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Original Article

Innovations in Electrophysiology

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OVER THE LAST FEW YEARS, THERE HAVE BEEN many advances in the field of non-invasive and invasive electrophysiology. Those publishing in this field have addressed a number of topics pertinent to children and young adults with congenital and acquired cardiac disease. In addition, there have been tremendous advances in our understanding of genetic testing in children with channelopathies at risk for sudden cardiac death. In this review, I discuss various aspects of these extensive reports.

Arrhythmias

Non-postoperative junctional ectopic tachycardia is a rare arrhythmia that, historically, has been difficult to treat, but is known to carry a high morbidity and mortality, especially in the neonatal cohort.[1] In an effort to ascertain the clinical impact of newer anti-arrhythmic agents, earlier diagnosis, and catheter ablative strategies, a large retrospective international multi-centric study coordinated by the Pediatric and Congenital Electrophysiology Society has addressed recent outcomes for 94 children with the problem.[2] While a variety of antiarrhythmic medications were used, most commonly amiodarone, with multiple medications used in over three-fifths of the cohort, only one-tenth of the patients had complete suppression of the abnormal rhythm. Much like incessant ectopic atrial tachycardia, medications achieved a clinically acceptable degree of rate-control. and reduced the frequency of tachycardia. Ablation was undertaken in 44 patients, using radiofrequency energy in 17 and cryoablation in 26. Both strategies achieved initial success in from 82 to 85% of the patients, with reoccurrence of the abnormal rhythm in 13 to 14%. Of those treated with radiofrequency energy, however, 3 acquired inadvertent complete atrioventricular dissociation, whereas no patient undergoing cryoablation developed atrioventricular block. The advent of cryoablation has undoubtedly changed the landscape for the paediatric electrophysiologist. There has been a marked reduction in morbidity of patients with parahisian accessory pathways, atrioventricular nodal reentrant tachycardia in the setting of structural heart disease, and junctional ectopic tachycardia as use of cryotechnology has become more prevalent. During a follow-up of 5 years, three-quarters of the patients with junctional ectopic tachycardia were doing well on no therapy, including those with spontaneous resolution as well as those having had an ablation. Of concern was the death of 4 neonates, all presenting with the abnormal rhythm below the age of 6 months, this finding supports the need for an aggressive pharmacological approach in these young patients.

Asymptomatic children with ventricular preexcitation are at a small but real risk of sudden cardiac death. While ablation of accessory pathways has become universal in symptomatic children; controversy exists over the optimal strategy for the management of asymptomatic patients. In the largest cohort studied to date, 184 children with a mean age of 10 years, and a range from 8 to 12 years, were followed up for a median period of 52 months following an electrophysiology study revealing presence of Wolff-Parkinson-White syndrome.[3] Of the cohort, 133 had no arrhythmic events, whereas 51 developed an arrhythmic event. Atrioventricular re-entrant tachycardia developed in 29 patients, and atrial fibrillation in 22 patients. Potentially life-threatening arrhythmias were observed in 19 of the 22 patients presenting with atrial fibrillation. Perhaps surprisingly, many of these had minimal or very vague cardiac-related

symptoms. In 3 asymptomatic patients, ventricular fibrillation was encountered, predicted by a short effective refractory period, less than 240 msec, for the accessory pathway, as well as the presence of multiple pathways. These findings support a more aggressive approach to the asymptomatic patient with Wolff-Parkinson-White syndrome, and provide strong evidence for consideration for a baseline electrophysiological study so as to identify the child with a potentially dangerous pathway.

Ablation Therapy

Ablation for supraventricular arrhythmias is no longer a novel procedure for children with isolated accessory pathways. Cryoablation, three-dimensional mapping, and improved catheter technology, have all facilitated ablation in children, with the rate of acute success now approaching 95%. Despite a relative commonality within the paediatric electrophysiology community to approaches for routine diagnosis and treatment of supraventricular tachycardia, advances in specific technology for ablation must be cautiously evaluated, and scrutinized in the context of excellent prior results achieved with minimal complications.

