Tetralogy Surgery - Back To Baltimore 70 Years Later: Melbourne Heritage and Group Tribute to Juan Comas

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Surgery for Tetralogy of Fallot progressed rapidly from the palliative arterio-pulmonary Blalock-Taussig shunt, introduced in Baltimore 70 years ago, to the "classic" complete transventricular repair technique, with which excellent early results were achieved soon thereafter. However, as duration of follow-up increased, so did the awareness of development of troubling late complications, including severe pulmonary insufficiency, right ventricular dilatation and dysfunction, and tricuspid valve insufficiency, all contributing to increasing incidence of late reoperations, as well as to arrhythmias and sudden death. This realization fueled the initial introduction of the transatrial–transpulmonary repair technique by Kawashima, as well as the subsequent firm establishment of this technique within the framework of an integrated surgical approach by Roger Mee in Melbourne. In turn, Mee's numerous trainees and associates led the dissemination of this approach and provided the impetus for the current wide adoption of a variety of right ventricular and pulmonary valve preservation techniques. In addition to the outstanding surgical results reported by individual centers adopting this surgical strategy, encouraging multi-institutional data are emerging regarding the benefits of these approaches for more favorable early and, most importantly, late outcome. One student and strong proponent of the Melbourne approach was our late colleague and friend Juan Comas, to whose memory this article can serve as tribute.
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Introduction

"We see more and farther than our predecessors, not because we have keener vision or greater height, but because we are lifted up and borne aloft on their gigantic stature." (Bernard of Chartres, 12th Century AD)

Although currently repair of Tetralogy of Fallot (TOF) is routinely achieved with minimal mortality and morbidity, controversies persist regarding the optimal strategy (including timing of surgery, role of palliation, and optimal surgical technique), with the goals of surgical innovation and discussion shifted from improving early mortality to achieving best long-term outcome and quality of life. It is widely accepted that the Melbourne strategy of transatrial–transpulmonary (TA/TP) repair of TOF represented an important advance in the management of TOF, with its core principle (namely, respect of the function of the pulmonary valve and right ventricle (RV)

Roger Mee, pioneer pediatric heart surgeon, established transatrial–transpulmonary repair.

Central Message

Transatrial–transpulmonary Tetralogy repair, established in Melbourne by Roger Mee, has gained wide acceptance and continues to be further refined, presaging improved late outcomes.

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as much as possible) now being adopted almost universally, including by the proponents of the classical transventricular repair. To appreciate the current state of the art of TOF surgery, it is helpful to review the important contributions of the many "giants", i.e., surgical pioneers whose contributions have made the excellent current results possible and have laid the foundations for further progress.

The goal of this article is to highlight important milestones in TOF surgery, from the pioneering palliative subclavian–pulmonary artery shunt, to the breakthrough of the classical transventricular repair (an accomplishment that coincided with the dawn of open heart surgery), to the emergence of the TA/TP repair. This last approach, focusing on maximal preservation of RV and pulmonary valve function, aims to optimize early and late outcome, minimizing the observed late complications of TOF repair. This surgical approach was firmly established by Roger Mee at the Royal Children's Hospital in Melbourne, Australia (from where outstanding early and medium-term results were reported), and from there, it was disseminated throughout the world by many of Mee's trainees and surgical associates. The wide adoption of this surgical strategy has also led to the recent development of more refined techniques of pulmonary valve preservation, as well as to the establishment of the suitability of this approach, initially performed in older infants, also in very young infants and even in selected neonates.

Naturally, this article only provides an overview of what the author felt constituted important and educational highlights, but it does not represent a comprehensive review of the subject and the pertinent literature. Consequently, the author assumes all responsibility for failing to acknowledge all the numerous other important contributions in this field.

The Development of TOF Surgery

Palliation

The era of TOF surgery was launched on November 29, 1944 with the Blalock Taussig-subclavian pulmonary artery shunt.[1] Even today, shunting, currently mostly performed in modified form by using a suitably sized PTFE graft between a systemic artery (subclavian, innominate, or the aorta) and the main pulmonary artery or one of its major branches, via either a thoracotomy or a sternotomy, remains an important tool for many subsets of patients with TOF. Despite the many theoretical advantages of primary complete repair, and numerous proponents with excellent reported results with this approach, palliative shunting is very much a reality in congenital heart surgery practice. In the European Congenital Heart Surgeons Association (ECHSA) Congenital Database, approximately 15% of operations for TOF are palliative shunts. Alternative palliative approaches for selected patients, such as ballooning of the pulmonary valve or right ventricular outflow tract (RVOT) stenting have been used more recently, but these approaches still lack universal acceptance because their long–term effects remain under scrutiny.

