Lung Reperfusion Injury in Patients after Balloon Angioplasty for Pulmonary Artery Stenosis

Saeed Yacouby, CRNA, DNP, Marcie Meador, RN, MS, and Emad Mossad, MD

Objectives: To determine the incidence and degree of acute lung reperfusion injury (ARI) in patients undergoing balloon angioplasty of branch pulmonary artery stenosis and to evaluate the correlation and efficacy of an oxygenation index in confirming the clinical diagnosis.

Design: Retrospective, single-center observational study.

Setting: Cardiac catheterization laboratory at a tertiary care children’s hospital.

Patients: Patients with congenital heart disease undergoing pulmonary artery balloon angioplasty.

Intervention: Review of patient medical and catheterization records.

Measurements and Main Results: The records of all patients with biventricular physiology undergoing balloon angioplasty of branch pulmonary artery stenosis over a period of 2 years (12/2006-12/2008) were reviewed. Data collection included demographics, details of pulmonary artery intervention, right ventricle/femoral artery systolic pressure (RV/FA) ratio, and post-procedure recovery condition. Markers of ARI, including clinical, radiographic, and blood gas analysis, were examined. Criteria for ARI were based on the International Society of Heart and Lung Transplantation (ISHLT) grading system, in which a PaO2/FIO2 of 200 to 300 indicates ARI. The distribution of PaO2/FIO2 after pulmonary artery intervention, the relation of clinical to laboratory manifestation of ARI, and the correlation among different oxygenation indices were examined.

During the study period, 46 patients with congenital heart disease and branch pulmonary artery stenosis were identified. Patient age ranged from 2 months to 25 years (mean 6.2 ± 6 years) and weight ranged from 5 to 86 kg (mean 23 ± 18 kg). ARI was identified in 10 of 46 patients (22%) using clinical criteria and correlated with ISHLT gas exchange criteria. Analysis of RV/FA ratio before (0.82 ± 0.34) and after (0.71 ± 0.22) balloon angioplasty revealed statistically significant decrease (p < 0.004). The degree of ARI was graded using ISHLT criteria and correlated with the presence of clinical symptoms (p < 0.002). As anticipated, the PaO2/FIO2 ratio had a strong correlation with A-aDO2 (r = 0.75) and SpO2/FIO2 (r = 0.7) and a strong specificity (0.78) to identify patients with clinical ARI.

Conclusion: ARI often can occur after pulmonary artery interventions. The PaO2/FIO2 is a valuable test for identifying patients at risk of developing ARI and can help guide the care of these patients in the postintervention period.

© 2014 Elsevier Inc. All rights reserved.

KEY WORDS: acute lung reperfusion injury, pulmonary artery angioplasty, pulmonary artery stenosis, congenital heart disease
RESULTS

The study sample consisted of patients with a diagnosis of pulmonary artery balloon angioplasty of one or more stenotic arteries both with and without stent placement. Patient age ranged from 2 months to 25 years (mean 6.2 ± 6 years) and weight ranged from 5 to 86 kg (mean 23 ± 18 kg). There were 18 (39%) females and 28 (61%) males. The primary diagnoses are summarized in Table 1. No patient in this series had a known or documented residual intracardiac shunt or communication.

In this study, of the 46 patients who underwent pulmonary artery angioplasty, 10 (22%) were identified clinically as having ARI during or immediately after the intervention. Seven patients developed pulmonary edema as evidenced by frothy serosanguinous exudate in their endotracheal tubes, and 1 patient presented with pulmonary hemorrhage. Two additional patients with pulmonary edema were identified after extubation in the anesthesia recovery unit. All 10 patients presented with oxygen desaturation requiring supplemental oxygen and/or mechanical ventilation and had diffuse chest radiograph (CXR) infiltrates consistent with pulmonary edema. All of the 10 patients who developed ARI were admitted to the cardiovascular intensive care unit (CVICU).