Cryoablation has undoubtedly become more prevalent in anatomic regions where delivery of radiofrequency energy is deemed to be less efficacious and/or safe. Cryoablation for paraHisian accessory pathways, and those residing within the coronary sinus, is potentially more advantageous than application of radiofrequency energy, given the proximity to the coronary arteries or formation of thrombus within the coronary artery itself. The large retrospective multicentric study discussed above[2] included 21 patients with accessory pathways located within the coronary sinus. Despite an acceptable initial success rate of 71% for these patients, clinical recurrences were quite high, occurring within 17 days in two-fifths of the cohort, with a range from 1 to 20 days.[4] A confounding factor in this study was the fact that many patients had combined radiofrequency and cryoablative lesions. To date, no prospective study has evaluated directly ablation of paraHisian accessory pathways by use of radiofrequency as opposed to cryoablative technology. Hopefully, the improved design of cryoablative catheters, permitting easier maneuverability, a better understanding of the need to make additional insurance lesions, knowledge of the required location for these insurance lesions, and better understanding of the freeze-thaw-freeze timing cycles, will minimize clinical recurrences while still achieving a high level of safety.

With an increasing number of children with congenitally malformed hearts living into adulthood, it is inevitable, and somewhat daunting, to note the complexity of arrhythmias that will challenge the electrophysiologist caring for these patients. The ability successfully to map and ablate these arrhythmias will not only challenge the electrophysiologist, but force the industry to improve technology so as to supplant previous modalities for mapping. While not necessarily designed for children, stereotaxis allows use of a floppy catheter that can be navigated into regions that may be quite difficult with manual, or even current steerable, catheters. In a limited cohort of 12 patients with atrial tachycardias in the setting of the congenitally malformed heart, 11 were successfully ablated with the Magnetic Navigation System developed by Stereotaxis Inc., St. Louis, Missouri, United States of America, although 3 had recurrences within 6 months.[5]

Similarly, the crossing of difficult anatomic repairs, baffles, and suture lines require a thorough understanding of the anatomy, surgical repair, and any residual lesions in order effectively to guide the ablation catheter to the area of interest. The imaging used may vary from standard fluoroscopy, angiography, integrated computerized tomography, magnetic resonance imaging and three-dimensional echocardiography, three-dimensional anatomical mapping, and intracardiac echocardiography. The latter modality has recently been used in conjunction with the CARTO system for treatment of 7 patients with either an atriopulmonary Fontan circuit or an atrial redirection procedure, achieving a high rate of success.[6]

Channelopathies

Over the last 15 years, there have been significant gains in the scientific understanding of the molecular substrate, and corresponding strategies for treatment, for patients with long QT syndrome, Brugada syndrome, arrythmogenic right-ventricular dysplasia, and catecholamine polymorphic ventricular tachycardia.

Catecholaminergic polymorphic ventricular tachycardia is a genetic disorder caused by a disruption in the calcium homeostasis of cardiac myocytes. Mutations in either the ryanodine receptor 2 gene or calsequestrin 2 gene may result in ventricular fibrillation under adrenergic stress.[7–9] Despite appropriate usage of β-adrenergic blocking agents, or Ca^{++} channel-blockers, many patients continue to have symptoms necessitating implantation of cardioverter defibrillators. Further compounding the problem is that such patients may develop storms should the device discharge, as the shock itself can release catecholamines. In a recent novel report 3 patients having arrhythmias recalcitrant to β-adrenergic

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blocking agents were shown to benefit from left cardiac sympathetic denervation.[10] Ablation of the lower part of the stellate ganglion along with the 2nd & 3rd thoracic ganglions interferes with the release of norepinephrine, and appears to be an effective strategy in conjunction with β-blockers and appropriate selection of an implantable cardioverter defibrillator.

Congenital Long QT syndrome most commonly arises from a mutation in a sodium or potassium ion channel, resulting in prolonged ventricular repolarization, and potentially leading to seizures, torsades de pointes, and sudden cardiac death. Patients, nonetheless, may be completely asymptomatic despite carrying a known channelopathy mutation.[11] Identifying risk in affected persons is critical, because it may alter a clinical decision that ranges from simple pharmacotherapy to implantation of a cardioverter defibrillator. In a large multicenter study involving the International LQT Registry, data was collected from 3,015 children aged from 1 to 12 years, assessing risk factors leading to either sudden cardiac death, or aborted cardiac arrest requiring external defibrillation.[12] The risk of both these problems during childhood was influenced by a QTc interval of greater than 500 msec, prior syncope, and male gender. Beta-blockers resulted in a reduction of over half in the risk of an aborted event or sudden death. Despite the apparent benefit of beta-blockade, a considerable proportion of children treated in this fashion continued to have life-threatening arrhythmias. Boys receiving beta-blockers who had syncope prior to the age of 6 years had a 12% chance of sudden cardiac death, or resuscitated from such events, within 7 years. It has previously been demonstrated[13] that male gender, a QTc interval greater than 500 msec, and syncope are significant risk factors that should prompt consideration for implantation of a cardioverter defibrillator.