Complete transventricular repair

Complete transventricular repair was first achieved by Walton Lillehei in his series of pioneering controlled cross-circulation operations in 1954.[2] Of course, further consistent progress in TOF surgery, as in all of congenital cardiac surgery, depended on the development of a reliable cardiopulmonary bypass system, as achieved by John Kirklin[3] at the Mayo Clinic. Within just a few years, in those early days of open heart surgery, excellent results (even by today's standards) for complete repair of TOF were reported: In 1966, Norman Shumway from Stanford reported a consecutive series of 50 patients with TOF with body weight ≥ 10 kg who underwent complete repair with 50% use of a transannular patch and zero operative mortality![4]

Many others have since established that TOF repair can be achieved with minimal mortality and excellent long-term survival, even after neonatal repair. Primary repair of TOF in infancy was introduced by Barrat-Boyes using profound hypothermia and circulatory arrest in the early 1970s.[5] Aldo Castaneda[6] firmly established infant repair of TOF in Boston, and many have followed this lead.[7-9]

Concerns regarding late outcome

However, despite the excellent early and even medium-term results, accumulating evidence from truly long-term follow-up studies demonstrated a substantial and ever-increasing rate of late reoperations, largely because of severe pulmonary valve insufficiency and RV dilation and dysfunction, necessitating pulmonary valve replacement. Perhaps surprisingly, the many theoretical arguments in favor of primary repair versus initial palliation, including benefits regarding avoidance of development of further ventricular hypertrophy or the detrimental effects of cyanosis on various organs, as well as the demonstrated feasibility of achieving excellent early results of even neonatal primary repair, have not been supported by observed long-term results. Many such important long-term data come from the Scandinavian countries, where the health care system achieves very complete and very long-term follow-up. In an important very long-term follow-up Norwegian study of 185 patients with TOF who had surgery between 1960 and 1987, there have been no significant differences in survival (from birth and also from TOF repair) between patients who had received a palliative procedure before complete repair and patients who had undergone primary TOF repair. In fact, increasing late mortality was seen three to four decades postoperatively.[10]

In another important long-term follow-up study from Norway, Lindberg and colleagues reported their single-center 50-year experience with TOF surgery, demonstrating improving early survival with each successive decennial of experience, but no statistically significant reduction in the very substantial frequency of late reoperations (up to 60% at 40 years). Importantly, there was a major increase in the rate of reoperation in the subgroup of patients who had undergone transannular patching.[11]

Accordingly, the excellent reported early results of TOF repair notwithstanding, prevention of the now well established late post-repair complications (severe pulmonary valve

insufficiency, residual RVOT obstruction, RV dilatation, RV dysfunction, tricuspid valve insufficiency) and consequent reoperations, arrhythmias, and sudden death remain as major challenges in TOF surgery.

TA/TP repair and the Melbourne legacy

The quest to minimize initially early surgical mortality and morbidity and, subsequently, late TOF complications and reoperations, led to the efforts of Hudspeth, who introduced the transatrial approach to total correction of TOF in 1963,[12] also reported by Edmunds in 1976,[13] and finally of Kawashima,[14] who introduced the TA/TP repair of TOF with or without minimal right ventriculotomy and with preservation or repair of the pulmonary valve.[15]

