Pediatric Cardiac Surgery Annual

The Congenital Heart Surgeons Society Datacenter: Unique Attributes as a Research Organization

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Over the last 25 years, the Congenital Heart Surgeons Society (CHSS) has evolved from an informal club to a mature organization. A central feature of the CHSS has been dedication to evaluating outcomes of congenital heart surgery across a wide array of clinical diagnoses. These research activities have been orchestrated through the CHSS Datacenter, which has developed a unique organizational structure that has strengths and weaknesses in comparison to other research organizational structures (eg, prospective randomized trials, registries, etc). This review will highlight the unique attributes of the CHSS Datacenter with emphasis on the Datacenter's strengths and weaknesses in comparison to other organizational structures.
Semin Thorac Cardiovasc Surg Pediatr Card Surg Ann 13:71-75

Background

The Congenital Heart Surgeons' Society (CHSS) Datacenter is a unique entity in the clinical world. The Datacenter is the product of a decades-long collaborative effort among congenital heart surgeons to address fundamental problems in creating new knowledge in the treatment of congenital heart disease. Specifically, the low prevalence of any particular lesion, the wide variety of anatomic and physiologic variations in presentation, and the wide array of available surgical strategies all contribute to the difficulties faced by any one surgeon (or program) in determining the optimal management strategy for a given lesion.

Because individual programs tend to focus on a limited set of management patterns, individual programs can only rarely make comparisons of a wide variety of management strategies. Acknowledging these fundamental difficulties, the CHSS embarked upon a collaborative venture in 1985 to share experiences and analyze aggregate data to improve the management of congenital heart disease.

The initial cohort of patients assembled by the CHSS (1985 to 1989) was dedicated to patients with transposition of the great arteries and included 985 neonates admitted to a CHSS institution within the first 2 weeks of life. This rapid accrual was on a voluntary basis without any form of remuneration to participating institutions. Undoubtedly, this enthusiastic participation was fueled by the sincere (and urgent) desire to rapidly develop a knowledge base on which to compare more traditional atrial switch strategies with the newer arterial switch strategies. The success of this cohort was followed by the development of eight other cohorts with over 5,400 patients enrolled. These cohorts have provided the data for numerous analyses and publication on behalf of the CHSS. These are available on our website at www.chssdc.org.

Current Structure of the Datacenter

To accomplish this task, the Datacenter currently employs a Research Program Manager, a Database Programmer with statistical expertise, two Clinical Research Project Assistants, a Data Entry Nurse (0.8 Full Time Effort [FTE]), and an additional part-time Clinical Research Assistant for troubleshooting Ethical Review Board problems (0.3 FTE). In 2001, a Research Fellow (the Kirklin/Ashburn Fellow) was added to the team (discussed below). The Datacenter has dedicated space within the Hospital for Sick Children in Toronto that includes 1,200 sq. ft. of office space with all required computers and information technology resources, as well as secure storage for all submitted data.

The Kirklin/Ashburn Fellowship

The addition of the Kirklin/Ashburn Fellow to the CHSS Datacenter represents a unique aspect of the CHSS research model.

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1092-9126/10/$-see front matter
doi:10.1053/j.pcsu.2010.01.007

Upon appointment of the first Fellow in 2001, there was an immediate and gratifying increase in academic productivity for the Datacenter and, importantly, the development of a mutually rewarding relationship between the Kirklin/Ashburn Fellow and member surgeons from across North America. The Fellowship is highly visible amongst congenital heart surgeons, and has allowed the intellectual firepower of future congenital heart surgeons to shine among their colleagues.

The Kirklin/Ashburn Fellows have studied in the Datacenter for 2 years and have enrolled in concurrent Masters or PhD programs at the University of Toronto. Their tenure in the Datacenter has been supported by intensive tutelage from Drs Eugene Blackstone and Brian McCrindle, and Sally Cai. Using this support network, the Fellows have forged new analyses of CHSS cohorts using state-of-the-art statistical techniques. The Fellows have led the analysis through collaboration with participating members from the inception of addressable questions, 'cleaning' of the data, development of an analysis plan, correspondence with working groups, creation of presentations, and writing of manuscripts. All these activities have been supported by the Datacenter staff in Toronto to provide the Fellows with mentorship, and help to focus their analyses and fine-tune interpretation of results.