Pacing

With the advent of thinner leads, and improvements in material used for insulation, transvenous pacemakers have been used with increasing frequency in children. Despite these innovations, endocardial leads may malfunction secondary to fractures, dislodgement, and breaks in insulation related to a more active life style and somatic growth. A large retrospective follow-up study conducted between 1994 and 2005 has now been reported based on implantation of 264 transvenous leads in 184 children.[14] Unlike earlier studies[15] that reported lead failures directly related to the presence of congenital cardiac surgery and younger age at implantation, these workers[14] identified lead fixation as the only multivariate risk causative of lead fracture. Of 19 fractures occurring in endocardial leads, 85% involved active-fixation leads. Over the next 5 years, additional information should reveal mid-term follow-up studies of the newer thinner brady-leads currently deployed.

Implantable Loop Recorders

Syncope is a common presentation to the paediatric cardiologist, and often results in a benign diagnosis that can be ascertained with a careful history and physical examination. Elucidating the exact mechanism of syncope with or without palpitations, nonetheless, can be difficult and time-consuming, requiring use of many non-invasive monitors. Implantable loop recorders offer an alternative investigation that may affirm or negate a malignant aetiology in a small subset of children with potentially dangerous recurrent syncope. A recent multicentric study collated findings from 33 young patients undergoing implantation of loop recorders for investigation of recurrent syncope and/or palpitations.[16] Their patients were grouped into those with a structurally normal heart, those undergoing reparative cardiac surgery, or those with suspected primary electrical disease. Correlation between symptoms and abnormal rhythms was observed in approximately half of the patients, necessitating catheter ablation, pacemaker implantation, or need for implantation of a cardioverter defibrillator. In 10 patients, recurrence of symptoms was correlated with a normal electrocardiogram, and no cardiac diagnosis was established beyond reassurance of the patient and the family. While additional non-invasive monitors used over an extended period of time may have yielded similar results, the timeliness of diagnostic yield was likely expedited, and in a few cases may have proven invaluable.

Implantable Cardioverter Defibrillators

These devices are extremely effective in preventing sudden cardiac death in children predisposed to life-threatening arrhythmias. Their complexity, nonetheless, with enhanced discriminator characteristics, increases the potential for malfunction compared to antibradycardic pacemakers. Advisories and recalls pose a particular challenge to the patient, family, and physician, who must together weigh the risk of malfunction and an inability appropriately to discharge if needed versus the complications related to explantation. Another retrospective study carried out on behalf of the Pediatric and Congenital Electrophysiology Society, in conjunction with local data, collated data from 236 affected devices.[17] Of these, 147 (62%) were left in place, while 89 (38%) were extracted, with 1 death and 1 patient requiring reoperation. Interestingly, none of the original advisories or recalls were identified, yet 2 patients were found to have a loose header-generator

connection. While the incidence of acute perioperative complications related to extraction secondary to recalls and advisories is quite low, at no more than 2%, note should be taken of the potential psychological trauma to the patient and the family should a "defective" device be left in place.

These implantable cardioverter defibrillators have clearly established a proven benefit in reducing the risk of sudden cardiac death in patients known to be at high risk. The performance of the leads, nonetheless, has come under tremendous scrutiny by patients, physicians, industry and most vociferously the media. The Medtronic Sprint Fidelis lead was first reported to have an excessively high rate of fractures of 2.3% at 30 months,[18] with a suspected higher rate in younger patients.[19] This higher observational rate in children should come as no surprise to paediatric electrophysiologists. Children with these devices as a whole are undoubtedly more active than their adult counterparts, thus exposing the lead-vessel interaction to greater stress and strain. In response to the higher fracture rate, the manufacturer recommended first the adjusting of the ventricular fibrillation detection/redetection settings to longer intervals, second the establishment of active patient alerts for pacing and impedance, and third that physicians should follow all available diagnostic trends.[20] Swerdlow and colleagues[21] subsequently described use of a downloadable algorithm using a lead-integrity measure to reduce inappropriate shocks.

