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Commentary

The in-depth and careful study of outcomes related to congenital heart disease and its management is of increasing importance, given the growing population of adult survivors. Studies of outcomes in adult patients who received follow-up in specialized clinics can be misleading, because the denominator or cohort from which these patients are derived is usually not defined. Likewise, outcomes studies from pediatric institutions tend to terminate near the age of 18 years. Studies such as that by El-Najdawi and associates, in which an entire inception cohort is carefully traced and followed to the present, are difficult but necessary to provide accurate information about prognosis and to identify potentially higher risk subgroups that may require altered surveillance and preventative management.

Nonetheless, the article is largely descriptive, with some important flaws in the data analysis that limit ready acceptance of some of their findings. The "Users Guides to the Medical Literature" series of articles succinctly highlights the key issues in the critical appraisal of an article concerning prognosis.[1] The study population is well defined and likely representative of patients who have undergone repair of partial atrioventricular canal defects. Because significant changes in diagnosis and management are likely to have occurred over the 40-year period, a more detailed analysis of outcomes and associated factors over time should have been included. Also, outcomes from smaller case series from a single institution are less likely to be generalizable to any other institution than outcomes from a larger case series pooled from a representative sample of institutions. The follow-up is sufficiently complete, given the limitations of tracing and contacting patients no longer being followed at the originating institution. Although the outcomes of death and reoperation are objective, left atrioventricular valve regurgitation and stenosis, left ventricular outflow obstruction, and supraventricular arrhythmias were mainly assessed in a subjective manner with evolving technologies and varying degrees of accuracy, completeness, and interpretation as recorded by multiple levels of providers in the medical record. The definitions for these latter outcomes are thus necessarily vague. More details about the medical questionnaire should be given, particularly regarding content, validity, and reliability as completed by the patients and nonstudy providers. In addition, the analysis of some of the morbidity outcomes as discretely timed events is erroneous, because these outcomes more accurately take on varying grades of severity that evolve over time. The patients (usually) do not suddenly experience the development of a threshold grade of left atrioventricular valve regurgitation or stenosis at a given date. Also, the dates used to define these outcome events (date of first notation in the medical record) are largely dependent on the providers' schedule of follow-up assessment. The error in this method for analyzing the data is clearly illustrated in Fig 3, *B*, of the article, in which it might appear that there is a significant trend toward earlier development of left atrioventricular valve regurgitation with the more recent experience, when, in fact, this probably represents improved detection with the advent of echocardiography.

An important aspect of an article about prognosis is the analysis of associated factors of prognostic importance; otherwise, the study is purely descriptive and of limited value. In the analysis of prognostic factors, the authors arbitrarily divided the cohort into 3 groups on the basis of the patients' date of repair procedure and entered this variable into models that assumed discretely timed events and presupposed that this provided adequate adjustment for changes that may have occurred over a 40-year period. The arbitrary categorization of continuously measured variables is rarely justified and diminishes both statistical power and the ability to elucidate more complex associations. Age at repair procedure, another potentially important prognostic factor, was also arbitrarily categorized. When exploring potential prognostic factors in multivariable analysis, it is very simplistic and often erroneous to assume that entering the date of repair into the model adequately adjusts for unmeasured trends over time in prognostic factors and outcomes. This is in addition to the fact that, before prognostic factors were examined,

the appropriate method of modeling of the outcome should have been performed (not a timed-event analysis), and the relationships between potential prognostic factors should have been explored.

How might the authors have improved the quantity and quality of evidence provided by their study? It would have been ideal if all surviving patients had undergone a standardized assessment in the same manner within a defined end-point interval, preferably performed at the study institutions by the dedicated investigators. This would supplement the study with important and more valid cross-sectional information about current outcomes in a defined cohort. A more detailed analysis of trends in patient characteristics and outcomes over time should have been performed. From the patients' perspective, outcomes begin at birth (and maybe even before birth), not at repair. Perhaps an analysis by birth cohorts (grouping the patients by their date of birth) should also have been performed, recognizing that the study results are relevant only to those patients with partial atrioventricular canal defects who underwent repair procedures. Other than survival and reoperation, the longitudinal aspects of this study are weak, given the limitations of the definitions. Statistical methods for the analysis of repeated or serial measurements are currently available for the modeling of evolving longitudinal outcomes and the testing of associated prognostic factors. The study should have collected more quantitative data longitudinally over all available assessments (particularly grade of valve regurgitation or stenosis and severity of left ventricular outflow obstruction) and used these analytic techniques. This was likely not feasible or sufficiently valid over the long period of the study. A less optimal but more feasible alternative would have been to improve the analysis of reoperation, particularly by identifying freedom from reoperation for particular causes. Although the definition of left atrioventricular valve residual or recurrent defects and left ventricular outflow obstruction may be subjective and problematic, one measure of the significance of these defects is the need for reoperation, an end point that is discrete and subject to less debate. The number of potential prognostic factors reported in this study is small; perhaps a more detailed and enriched data set might have been created. Health status and quality of life are important outcomes to patients; perhaps patients might have completed one of the currently available validated questionnaires, especially because most of the subjects were either seen at the study institution or were contacted to complete a medical questionnaire.

Despite these missed opportunities, the study by El-Najdawi and associates represents an excellent attempt at a more valid and comprehensive assessment of outcomes, and the authors are to be commended on the excellent follow-up of a well-defined patient series. Nonetheless, the reported results related to medical morbidity must be viewed in light of important threats to validity. It should also be recognized that if only perfect studies were published, much of the available evidence currently guiding medical practice would not exist.

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