Building a training program into the structure of the Datacenter has promoted academic output and helped to keep the CHSS Datacenter as a hub of activity within the CHSS.

Unique Attributes of the CHSS Datacenter

Diagnosis-Based Cohorts

A unique attribute of cohorts followed by the CHSS is that diagnosis-based cohorts are strongly preferred over procedure-based cohorts (with one exception in the recent cohort based on the use of a RV-PA conduit). The importance of a diagnosis-based cohort cannot be overestimated as it allows evaluation of important patient subsets that are typically excluded from procedure-based surgical reports. For example, inclusion of non-operated patients in the diagnosis-based cohorts allows an evaluation of the management of all patients with the diagnosis, rather than a filtered group of selected patients chosen to undergo a specific surgical procedure. One institution may exclude certain patient subsets from consideration for surgical therapy, whereas another institution may choose to provide therapy – with a diagnosis-based cohort, comparison can be made between operative and non-operative therapy. An example of the importance of inclusion of all patients is demonstrated in an analysis of the CHSS pulmonary atresia cohort.[1] In Fig. 1, the transition from entry in the study (diagnosis) to a definitive single-, 1.5-, or two-ventricle repair is shown. Note that a large proportion of the patients never made it to one of these end-states. Consequently, a procedure-based surgical report describing a 'definitive' operation would have neglected to account for the substantial proportion of patients who have died without undergoing a 'definitive' procedure (indeed, the largest group of patients was the group that did not survive to a definitive end state!).

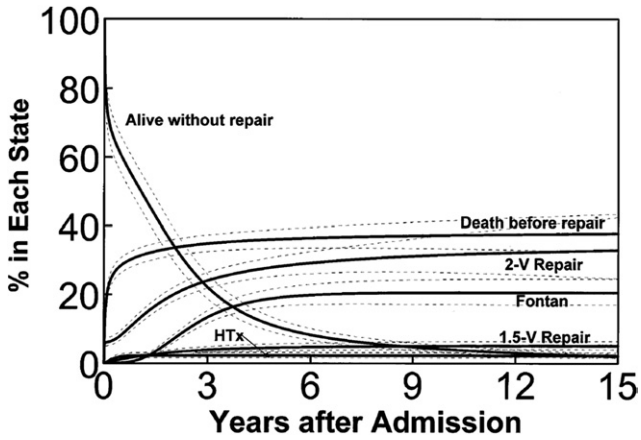

Figure 1 Non-risk-adjusted competing-risks depiction of end states in 408 neonates with pulmonary atresia with intact ventricular septum (PAIVS), illustrating the proportion of children reaching each end state over time after initial hospital admission. All patients begin alive at the time of initial admission (time = 0) and migrate to an end state at a time-dependent rate defined by the hazard functions. At 5 years, the estimated prevalences of end states are as follows: two-ventricle repair, 28%; Fontan operation, 19%; 1.5-ventricle repair, 5%; cardiac transplantation, 2%; death before reaching a repair state, 36%; and alive without end state, 11%. (Reprinted with permission.[1])

Analysis of Complex Management Strategies

A second important attribute of the diagnosis-based cohorts utilized in the CHSS Datacenter is the potential for comparison of multiple management strategies rather than a limited evaluation of a single comparison as is typically utilized in a prospective randomized trial. For example, the recent Pediatric Heart Network-funded Single Ventricle Reconstruction Trial is a fine example of a study that has rigorously addressed a direct comparison of neonates meeting entry criteria who were randomized to right ventricle to pulmonary artery conduits (Sano procedure) or more conventional modified Blalock-Taussig shunts. This focused comparison is well-suited for a prospective randomized trial. However, such a trial does not evaluate the large proportion of patients who died before enrollment, failed to meet enrollment criteria, or were managed with alternative strategies including transplant and hybrid palliation. In contrast, the CHSS enrolled patients with aortic atresia and critical aortic stenosis (1994 to 2001) in a diagnosis-based cohort that allowed comparison of multiple management strategies.[2]

