Cardiol Young 2005; 15 (Suppl. 1): 161–164

ISSN 1047-9511

Data, dogma, or latest fashion? How scientific meetings and peer-reviewed literature affect cardiac surgical practice

Thomas L. Spray

Children's Hospital of Philadelphia, Philadelphia, Pennsylvania, United States of America

FOR MANY YEARS, SURGEONS HAVE BEEN ABLE TO implement new techniques and treatments with minimal oversight. Although regulatory control over application of new strategies for treatment is far different today, surgeons have enjoyed a greater degree of freedom than other specialists. The laboratory of the surgeon, and particularly the congenital cardiac surgeon, is often the operating room, since appropriate animal models are not available. Thus, the congenital cardiac surgeon has often been stimulated to modify existing techniques, or create new surgical approaches, to improve the perceived limitations of previously known surgical strategies.[1] The introduction of a new surgical technique has often taken the strong ego and persistence of a surgical innovator, and has subjected the surgeon to criticism from medical colleagues. Although innovation is a proud heritage of the development of congenital cardiac, it now seems appropriate, as we are more cognizant of the past accomplishments in the development of repairs for congenital cardiac malformations, to evaluate how surgical techniques become widely adopted, often with only minimal data to suggest improvement over previously accepted procedures.

While innovation is a desirable quality, it is important to recognize that innovation in itself does not always equal progress. Countless examples of new surgical procedures and modifications of older techniques over the years have been abandoned due to data accrued from follow-up suggesting little improvement, or in fact even worse outcomes. An excellent example of such a situation is the development of the Starr-Edwards prosthesis for replacement of the aortic and mitral valves.[2] The initial prosthesis, as used in the 1960s, comprised a silastic ball inside a metal cage. While this pioneering technology resulted in the ability to implant a valvar prosthesis orthotopically in otherwise untreatable patients, there was a significant incidence of swelling of the silastic ball causing fracture and embolization, in addition to a risk of thromboembolism requiring chronic anticoagulation. In order to improve upon these undesirable effects, several innovative technologies were added. Initially, the metal struts were covered with cloth, to encourage intimal in-growth and decrease the need for anticoagulation. After several hundred valves had been implanted, it became apparent that the ball inside the cage gradually wore the cloth, causing fraying, and eventually increasing the risk of thromboembolism and haemolysis, rather than decreasing the risk as had been originally expected. In addition, in order to prevent swelling of the silastic ball, a hollow metal ball was introduced, which only made the situation worse. For each of these "innovations", several hundred patients underwent implantation of the new devices with "improved" immediate post-operative outcomes; the disadvantages showing up only several years later. In order to prevent wear on the cloth, a metal track was instituted for the metal ball to follow. The noise created by this modification, however, was severe, and dissatisfaction amongst the patients was great. In addition, small struts were created at the base of the valve to allow the metal ball to avoid contact with the fabric used to cover the struts. These struts also wore gradually and again caused fraying of the fabric. After over 15 years of "innovation and improvements", therefore, the Starr Edwards valve went back to its original design of a bare metal cage with a silastic ball, albeit with introduction of a new process to cure the ball which seemed to inhibit the swelling and fracture seen in the original design.

Correspondence to: Thomas L. Spray MD, Cardiac Surgery, Children's Hospital of Philadelphia, 34th Street and Civic Center Boulevard, Philadelphia, PA 19104-439, USA. Tel: +1 215 590 2708; Fax: +1 215 590 2715; E-mail: spray@email.chop.edu

This valve has since proved durable, and shown to carry a low risk for thromboembolism.

