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Editorial

Pulmonary Valve Replacement in Patients with Repaired Tetralogy of Fallot: What Are the Benefits?

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▸ See the article "Effect of Pulmonary Valve Replacement in the Repaired Tetralogy of Fallot Patients with Trans-annular Incision: More than 20 Years of Follow-up" in volume 51 on page 360.

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Repair of tetralogy of Fallot (TOF) often results in pulmonary regurgitation (PR), which can lead to right ventricular (RV) dilatation, RV dysfunction, left ventricular (LV) dysfunction, arrhythmias and sudden cardiac death.[1] Pulmonary valve replacement (PVR) is being performed with increasing frequency in patients with repaired TOF to prevent or reverse the deleterious consequences of chronic PR. During the past decade, a substantial number of studies dealing with issues of PVR in this population have been published.[2-4] Indications and optimal timing of PVR have been refined, mostly based on pre-PVR cut-off values of RV volume indexes for post-PVR normalization of RV volume indexes and ejection fraction (EF).[5] It is now firmly established that PVR in this population consistently leads to significant reduction in RV volumes and improvement in subjective functional class. What remains unknown is whether these benefits of PVR will translate into improved long-term survival. Until now, no study clearly answered this question. Reported survival rates at 15 years after PVR range between 70% and 96%.[6-8] Prospective randomized studies to answer this question may not be possible in the future and seem to be unethical.

In this issue of the *Korean Circulation Journal*, Kwak and colleagues[9] report long-term outcomes of transannular TOF repair and effects of PVR on these outcomes. Between 1991 and 1997, 180 out of 196 patients (excluding 10 early deaths after TOF repair and 6 patients who underwent pulmonary valve repair during follow-up) with a median age of 14 months at TOF repair were included in the study. The median follow-up duration was 24.8 years and the overall survival at 25 years was 88.4%. Eighty-one patients underwent PVR at a median age of 13.5 years. The freedom from reoperation for PR at 25 years was 53.5%. Among these, 63 patients (78%) underwent pre-PVR magnetic resonance imaging (MRI), although the mean RV volume indexes and EF of these entire patients are not presented in the study. As expected, RV volume indexes decreased significantly after PVR, but not to normal level. In the entire cohort (n=196), the authors compared long-term survival between the unmatched PVR and non-PVR groups and observed better survival in the PVR group (100% vs. 88.7% at 20 years). In an unmatched subgroup analysis (n=180), the PVR group also showed better long-term survival. Age less than 1 year at TOF repair and prior aortopulmonary shunt were associated with shorter time to PVR after TOF repair. Based on these data, the authors concluded that early PVR might be beneficial for long-term survival in patients with repaired TOF and significant PR.

Data Sharing Statement
The data generated in this study is available from the corresponding author upon reasonable request.

This is an important study in a sense that it scrutinized long-term outcomes of transannular TOF repair and effects of PVR on these outcomes. The authors should be commended on their arduous effort to collect the old data for this kind of long-term follow-up study. It is valuable information that nearly 50% of the patients who underwent transannular TOF repair will require PVR by 25 years after repair. The median age at PVR (13.5 years) was quite lower compared with other studies,[2-4)6-8)10)] although it is not clear whether this reflects their center's policy toward early PVR, or this simply means early need for PVR for some reason. Looking into the pre-PVR MRI data (n=34), the mean RV end-diastolic and end-systolic volume index was 179 and 106 mL/m^2, respectively, which are rather high considering the relatively young age of this cohort and other studies.[2-4)8)] RV systolic dysfunction was already evident with a mean RV EF of 41%. It is probable that the factors other than volume overload by chronic PR, such as large RV incision with subsequent large RV outflow tract patch and inadequate myocardial protection at the time of initial repair, might have contributed to the observed MRI parameters. This speculation is based on the early mortality of 5.1% (10 out of 196) and low cardiac output syndrome as a predominant cause of the early deaths (7 out of 10). However, the survival after PVR was good, with only 1 late death, although the mean follow-up duration after PVR is not presented.

There are several limitations that need to be mentioned for cautious interpretation of this study. First, the follow-up completeness was suboptimal and 25% of the study population could not be followed-up within 5 years of the closing date of the study. Although the authors tried to confirm the survival status of the patients who had been lost to follow-up from the National Health Insurance Service, it was not mentioned how many late deaths were identified by this method. Second, the causes of the 11 late deaths are unclear. Only clinical problems that developed in these patients during follow-up were described. This is somewhat understandable if some of the late deaths were identified from the National Health Insurance Service, because of the well-known limitations of this kind of administrative database. The authors just speculated that 5 of the 11 late deaths seemed to be sudden deaths based on the observations that they had experienced temporary ventricular arrhythmias. However, all documented ventricular arrhythmias were isolated monomorphic premature ventricular contractions, not sustained ventricular tachycardia. QRS durations of these patients were not presented. All of the late deaths occurred in the first or second decade of age. Considering the general observation that chronic PR is well tolerated during this period, it is probable that the late deaths mostly observed in the non-PVR group might have been largely due to the deleterious consequences of the initial TOF repair, not due to the consequences of chronic PR after uncomplicated repair. Third and most importantly, this study is seriously limited by the fact that the 2 groups were not matched for fair comparison of outcomes. For fair and meaningful comparison of outcomes in this kind of retrospective study, baseline characteristics should be carefully matched, and follow-up should start at the time of PVR.[6)10)] Important baseline characteristics such as date of birth, age at repair, QRS duration, and follow-up duration were not matched in this study. All the Kaplan-Meier curves presented in the study start from the time of TOF repair, instead of the time of PVR. Therefore, I would say that one of the conclusions of this study stating "The early, adequate timing of PVR could be beneficial for long-term survival in the patients who have significant PR after TOF repair..." is not supported by the data presented. This is not to deny the role of PVR in patients with repaired TOF or discourage the authors. Currently, there is no clear evidence that PVR improves survival of this patient population, although this can be viewed as disappointing. Long-term follow-up results of carefully designed studies, such as those from the INDICATOR registry,[4)] are needed to draw meaningful conclusions on this important issue.

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