Evaluation of diverse management paths in the aortic atresia/critical aortic stenosis cohort was conducted by initial creation of statistical models to control for neonatal anatomic characteristics. The pathways depicted in Fig. 2 were evaluated and grouped into one- and two-ventricle pathways. Separate models were constructed for the one- and two-ventricle management paths, and comparisons of these models can be used to assist in clinical decision-making for an individual patient. Importantly, these data are derived from clinical practice across a broad range of academic institutions and may more closely reflect more broadly generalizable outcomes than data derived from a small

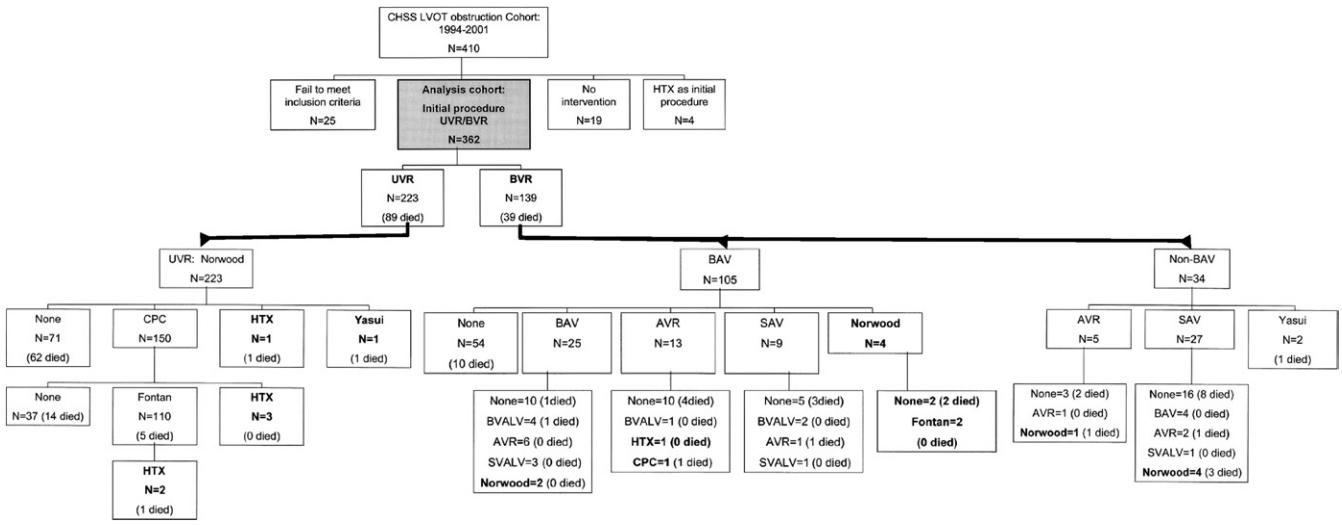

Figure 2 A wide variety of management strategies were utilized in the care of 410 patients enrolled in a diagnosis-based cohort of neonates with aortic stenosis and aortic atresia between 1994 and 2001. (Adapted and reprinted with permission.[2])

number of highly motivated institutions participating in a prospective randomized clinical trial.

Another example of an examination of diverse management pathways is a recent analysis of pulmonary atresia with intact ventricular septum.[1] A strong advantage of the current CHSS methodology is evident when we analyzed the relationship between the wide array of management decisions made at different institutions and tricuspid valve z-score. In this study, we collected data from member institutions where patients were treated according to each institution's particular management strategy. 'Accepted medical practice' at each institution was quite varied when comparing between institutions. The breadth of decision-making patterns permitted a comparison of wide array of management strategies that would have been impractical (if not impossible) if each institution had to agree upon randomization to each of the identified management strategies. Thus, the CHSS Datacenter is well suited to evaluate complex management strategies and can exploit inter-institutional differences in these complex management strategies to identify practice patterns that are associated with improved patient outcomes (Fig. 3).