In Table 1, patients with ARI (diagnosed by clinical findings) were compared with patients with no RI both before and after pulmonary artery balloon angioplasty. When comparing RV/FA pressures, a significantly higher absolute ratio was noted in the ARI group both before and after the intervention. The percent change in RV/FA pressure was not noted in the ARI group both before and after the intervention. However, those who developed ARI had significantly lower in the ARI group compared with relatively normal values in the no-RI group both before and after interventions. There was no significant difference in the number of segments dilated or stents placed between groups. However, those who developed ARI had undergone significantly longer procedures. The ISHLT criteria (CXR and PaO2/FIO2) were used to examine grades of gas exchange and showed a significant difference among patients with and without clinical ARI (p = 0.002) (Table 2). As anticipated, the PaO2/FIO2 ratio had a significant negative correlation to A-aDO2 (r = -0.75) and a positive correlation to SpO2/FIO2 (r = 0.7) (Fig 2). In Table 3, the correlation of the PaO2/FIO2 was examined and found to have a sensitivity of 0.60 to clinical ARI and specificity of 0.78 in its absence.

DISCUSSION

In this study the authors identified 10 of 46 patients who developed ARI after pulmonary artery angioplasty, an incidence of 22% in this cohort. In another study, Geggel et al reported a 15% incidence of transient pulmonary edema after pulmonary artery balloon angioplasty in children with Williams syndrome. Interestingly, 75% of the patients (3 of 4) who had Williams syndrome in this study developed clinical ARI after pulmonary artery balloon angioplasty, indicating these patients may be at higher risk for ARI. The etiology of developing ARI after pulmonary artery interventions may be due to the reperfusion effect, exposure of the pulmonary circulation to higher pressure after angioplasty, or, potentially, the increase in end-diastolic volume of a noncompliant left ventricle.

<table>
<thead>
<tr>
<th>Variable N = 46</th>
<th>No ARI (n = 36)</th>
<th>ARI (n = 10)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>6.7 ± 5.7</td>
<td>4.4 ± 5.4</td>
<td>0.3</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>23 ± 15</td>
<td>21 ± 26</td>
<td>0.8</td>
</tr>
<tr>
<td>Number of branches dilated</td>
<td>1.6 ± 0.7</td>
<td>1.7 ± 0.7</td>
<td>0.6</td>
</tr>
<tr>
<td>Stent placed (%)</td>
<td>13 (36)</td>
<td>3 (30)</td>
<td>NS</td>
</tr>
<tr>
<td>Case time (minutes)</td>
<td>284 ± 93</td>
<td>353 ± 74</td>
<td>0.02</td>
</tr>
<tr>
<td>RV/FA preintervention</td>
<td>0.72 ± 0.30</td>
<td>1.13 ± 0.23</td>
<td>0.001</td>
</tr>
<tr>
<td>RV/FA postintervention</td>
<td>0.60 ± 0.29</td>
<td>1.03 ± 0.29</td>
<td>0.003</td>
</tr>
<tr>
<td>% Change in RV/FA</td>
<td>15 ± 21</td>
<td>6.25 ± 26</td>
<td>0.45</td>
</tr>
<tr>
<td>A-aDO2 postintervention</td>
<td>176 ± 167</td>
<td>314 ± 197</td>
<td>0.20</td>
</tr>
<tr>
<td>PaO2/FIO2 preintervention</td>
<td>408 ± 101</td>
<td>274 ± 152</td>
<td>0.02</td>
</tr>
<tr>
<td>PaO2/FIO2 postintervention</td>
<td>417 ± 143</td>
<td>262 ± 140</td>
<td>0.01</td>
</tr>
<tr>
<td>CXR infiltrate n (%)</td>
<td>2 (5)</td>
<td>10 (100)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Abbreviations: ARI, acute reperfusion injury; No ARI, no acute reperfusion injury; NS, not statistically significant; RV/FA, right ventricle-to-femoral artery pressure ratio; CXR, chest x-ray.

Fig 1. Frequency of primary cardiac diagnoses. DORV PA, double-outlet right ventricle and pulmonary atresia; PPS, peripheral pulmonary stenosis; TGA, transposition of the great arteries; TOF, tetralogy of Fallot; Truncus, truncus arteriosus; Williams, Williams syndrome.
Pulmonary artery balloon dilation is considered effective if the ratio of right ventricle (RV)-to-femoral artery (FA) pressure decreases by 20% and the vessel diameter increases by at least 50%. In this study, the overall decrease in RV/FA pressure was 13% (p = 0.003) after dilation. Data on vessel diameter were incomplete and thus not reported. However, the appearance of the pulmonary artery waist on angiography during balloon dilation served as an endpoint for balloon expansion. Geggel et al evaluated the effectiveness of pulmonary artery balloon angioplasty in children with Williams syndrome and found that, despite a greater than 50% increase in vessel diameter in the majority of cases, the ratio of RV-to-aortic peak pressure increased by >50%. In this study, the overall decrease in RV/FA pressure was 13% (p = 0.003) after dilation. Data on vessel diameter were incomplete and thus not reported. However, the appearance of the pulmonary artery waist on angiography during balloon dilation served as an endpoint for balloon expansion. Geggel et al evaluated the effectiveness of pulmonary artery balloon angioplasty in children with Williams syndrome and found that, despite a greater than 50% increase in vessel diameter in the majority of cases, the ratio of RV-to-aortic peak pressure increased by >50%.

