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

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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 PaO_2/F_IO_2 of 200 to 300 indicates ARI. The distribution of PaO_2/F_IO_2 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 $\pm$ 6 years) and weight ranged from 5 to 86 kg (mean 23 $\pm$ 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 $\pm$ 0.34) and after (0.71 $\pm$ 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 PaO_2/F_IO_2 ratio had a strong correlation with A-aDO_2 ($r = 0.75$) and SpO_2/F_IO_2 ($r = 0.7$) and a strong specificity (0.78) to identify patients with clinical ARI.

Conclusion: **ARI often can occur after pulmonary artery interventions. The PaO_2/F_IO_2 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.**

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

THE PAST 2 DECADES have witnessed an advance in the application of catheter interventions in patients with congenital heart defects (CHD), with the development of new devices, stents, and catheters. The interventions are conducted on sicker patients with more complex lesions, increasing the risk of postprocedure complications.[1]

Pulmonary artery angioplasty has come to be accepted as the treatment of choice in children with CHD and pulmonary artery stenosis.[2] Patients undergoing pulmonary artery balloon angioplasty are at risk of developing acute lung reperfusion injury (ARI). The incidence and degree of lung ARI are not clear, and the appropriate method to confirm the clinical diagnosis of such injury is important.[1,3]

In this study, the authors examine the incidence of ARI in patients after pulmonary artery balloon angioplasty and investigate the validity and reliability of laboratory measurements of gas exchange as tools to confirm the clinical diagnosis.

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METHODS

After institutional review board approval, the records of all pulmonary artery angioplasty cases from the pediatric cardiac catheterization laboratory at Texas Children's Hospital over a 2-year period (12/2006-12/2008) were selected and reviewed. Excluded from the study were patients with functional single ventricles and persistent intracardiac mixing and those who had a palliative aortopulmonary shunt, which interferes with standard equations of gas exchange used to determine ARI. Within the review period, a final sample of 46 cases was identified. Data were collected retrospectively and included demographics, number of pulmonary artery segments dilated, pre- and postintervention hemodynamic and clinical variables, and arterial blood gas analysis. All patients were managed with endotracheal intubation, primary inhalation anesthetic, and intermittent positive-pressure ventilation. Using the collected data, markers of gas exchange were calculated using standard equations for alveolar-to-arterial oxygen difference/gradient (A-aDO_2), PaO_2/F_IO_2, and SpO_2/F_IO_2.[4]

The criteria by which ARI is diagnosed vary in different reports.[4–6] In this study, criteria for ARI were based on the International Society of Heart and Lung Transplant (ISHLT) grading, in which a PaO_2/F_IO_2 ratio of 200 to 300 indicates ARI and a ratio of less than 200 indicates severe reperfusion injury (RI).[5] Although the ISHLT criteria are for whole-lung graft reperfusion, they are the best available to identify and grade segmental ARI. Additionally, in this study the presence of postintervention pulmonary edema or hemorrhage, unilateral or bilateral chest radiograph infiltrates, ICU admission, and unplanned intubation and postoperative mechanical ventilation were considered as predictive clinical features of ARI.[6,7]

All data were expressed as mean $\pm$ SD. Descriptive analyses included *t* tests for continuous variables and Chi-square Fisher's exact for categoric variables. A value of $p < 0.05$ was considered statistically significant. A Pearson *r* coefficient was calculated to analyze the correlation between A-aDO_2 and PaO_2/F_IO_2 and SpO_2/F_IO_2. The

validity of the PaO_2/F_IO_2 was analyzed from a 2 × 2 matrix with sensitivity and specificity analysis. Statistical analyses of the data were performed using STATA 10.1 SE (StataCorp, College Station, TX).

RESULTS

The study sample consisted of patients with a diagnosis of pulmonary artery stenosis who had undergone 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 Figure 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. However, the percent change in RV/FA pressure was not significant in either group. The PaO_2/F_IO_2 ratio was significantly lower in the ARI group compared with relatively normal measures of the no-RI group both before and after interventions. This signifies potential lung perfusion compromise in the ARI group even before dilation. 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 PaO_2/F_IO_2) 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 PaO_2/F_IO_2 ratio had a significant negative correlation to A-aDO2 ($r = -0.75$) and a positive correlation to SpO_2/F_IO_2 ($r = 0.7$) (Fig 2). In Table 3, the correlation of the PaO_2/F_IO_2 was examined and found to have a sensitivity of 0.60 to clinical ARI and specificity of 0.78 in its absence.

Table 1. Comparison of Patients Who Developed Acute Reperfusion Injury (ARI) Versus Those Who Did Not

Variable N = 46	No ARI (n = 36)	ARI (n = 10)	p Value
Age (years)	6.7 ± 5.7	4.4 ± 5.4	0.3
Weight (kg)	23 ± 15	21 ± 26	0.8
Number of branches dilated	1.6 ± 0.7	1.7 ± 0.7	0.6
Stent placed (%)	13 (36)	3 (30)	NS
Case time (minutes)	284 ± 93	353 ± 74	0.02
RV/FA preintervention	0.72 ± 0.30	1.13 ± 0.23	0.001
RV/FA postintervention	0.60 ± 0.29	1.03 ± 0.29	0.003
% Change in RV/FA	15 ± 21	6.25 ± 26	0.45
A-aDO_2 postintervention	176 ± 167	314 ± 197	0.20
PaO_2/F_IO_2 preintervention	408 ± 101	274 ± 152	0.02
PaO_2/F_IO_2 postintervention	417 ± 143	262 ± 140	0.01
CXR infiltrate n (%)	2 (5)	10 (100)	0.001

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.

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.[8] 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

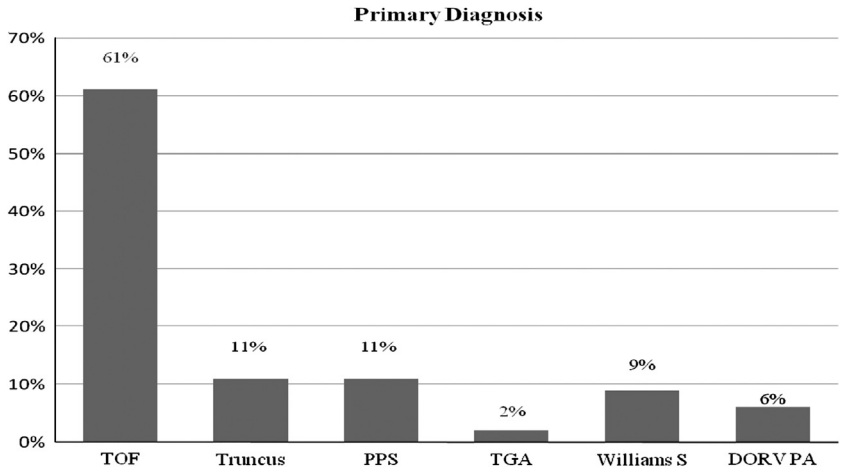

Fig 1. Frequency of primary cardiac diagnoses. DORV PA, double-outlet right ventricle and pulmonary atresia; PPS, peripheral pulmonary stenosis; TGA, transposition of the great arteries; TOF, tetralogy of Fallot; Truncus, truncus arteriosus; Williams, Williams syndrome.