Evaluation of Uncommon Lesions

The CHSS Datacenter is well-suited to examine uncommon lesions that have diverse management pathways in current clinical practice. For example, the CHSS assembled a large cohort of patients with interrupted aortic arch. A subset analysis of this cohort examined the combination of interrupted aortic arch and aortopulmonary window.

Out of 472 patients with interrupted aortic arch, concomitant aortopulmonary window was identified in 20 patients. Although a small subset, examination of this group provides important insights into this rare combination, which could not be easily accomplished by any clinical institution working in isolation (Fig. 4).

Another excellent example of a rare lesion that will be studied in a currently evolving project is a multicentre prospective inception cohort of patients with anomalous origin of the coronary arteries arising from the opposite aortic sinus (Fig. 5). This is a relatively rare lesion, but it provokes intense anxiety among patients (and clinicians) because there are no clearly defined management algorithms and the potential for sudden death is not well-defined. A recent survey of management patterns among clinicians demonstrated very little consensus in terms of diagnostic criteria, indications for surgery, and non-operative considerations. The large number of CHSS institutions will allow rapid accrual of a large cohort to characterize the natural and 'unnatural' (eg, postsurgical) history of this disease. Because of the 'urgency' faced by our membership to obtain answers to important clinical questions with regard to this disease, we anticipate a brisk enrollment.

Voluntary Contribution of Data

Another important attribute of the CHSS Datacenter is that it relies on voluntary contribution of data. This can easily be construed as a weakness of the CHSS organizational structure as the potential for failure to include all eligible patients in a cohort is omnipresent. The parameters that influence enrollment are not well-studied, but are likely to include the clinical urgency associated with the research question that was the rationale for inception of the cohort. For example, as noted above, the transposition cohort acquired patients with extreme velocity (985 neonates were enrolled from 100% of all CHSS institutions [24 at that time] within 4 years). In contrast, a recent inception cohort of patients with critical LVOTO has enrolled relatively slowly (341 patients, 16 institutions, 4 years). The LVOTO enrollment can be compared with the single ventricle reconstruction (SVR) trial, which had a more narrow diagnostic range of entry criteria and fewer participating institutions. Nevertheless, the SVR trial enrolled 555 patients (15 institutions over 3 years; Rick Ohye, personal communication). It is likely that the presence of paid coordinators 'on the ground' in each institution with scrutinized enrollment rates, and potential for financial penalties for failure to enroll, contributed to the far more com-

