In this issue of Circulation: Cardiovascular Interventions, Borik et al review the intermediate and long-term echocardiographic, MRI and cardiopulmonary exercise results in a cohort of 51 patients followed for a mean of 4.5±1.9 (0.9–6.9) years after percutaneous pulmonary valve implantation (PPVI). The majority of patients had mixed pulmonary stenosis (PS) and pulmonary regurgitation (PR; 32/51) or predominant PS (16/51). The cohort is divided into patients <16 years of age and those >16 years. Clinical outcomes are favorable in the overall cohort, no differences were noted in the need for reintervention or reoperation between the younger and older groups and there was only one episode of endocarditis. Incremental improvements in right ventricular size by echo and MRI were noted in younger patients and there was a trend toward improvement in right ventricular ejection fraction in patients <16 years of age. Moreover, the authors noted greater improvement in maximum oxygen consumption in younger patients, those with lower preimplantation right-sided pressures, and those with better ventricular function and aerobic capacity before implantation. The improvements in aerobic capacity occurred within the first year and plateaued thereafter. The authors concluded that PPVI in younger patients with right ventricular outflow tract (RVOT) dysfunction is associated with improved aerobic exercise capacity and right ventricular dimensions.

See Article by Borik et al

There is general consensus among experts in congenital heart disease that symptomatic patients with RVOT dysfunction should undergo pulmonary valve replacement. Symptomatic patients include those with decreased functional capacity, evidence of heart failure, and arrhythmias. The timing of pulmonary valve replacement in asymptomatic patients with RVOT dysfunction is more controversial. Coats et al demonstrated that patients with RVOT obstruction, defined as an echo Doppler-derived peak systolic gradient ≥50 mmHg, benefited from PPVI with resultant immediate reductions in RV pressure and short-term improvement in RV size, right ventricular ejection fraction, aerobic exercise capacity and anaerobic threshold. Lurz et al also demonstrated short-term improvements in exercise capacity and right ventricular ejection fraction in patients with predominant PS, but no such improvements were seen in patients with predominant PR. Although patients with PR did demonstrate improvement in RV diastolic volume, this did not translate into improvements in exercise capacity or ejection fraction. Batra et al evaluated cardiopulmonary exercise capacity pre and 6 months post Melody PPVI in a multicenter cohort and demonstrated no significant change in peak oxygen consumption or oxygen pulse (a surrogate for RV stroke volume). The degree of PR was not associated with baseline oxygen consumption in this cohort.

Several studies have evaluated the timing of surgical pulmonary valve replacement in patients with predominant PR and have suggested that normalization of RV volume and systolic function is likely to occur after valve replacement in patients with right ventricular end-diastolic volume index of 150 to 170 mL/m², right ventricular end-systolic volume index of 80 to 90 mL/m² or right ventricular end-diastolic volume twice left ventricular end-diastolic volume. It is important to note that normalization of RV volume has not been correlated with improved clinical outcomes, such as reductions in mortality, arrhythmia burden, or heart failure episodes; however, functional capacity (New York Heart Association class) improvements are expected. Given the available evidence, it stands to reason that asymptomatic patients with RVOT stenosis (peak Doppler systolic gradient ≥50 mmHg) could undergo intervention with an expected improvement in exercise capacity. The timing of intervention in asymptomatic patients with predominant PR is based on data demonstrating improved RV volumes at certain MRI-derived volumetric thresholds and not on evidenced improvements in clinical outcomes. The study by Borik et al suggests that earlier intervention results in improved functional and volumetric measures; however, the majority of the study population consists of patients with either predominant RVOT stenosis or mixed PS and PR. As a matter of fact, only 2 patients in the entire cohort, both >16 years, had predominant PR. Therefore, one cannot conclude, from the data provided, that intervention at a younger age for predominant PR is associated with improved exercise and volumetric outcomes. However, the data provided by Borik et al does support the assertion that earlier intervention in patients with PS or mixed stenosis/regurgitation is associated with greater improvements in exercise capacity, RV size and RV function.

