Introduction

Post operative pulmonary hypertension is a feared complication after heart surgery in children in whom increased pulmonary blood flow, pulmonary venous obstruction, or both, have caused increased pulmonary vascular resistance (PVR) and reactivity.\textsuperscript{1,2} The operative trauma (e.g., the endothelial injury caused by cardiopulmonary bypass [CPB])\textsuperscript{3} may further increase pulmonary vascular reactivity and create a situation in which moderate postoperative stress dramatically increases PVR. In children with decreased right ventricular contractility, this may result in acute right ventricular dilation, circulatory collapse and death.

Corrective surgery on younger children and improvements in perfusion technology and perioperative care have both decreased the risk of severe pulmonary hypertension and improved its outcome. Intraoperative ultrafiltration\textsuperscript{4} and selective decrease of pulmonary vascular resistance by use of nitric oxide\textsuperscript{5,6} have shown promising results so far. The creation of larger paediatric surgery programmes has promoted early recognition and treatment of pulmonary hypertension, thus increasing the chances of a positive outcome.\textsuperscript{7}

Aims and Objectives

To determine the outcome of patients with severe pulmonary hypertension in terms of
1) inotropic support,
2) duration of intensive care unit stay and
3) outcome.
Severe pulmonary hypertension was said to exist when there was an increase in the mean pulmonary arterial pressure to the level of mean systemic arterial pressure or greater.

**Inclusion Criteria**
1) All paediatric patients less than 15 years of age, with operable congenital heart diseases with clinical features suggestive of pulmonary hypertension.
2) Any child with left to right shunt with pulmonary hypertension

**Exclusion Criteria**
1) Patients older than 15 years.
2) Patients who refuse consent to undergo surgery
3) Patients with cardiac anomalies or had undergone corrections not compatible with pulmonary hypertension, e.g. tetralogy of Fallot, pulmonary stenosis or atresia, cavopulmonary connections, and the Norwood procedure for hypoplastic left heart syndrome

**Material and Methods**
This retrospective study was conducted at our institution over a 1 year period from January 2007 to December 2007. The data collected during this one year period was retrieved from the records of cardiothoracic surgery operation theatre and intensive care unit attached to it. A total of 193 patients' records were obtained, whose age group was below 15 years and they underwent cardiac surgery at our institute. The children were classified according to risk as recommended by Swedish National Board of Health and Welfare (Table 1).

To select children with or at risk for clinically important PH, we studied all children who were monitored after the operation (n = 191), who needed mechanical ventilation longer than 4 postoperative days (n = 42) or who died in the operating room or

**Table 1 : Paediatric heart operations according to the risk classification used by the Swedish National Health Institute**

<table>
<thead>
<tr>
<th>Group 1</th>
<th>Group 2A</th>
<th>Group 2B</th>
<th>Group 2C</th>
<th>Group 3A</th>
<th>Group 3B</th>
<th>Group 3C</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASD Secondary</td>
<td>TOF</td>
<td>TOF + conduit</td>
<td>Switch</td>
<td>VSD + conduit</td>
<td>Fontan or TCPC</td>
<td>Prematurity</td>
</tr>
<tr>
<td>ASD Primary</td>
<td>VSD + AS</td>
<td>Peripheral PS</td>
<td>Mustard</td>
<td>Bidirectional Glenn</td>
<td>Complex Glenn + VSD</td>
<td>AS + LV hypoplasia</td>
</tr>
<tr>
<td>VSD</td>
<td>VSD + PS</td>
<td>DORV</td>
<td>Senning</td>
<td>PA + VSD</td>
<td>Complex switch</td>
<td>HLHS</td>
</tr>
<tr>
<td>PS, age &gt; 1 month</td>
<td>ASD + PAPVD</td>
<td>Multiple VSD</td>
<td></td>
<td>PA + IVS</td>
<td>Truncus arteriosus</td>
<td></td>
</tr>
<tr>
<td>AS, age &gt; 1 year</td>
<td>AS &lt; 1 yr</td>
<td>MS, MR &gt; 1yr</td>
<td>Absent pulmonary valve</td>
<td>Atrial septectomy</td>
<td>Aortic root reconstruction</td>
<td></td>
</tr>
</tbody>
</table>

