Impact of Pulmonary Flow Study Pressure on Outcomes After One-Stage Unifocalization

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Background. **The purpose of this study was to evaluate the accuracy of the pulmonary flow study in (1) predicting the feasibility of concomitant intracardiac repair after one-stage unifocalization; and in (2) predicting long-term survival and the onset of right ventricular dysfunction after surgery.**

Methods. **Between October 1996 and July 2015, a flow study was obtained in 95 patients undergoing complete one-stage unifocalization for pulmonary atresia with ventricular septal defect and major aortopulmonary collaterals. The ability to achieve 100% flow (approximately 2.5 L · min^{-1} · m^{-2}) into the pulmonary bed at a mean pressure of 30 mm Hg or less was utilized as an indicator for acceptability of ventricular septal defect closure.**

Results. **Overall survival was 78% ± 6% at 15 years. Sixty-four patients underwent successful one-stage intracardiac repair. The flow study accurately predicted suitability for VSD closure (area under the curve = 0.855). After one-stage ventricular septal defect closure, no difference in survival was observed after stratification according to flow study pressures (25 mm Hg or less versus greater than 25 mm Hg, log rank p = 0.20). At a median follow-up of 7 years, no association was found between flow study pressure and the onset of right ventricular dysfunction (p = 0.21). Overall, the inability to achieve final intracardiac repair was a strong predictor of death (hazard ratio 9.14, 95% confidence interval: 1.98 to 42.07, p < 0.0001).**

Conclusions. **Suitability for ventricular septal defect closure is reliably defined by the flow study with a cutoff of 30 mm Hg. Flow study pressure values do not affect long-term outcomes. The ability to obtain intracardiac repair (in either one or more stages) is the strongest predictor of survival.**

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Pulmonary atresia with ventricular septal defect (VSD), diminutive or absent central pulmonary arteries, and major aortopulmonary collateral arteries (MAPCAs) is a complex congenital heart disease with varying iterations of segmental pulmonary blood supply. Although the management of this condition is still quite controversial, the prevailing surgical strategy is to perform a one-stage unifocalization procedure to centralize the multifocal pulmonary blood supply, provide an egress from the right ventricle to the neopulmonary arterial bed and close the VSD, whenever possible. Over the past 2 decades, optimism has stemmed from several surgical series [1–5] in which the majority of patients have been managed with one-stage repair in early infancy. From the surgical standpoint, once unifocalization is complete, an objective assessment must be made regarding whether VSD closure will be tolerated at a reasonably low right ventricular pressure.

In 1997, Reddy and colleagues [6] proposed the utilization of the intraoperative flow study as a functional measure of pulmonary vascular performance and candidacy for VSD closure. During the flow study, the mean pulmonary artery pressure (mPAP) was recorded while incremental volumes of blood were pumped through the unifocalized pulmonary arteries at a cardiac index of 2.5 L · min^{-1} · m^{-2}. Mean PAP values of 30 mm Hg or less were selected for VSD closure at a reasonable postoperative right ventricular pressure [7]. Recently, Honjo and associates [8] demonstrated that the functional intraoperative flow study is highly correlated with postoperative hemodynamics, and more accurately predicts successful VSD closure than anatomic indices [9–12]. In addition, Zhu and colleagues [13] explored the flow study accuracy as a predictor of medium term survival after unifocalization, concluding that pressures of 25 mm Hg or greater are associated with an increased

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hazard of death (hazard ratio 9.8, 95% confidence interval: 1.14 to 83.30).

Since October 1996, we adopted the functional intraoperative flow study to assess the feasibility of VSD closure at the time of complete unifocalization. In this study, we sought to evaluate the accuracy of the functional flow study in predicting the tolerability of VSD closure at the time of unifocalization and investigated the relationship between flow study pressures and long-term outcomes.

Patients and Methods

Patients

After approval by the Institutional Review Board at the Bambino Gesù Children's Hospital, who waived the need for informed patient consent, we reviewed the medical records of 95 patients with pulmonary artery/VSD/MAPCAs who underwent intraoperative flow study at the time of unifocalization between October 1996 and July 2015. For patients who achieved VSD closure at the time of unifocalization, right ventricular fractional area change (RVFAC) was manually calculated off line by an experienced pediatric cardiologists based on the last echocardiographic dataset available. Xcelera analysis software version 1.3 (Philips HealthCare, Eindhoven, Netherlands) was utilized, and any RVFAC value above 35% was considered normal.