Shortly after the fractures were reported for the Sprint Fidelis lead, concerns began to plague St. Jude over the performance of the Riata lead, with one group reporting an incidence of 1.9% for significant perforations over a period of 20 months.[22] While other investigators did not corroborate these initial concerns,[23,24] the exposure and concerns already left the barn door open to the public.

Tremendous demands are placed on leads for implantable cardioverter defibrillators, and it is unreasonable to expect 100% reliability. Increased surveillance with utilization of home-monitoring will hopefully identify complications and malfunctions of leads before they result in inappropriate shocks. In addition, as a paediatric cardiologic community, we should be diligent in our reporting of such complications so as to be able to distinguish the anecdotal case report from those leads that are clearly performing at a suboptimal level.

Cardiac Resynchronization Therapy

Cardiac resynchronization therapy has been extensively studied in adults with cardiac failure and dysynchrony. Use of the technique in adults with a cardiomyopathy and ejection fraction of less than 35% have shown marked improvement in ventricular function and measures of quality of life. The heterogeneous nature of cardiac failure in children has made it not only difficult to accurately establish specific guidelines for this treatment, but also to identify a cohort which is likely to benefit from the therapy. Studies of resynchronization following congenital cardiac surgery have shown an acute haemodynamic benefit in certain cohorts, albeit that mid-term data is limited.[25–29]

A retrospective analysis of 60 consecutive children undergoing resynchronisation between 2002 and 2007 at Children's Hospital, Boston, evaluated the functional and clinical outcome of biventricular pacing at 3 months after implantation on the basis of an improvement of at least 10% in ejection fraction, or advancement by one ordinal point in the classification of the New York Heart Association.[30] Patients were further categorized as having a systemic left, right, or solitary ventricle. A variety of transvenous, epicardial, and hybrid systems were deployed for resynchronisation. Of the patients, more than three-quarters had structural heart disease, with more than half comprised of either those with functionally single ventricles or congenitally corrected transposition. In the patients with systemic left ventricles, resynchronization resulted in an increase in the ejection fraction from 35% at baseline to 43% after 3 months. This positive response was in contrast to those patients with a systemic right ventricle, of whom only 2 of 9 enjoyed a long-term benefit. Of the 13 patients with functionally single ventricles, 11 demonstrated an improvement in their functional classification, with the ejection fraction increasing from a median of 37% to 47% within the first year subsequent to resynchronisation. Interestingly, the group of patients undergoing treatment at a remote time from the surgical procedure fared better than those having therapy as part of a combined surgical procedure. The lack of response in patients with systemic right ventricles is out of sequence with earlier reports showing a hemodynamic benefit. It is plausible that the older age at which some of the devices were deployed in the Boston experience may account for some of the disparity. Additionally, the absence of uniformity in placement of leads, along with atrioventricular and V–V optimization, may account for some of the findings. While the results of this study represent no more than mid-term outcomes, and the it suffers from absence of a control group not undergoing resynchronization, the results are promising for patients in cardiac failure with systemic left and functionally single ventricles. Future understanding of optimal placement

of leads, with improved understanding of echocardiographic dysynchrony in patients with congenitally malformed hearts, may help guide appropriate choice of candidates for resynchronisation.

Congenital Cardiac Surgery and Electrophysiology

Many patients following surgery for tetralogy of Fallot are exposed to right ventricular volume overload as a result of progressive pulmonary valvar regurgitation. Such chronic right ventricular volume overload results in exercise intolerance, serves as an arrythmogenic substrate, and even leads to mortality. Placement of a valved pulmonary conduit reverses the ventricular dilation, and reduces the risk of ventricular arrhythmias.[31] The timing of replacement is often left to the primary cardiologist, without clear guidelines as to exact recommendation for such a procedure. In an effort to address these issues, the group working at Children's Hospital, Boston, identified 98 patients with right ventricular dilation undergoing late replacement of the pulmonary valve after correction of tetralogy of Fallot, comparing them with matched controls with tetralogy and dilated right ventricle who did not undergo pulmonary valvar replacement.[32] Overall, freedom from death, ventricular tachycardia, or both after 5 and 10 years was 80% and 41%, respectively. There was no significance difference in the incidence of death and/or ventricular tachycardia in the control group, and no change was observed in the duration of the QRS complex following pulmonary valvar replacement. This study is somewhat concerning, in that there is no clear evidence that replacement of the pulmonary valve for clinically indicated reasons in patients with pulmonary regurgitation after repair of tetralogy of Fallot reduces the risk of death and/or ventricular tachycardia. It is possible that the protective effect of such an intervention may not be seen for some time, or that earlier timing of replacement and earlier ventricular remodeling may be more beneficial.