ASD : atrial septal defect; AVSD : atrioventricular septal defect; TOF : tetralogy of Fallot; VSD : ventricular septal defect; TCPC : total cavopulmonary connection; AS : aortic stenosis; TAPVD : total anomalous pulmonary venous return; UVH : univentricular heart; PS : pulmonary stenosis; PA : pulmonary atresia; LV : left ventricular; DORV : double-outlet right ventricle; CTGA : congenital corrected transposition of the great arteries; PAPVD : partial anomalous pulmonary venous return; IVS : intact ventricular septum; HLHS : hypoplastic left heart syndrome; MS : mitral stenosis; MR : mitral regurgitation

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intensive care unit (ICU, n = 4). Inclusion of children who were continuously monitored after the operation was likely to select most patients with severe PH, because pulmonary artery catheters were routinely placed in children deemed at risk for postoperative PH and in whom intraoperative, postbypass cardiac pressure recordings indicated such a risk.

The degree of pulmonary hypertension was classified as follows in the total of 193 patients.

— none or mild when mean PAP was normal or only transiently elevated above 30 mm Hg,
— as moderate when mean PAP exceeded 30 mm Hg on more than 3 occasions after the operation but did not reach MAP levels,
— as severe when mean PAP was at least as great as MAP, and
— as a PH crisis when mean PAP equal to or greater than MAP was combined with a decrease in MAP.

Perioperative or early mortality was defined as death occurring during the operation or within 30 days of the operation. ICU morbidity was expressed as duration of ventilatory support, duration of ICU stay, and number of registered complications. The latter were classified as follows:

— circulatory complications were noted when at least two inotropic drugs were used or a myocardial infarction was diagnosed in the postoperative period;
— respiratory complications were noted when stridor, obstruction, pulmonary secretion, pulmonary oedema, respiratory bronchitis, pneumothorax, haemothorax, atelectasis, or pulmonary aspiration occurred and required specific treatment;
— infectious complications were noted when septicaemia, wound infection, gastroenteritis, urinary tract infection, or upper airway infection was diagnosed;
— renal complications were noted when haemodialysis or peritoneal dialysis was used;
— and neurologic complications were noted when seizure, cerebral infarction, cerebral bleeding, peripheral nerve palsy, or clinical disturbance of consciousness or motor function was recognized.

Intraoperative anaesthetic management

After confirming starvation and checking consent, patients were taken into the operation theatre. Regular and cardiac monitors were attached. Anaesthesia was induced and maintained with weight dependent moderate doses of Inj. Midazolam, Inj. Fentanyl and Inj. Pancuronium for muscle relaxation. Patients were intubated with appropriate sized cuffed or uncuffed endotracheal tubes. All patients received intraoperative antibiotics prior to the surgery. Right internal jugular vein was cannulated for central venous pressure with 5 Fr triple lumen catheter. Right femoral artery was cannulated to record the invasive blood pressure readings. Patients were ventilated with oxygen with intermittent inhalational agents. Cardiopulmonary bypass was managed with a paediatric CPB circuit, in a nonpulsatile perfusion, with a membrane oxygenator and filters. The CPB circuit was primed with blood, crystalloids, and manifold, to keep a higher haemoglobin concentration. Cold cardioplegia rich in potassium was used in all patients who required aortic cross clamping. Ultrafiltration was used in all the paediatric CPB circuits in order to avoid fluid overload and provide haemoconcentration.

