International Journal of Cardiology 171 (2014) 351–360

Contents lists available at ScienceDirect

International Journal of Cardiology

journal homepage: www.elsevier.com/locate/ijcard

Clinical research priorities in adult congenital heart disease ☆,☆☆

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ARTICLE INFO

Article history:
Received 15 November 2013
Accepted 14 December 2013
Available online 24 December 2013

Keywords:
Congenital heart disease
Tetralogy of Fallot
Transposition of the great arteries
Fontan procedure
Survey

ABSTRACT

Background: Adult congenital heart disease (ACHD) clinicians are hampered by the paucity of data to inform clinical decision-making. The objective of this study was to identify priorities for clinical research in ACHD.
Methods: A list of 45 research questions was developed by the Alliance for Adult Research in Congenital Cardiology (AARCC), compiled into a survey, and administered to ACHD providers. Patient input was sought via the Adult Congenital Heart Association at community meetings and online forums. The 25 top questions were sent to ACHD providers worldwide via an online survey. Each question was ranked based on perceived priority and weighted based on time spent in ACHD care. The top 10 topics identified are presented and discussed.
Results: The final online survey yielded 139 responses. Top priority questions related to tetralogy of Fallot (timing of pulmonary valve replacement and criteria for primary prevention ICDs), patients with systemic right ventricles (determining the optimal echocardiographic techniques for measuring right ventricular function, and indications for tricuspid valve replacement and primary prevention ICDs), and single ventricle/Fontan patients (role of pulmonary vasodilators, optimal anticoagulation, medical therapy for preservation of ventricular function, treatment for protein losing enteropathy). In addition, establishing criteria to refer ACHD patients for cardiac transplantation was deemed a priority.
Conclusions: The ACHD field is in need of prospective research to address fundamental clinical questions. It is hoped that this methodical consultation process will inform researchers and funding organizations about clinical research topics deemed to be of high priority.

☆ All authors take responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.
☆☆ Dr. Aboulhosn receives grant support from Actelion Pharmaceuticals.

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http://dx.doi.org/10.1016/j.ijcard.2013.12.034

1. Introduction

Adult congenital heart disease (ACHD) clinicians are hampered by the paucity of robust data to inform clinical decision-making. The American College of Cardiology/American Heart Association 2008 Guidelines for the Management of Adults with Congenital Heart Disease have been an important effort in standardizing ACHD care, although limited by a lack of strong evidence to support many of the recommendations. The document consists of 513 individual recommendations, of which 5 (0.97%) are based on level A evidence (multiple randomized trials or meta-analyses), 161 (31.4%) based on level B evidence (a single randomized trial or nonrandomized studies), and 347 (67.6%) based on level C evidence (expert opinion, case studies, or standards of care) [1].

To date, the vast majority of multi-center research studies in ACHD have been descriptive or observational. However, newer efforts including notable examples from pediatric cardiology and congenital cardiac surgery have demonstrated the feasibility of prospective, randomized trials [2,3]. The development of large, nationwide registries, such as the Dutch CONCOR registry and others has contributed importantly to our understanding of prevalence and natural history of CHD [4]. The Alliance for Adult Research in Congenital Cardiology (AARCC) has also pooled resources to complete multicenter studies [5]. As prospective, randomized trials are expensive and time-intensive, careful prioritization of potential study topics is prudent.

Given scarce resources for executing studies, it is worthwhile to focus on topics with the greatest potential to positively impact clinical management. Therefore, the aim of this study was to methodically pool opinions of key stakeholders, including both patients and providers, in identifying top priorities in clinical ACHD research.

2. Methods

Initially, a list of potential clinical research questions was generated through "brainstorming" sessions by AARCC investigators based on a list of congenital heart defects and general topics to ensure comprehensive consideration of all lesions. Distinct and specific research questions were generated for each, rather than general issues. Questions were circulated and revised over several iterations during a 12-month period. Overlapping questions were consolidated. From this initial list, general approximations of potential impact (considering both frequency of the population to be studied and the impact on clinical management) and feasibility were determined by consensus. From a total of 86 research questions initially posed and ranked on the basis of impact and feasibility, the top 45 questions were retained for further consideration. This number was selected based on natural break points in the order list, and included all questions considered to have either very high feasibility or very high impact.