The PaO2/FIO2 ratio has been used extensively in studies attempting to identify and define ARI severity. There are, however, differing opinions on its ability to do this accurately. Using mathematic models, Karbing and colleagues studied the validity of the PaO2/FIO2 ratio with varying FIO2 concentrations. They reported that for a given FIO2, the PaO2/FIO2 overestimated the presence and/or severity of ARI. El-Khatib et al assessed the reliability of traditional oxygen indices, including the PaO2/FIO2. They reported that a new oxygenation factor that incorporates mean airway pressure into the PaO2/FIO2 ratio might be more reliable in assessing severity of lung disease. Conversely, many studies have reported the PaO2/FIO2 to be a reliable index of oxygen exchange and its use is documented throughout the literature.

In this study, the PaO2/FIO2 ratio was useful as a measure to identify and confirm ARI and provided a means to evaluate oxygenation at different FIO2 fractions. It strongly correlated with A-aDO2, another standard measure of oxygenation and lung injury. However, the PaO2/FIO2 ratio was limited by the inability to apply it in the presence of intracardiac shunting and mixing lesions. It is also a calculation that requires an invasive method to obtain arterial blood gas sampling. Other studies have reported the reliability of the noninvasive SpO2/FIO2 ratio in identifying ARI and showed a strong correlation with PaO2/FIO2 ratio. In this study the SpO2/FIO2 ratio had a weaker correlation despite excluding patients with higher pulse oximetric readings (>98%, as in other reports). This difference may have been due to the smaller number of observations in this study compared with previous studies and the extent of ARI in these patients, which was limited compared with patients with significant lung injury in other reports.

Examination of the validity of the PaO2/FIO2 as a measure of ARI revealed that it was moderately sensitive (0.6) in its presence and specific (0.78) in its absence, which is adequate for excluding the diagnosis of ARI but is not as strong a positive diagnostic tool. It can be useful in confirming the diagnosis of ARI after intervention and can guide the decision process for the intensity and location of postprocedure recovery for these patients.

The limitations of this study were those inherent to a retrospective design. First, measures were not taken in real time but rather from patient records as many as 2 years after the intervention. Second, a number of patients were excluded from the study because of either lack of data or missing records. Also excluded were patients with single ventricle physiology or intracardiac mixing because gas exchange calculations would not have accurately reflected gas exchange impairment. Exclusion of patients for the various reasons discussed provides a potential
threat to the validity of the results and conclusions. Third, the study population (46 patients) and those developing ARI (10 patients) did not permit an examination of the relation of underlying diagnosis to the risk of developing ARI after pulmonary artery angioplasty. Future multicenter or database-based study.

Strengths of this study included establishing the incidence of ARI in a tertiary care children’s hospital, laying the groundwork for future prospective studies that also can examine interventions to limit the degree of ARI with these procedures.15 Future studies of ARI also can consider the inclusion of patients with single-ventricle physiology and intracardiac mixing. This can be accomplished by using pulmonary venous blood gas measurements in place of peripheral arterial blood gas measurements.

CONCLUSION

Although pulmonary artery balloon angioplasty is safe and effective in the majority of patients who undergo the procedure, the risk of developing ARI is significant. As such, awareness and early recognition of ARI after this procedure are paramount. When clinical symptoms of ARI are evident, the management strategies for postintervention care are clear. However, when the signs and symptoms of RI are not readily apparent after intervention, the decisions regarding care must be made using other means. In those situations in which ARI is suspected but not confirmed, the PaO2/FiO2 ratio may provide insight into the presence of subclinical RI and help to guide postintervention care.

REFERENCES