A major advance in the reporting of valvar complications was instituted when surgeons, who recognized the difficulty in comparing types of valves based on outcomes limited to survival, created a standardized set of reporting characteristics for long-term outcomes looking at event-free survival and valvar related complications of all types, thus permitting comparison of valves that may have different potential complications over their lifetimes. It is now possible, therefore, to compare the overall event-free survival of tissue and mechanical valves, which have vastly different complications.[3]

Most surgical innovation and change, nonetheless, enters clinical practice without rigid collection and analysis of data. In part, this is due to the fact that congenital cardiac disease affects a relatively small population of patients, and variations in institutional approach, and the individual experience and ability of the surgeon and the institution, may affect outcomes even with the same operative procedure. Thus, can we really use surgical outcomes from one center reported in the peer-reviewed literature to ascertain whether a new surgical approach is superior to old "tried and true" approaches? Are randomized, prospective, multi-institutional, controlled studies, such as now are becoming popular in the adult cardiological scene, the goal for introduction of new surgical techniques? Does a "rational" belief in potential advantages of a new surgical approach warrant its introduction before any clinical data is accrued? These questions will continue to drive the evolution of the specialty of paediatric cardiothoracic surgery.

An example of the rapid spread of new surgical techniques into the surgical armamentarium without definitive evidence of superior outcomes is the use of the extracardiac Fontan operation for functionally single ventricle. When this technique was introduced in the early 1990s, it was rapidly accepted by most centers, although there has not yet been adequate follow-up data to suggest that the technique will live up to the potential advantage of decreasing late atrial arrhythmias. The technique was introduced because there were theoretical advantages of lack of exposure of the atrium to higher than normal venous pressures, the concept being that this should not stimulate as much atrial hypertrophy, and therefore could potentially decrease the risk of late atrial arrhythmias. In addition, the "less or no" atrial suture lines were thought to be likely to decrease the incidence of atrial arrhythmias, which had been related to creation of surgical block in the atrium from previous atrial suture lines with lateral tunnel or atriopulmonary techniques. Streamlining of venous flow was also suggested as an advantage of the extracardiac technique. While these advantages may in fact be real, since atrial arrhythmia occurs infrequently until 8–10 years after the Fontan operation, and since concurrent studies comparing lateral tunnel and extracardiac conduits by the same group of surgeons in single institutions over the same time frame have not yet been reported, it is not yet clear whether this technique will have overwhelming advantages over the lateral tunnel techniques. In addition, the effects of conduits on the right side of the heart, which have been known to cause problems in other cardiac conditions, are not yet known over the long-term after these procedures. Introduction of new technologies, including the intra-cardiac tunnel created using interventional catheter techniques, are also in their infancy. The effects on early complications and late issues after the Fontan operation are completely unknown. Nevertheless, these techniques are becoming commonplace, and are gaining rapid adoption around the country, because of the "perceived benefits" of their "non-invasiveness".

Recently, Sano et al., from Okayama in Japan, have demonstrated in a small series of patients an improved outcome in their center with use of a connection from the right ventricle to the pulmonary arteries at the first stage of the sequence of operations used for definitive palliation of hypoplastic left heart syndrome. In their center, the adoption of this technique resulted in much improved early postoperative haemodynamic stability, and improved early outcome.[4] Based upon this success, and continued poor results in some centers with the standard Norwood operation, there has been a rapid adoption of the use of this technique in many centers throughout the world. The potential advantages of the technique, including elevated diastolic blood pressure, and improved flow of blood to the lungs, with a lower volume load on the functionally single ventricle, have theoretical appeal. It was hoped that adoption of this technique would improve growth of the pulmonary arteries, and decrease the incidence of inter-stage mortality following the first-stage Norwood operation. But despite enthusiastic adoption of this technique in many centers, no direct comparison in a contemporaneous group in the same institution has yet been reported. As in many new surgical techniques, the center decides to adopt a new approach, and therefore concurrent control operations with the older technique are not performed as the learning curve for adoption of the new technique is paid. The potential deleterious affects of an incision in the right ventricle might not be known for many, many, years and early improvements in outcome, if seen in this technique, could be nullified by late complications which may not be known for some time. In addition,

