LETTERS TO THE EDITOR

Repairing Tetralogy of Fallot—Does Age Matter?

We read with interest the article by Munkhammar et al. (1). The authors attempted to answer an important question for clinicians who take care of patients after complete repair of tetralogy of Fallot (TOF): what are the variables related to restrictive right ventricular (RV) physiology? Although the authors examined many possible “determinants for restrictive RV physiology,” they “focused on age at repair and its possible association to later diastolic RV physiology.” Unfortunately, their study design suffers from serious selection bias and the subsequent analysis is open to methodologic questions.

An initial selection bias is introduced by including patients from two hospitals: 27 patients from Lund (1985–1996) and 20 patients from the Hospital for Sick Children (1994–1996). The variables related to different institution, surgeon and era (Lund clearly covers a much wider period) were not explored. Although different surgical techniques were compared, other important operative variables such as cardiopulmonary bypass time, aortic cross-clamp time and myocardial preservation technique were not studied.

A more serious problem in subject selection arises from the arbitrary selection of only infants (<1 year of age) as the study group. This is particularly worrisome because the authors find a major effect of “age” on RV restrictive physiology. We have studied age at operation for infants and children in California and have found that the age distribution for complete TOF repair does not follow a normal distribution (2). In addition, the distribution of age at TOF repair for subgroups of patients, such as patients with restrictive RV physiology and patients with nonrestrictive physiology, is unknown. Using 1 year as an arbitrary age cutoff may select different portions of the distribution curves for restrictive and nonrestrictive groups, distorting any comparison of mean age between the two groups. Furthermore, the authors found p < 0.05 for the difference in age at repair for restrictive (mean 0.77 months) and nonrestrictive (mean 0.64 months) groups. The presentation of the data as the mean value ± SD implies that the authors used the Student t test to compare the ages of the two groups. This would not be an appropriate comparison if age at repair for TOF is not normally distributed. In addition, there was a large difference of <2 months (6 months vs. 8 months) in mean age between the two groups, with a wide standard deviation in both groups, making the meaning of p < 0.05 by the Student t test questionable.

After comparing preoperative, operative, postoperative and echocardiographic variables, the only conclusion the authors could draw was that “restrictive RV physiology is inversely related to age at repair.” With the selection bias and methodologic problems in statistics used, we believe the study does not support the conclusion the authors have reached. The results of this study should be interpreted with extreme caution by the readers of the Journal.

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REFERENCES

REPLY

Thank you for your interest in our paper on right ventricular (RV) diastolic physiology after tetralogy of Fallot repair (1). We do agree that the initial selection of patients from two hospitals may cause problems in data interpretation, which we have stated in the limitations of the study. However, we do not agree that this should invalidate our results for the following reasons. In two recent studies we explored several factors characterizing early and mid-term restrictive RV physiology after tetralogy repair, including details on cardiopulmonary bypass time, aortic cross-clamp time and different myocardial protection (2,3). Surprisingly, none of these factors were related to subsequent restrictive RV physiology. It is therefore unlikely that possible differences between the two hospitals in these surgical factors should influence subsequent diastolic physiology. The wider period on patients from Lund could represent a methodologic problem if restrictive RV physiology was related to length of follow-up. This is not the case; the pattern of diastolic RV physiology does not change much with time, as we have shown recently (4).

We definitively do not share your view on selecting patients <1 year of age for the study, even if age is not normally distributed in these patients. Because age at repair is declining and transannular patch (TAP) repair usually is needed in infancy, we believe it is of particular importance to study this well-defined and clinically important age group. The selection is not particularly worrisome because we suggested a relation of restriction to age at repair. What may be worrisome are the consequences of early repair on long-term RV function if early repair subsequently leads to more pulmonary regurgitation. However, we partly share your methodologic comments on the use of statistics. The comparisons for all patients were done using the Student t test (Table 1 of our article), requiring that the data have an approximately normal distribution. The standard deviations for age and pulmonary stenosis are far below 50% of the mean, thus suggesting a normal distribution of the data. For data with a standard deviation >50% of the mean and for data on patient subgroups with TAP repair, the nonparametric Mann-Whitney U test was used. The presentation of the data in Table 1 using the mean value ± SD can be misleading. Nonrestrictive patients with TAP repair were significantly younger at repair and had less severe preoperative pulmonary stenosis analyzed using nonparametric methods. These are the most important patients to follow because the consequences of nonrestriction may be more pronounced (3).

We also share your caution in interpreting small differences, which should be clear by reading our report carefully. Age at repair is not our