Induction of Right Ventricular Hypertrophy With Obstructing Balloon Catheter

Nonsurgical Ventricular Preparation for the Arterial Switch Operation in Simple Transposition

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**Background.** Recently, a successful result with a rapid two-stage arterial switch operation (ASO) was reported for patients with transposition of the great arteries (TGA) with low left ventricular pressure. In this procedure, the interval between pulmonary arterial banding and ASO was approximately 1 week. This successful result indicates the possibility of a nonsurgical ventricular preparation procedure using an obstructing balloon catheter prior to ASO.

**Methods and Results.** A 5F atrioseptostomy catheter was inserted directly into the main pulmonary artery in six lambs aged 20 to 38 days. After the chest was closed, the balloon was inflated twice a day for a period of 2 to 2.5 hours. This procedure was performed for 4 consecutive days. After the final inflation, the ratio of right ventricular weight to total ventricular weight was compared with that in an age-matched control group. After the final inflation, the peak systolic right ventricular pressure and the percentage of peak systolic right ventricular to peak systolic aortic pressure rose to 85.6±4.7 mm Hg (mean±1 SD) and 79.6±8.6%, respectively. The percentages of the right ventricular weight to the total ventricular weight were significantly higher after the balloon inflation than those in the control group in terms of wet heart weight (29.5±1.2% versus 23.0±1.0%; *P*<.0001) and dry heart weight (27.0±2.0% versus 21.0±1.1%; *P*<.0001).

**Conclusions.** The myocardial mass in the right ventricle increased after 4 days of intermittently applied pressure overload. Nonsurgical preparation of the ventricle for ASO in TGA is feasible. *(Circulation. 1993;88(part 1):1765-1769.)*

**Key WORDS** • transposition, great arteries • surgery • balloons

Several recent reports1-5 have revealed good early or midterm results of the one-stage arterial switch operation (ASO) for neonates with simple transposition of the great arteries (TGA). Some investigators7-10 have also reported several serious complications after the ASO, such as right ventricular dysfunction, arrhythmia followed by sudden death, and systemic or pulmonary venous obstructions. Although it is too early to determine the best treatment for children with simple TGA, the one-stage ASO is likely to become the first choice of treatment. However, this procedure should be performed within a few weeks after birth, when pulmonary vascular resistance is still high. Beyond this period, a ventricular preparation procedure like pulmonary arterial banding (PAB) is necessary prior to the ASO. Investigators11,12 have recommended that the interval between PAB and ASO be more than a few months. However, the length of time for the ventricular preparation for ASO is still unclear. Several studies13-16 have reported that the myosin genes in cardiac cells responded to acute pressure load quickly, after hours or days. Jonas et al17-19 have recently reported the rapid two-stage ASO, in which the interval between PAB and ASO is approximately 1 week. Several preliminary studies20,21 have shown the possibility of ventricular preparation with a balloon catheter prior to ASO. We have conducted studies to determine if the obstruction to flow in the pulmonary artery using a balloon catheter can create ventricular hypertrophy and have examined the feasibility of this procedure for the ventricular preparation for the ASO.

**Methods**

This study adhered to the guidelines for experimental animals published by the American Physiological Society.

Six lambs aged 20 to 38 days (28.0±6.2 days; mean±1 SD) were selected for this study (balloon inflation group). Six additional age-matched lambs (28.2±9.5 days) were selected for the measurement of heart weight as control models (control group).

**Insertion of Catheters**

After sedation with an intravenous injection of 10 mg/kg methohexital sodium, the lambs were intubated...
and ventilated with \( F_{\text{IO}} \), 0.985 to 0.995 and 0.5% to 1.5% halothane. Through a left thoracotomy, the chest was opened, a 5F Millar Mikrotip transducer (Millar, Houston, Tex, PC-350) was inserted into the proximal side of the main pulmonary artery and advanced to the right ventricle retrogradely, a 5F atrioseptostomy catheter with a 4-mL balloon (Baxter Edwards, LIS Division, Irvine, Calif) was inserted into the main pulmonary artery 2 cm above the pulmonary valve and secured with a purse-string suture, and fluid-filled catheters were inserted into the aorta and into the superior vena cava through the left carotid artery and the left jugular vein, respectively.