References

1. Villain E, Vetter VL, Garcia JM, Herre J, Cifarelli A, Garson A Jr. Evolving concepts in the management of congenital junctional ectopic tachycardia. Circulation 1990; 81: 1544–1549.
2. Collins KK, Van Hare GF, Kertesz NJ, Law IH, Bar-Cohen Y, Dubin A, et al. Pediatric nonpost-operative junctional ectopic tachycardia. J Am Coll Cardiol 2009; 53: 690–697.
3. Santinelli V, Radinovic A, Manguso F, Vicedomini G, Gulletta S, Paglino G, Mazzone P, Ciconte G, Sacchi S, Sala S, Pappone C. The natural history of asymptomatic ventricular pre-excitation. J Am Coll Cardiol 2009; 53: 275–280.
4. Collins KK, Rhee EK, Kirsh JA, Cannon BC, Fish FA, Dubin AM, Van Hare GF. Cryoablation of accessory pathways in the coronary sinus in young patients: A multicenter study from the pediatric and Congenital Electrophysiology Society's Working Group on Cryoablation. J Cardiovasc Electrophysiol 2007; 18: 592–597.
5. Schwagaten B, Jordaens L, Witsenburg M, Duplessis F, Thornton A, Van Belle Y, Szili-Torok T. Initial experience with catheter ablation using remote magnetic navigation in adults with complex congenital heart disease and in small children. PACE 2009; 32: S198–S201.
6. Peichl P, Kautzner J, Gebauer R. Ablation of atrial tachycardias after correction of complex congenital heart disease: utility of intracardiac echocardiography. Europace 2009; 11: 48–53.
7. Priori SG, Napolitano C, Tiso N, et al. Mutations in the cardiac ryanodine receptor gene (hRyR2) underlie catecholaminergic polymorphic ventricular tachycardia. Circulation 2001; 103: 196–200.
8. Laitinen PJ, Brown KM, Piippo K, et al. Mutations of the cardiac ryanodine receptor (RyR2) gene in familial polymorphic ventricular tachycardia. Circulation 2001; 103: 485–490.
9. Postma AV, Denjoy I, Hoorntje TM, et al. Absence of calsequestrin 2 causes severe forms of catecholaminergic polymorphic ventricular tachycardia. Circ Res 2002; 91 (8): e21–e26.
10. Wilde AA, Bhuyan ZA, Crotti L, Facchini M, De Ferrari GM, Paul T, et al. Left cardiac sympathetic denervation for catecholaminergic polymorphic ventricular tachycardia. N Engl J Med 2008; 358: 2024–2029.
11. Schwartz PJ, Moss AJ, Vincent GM, Crampton RS. Diagnostic criteria for the long QT syndrome: an update. Circulation 1993; 88: 782–784.
12. Goldenberg I, Moss AJ, Peterson DR, McNitt S, Zareba W, Andrews ML, et al. Risk factors for aborted cardiac death in children with congenital long-QT syndrome. Circulation 2008; 117: 2184–2191.
13. Locati EH, Zareba W, Moss AJ, Schwartz PJ, Vincnt GM, Lehmann MH, et al. Age-and sex-related differences in clinical manifestations in patients with congenital long-Qt syndrome: findings from the International LQT Registry. Circulation 1998; 97: 2237–2244.
14. Olgun H, Karagoz T, Celiker A, Ceviz N. Patient- and lead-related factors affecting lead fracture in children with transvenous permanent pacemaker. Europace 2008; 10: 844–847.
15. Fortescue EB, Berul CI, Cecchin F, Walsh EP, Triedman JK, Alexander ME. Comparison of modern steroid-eluting epicardial and thin transvenous pacemaker leads in pediatric and congenital heart disease patients. J Interv Card Electrophysiol 2005; 14: 27–36.
16. Sreeram N, Gass M, Apitz C, Ziemer G, Hofbeck M, Emmel M, et al. The diagnostic yield from implantable loop recorders in children and young adults. Clin Res Cardiol 2008; 97: 327–333.
17. Mahajan T, Dubin AM, Atkins DL, Bradley DJ, Shannon KM, Erickson CC, et al. Impact of manufacturer advisories and FDA recalls of implantable cardioverter defibrillator generators in pediatric and congenital heart disease patients. J Cardiovasc Electrophysiol 2008; 19: 1270–1274.
18. Patient Management Recommendations for Sprint Fidelis Leads. Available at: http://www.medtronic.com/fidelis/appendixChtml. Accessed October 28, 2007.
19. Cantanchin A, Anderson L, Jones S, et al. The higher than expected early failure rate of the Sprint Fidelis implantable cardioverter defibrillator lead (model 6949, Medtronic Inc). Heart Rhythm 2008; 5: 167–168.
20. Urgent medical device information. Sprint Fidelis lead patients' management recommendations. Available at: http://www.medtronic.com/fidelis/physiican-letter.html. Accessed January 28, 2008.
21. Swerdlow CD, Gunderson BD, Ousdigian KT, Abeyratne A, Stadler RW, Gillberg JM, Patel AS, Ellenbogen KA. Downloadable