new strategies for management of the patient with hypoplasia of the left heart have now had to be introduced because of the tendency for patients with the Sano modification to develop cyanosis, thus requiring earlier intervention for the second stage. The affects on morbidity of requiring reconstruction of the second stage at two to three months of age, in patients who have very low birth weight at the initial operation, have not yet been evaluated. Very young age at the second stage, nonetheless, has been associated with evidence of increased morbidity, although not necessarily increased mortality. The relative trade-off of these techniques, therefore, has still to be evaluated. Optimal evaluation of the new techniques requires a prospective randomized trial in centers where traditionally good outcomes were obtained with the standard Norwood operation so that the new technique can be compared to a recent benchmark. In addition, contemporary collection of data would allow long-term follow-up of these patients to look at late outcomes in both groups. In spite of the inherent appeal of such a trial, it has been notoriously difficult to engage surgeons and institutions in multi-institutional studies requiring randomization of surgical techniques. Before such a trial could be accomplished, the techniques may change again, such as the "off-pump" banding of the pulmonary trunk, and stenting of the arterial duct now being introduced in some centers.

What about the use of randomized prospective trials, and their impact on surgical approaches? Perhaps the best known, and probably best performed, randomized prospective trial in the field of congenital cardiac surgery is the Boston Circulatory Arrest Trial, which compared the neurodevelopmental outcomes of deep hypothermic circulatory arrest versus conventional cardiopulmonary bypass in a reasonably large cohort of patients with transposition, specifically concordant atrioventricular and discordant ventriculo-arterial connections, treated at a single institution.[5] This landmark study was funded by the National Institutes of Health, and required many millions of dollars over several years adequately to follow-up the patients. As a randomized prospective trial of one surgical therapy, it was rigidly crafted in that the patients were relatively uniform, having a single diagnosis of transposition with or without ventricular septal defect, and two surgical strategies were utilized for perfusion over the time course of the study in one institution. Even then, the cohort included mostly white male patients. This study concluded that, at early follow-up, patients who underwent deep hypothermic circulatory arrest as the predominant strategy for perfusion strategy had worse neurodevelopmental outcomes than those patients who had continuous cardiopulmonary bypass with only a very brief period of circulatory arrest.[5] This conclusion was picked up rapidly, and perhaps erroneously, by the surgical community to suggest that deep hypothermic circulatory arrest was a poor strategy, and should be completely abandoned. In fact, many institutions and surgeons became fanatically driven to perform all cardiac operations without even the shortest periods of circulatory arrest, thus hoping to avoid the "deleterious" effects on the brain of lack of flow of blood.

When the papers that emerged from the study are carefully analyzed, while it is true that the patients with a predominant perfusion strategy of deep hypothermic circulatory arrest had a different neurodevelopmental outcome than the other group, there were several other very important findings that were not readily adopted and recognized by the surgical community. The first, and most obvious, finding was that anatomy and socioeconomic status of the patients were more important than the strategy for perfusion in determining outcome.[6] Patients with transposition and ventricular septal defect had a significantly poorer neurodevelopmental outcome than did patients in whom the ventricular septum was intact, no matter what strategy was used for perfusion. Secondly, it was somewhat ignored that some patients had adverse neurodevelopmental outcomes even when no deep hypothermic circulatory arrest was used. Thus, is it the technique of perfusion, or the anatomy and physiology of the specific patient that lead to identifiable neurodevelopmental defects over long-term follow-up? While the authors acknowledged in the body of one paper that deep hypothermic circulatory arrest, and its duration, was a relatively small determinant of overall neurodevelopmental outcome, this conclusion was not emphasized in the conclusions. Each study, in fact, suggested that deep hypothermic circulatory arrest was a major contributor to a poor outcome. Only in the most recent studies from this same group, after follow-up extending out to 8 years, have the authors recognized that there was "not the ability to discriminate an adverse neurologic outcome between the two groups if circulatory arrest times were under 45–50 minutes".[7,8] Thus most of the reported adverse outcomes in those having circulatory arrest over years of these studies were concentrated in a relatively few patients who had prolonged intervals of circulatory arrest. Whether these prolonged intervals were markers for other problems, such as technical difficulties, or other physiologic variables, was not readily apparent. Despite this finding, there were clear differences in the types of neurodevelopmental changes seen in the two groups, and it has become apparent that bypass alone has been associated with certain kinds of behavioral difficulties in other studies, thus

confirming the results reported from Boston.[9] The conclusion of the most recent study was that the authors could "not identify" a "safe" period of deep hypothermic circulatory arrest.[8] While true, this statement continues to be taken by many cardiac surgeons as a complete condemnation of a technique that has been used safely for cardiac repairs in many institutions for many years.[10]