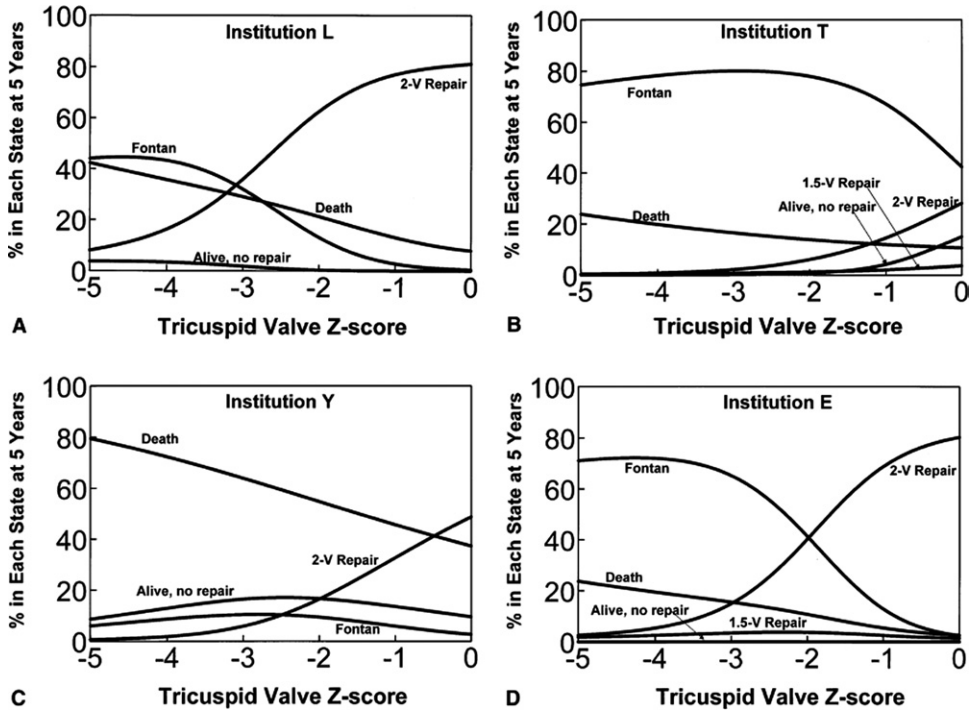

Figure 3 A competing risks analysis is used to examine the relationship between tricuspid valve z-score, inter-institutional management patterns, and a group of mutually exclusive endstates. Using this analysis, it is apparent that there are differences in the relationship between tricuspid valve z-score and death between institutions. Importantly, it is also apparent that some institutions (eg, Institution T) use a Fontan strategy across a wide spectrum of tricuspid valve z-scores with a low death rate, but at the expense of failing to offer two-ventricle palliation to patients with relatively large tricuspid valves (eg, z-scores between 0 and −2). In contrast, Institution L more frequently chose two-ventricle repairs (and less frequent Fontan strategies) in patients with small tricuspid valves, with a relative increase in the death rate in the patients with the smallest tricuspid valves. Finally, Institution E had a balanced strategy with two-ventricle repairs in patients with larger tricuspid valves and Fontan strategies in patients with smaller tricuspid valves – and a corresponding low death rate across the spectrum of tricuspid valve z-scores.

plete enrollment in the funded SVR trial when compared with the voluntary CHSS cohort.

Centralized Abstraction of Data

Another unique attribute of the organization structure the Datacenter is the abstraction of medical records within the Datacenter as compared with data abstraction, and the use of data forms at each member institution. In the Datacenter, medical records for each patient are collected and stored. Data are abstracted by specially trained personnel and then added to forms for analysis. The importance of this distinction is two-fold. First, the data abstraction process is performed by a limited number of

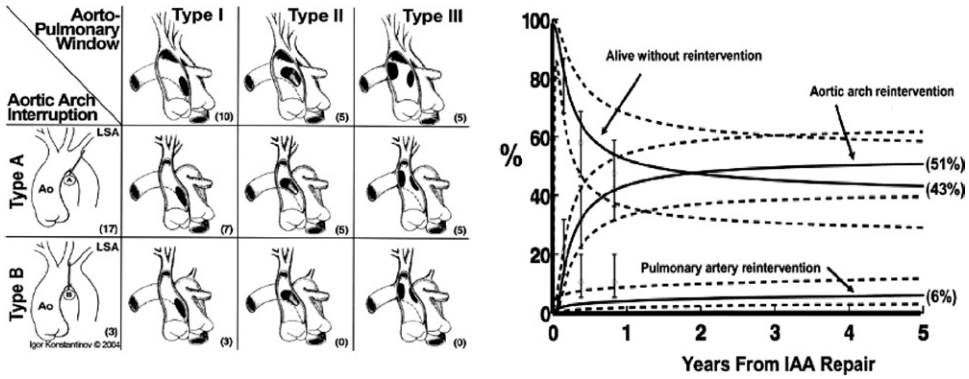

Figure 4 Rare combinations of lesions can be examined within larger CHSS cohort. Konstantinov et al[3] examined outcomes in patients with interrupted aortic arch and concomitant aortopulmonary window and were able to make important inferences to assist in clinical decision-making. This would be difficult or impossible for any single institution to perform because of the rare prevalence of this combination of lesions.

