectively [6]. In a Malian series for rheumatic valve disease surgery, we found that: 19.1% had PASP between 35 and 50 mmHg and 25% had PASP > 50 mmHg [7]. Lindberg *et al.* [8] were found a 2% incidence of severe PH and a 0.7% incidence of PH crisis after cardiac surgical procedures.

This high prevalence could be explained, among other things, by delays in treatment and limited access to surgery in these regions of the world. In our series, 62.8% of patients waited between 1 and 5 years to receive surgical treatment. Kingué *et al.* reported that patients were seen late in the course of the disease, with 40% presenting with heart failure and in New York Heart Association class III or IV [9].

PH is an independent predictor of increased morbidity and mortality (4% - 24%) following surgery, and these patients are high-risk candidates depending on severity of disease and surgical procedure [10].

The assessment of perioperative risk depends on the type of surgery, the severity of PH, and the functional status of the patient. The outcomes of major surgeries showed mortality and short-term morbidity rates of 7% and 42%, respectively [4].

Perioperative risk factors for PH after cardiac surgery and CPB include preoperative PH, fluid overload, acidosis, hypoxia, positive pressure ventilation, elevated sympathetic tone, ischemia-reperfusion injury, pulmonary reperfusion syndrome, left ventricular diastolic or systolic failure, acute respiratory distress syndrome, embolism such as air embolism, thromboembolism, amniotic fluid embolism, and CO₂ embolism, systemic inflammatory response, the necessity of blood

transfusions, mechanical failure, loss of vasculature such as pneumonectomy, duration of CPB, and pharmacological agents [11]. In addition, hypoxia, hypercarbia, and pulmonary embolism which can appear before, during, or after CPB are contributors to PH development. When hypoxia is present, pulmonary vessels tend to constrict due to a direct effect on the microcirculation [2]. Inflammation has also been identified to play a role in PH after cardiac surgery and CPB [2]. There are several mechanisms that cause inflammation during cardiac surgery with CPB. Mechanisms that cause inflammation during cardiac surgery include blood exposure to synthetic surfaces during CPB, lung damage due to ischemia-reperfusion, splanchnic hypoperfusion-induced endotoxemia, blood recirculation during cardiotomy suction, utilization of protamine, and injury to the surgical tissue.

Although PAP may decrease after valvular surgery, the period immediately after separation from CPB may be complicated by a higher PAP, particularly among patients with pre-existing PH. PVR may increase after CPB because of atelectasis, ischemia-reperfusion injury, endothelial damage, and the release of inflammatory mediators that increase capillary permeability. Ventricular dysfunction, which is common in the immediate post bypass period [2].

Different therapeutic classes are used to treat these PHs depending on their pathophysiological classes, clinical status, and, of course, the availability of therapies. [4]. These are:

Group 1: Anticoagulation, diuretics, oxygen therapy, and digoxin. Therapeutic approach is guided by functional status and objective testing as follows: **Low risk, functional Class I - III** patients may be treated with oral Phosphodiesterase-5 (PDE-5) inhibitors, oral endothelin receptor antagonists (ERAs), or inhaled prostacyclins.

High risk, functional Class III - IV patients should be treated with intravenous (IV) or subcutaneous prostacyclins.

Group 2: They are managed with therapies for left heart failure. A small trial suggested potential benefit of PDE-5 inhibitors in patients with heart failure and a preserved ejection fraction. ERAs and prostacyclins should not be used.

Group 3: Management is directed at the underlying lung disease. Pulmonary vasodilators do not have a role and worsens ventilation perfusion (VQ) matching in these patients.

Group 4: PH is potentially curable with pulmonary thromboendarterectomy. There may be a role for pulmonary vasodilators in those who are not surgical candidates.

Group 5: Management is directed at the underlying disease.

Studies have demonstrated the success of Inhaled NO (iNO) in treating postoperative PH as a selective pulmonary vasodilator for patients undergoing cardiac surgery and CPB. In a study, it was concluded that iNO greatly decreases mPAP in patients with postoperative PH, helps with vasodilation, and does not cause hemodynamic complications [2].

Several studies have shown sildenafil to be successful in treating postoperative PH. Sildenafil, a PDE5 inhibitor, has been shown to be promising in treating PH due to mitral valve surgery. In a double-blind, placebo-controlled randomized trial, it was found that giving sildenafil postoperatively is safe and that it lowers pulmonary vascular pressure and mean pulmonary pressure without causing ventilation–perfusion mismatch or systemic hypotension [12]. A meta-analysis studying the role of sildenafil in pulmonary hypertension [13] retrouvait: Sildenafil treatment resulted in a significant improvement in the Six-Minute Walk Distance (6 MWD). Quality of Life (QOL) assessment, using the Chronic Heart Failure Questionnaire, revealed improvements in breathlessness, fatigue, emotional function, and overall score with sildenafil. New York Heart Association (NYHA) Classification improved with sildenafil in one study while another study found no re-classification.

Milrinone has been demonstrated to be effective in treating postoperative PH for patients undergoing mitral valve surgery. A study found that IV milrinone is superior to oral sildenafil in managing PH after pediatric cardiac surgery and ending pulmonary hypertensive crisis [14].

In our context, therapies such as ERAs, inhaled prostacyclins, subcutaneous prostacyclins, or inhaled nitric oxide (NO) are not available. Hence the implementation of this protocol (sildenafil + furosemide preoperatively and weaning from CPB under milrinone). Our protocol appears to be yielding good results, with a significant decrease in sPAP values. Furthermore, no hypertensive crises were observed during the perioperative period.

6. Limitations of the Study

This study is an ambitious undertaking, but it does have a number of practical limitations that we feel are important to highlight here. It is a retrospective study that was conducted in a single center (monocentric, the only cardiac surgery center in the country). The fact that pulmonary pressure measurements were taken by echocardiography rather than right heart catheterization may have an impact on the assessments, but has the advantage of being practical, since echocardiography is the method available to us and the one we use on a daily basis.

7. Conclusion

PH complicates rheumatic valve disease and certain congenital heart diseases. It is common in our resource-limited setting, where access to cardiac surgery is insufficient. It is associated with high perioperative morbidity and mortality. Management is well codified, but the therapeutic classes are sometimes unavailable in our countries. The postoperative protocol of furosemide + sildenafil and milrinone appears to give good results.

Ethical Considerations

Patient confidentiality was respected throughout the conduct of this work. Pa-

tients or their legal representatives authorized the use of their data in this work. Authorization from the local ethics committee of the “LE LUXEMBOURG” Mother and Child University Hospital, Bamako was obtained prior to the conduct of this work.

Conflicts of Interest

The authors report no conflicts of interest in relation to this work.

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