Surgical Technique

One-stage unifocalization was pursued through a median sternotomy in all patients with abnormal arborization of the native pulmonary arteries or dominant MAPCAs at a body weight greater than 5 kg, regardless of the patient's age. Conversely, patients with confluent, fully arborizing (ie, dominant), yet diminutive native pulmonary arteries, initially underwent pulmonary artery rehabilitation procedures. The decision whether to close the VSD after unifocalization was determined by the functional intraoperative flow study. At the conclusion of intracardiac repair, a transthoracic pressure catheter was placed for calculation of the right ventricular systolic pressure (RVSP) to systolic blood pressure (SBP) ratio.

Conduct of Functional Intraoperative Pulmonary Flow Study

A line derived from the arterial port of the oxygenator was introduced into the valved conduit sutured to the neopulmonary arterial confluence, together with pressure-monitoring recording. We routinely utilized quarter-inch tubing without any additional cannula to avoid any pressure drop along the circuit. With lungs deflated and the heart beating and fully vented, the test was started at a nasopharyngeal temperature of 25°C. By an incremental stepwise 25% increase, a maximum flow of oxygenated blood equal to 2.5 $L \cdot min^{-1} \cdot m^{-2}$ was pumped into the reconstructed pulmonary bed and the mPAP was simultaneously recorded. If recorded pressure was higher than 30 mm Hg at any incremental step in the blood flow study, the test was terminated and intracardiac repair was not performed. For pressure values within 30 mm Hg, concomitant VSD closure was carried out and weaning from cardiopulmonary bypass was based on continuous RVSP/SBP monitoring. If the ratio was consistently above 0.75, careful pulmonary hygiene was performed, and aggressive ventilation with inhaled nitric oxide (when available) was initiated. If no response to these maneuvers occurred, unrestrictive VSD patch fenestration was carried out.

The original method to perform the functional flow study was tested in animal experiments, extended to humans, and reported in the literature by Reddy and associates [6] in 1997. We fully embraced this method from the very beginning of our experience and kept it unchanged over time. During such a test, the use of oxygenated blood and the low hematocrit level of the pump prime should somehow counterbalance the potential increase of the pulmonary vascular resistance related to low temperatures, nonpulsatile flow perfusion, and absent lung ventilation. Correct intraoperative flow study execution may be problematic in patients exceeding 1 m^2 body surface area, owing to the need for excessive pump priming and to the ability of the pump oxygenator to sustain adequate flow. Potential systemic hypoperfusion during test execution may result in organ damage, especially in patients with persistent systemic-to-pulmonary collateral circulation. Although our current elective approach to one-stage unifocalization includes almost exclusively patients in infancy, late referrals exceeding 1 m^2 body surface area are more appropriately managed by preoperative cardiac magnetic resonance imaging with the pulmonary to systemic flow ratio (Qp:Qs) calculation, and VSD closure is decided accordingly [14] if Qp:Qs values are greater than 1.5:1 [15, 16].

Statistical Analysis

Categoric variables are reported as frequency and percentage. Continuous variables are presented as mean with standard deviation or median with range. Correlations were determined using Spearman's rank correlation test. The primary endpoint was all-cause mortality. The secondary endpoints included both survival according to pulmonary pressure (less than 25 mm Hg versus 25 to 30 mm Hg) on the flow study and RVFAC in patients who achieved one-stage intracardiac repair. The accuracy of the functional flow study in predicting the feasibility of VSD closure was analyzed by the area under the receiver-operating characteristics curve. Freedom from death was analyzed using Kaplan-Meier survival analysis, and the survival estimates were compared using the log rank test.

Univariable Cox proportional hazards analysis was utilized to assess candidate risk factors affecting outcomes. The last follow-up ended on February 1, 2017. Patients' data were censored at the time of last contact, and among survivors, follow-up was 79.4% complete. The IBM SPSS Statistics for Windows 21 (IBM Corporation, Armonk, NY) and STATA version 11.1 data analysis and