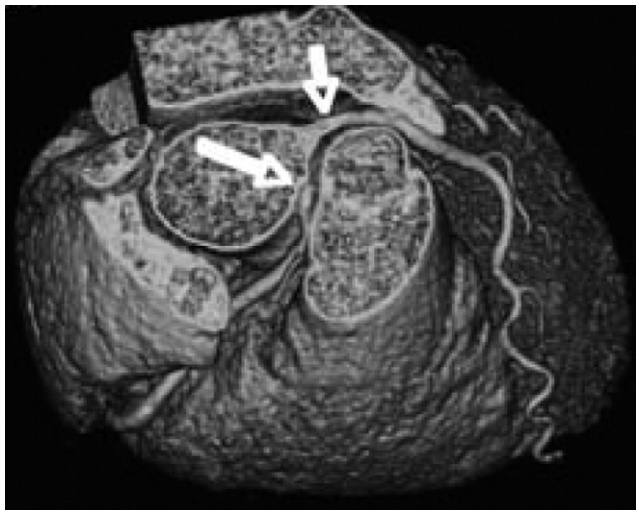

Figure 5 Anomalous aortic origin of the right coronary artery from the left coronary sinus. (Reprinted with permission.[4])

personnel, which allows quality control without needing on-site audits of member institutions. Secondly, and most importantly, the presence of stored medical records in the Datacenter allows future analysis of the cohort in ways that may not have been envisioned at the time of the inception of the cohort. Because the records are available for review, a 'follow-on' unplanned analysis can be undertaken whenever needed. For example, a detailed analysis of the aortic valve stenosis/aortic valve atresia cohort enabled a complex analysis of the role of the Ross-Konno and Yasui procedures many years after inception of the cohort. For this subset of patients, unique data fields were required and the analysis would have been impossible if the raw data were not available in the Datacenter.

Low Cost of Incremental Studies

A final important attribute of the CHSS Datacenter is the relatively low cost of adding additional cohorts for study. Because the infrastructure is in place to follow patients, the incremental cost to addition of new cohorts is relatively low. In fact, there was no net increase in expenses for the addition of the last two cohorts launched by the Datacenter. The additional work load has been offset by improvement in the efficiency of follow-up (eg, automated communications, batch e-mail, etc). Although trading efficiency for increased workload cannot continue indefinitely, it has been effective in the past. Prospectively, the addition of new cohorts has required the provision of funding to increase personnel in the Datacenter on a modest basis. For example, the anomalous aortic origin of the coronary arteries (AAOCA) cohort described above will require a single FTE to conduct the entire study, which is anticipated to enroll patients from up to 60 institutions. Personnel management, statistical support, data management, office space, relationships with member institutions, and all other aspects of infrastructure are already in place. To start a de novo registry would require a team of coordinators, managers, and statistical consultants. The low incremental cost for additional studies makes the Datacenter an attractive support venue for launching inception cohorts with plans for long-term follow-up.

Further efficiencies in the Datacenter will include the renovation of our web site (www.CHSSdc.org). Through direct contact with our patients followed on a yearly basis for up to 25 years, it has become apparent that there is a strong desire among participants to communicate with other participants within the Datacenter website venue. Indeed, the desire to communicate ranges from anxious parents of newly enrolled neonates to neonatal enrollees who are now transitioning into adulthood! The potential to facilitate communications between patients and parents within the Datacenter website will have important implications in terms of increasing the efficiency in terms of patient follow-up by monitoring (and participating) in web-based communication. Importantly, the potential to offer 'value added' for enrolling in CHSS cohorts will give our members something tangible to offer prospective enrollees: the opportunity to participate in a web-based community of people with similar congenital heart problems under the umbrella of a well-established organization that can provide the participants with up-to-date scientific information – which the enrollees themselves have helped to generate!

Conclusion

The CHSS Datacenter is a unique research organization with attributes that favor analysis of uncommon lesions with complex management algorithms. Using a low-cost platform, the Datacenter can rapidly accrue inception cohorts and compare management strategies across a broad range of institutions, enabling analysis that no single institution could perform in isolation. The voluntary nature of the participation is the chief limitation, which could be overcome with appropriate funding to strengthen the well-developed infrastructure and better capture eligible patients for enrollment.

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