Inflation of Balloon

The awake, nonsedated lambs were placed in a nylon mesh cradle. The aortic and the right ventricular pressures were monitored using a Statham P23Gb and a Millar microtip transducer, respectively. The balloon was inflated with a Meditech hyperinflation syringe twice a day for a period of 2 to 2.5 hours. We tried to increase right ventricular pressure as high as possible without the emergence of serious complications, such as systemic hypotension, arrhythmias, bradycardia, respiratory distress, and agitation. After each inflation, the balloon was partially deflated at a peak systolic right ventricular pressure level of approximately 50 mm Hg. These procedures were performed for 4 consecutive days (Fig 1). During balloon inflation, the right ventricular pressure and the aortic pressure were continuously recorded on a paper chart recorder. The data of the pressures were taken at 30-minute intervals and stored in digitized form. Samples for blood gas analysis were obtained during inflation. The fluid-filled catheters were flushed with heparin twice a day. After the final balloon inflation, the lamb was anesthetized, intubated, and ventilated as described previously. The chest was opened through a median sternotomy, an electromagnetic flow probe (Carolina Medical Electronics, King, NC, model EP 300) was placed around the ascending aorta, and cardiac output was measured before and after a balloon inflation.

Measurement of Ventricular Weight

After the final inflation, the lamb was killed, the whole heart and both lungs were harvested, and cardiovascular anatomy was examined. The weight of the ventricles was measured with the methods described by Fulton et al. After the whole heart was removed, epicardial fatty tissue was carefully dissected away. The aorta and the pulmonary artery were separated from the ventricles at the level of the semilunar valves. The supraventricular components were separated from the ventricles along the atrioventricular groove. Valvular tissues were also removed from the ventricles. The right ventricular free wall was separated from the ventricular septum along the anterior descending branch of the left coronary artery and the posterior descending artery. The moderator band was cut at its septal end. After separation of the right ventricular free wall from the ventricular septum and the left ventricle, the right and left ventricular portions were weighed and subsequently dried at 100°C for 24 hours, and dry weights were compared.

Statistical Analysis

Differences in ventricular weights between the balloon inflation and control groups were analyzed using unpaired Student's \( t \) test. Changes in \( P_{\text{O}_2} \), pH, and cardiac output after inflation were analyzed with paired Student's \( t \) test.

Results

No cardiovascular anomalies were found, no lung embolism was observed macroscopically, and no serious complication occurred. Specifically, no changes were noted in any of the cardiac valves. The mean peak systolic right ventricular pressure before balloon inflation was 34.2±4.1 mm Hg. The mean peak systolic right ventricular pressure rose immediately to approximately 60 mm Hg (58.0±2.6 mm Hg). Further inflation generated only transient elevation in the systolic right ventricular pressure, and excessive inflation resulted in the fall of the aortic pressure without increasing systolic right ventricular pressure. Thereafter, the mean peak systolic right ventricular pressure gradually rose with successive inflations. The mean peak systolic right ventricular pressure reached 85.6±4.7 mm Hg after the final inflation (Fig 2, top). The percentage of the mean peak systolic right ventricular pressure to the mean peak systolic aortic pressure (RVP/AoP) also rose from 30.9±2.5% to 53.7±7.7% after the first inflation and exceeded 75% after the final inflation (79.6±8.6%) (Fig 2, bottom). Mean peak systolic aortic pressure did not change significantly during balloon inflation. No administration of positive inotropic agents was necessary in any animal. Cardiac output was measured in four lambs and and did not change before or after balloon inflation (1.23±0.23 versus 1.22±0.17 L/min).

The percentages of right ventricular weight to the total ventricular weight were significantly higher in the balloon inflation group than those in the control group in terms of wet heart weight (29.5±1.2% versus
The peak systolic RVP elevated gradually and reached more than 80 mm Hg after the final inflation. Systolic pressure ratio showed similar changes as peak systolic RVP and reached to nearly 80% after the final inflation. These data satisfied clinical criteria for arterial switch operation in the latest studies.

23.0±1.0%; P<.0001) and dry heart weight (27.0±2.0% versus 21.0±1.1%; P<.0001) (Fig 3).

Mild hypoxemia was observed before balloon inflation (77.0±9.3 mm Hg) and was slightly aggravated during balloon deflation (67.8±7.3 mm Hg; P<.0005). Twenty minutes after deflation, P02 increased significantly from values obtained at the end of each inflation (68.1±6.6 mm Hg versus 74.2±7.1 mm Hg; P<.0005) (Fig 4). The range of pH values observed during balloon inflation was 7.35 to 7.52; no acidosis was observed throughout the procedure (Fig 5).