All through the surgery, the patients were regularly monitored with continuous arterial
and central venous pressures, in addition to oxygen saturation, ECG, (> 2 leads) and regular blood sugars and arterial blood gases. Intraoperatively, cardiac supports were infused as and when required, mainly Inj. Dopamine and Inj. Dobutamine. Patients were shifted with the supports to post operative intensive care unit on ventilator.

Postoperatively, these patients were not extubated, were deeply sedated and ventilated with Vela paediatric circuit or Bear Cub ventilator. Patients were extubated after 24-48 hours, depending on the severity of the cardiac lesion and the complexity of the repair. Postoperative supports were weaned off as haemodynamic stability improved.

Patients with pulmonary hypertension crisis reactions were treated with manual hyperventilation with 100% oxygen and intravenously administered opiates (usually fentanyl at 5-10 µg/kg body weight.

Patients were shifted to ward after ensuring adequate weaning off of ventilator support and stable haemodynamics and when invasive monitoring was no longer needed.

Statistics
Data were analyzed with the STATISTICA for Windows software package. Descriptive statistics are expressed as median and range. The Mann-Whitney U test was used for comparisons of quantitative variables and followed by Bonferroni correction when multiple comparisons were done. Qualitative variables were compared with the Chi square test (Table 2 and Fig. 1).

Results
During the study period, a total of 191 patients underwent cardiac surgical procedures.

Severe PH was observed in 26 patients, for an overall incidence of 11.0% (n = 26/191).

<table>
<thead>
<tr>
<th>Table 2 : Category wise distribution of patients</th>
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</thead>
<tbody>
<tr>
<td>Category/Group</td>
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<tr>
<td>----------------</td>
</tr>
<tr>
<td>1</td>
</tr>
<tr>
<td>2A</td>
</tr>
<tr>
<td>2B</td>
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<tr>
<td>2C</td>
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<tr>
<td>3A</td>
</tr>
<tr>
<td>3B</td>
</tr>
<tr>
<td>3C</td>
</tr>
<tr>
<td>Total</td>
</tr>
</tbody>
</table>

Fig. 1 : Category wise distribution of patients

The PH classification was based on direct measurements of PAP in all the cases and on intraoperative pressure measurements and postoperative Doppler measurements. Four infants with severe PH died post operatively. All the deaths occurred immediately after correction in the post operative intensive care unit. At the end of the correction both infants had severe PH, and inotropic support and prolonged mechanical support with low-flow CPB were both ineffective. This shows that inspite of multi pronged approach towards treatment, the deaths could not be prevented.

Children with severe PH were younger, mostly in the age group of 1 month to 1 year, needed longer postoperative ventilation (mean = 4 days) stayed longer in the ICU (mean = 7.2 days), and had more circulatory
and renal complications than did the other children.

153 patients had mild degree of pulmonary hypertension, which did not require any treatment apart from surgical correction. Most of these patients were in the age group of 1 year to 15 years. A total of 12 patients in our study had a moderate degree of pulmonary hypertension, which required supportive treatment apart from surgical correction. Most of these patients were in the age group of 1 month to 1 year of age.

Severe degree of pulmonary hypertension was seen in 26 patients, mainly in the age group of 1 month to 1 year (Table 3 and Fig. 2). There were 4 deaths among these 26 patients (Table 4).

The intra operative and post operative variables were compared in between all the patients and the patients with severe PH, in terms of total bypass time, aortic cross clamping time and duration of mechanical ventilation post operatively, and the total

<table>
<thead>
<tr>
<th>Degree of PH</th>
<th>Age &lt; 1 month</th>
<th>1 month - 1 yr</th>
<th>1 yr to 15 yrs</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>Nil</td>
<td>2</td>
<td>151</td>
<td>153</td>
</tr>
<tr>
<td>Moderate</td>
<td>Nil</td>
<td>2</td>
<td>12</td>
<td>12</td>
</tr>
<tr>
<td>Severe</td>
<td>3</td>
<td>21</td>
<td>2</td>
<td>26</td>
</tr>
<tr>
<td>Total</td>
<td>3</td>
<td>25</td>
<td>165</td>
<td>191</td>
</tr>
</tbody>
</table>