Kawashima described various methods to preserve pulmonary valve function during TOF repair: commissurotomies in tricuspid or bicuspid pulmonary valves, minimal annular division and use of pericardium to replace or to supplement pulmonary valve leaflets, and performing a "mini-transannular patch." Roger Mee, working at the Royal Children's Hospital of Melbourne in the 1980s and early 1990s, standardized the technique of TA/TP repair of TOF. This involves transatrial ventricular septal defect closure, transatrial and, when necessary, transpulmonary RVOT resection, transpulmonary pulmonary valvotomy, minimal division of the pulmonary annulus to achieve a diameter of just over mean normal, and reconstruction of the RVOT and pulmonary valve annulus with a "mini transannular patch." using fresh autologous pericardium. Monocusp pulmonary valves were used in a few select cases of small pulmonary arteries or distal pulmonary artery stenoses. In the landmark Melbourne series of 366 consecutive patients who underwent TA/TP repair of TOF between 1980 and 1991, including all patients with TOF type double outlet RV, operative mortality was 0.5%, actuarial survival was 97.5% at 42 months (four late deaths), and freedom from reoperation was 95% at 10-year follow-up.[16] These results, remarkable for the achieved minimal early mortality and morbidity, were also highly promising for favorable long-term outcome, and were based on Roger Mee's aforementioned standardized and well-reproducible surgical technique as well as on his selective patient management strategy, individualized to the patient. Mee's approach was taught to numerous trainees and associates and thus spread from Melbourne around the world.

Soon, many publications confirmed and further reinforced the early Melbourne findings. Tom Karl, succeeding Roger Mee in Melbourne, expanded the TOF series to 611 consecutive TA/TP repairs and demonstrated the effectiveness of the method, even in the presence of significant coronary anomalies, which would have necessitated conduit repairs if a traditional transventricular approach had been used.[17]

In Europe, Giovanni Stellin and the Padova group demonstrated excellent results with TA/TP repair of TOF in the first 6 months of life, with improved RV function when compared with the transventricular approach.[18]

In the United States, Charles Fraser and his group at the Texas Heart Institute (Houston, TX) reported a consecutive series of 144 operations for TOF, including patients with TOF/complete atrioventricular canal defect, using a patient management algorithm individualized to the patient, in the Melbourne tradition. There were 94 one-stage complete TA/TP repairs, and 39 repairs after initial Blalock-Taussig shunting with no mortality and 3% reoperation at 5 years.[19]

In Athens, our group introduced TA/TP repair of TOF at a new congenital cardiac program in Greece in 1997, and soon we reported our early results in a consecutive series of 96 repairs with zero operative mortality and excellent functional outcome.[20]

Our updated report from the Athens Heart Surgery Institute 10 years later confirmed that, in the series of 245 consecutive patients with TOF (including 6.5% patients previously shunted elsewhere and 6.5% with new shunts), 213 TA/TP repairs were performed with no operative mortality and minimal morbidity. Probably most importantly, the reoperation rate was 10% at 14 years with excellent RV functional preservation.[21]

Persistent controversies and recent innovations

Despite the increasing influence of the Melbourne tradition in TOF surgery and numerous reports of excellent results from many centers, "real-life" registry data show that this strategy is far from having become the dominant procedure over the last decade. In fact, in our report from the ECHSA European Congenital Cardiac Surgical Database, of 6,350 reparative operations for "classical" TOF, only 18.2% were TA/TP repairs. Of note, hospital mortality for these was only 1.48%, compared with 3.11% for the traditional repair subgroup (transventricular repair with transannular patch).[22]

Thus, although many surgeons have been adopting the TA/TP strategy, and despite the realization that the current focus in TOF surgery has shifted from improving early results (which are generally excellent regardless of the approach) to optimizing long-term functional outcome, several controversies persist. These involve the question of timing of surgery, the role of early palliation, the ideal surgical technique, particularly regarding management of the pulmonary valve, and indications for and management of reoperation. During the 2015 American Association of Thoracic Surgery annual meeting, an expert panel comprehensive discussion of remaining such controversies surrounding TOF management was organized by Charles Fraser and subsequently published.[23] Regarding timing, there was general consensus that the asymptomatic patient with TOF is best served by early but not neonatal repair. For the symptomatic neonate, the prevailing opinion is that shunting is preferred. Primary neonatal repair can indeed be achieved with low mortality, but at the cost of higher morbidity and almost universal transannular patching, which is undesirable in terms of long-term complications. Stenting of either a patent ductus or the RVOT as a means of palliating selected symptomatic neonates with TOF may be an option in some centers in lieu of traditional shunting, but this practice has not gained wide acceptance. In particular, there is concern about long-term outcome with RVOT stenting because it necessarily results in destruction of the pulmonary valve and placement of a transannular patch at the time of eventual

complete repair. Nonetheless, there seems to be consensus on the essential principles of the TA/TP approach. Selective patient management is indicated, and repair should both avoid or at least minimize a right ventriculotomy and maximally preserve the pulmonary valve.