Discussion

After 4 days of intermittent balloon inflation, the percentage of right ventricular weight to total heart weight was significantly higher in the balloon inflation group than that in the control group. These findings are consistent with the results of previous studies of aortic banding\(^{13,16}\) or PAB.\(^{24}\) The increase in right ventricular wet heart weight might be due to edema of the myocardium, but the increase in right ventricular dry heart weight strongly suggests hypertrophy of the right ventricle. The magnitude of the increase in ventricular hypertrophy necessary for ASO remains unclear.\(^{11,12,25}\) Yasui et al\(^{25}\) reported that criteria for ASO includes a left ventricular pressure more than 65 mm Hg or the ratio of left ventricular to right ventricular systolic pressure...
more than 80%. Jonas et al reported that patients whose left ventricular pressure was at least 75% of systemic pressure. Our data after the final inflation satisfied these criteria.

Investigators have reported that a sudden increase in afterload to the right ventricle results in the right ventricle being unable to generate a systolic pressure more than 60 mm Hg without an increase in right ventricular mass. In this study, the right ventricular systolic pressure was near 60 mm Hg after the first inflation. This pressure might be the upper limit of right ventricular pressure without a positive inotropic agent. Thereafter, the right ventricular pressure gradually increased as the balloon was further inflated. Lange et al reported that a slow progressive increase of afterload did not impair the ventricular function. Our data showed a smooth elevation of right ventricular pressure and no drop of aortic pressure or cardiac output, although the rate of progressive pressure load in this study was much greater than that in the study by Lange et al. This should be one of the advantages of this maneuver.

Previous studies with the two-stage ASO have reported that hypoxia and metabolic acidosis after PAB were common and a systemic-pulmonary shunt was necessary in many cases. In our study, mild hypoxemia was observed, but acidosis was not observed. Intermittent inflation with 2 to 2.5 hours of inflation period may avoid the onset of severe hypoxemia or metabolic acidosis. Lange et al reported that right ventricular end-diastolic pressure increased less with slow progressive pressure loading. Compared with PAB, our maneuver is expected to leave the left ventricular end-diastolic pressure and left atrial pressure low. This may help to maintain a balanced interatrial shunt. Furthermore, we can deflate the balloon at any time if necessary, promoting the correction of hypoxemia as previously discussed. Some investigators have reported that PAB alone did not increase the left ventricular pressure in some cases with relatively small left ventricles. Ilbawi et al reported that the combination of pressure and volume overload was the best to create ventricular hypertrophy. However, pressure overload is considered the major factor to increase ventricular mass. With normal ventricular size, pressure overload may be able to increase ventricular mass sufficiently to perform ASO.

Another possible problem is the placement of the balloon at the optimal position in the main pulmonary artery. In one animal, the peak systolic right ventricular pressure rose to 70 mm Hg with full inflation of the balloon. After the lamb moved slightly, the peak systolic right ventricular pressure suddenly dropped to 40 mm Hg with full inflation. During these changes, aortic pressure did not change. We speculated that the balloon wedged in one of the pulmonary branch arteries. In patients with simple TGA, a balloon must advance to the right atrium, left atrium, left ventricle, and pulmonary artery in sequence. It may be more difficult to position a balloon at an optimal position in the main pulmonary artery through this complicated route. A catheter with balloons of special configurations as shown in Fig 6 may be necessary to resolve this problem.

Aortic regurgitation has been reported in patients after the two-stage ASO. Lange et al reported enlargement of the pulmonary artery at the site of PAB and that the enlargement might be related to aortic regurgitation. A nonsurgical maneuver may reduce the incidence of aortic regurgitation after ASO. This maneuver will also prevent adhesion at the site of PAB. However, the biggest advantage of this maneuver is, of course, to obviate the need for two thoracotomies in those patients requiring a two-stage ASO. Recently, a clinical case with success using this maneuver was reported in a brief report. This success emphasizes the feasibility of this maneuver.

In conclusion, 4 days of intermittent pressure overload increased ventricular mass in this study. Nonsurgical ventricular preparation for ASO using an obstructing balloon catheter is feasible.

Acknowledgment
This work was supported by NIH grant R-01-HL-35389.

References
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Circulation. 1993;88:1765-1769
doi: 10.1161/01.CIR.88.4.1765

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1993 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

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