**Table 3 : Age wise distribution of Pulmonary Hypertension.**

<table>
<thead>
<tr>
<th>Degree of PH</th>
<th>No. of patients</th>
<th>No. of deaths</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe PH</td>
<td>26</td>
<td>4</td>
<td>15.2 %</td>
</tr>
</tbody>
</table>

**Table 4 : Percentage of deaths in severe PH**

<table>
<thead>
<tr>
<th>Bypass time ± (mean ± SD) min</th>
<th>All children</th>
<th>Severe PH</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>94 ± 41</td>
<td>98 ± 46</td>
<td>&gt; 0.05 (not significant)</td>
<td></td>
</tr>
<tr>
<td>Aorta cross clamp time (mean ± SD) min</td>
<td>59 ± 33</td>
<td>64 ± 38</td>
<td>&gt; 0.05 (not significant)</td>
</tr>
<tr>
<td>Post operative mechanical ventilation (no. of days). Mean</td>
<td>1.3</td>
<td>4.0</td>
<td>&lt; 0.01 (extremely significant)</td>
</tr>
<tr>
<td>Duration of ICU stay</td>
<td>4.3 days</td>
<td>7.2</td>
<td>&lt; 0.01 (extremely significant)</td>
</tr>
</tbody>
</table>
duration of ICU stay (Table 5 and Figs. 3 and 4). There was no significant difference in the intra operative variables, namely the total cardiopulmonary bypass time and the aortic cross clamping time in between the two groups as shown in the Table. However, significant differences were found in the post operative variables, with the duration of mechanical ventilation and the length of ICU stay being significantly higher in patients with severe PH (p < 0.01, extremely significant). This implies that the patients with severe degree of pulmonary hypertension pre operatively, needed a longer duration of post operative mechanical ventilatory support and were monitored in the intensive care unit for a longer time than the other patients, with a longer ICU stay. The requirement of inotropic support was similar in both the groups and in all the patients.

Discussion

Pulmonary endothelium plays a crucial role in the adaptation and regulation of pulmonary vascular tone in both the normal and hypertensive circulations. There are a number of physiological factors, which influence pulmonary artery pressure (PAP) and PVR and there are a number of specific manoeuvres, which have been used to reduce the PVR when elevated.

Carbon dioxide tension and hydrogen ion concentration are important determinants of PVR. Alkalosis produces pulmonary vasodilatation and acidosis results in pulmonary vasoconstriction. For some time, it was unclear whether the stimulus for vasoconstriction was an elevated carbon dioxide tension or resultant changes in hydrogen ion concentration. In an elegant study of children with trisomy 21 and increased propensity to PHT following the atroventricular valve repair, Chang et al. allowed the arterial carbon dioxide tension to rise to > 7.3 kPa (56 mmHg) resulting in PHT, which then decreased with i.v. administration of a sodium bicarbonate despite allowing the P_a CO_2 to stay elevated. PVR decreased in spite of a high P_a CO_2 confirming hydrogen ion concentration to be the primary determinant of PVR.

In normal lungs, a sufficiently large reduction in alveolar oxygen tension will provoke hypoxic pulmonary vasoconstriction (HPV). The relationship between alveolar oxygen tension and PVR is not linear. An increase in PVR occurs only below an alveolar oxygen tension of about 60 mmHg. Furthermore, this response is pH-dependent. As the pH is reduced, the increase in PVR in response to a given reduction of P_a O_2 is greater. The HPV response appears to be mainly because of changes in alveolar oxygen tension rather than pulmonary arterial or pulmonary venous oxygen tension.