So, how should we introduce new and innovative techniques into the practice of paediatric cardiothoracic surgery? Must we demand data over a significant time frame before adopting a new surgical technique? Should we accept dogma from surgical pioneers who taught the advantages of new surgical approaches without collecting ongoing data regarding complications and late events? And can we trust peer-reviewed literature to provide us with guidance about which new therapies hold the most promise? Ultimately, perhaps, the answer is that we must always keep an open mind. Innovation often flies in the face of accepted wisdom, and there is a tendency for all surgeons to wish to try out new techniques and procedures to garner potential advantages for their patients. It is probably unrealistic to expect modifications of surgical techniques to undergo approval from Institutional Review Boards before their introduction, since there is no way effectively to model most of these patients for laboratory studies prior to their introduction in the clinical arena. Multi-institutional prospective randomized trials of major surgical innovations may well be desirable, but will always be limited by the variation in anatomy in congenital cardiac disease, and by the variations in surgical techniques and ability and medical management between institutions. The overall rarity of complex congenital malformations makes collection of very large cohorts of patients, like the thousands of patients enrolled in major cardiologic trials of interventional procedures for coronary arterial disease, to be an impossible dream for our specialty. Opportunities for funding large-scale multi-institutional studies are likely to become increasingly unavailable, further limiting our ability directly to compare outcomes in contemporaneous cohorts of patients. Thus, perhaps the only real service we can do to advance the field and evaluate our surgical innovation is to commit ourselves to collect data on the patients. In spite of our obligation to collection of follow-up information, even this is currently being thwarted by regulatory agencies. Nevertheless, unless we adopt such approaches, especially when introducing new modifications of surgical techniques, we may find that our best intentions are thwarted by late outcomes that may not live up to our expectations.

References

1. Bove EL. Facts and fantasies of congenital heart surgery: Thoughts on advances in heart surgery and those who make them. Semin Thorac Cardiovasc Surg Pediatr Card Surg Annu 2003; 6: 184–189.
2. Lefrak EA, Starr A. Cardiac Valve Prostheses. Appleton-CenturyCrofts, New York , NY, 1979.
3. Grunkmeier G, Wu YX, Ruyun J. Statistical analysis of heart valve outcomes. J Heart Valve Dis 2002; 11 (Suppl I): S2–S7.
4. Sano S, Ishino K, Kawada M, et al. Right ventricle-pulmonary artery shunt in first stage palliation of hypoplastic left heart syndrome. J Thorac Cardiovasc Surg 2003; 126: 504–510.
5. Bellinger DC, Rappaport LA, Wypij D, et al. Patterns of developmental dysfunction after surgery during infancy to correct transposition of the great arteries. J Dev Behav Ped 1997; 18: 75–83.
6. Forbess JM, Visconti KJ, Hancock-Friesen, et al. Neurodevelopmental outcome after congenital heart surgery: Results from an institutional registry. Circulation 2002; 106 (Suppl I): 95–102.
7. Bellinger DC, Wypij D, duPlessis AJ, et al. Neurodevelopmental status at eight years in children with dextro-transposition of the great arteries: The Boston Circulatory Arrest Trial. J Thorac Cardiovasc Surg 2003; 126: 1397–1403.
8. Wypij D, Newburger JW, Rappaport LA, et al. The effect of duration of deep hypothermic circulatory arrest in infant heart surgery on late neurodevelopment: The Boston Circulatory Arrest Trial. J Thorac Cardiovasc Surg 2003; 126: 1397–1403.
9. Karl TR, Hall S, Ford G, et al. Arterial switch with full-flow cardiopulmonary bypass and limited circulatory arrest: Neurodevelopmental outcome. J Thorac Cardiovasc Surg 2004; 127: 213–222.
10. Ungerleider RM, Gaynor JW. The Boston Ciculatory Arrest Study: An analysis. J Thorac Cardiovasc Surg 2004; 127: 1256–1261.