algorithm to reduce inappropriate shocks caused by fractures of implantable cardioverter-defibrillator leads'. Circulation 2008; 118: 2122–2129.
22. Danik SB, Mansour M, Heist EK, Ellinor P, Milan D, Singh J, et al. Timing of delayed perforation with the St. Jude Riata lead: A single-center experience and a review of the literature. Heart Rhythm 2008; 5: 1667–1672.
23. Epstein AE, Baker II J, Beau SL, Deering TF, Greenberg SM, Goldman DS. Performance of the St. Jude Medical Riata leads. Heart Rhythm 2008: 1–6.
24. Corbisiero R, Armbrister R. Does size really matter? A comparison of the Riata lead family based on size and its relation to performance. PACE 2008; 31: 722–726.
25. Pham PP, Balaji S, Shen I, Ungerleider R, Li X, Sahn DJ. Impact of conventional versus biventricular pacing on hemodynamics and tissue Doppler imaging indexes of resynchronization postoperatively in children with congenital heart disease. J Am Coll Cardiol 2005; 46: 2284–2289.
26. Strieper M, Karpawich P, Frias P, Gooden K, Ketchum D, Fyfe D, Campbell R. Initial experience with cardiac resynchronization therapy for ventricular dysfunction in young patients with surgically operated congenital heart disease. Am J Cardiol 2004; 94: 1352–1354.
27. Zimmerman FJ, Starr JP, Koenig PR, Smith P, Hijazi ZM, Bacha E. Acute hemodynamic benefit of multisite ventricular pacing after congenital heart surgery. Ann Thorac Surg 2003; 75: 1775–1780.
28. Khairy P, Fournier A, Thibault B, Dubuc M, Theirein J, Vobecky SK. Cardiac resynchronization therapy in congenital heart disease. Int J Cardiol 2005; 46: 277–283.
29. Dubin AM, Janousek J, Rhee E, Strieper MJ, Cecchin F, Law IH, et al. Resynchronization therapy in pediatrics and congenital heart disease. J Am Coll Cardiol 2005; 46: 277–283.
30. Cecchin F, Frangini PA, Brown DW, Fynn-Thompson F, Alexander ME, Triedman JK, et al. Cardiac resynchronization therapy (and multisite pacing) in pediatrics and congenital heart disease: Five years experience in a single institution. J Cardiovasc Electrophysiol 2009; 20: 58–65.
31. Therrien J, Siu SC, Harris L, Dore A, Niwa K, Janousek J, Williams WG, Webb G, Gatzoulis MA. Impact of pulmonary valve replacement on arrhythmia propensity late after repair of tetralogy of Fallot. Circulation 2001; 103: 2489–2494.
32. Harrild DM, Berul CI, Cecchin F, Geva T, Gauvreau K, Pigula F, Walsh EP. Pulmonary valve replacement in tetralogy of Fallot: Impact on survival and ventricular tachycardia. Circulation 2009; 119: 445–451.