Hypoxic pulmonary vasoconstriction is a fundamental mechanism to instantaneously match pulmonary perfusion to ventilation. The pathophysiological mechanism of HPV is thought to be due to the Redox regulation of O_2/K-sensitive channels of mitochondrial sensors in resistance artery, and smooth muscle cells (SMC). Similarly, the low PO_2 environment favours in utero pulmonary vasoconstriction, whereas increased alveolar PO_2 secondary to the first few breathes instantaneously vasorelaxes the pulmonary circulation.

During anaesthesia or resuscitation, at low lung volumes, PVR increases because of the surrounding uninflated lungs compressing intrapulmonary blood vessels. As the lungs are expanded, PVR falls and is lowest at the functional residual capacity. However, with overdistension, PVR increases again as a result of stretching the intrapulmonary vessels.
Previous studies have thus reported both higher incidences of and higher mortalities associated with severe PH. In 1991, Hopkins and colleagues prospectively investigated the incidence of PH crisis and observed a mortality of 54.5% among children with PH crisis. These authors used a more generous definition of severe PH (with a PH event defined as PH crisis or systolic PAP more than 50% of MAP continuing for 6 hours after repair) and found a mortality of 18.5% (n = 10/54) in 1980 through 1984 and a mortality of 35.5% (n = 11/31) in 1990 through 1994.12

Whereas, in our study, severe PH was defined as a mean PAP least as great as MAP. We found a 15.2% incidence of deaths among the patients with severe PH. Patients with severe PH needed longer postoperative ventilation (mean = 4 days) stayed longer in the ICU (mean = 7.2 days), with a p value of < 0.01, considered extremely significant.

CPB induces pulmonary endothelial cell injury and pulmonary dysfunction, probably from hypoperfusion of the lung during CPB or activation of the systemic inflammatory response, which exacerbates the reactivity of the pulmonary vascular bed. This may result in inhibition of NO production and increase in the production of endothelin 1 after CPB. Several interventions, including dexamethasone, ultrafiltration, aprotinin, leukocyte depletion, antioxidants, and heparin-coated circuits, may decrease the inflammatory response during CPB, but more studies are needed to clarify whether their use is really cost-effective.13,14

Treatment for PH can be regarded as a bridge until the increase in PVR has subsided or the right ventricle is able to cope with the increased PVR. In our study 4 patients with severe PH died in the ICU, indicating that treatment modalities need to be reviewed.

Inhalation of NO can selectively decrease mean PAP and improve arterial and venous oxygen saturation, and it is the preferred treatment for severe postoperative PH in many centres. In Sweden, NO treatment is only allowed when conservative treatment is ineffective and the patient has life-threatening PH.15 However, NO is not used in our set up.

Although the immediate outcome of patients with severe PH were good, all had long ICU stays and longer post operative mechanical ventilation.

Conclusion

Patients with severe degree of pulmonary hypertension diagnosed pre operatively, required a longer post cardiac surgery mechanical ventilatory support and a longer duration of intensive care unit stay, indicating the need for continuous monitoring in the post operative period. Also, treatment modalities need to be reviewed to avoid the mortality from severe PH and to avoid the prolonged ventilator support which has its own inherent complications.

Acknowledgements

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2) Dr. A.M. Patwardhan, Professor and Head, Department of Cardiothoracic and Vascular Surgery, Seth G S Medical College and KEM Hospital, Mumbai.

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**3D ECHOCARDIOGRAPHY: THE MOST POWERFUL PREDICTOR OF MASKED CVD IN METABOLIC SYNDROME**

Metabolic Syndrome is associated with masked cardiovascular disease (CVD) as evident by 3D Echo in this series of patients. LVMPI was an early indicator and the most robust marker of early LVDD. Impaired relaxation was highly prevalent; while LAVi was less robust predictor of LVDD in this series of patients. Concentric left ventricular remodelling was the most common pattern of LVH. Most of our series of patients had increased Composite CCIMT. Thus 3D Echocardiography has great potential and is very useful for early detection and timely therapeutic interventions in patients with sub clinical CVD in MetS.