A survey was then generated using these 45 questions and administered to attendees at the 2012 International Symposium on Congenital Heart Disease in the Adult held in Toronto, Canada. A hard copy version was distributed to all attendees, including faculty, and collected at the end of the conference. Respondents were asked to rate the feasibility and impact of each topic using a 5-point Likert scale (5 = highest impact/priority). Space was provided for notes and additional feedback. Each respondent was also asked to provide the percentage of clinical time they spent treating ACHD patients (<25%, 25–50%, 50–75%, or >75%) and their academic position (RN, NP/PA, MD/DO, or other).

Responses were entered into a database, including write-in questions/comments. Each response was weighted by the respondent's time spent in ACHD (1–4 scale based on the indicated percentage). Weighted feasibility and impact scores were averaged for each question and then added to generate an overall score. Write-in questions and comments were reviewed and incorporated whenever possible. Corrections or rewordings were made as necessary.

In parallel, patient input was sought via the Adult Congenital Heart Association (ACHA). Research priorities were discussed at several in-person community meetings attended by a large cross-section of ACHA membership in different geographic locations, as well as through online forums. Through these collective efforts, patients were provided with a list of general research topics and asked to rank them by perceived importance (1–5 scale). The average score for each topic was calculated (Table 1), and categories ranked accordingly. These results were then factored into weighing the Toronto survey. Each research question from the provider survey was reviewed for its relevance to general categories selected by the ACHA. The sum of the final physician and patient ranks was used to determine a final priority score.

The 25 top ranking questions were then sent to large list of self-identified ACHD providers worldwide in the form of an online survey (surveymonkey.com). Each question was re-ranked on a scale of 1 to 5 based on perceived priority (low, intermediate, high, very high, and top priority). Respondents were specifically encouraged to use the entire spectrum of scores. Options for write-in comments or additional questions were provided, and respondents were again asked to estimate their amount of time spent in ACHD care.

Table 1
Classification of research priority categories from patient surveys.

General topic	Mean score	Rank
Heart rhythm problems	4.6	1
Surgery	4.6	2
Insurance	4.3	3
Devices	4.3	4
Quality of life/social/psychological concerns	4.2	5
Physical symptoms	4.1	6
Medications	4.0	7
Pregnancy	3.9	8
Exercise	3.9	9
Kidney and liver function	3.6	10
Sexual function	3.2	11

A reminder to complete the survey was issued 4 weeks later such that the survey was open for a three-month period of time, until no additional responses were received.

2.1. Data analyses

Data are presented as frequencies and percentages. All responses were weighted according to the relative proportion of time spent in ACHD care using an ordinal scale (i.e., 0.25, 0.5, 0.75, and 1.0). Research questions were then ranked by score to generate a final priority list. Comments and write-in questions were reviewed and qualitatively incorporated in results.

3. Results

A total of 57 surveys were received from the Toronto conference. Respondents included 43 MD/DO, 8 RN, 5 NP/PA, and 1 other. Of these, the time spent in ACHD care was >75% for 44% of respondents, 50–75% for 19% of respondents, 25–50% for 12% of respondents, and <25% for 23% of respondents. The top 25 ranked questions that were further considered are listed (Table 2).

The online survey yielded 139 responses. Of these 50 (36%) reported >75% of time spent in ACHD care, with 15%, 27%, and 22% of responders indicating 50–75%, 25–50%, or <25% of time in ACHD care, respectively. No questions were left blank by any respondent. The top 10 ranked questions were retained for discussion in this manuscript. Two relate to tetralogy of Fallot, 3 to patients with a systemic right ventricle (RV), 4 to Fontan palliation, and 1 with general application.

Of the write-in questions, some lent themselves to inclusion within existing questions, or helped to correct/clarify existing topics. Comments that were not included were: 1) too broad or general to lend themselves to specific research topics, 2) previously included in the original brainstorm list, 3) felt not to be feasible, or 4) previously addressed or the subject of ongoing studies. One respondent wrote "All the topics listed above are important with very little variations in their priority," which is an important reminder that topics not included in the final selection should not necessarily be viewed as unimportant. Many respondents spontaneously expressed interest in participating in multicenter research trials.

4. Discussion

While no list can incorporate all potential important research questions of interest, our objective was to highlight research topics deemed to be of high priority by a methodical consultation process of relevant stakeholders. Each of the top 10 research questions is discussed in greater detail, in random order, below.

4.1. What is the optimal timing of surgical pulmonary valve replacement in tetralogy of Fallot?

Despite intense interest and numerous publications during the past 15 years on pulmonary valve replacement (PVR) in adults with repaired tetralogy of Fallot (TOF), optimal timing remains uncertain [6–8]. There