Although the timing of RVOT intervention in asymptomatic patients is mostly predicated on the presence of RVOT...
dysfunction, enlarged RV size, and RV systolic dysfunction, other considerations should also be taken into account. Placement of a transcatheter pulmonary valve may improve conduit or bioprosthetic valve stenosis and regurgitation; however, this does come at a cost. The effective maximum internal circumference of the conduit or bioprosthesis is inevitably decreased after valve placement. Lurz et al\textsuperscript{13,14} demonstrated excellent long-term survival post Melody pulmonary valve replacement; however, 27% of patients did require reintervention at 70 months of follow-up, the highest risk for reintervention was in those with residual RVOT gradient >25 mmHg and in the first 50 cases performed. It would stand to reason that percutaneous pulmonary valve function, as is the case with surgically placed bioprosthetic valves or conduits, will deteriorate over time and that replacement will be needed in the majority of patients within 1 to 2 decades. For example, a child with a dysfunctional 18-mm homograft that undergoes Melody valve placement at 10 years of age may require at least 3 future valve replacements during the next 60 years of life. Thus, one would expect the gradual development of worsening conduit stenosis with multiple PPVI procedures and eventual need for surgical conduit revision. The long-term consequences of multiple surgical RVOT interventions include ventricular diastolic dysfunction and a significant increase in atrial and ventricular arrhythmias, sudden cardiac death, and need for defibrillator placement.\textsuperscript{13,14} Therefore, when taking atrial and ventricular arrhythmias, sudden cardiac death, and ventricular diastolic dysfunction and a significant increase in consequences of multiple surgical RVOT interventions include ventricular diastolic dysfunction and a significant increase in atrial and ventricular arrhythmias, sudden cardiac death, and need for defibrillator placement.\textsuperscript{13,14} Therefore, when taking atrial and ventricular arrhythmias, sudden cardiac death, and ventricular diastolic dysfunction and a significant increase in atrial and ventricular arrhythmias, sudden cardiac death, and need for defibrillator placement.\textsuperscript{13,14} Therefore, when taking atrial and ventricular arrhythmias, sudden cardiac death, and ventricular diastolic dysfunction and a significant increase in atrial and ventricular arrhythmias, sudden cardiac death, and need for defibrillator placement.\textsuperscript{13,14} Therefore, when taking the long view on percutaneous pulmonary valve replacement, it is imperative to consider the size of the existing RVOT, the potential need for subsequent reintervention and the resultant eventual and inevitable stenosis of the existing RV to PA communication. The risk of infective endocarditis in patients that have undergone Melody valve placement must also be considered. Although only one patient in this cohort (2\%) had infective endocarditis, infective endocarditis has been shown to occur with an estimated annualized rate as high as 2.4\% per patient year.\textsuperscript{15,16}

Is earlier PPVI better? It depends. If the patient is symptomatic or has decreased functional capacity then intervention is certainly indicated. If the patient has significant RVOT stenosis or mixed PS/PR then one would expect improvement in exercise capacity with intervention. Patients with predominant PR may also benefit but there is little data to suggest early intervention is associated with improved clinical or functional outcomes in those with normal functional capacity (New York Heart Association class I). The existing data supports intervention at certain volumetric thresholds or in those with reduced right ventricular ejection fraction to normalize RV volume and improve systolic function but not to reduce hard clinical endpoints. This article demonstrates that early valve placement in younger patients with predominant PS or mixed PS/PR is associated with improved exercise and volumetric outcomes but, similar to previous studies, does not demonstrate improved clinical outcomes. The long-term impact of early PPVI and the need for subsequent valve in valve implants with eventual luminal stenosis should also be considered. This may not be as important of a consideration in patients with native RVOTs or patches where there is no absolute size limitation imposed by a surgically placed conduit or bioprosthetic valve. As there may be significant benefits to earlier PPVI, this article provides more impetus for a well-controlled study of the long-term benefits of earlier PPVI. However, because early PPVI also has risks and disadvantages, these interventions must be carefully planned and studied.

Are we starting to see a paradigm shift toward earlier PPVI? Because Melody PPVI has been shown to be safe and effective with excellent short- and intermediate-term outcomes and favorable risk profile,\textsuperscript{12,17,18} we have seen congenital cardiologists sending patients earlier for PPVI than they did for surgical pulmonary valve implantation. Is earlier pulmonary valve replacement justified now that this procedure can be done in a transcatheter fashion? It is impossible to make definitive recommendations based on the data from this article by Borik et al\textsuperscript{5}: this retrospective data includes a mixed population of patients with PS/PR with only 23 patients <16 years of age, 28 patients >16 years of age, and with data available on only a fraction of these patients and no control subjects. Nonetheless, the authors clearly show that younger patients may benefit from earlier PPVI and it is reasonable to continue to study the effects of lowering the bar for PPVI.

Disclosures

None.

References


Percutaneous Pulmonary Valve Implantation: Is Earlier Valve Implantation Better?
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