In fact, in many centers, current efforts focus on different approaches to further enhance pulmonary valve preservation in the context of TA/TP repair. In Spain, Juan Comas was able to expand the scope of pulmonary valve preservation accepting higher initial RV to LV pressure ratios, and demonstrated that, after a valve-sparing TOF procedure, there was a statistically significant reduction of this ratio at mid-term follow-up. Furthermore, this reduction was seen in all patients, including the subgroup with the highest early postoperative ratio.[24] These findings strengthen the efforts to preserve the pulmonary valve even accepting some residual obstruction instead of abolishing obstruction at the expense of a large transannular patch.

Over the last few years, an additional surgical strategy has emerged to achieve pulmonary valve preservation in the context of a TA/TR approach even in selected cases where at least a mini-transannular incision would have been necessary. This involves intraoperative balloon dilatation of the pulmonary valve annulus, as introduced by Giovanni Stellin and the Padova group. They were able to demonstrate that the integrity and function of the PV can be preserved in selected patients during early repair of TOF by concomitant balloon dilation, leading to a better mid-term RV function.[25,26]

The Padova group further introduced more elaborate pulmonary valve reconstruction techniques, such as what they termed "delamination plasty," which involves in-situ augmentation of the native pulmonary valve leaflets "delaminating" them from the RVOT muscle, in a maneuver reminiscent of the mobilization of the tricuspid valve during Ebstein repair. These techniques promise to permit further extension of the applicability of pulmonary valve preservation.[27,28]

Tribute to Juan Comas

In this exposition of the Melbourne legacy in the surgical management of TOF, it is fitting to pay tribute to our late friend and colleague Juan Comas, an active supporter and promoter of this approach in Spain and around the world. His unexpected and untimely death in Madrid a year ago, on June 15, 2015, shocked his family, his friends, and all of our congenital community. An article in his memory was published soon thereafter in the *World Journal for Pediatric and Congenital Heart Surgery*.[29]

Juan, Catalonian by birth, trained in Spain, France, England, and Australia, and worked in Madrid, where he established and led an outstanding congenital program at the 12th of October University Hospital. In his numerous academic leadership positions, such as in the ECHSA and the European Association for Cardio-Thoracic Surgery, where he served as a most effective Chair of the Congenital Domain, he championed the closer cooperation between the various subspecialties in our field, as well as that between the various academic cardiac surgical societies across continents. With incredible energy, Juan worked to improve pediatric cardiac surgery not only in Spain, but also in several other countries, where he systematically assisted developing centers in humanitarian missions. In this context, he was active in spreading the Melbourne tradition in the management of TOF. Juan excelled as a pediatric heart surgeon and also found time to enjoy life to the fullest, appreciating art, music, and sport. A man with great intellect, humor, and a most friendly and open personality, he was loved by all. A very much devoted family man, he left his beloved wife Montserrat and his son Jan. The congenital cardiac surgery community, along with his family and friends, all miss Juan and will remember him with great affection.

Conclusions

Currently, repair of TOF can be achieved with very low morbidity and mortality, even in infancy. Although even neonatal repair for symptomatic patients is feasible with low mortality (at a cost of a greater morbidity), concern for adverse long-term consequences of the relevant required transannular patch still provides support for persisting significant prevalence of palliative procedures (as demonstrated in large international registries) in selected cases. Most palliation involves shunting, with the role of newer options such as ductal or RVOT stenting still being explored. Overall, a selective surgical management strategy individualized to the patient in the Melbourne tradition is gaining wide acceptance, even though the no-ventriculotomy TA/TP approach is far from having been universally accepted. Still, there seems to emerge general agreement on the basic principles of the Melbourne heritage, namely, that one should preserve the function of the RV and the pulmonary valve as much as possible during TOF repair to minimize long-term TOF repair complications and reoperations. In these efforts, new techniques of intraoperative balloon dilatation of the pulmonary valve and pulmonary valve leaflet plasty techniques may offer advantages complementing the benefits of TA/TP repair.

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