Call for a Disease-Specific Patient-Reported Outcome Tool in Adult Congenital Heart Disease

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Those who care for patients with adult congenital heart disease (ACHD) need a valid and sensitive measure to better quantify the effect of ACHD on patients’ health status, their symptoms, function, and quality of life (QOL). These insights are critical in evaluating the success of novel treatments, monitoring patients over time, and comparing treatment success across providers as a foundation for quality improvement. Given the unique and myriad manifestations of various forms of ACHD, generic QOL measures are likely inadequate and the time has come to create an ACHD-specific patient-reported outcome (PRO) tool.

The prevalence of ACHD is expanding rapidly in the developed world. As a result of medical and surgical advances over the last half century, patients who previously would have succumbed to their cardiac abnormality in early childhood now live well into adulthood. Currently, it is estimated that there are more adults living in the United States with congenital heart disease than there are children. Although medical and surgical advances have led to dramatic improvements in survival, these patients are not cured and live with various limitations and symptoms that require ongoing monitoring and treatment.

The growth of this unique population of patients with chronic heart disease creates a need for new research strategies to optimize care and improve outcomes. Like other patients with chronic heart disease, patients with ACHD have been demonstrated to have rapidly rising rates of hospitalization and medical resource utilization. Current data support the notion that appropriate disease-specific care improves both health outcomes and resource utilization. Current data support the notion that appropriate disease-specific care improves both health outcomes and resource utilization. The recent demonstration that specialized ACHD care may result in more positive outcomes for ACHD patients suggests that these patients may benefit from novel disease-specific pharmacological and device therapies analogous to improvements in outcomes realized in patients with acquired heart disease.

To facilitate identification of new therapeutic approaches and to address the need for improved research in ACHD healthcare quality, an ACHD-specific PRO is critical. ACHD clinical research arguably remains in its infancy. The great majority of research in the field is retrospective and nonrandomized. Although changes in practice based on such research have clearly benefited ACHD patients, further improvements will require better outcome data on quality, including the symptom, function, and QOL status of patients. The limited number of well-conducted, randomized, placebo-controlled trials in ACHD have largely failed to demonstrate the efficacy of modern neurohumoral modulation in decreasing hospitalization or mortality in this population. These failures may well indicate inefficacy of the tested interventions. There are nevertheless trends present in these studies, indicating that patient heterogeneity, inadequate study power, and non ACHD-specific outcomes may have contributed to their failure to yield statistically significant results. As the first 2 variables are nearly unresolvable in ACHD research, it is necessary to expand our measurement of outcomes to include novel measures that are clinically relevant, associated with other hard outcomes, and meaningful to patients.

In this regard, PRO tools are ideally suited to facilitate further progress in ACHD research. PRO tools have been widely used as outcomes in acquired chronic heart disease research. In this setting, optimally designed tools have been shown to be both predictive of hard outcomes and sensitive to changes in patients’ health status; a major therapeutic goal of treatment. In ACHD research, exercise tolerance has been widely adopted as a surrogate for hard outcomes because of its good correlation with event-free survival. The heterogeneity of exercise tolerance in the ACHD population, however, makes prognosticating based on exercise capacity alone problematic. Moreover, by design, exercise tolerance measures what patients are capable of performing, but not how they routinely perform. It does not directly assess symptoms or patients’ perceived health-related QOL. There is, however, a growing appreciation that health-related QOL is an essential outcome metric in clinical research. The capacity of PROs to measure QOL, potentially including domains to assess depression or anxiety, is particularly important in the US ACHD population, which is recognized to be susceptible to psychological disorders. Despite its correlation with hard outcomes, exercise tolerance performs poorly in predicting health-related QOL among ACHD patients.

This is not to suggest that the importance of health-related QOL has been ignored by the ACHD community. In fact, there are multiple examples of trials that have used existing QOL assessment tools in various clinical scenarios. Nearly all existing studies in ACHD that have used QOL as an end point, however, have used generic health-related QOL tools, such as the 36 question short form (SF-36). Although these tools...
are better assessments of QOL than other clinical variables, they are not designed to measure the unique manifestations of ACHD on patients’ health status and are insensitive to clinical changes that are important to ACHD patients and those who treat them.21,42,43 Disease-specific PRO tools, in contrast, may have the advantage of both accurately assessing QOL and sensitively capturing changes in patients’ health status.44

We think that the time is right for the ACHD research community to focus on developing a well-designed and validated, ACHD-specific, PRO tool. Although some domains of symptoms and physical function may be captured well by existing disease-specific tools for heart failure, other domains need to be considered and new domains will likely warrant quantification. For example, the psychological effects of chronic heart disease are significantly different in patients who acquired their disease, as compared with ACHD patients, who have never known a disease-free life.45 Acquired chronic heart disease has a profound effect on all aspects of QOL, and QOL in this population correlates strongly with disease severity, activity, and duration.46–49 In contrast, QOL in patients with ACHD correlates poorly with disease complexity or degree of cardiac dysfunction.50,51 In fact, outside of the physical domain, ACHD patients demonstrate little difference in their reported QOL compared with the general population.52,53 Furthermore, anxiety and depression are common among patients with acquired chronic heart disease and have a strong correlation with clinical outcomes.54–56 In contrast, studies investigating the prevalence of depression and anxiety in ACHD patients have had conflicting results, and no study has specifically investigated correlations between depression or anxiety and clinical outcomes.57 The psychological differences between patients with acquired chronic heart disease and ACHD would therefore be anticipated to decrease the probability that existing tools will be useful in the latter group of patients.

The unique anatomy and sequelae of ACHD would further confound employment of existing PRO tools in this population. As a result of their underlying anatomy, ACHD patients as a group are more likely to experience progressive right ventricular failure and cyanosis than are patients with acquired heart disease. These problems would be anticipated to be associated with distinct symptoms, which differ from those experienced by patients with progressive acquired heart disease. In addition, the anatomic and physiological heterogeneity which characterize ACHD would limit the validity and responsiveness of any questionnaire designed specifically for a single disease process. Hospital admissions among patients with ACHD are nearly equally divided between those for arrhythmia, coronary artery disease, and congestive heart failure.7 Retrospective data and experience would suggest that the probability of hospitalization for each of these reasons differs significantly depending on underlying anatomy and repair. Furthermore, within a group of patients with similar anatomy and repair, >1 existing PRO may provide relevant information. For example, patients with complete transposition of the great arteries who have undergone an atrial level repair would likely be ideally evaluated using PRO tools specific for both heart failure and arrhythmia. An ideal PRO for ACHD would likely require a core set of measures that are relevant to all patients with ACHD, supplemented by disease-specific modules for specific anatomic and physiological subsets of this heterogeneous population.

The unique character of the ACHD population thus demands a unique approach to the development of an ACHD-specific PRO tool. We propose using an iterative process for the development of this tool in 4 distinct steps:

Step 1: ACHD healthcare professional survey. To help build a conceptual model for constructing a modular PRO platform for ACHD, physicians and nurses who care for these patients should be surveyed to help categorize the range of ACHD into groups based on the clinical manifestations that they perceive patients experience. They should also provide a list of symptoms that they think are reflective of clinical deterioration and have a significant effect on a patient’s QOL. In addition, they will be asked to provide a list of acute medical stressors, events such as recent hospitalizations, surgeries, or device placement procedures that may affect PRO responses. These symptoms and stressors will be compiled into a patient survey.

Step 2: ACHD patient survey. During this step, the survey constructed as a part of Step 1 should be given to ACHD patients, along with open-ended opportunities for patients to elaborate on how they perceive their disease to affect their lives. Patients should rank the symptoms and stressors identified by ACHD professionals in order of greatest effect on their QOL. In addition, they will be asked to provide a list of symptoms not mentioned on the questionnaire, but which they feel are of significance in their QOL. Survey responses will be grouped based on underlying patient anatomy and repair to confirm the construct validity of ACHD types proposed by clinicians.

Step 3: Construction of questionnaires. Using the data compiled during Steps 1 and 2, preliminary PRO questionnaires should be constructed. We anticipate that, in spite of the heterogeneity in this patient population, certain common symptom complexes will emerge. These symptom complexes will have a variable effect on QOL depending on underlying diagnosis and repair. These symptom complexes should be used to construct modular questionnaires that can be variously applied, depending on underlying ACHD diagnosis and repair. These questionnaires will then be subjected to cognitive debriefing in patient focus groups to optimize accuracy, interpretability, and validity.

Step 4: Validation of questionnaires. Any proposed PRO needs to demonstrate adequate psychometric properties, including validity, reliability, responsiveness, and interpretability. To establish these properties, any proposed ACHD-specific PRO modules will need to be administered to ACHD patients, including those with different anatomic and physiological states. This should be performed over time, ideally at each outpatient visit at multiple centers over the course of several years and before and after therapeutic interventions. ACHD patients could also be asked to complete other, standard PROs at these visits to better support, compare, and contrast the benefits of the new tools over and above existing instruments.55,61,62 During this period, hospitalization and mortality data should be recorded for respondents to establish the predictive validity of the various tools being tested.

The derivation of an ACHD-specific PRO tool represents a unique challenge for the community providing care to ACHD
patients, but is one that it is necessary to accomplish as we strive to improve care and treatment for this growing population of patients. Disease heterogeneity in the ACHD population and psychological differences between this population and that of patients with acquired chronic heart disease represent significant obstacles to be overcome. Nevertheless, the rising social and financial burden of ACHD in the United States demands that the community of ACHD providers step up to improve the quality and relevance of research in ACHD. The development of an ACHD-specific PRO is a key missing piece to meeting this demand.

Disclosures

Ari Cedars receives research support from Actelion Pharmaceuticals, Gilead Pharmaceuticals, and Jazz Pharmaceuticals. John Spertus has a research contract from the American College of Cardiology Foundation and has a copyright on the Seattle Angina Questionnaire, Kansas City Cardiomyopathy Questionnaire, and the Peripheral Artery Questionnaire.

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_Circ Cardiovasc Qual Outcomes_. 2014;7:971-974; originally published online October 14, 2014;
doi: 10.1161/CIRCOUTCOMES.114.001406

_Circulation: Cardiovascular Quality and Outcomes_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 1941-7705. Online ISSN: 1941-7713

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