Circulation: Arrhythmia and Electrophysiology

REVIEW

Year in Review in Cardiac Electrophysiology

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In the past year, there have been key advances in our understanding of arrhythmia mechanisms and diagnosis and important new therapies. We have seen advances in basic cardiac electrophysiology with demonstration of optogenetic targeting of atrial fibrillation (AF) rotors, induced pluripotent stem cell–based biological pacemakers, small-conductance Ca^{2+}-activated K^+ (SK) channels as targets for AF treatment, and reductions in inward rectifier potassium current in promoting ventricular fibrillation. Hand-held ECG devices and implantable loop recorders have been shown to detect subclinical AF. Catheter ablation of AF in patients with left ventricular dysfunction improves outcomes compared with medical therapy. Both hybrid thoracoscopic surgical and catheter ablation procedures and off-pump surgery for AF have demonstrated efficacy. Anticoagulation with uninterrupted dabigatran had a lower major bleeding rate compared with uninterrupted warfarin after AF ablation. Studies have examined optimizing access to automatic external defibrillators by identifying optimal locations for placement and possibility of using a drone delivery network. In long-QT syndrome, there are advances in understanding of ECG predictors of arrhythmic events, the role of the role of gene variants in conferring arrhythmic risk, and effect of age and sex on QTc interval. There are numerous advances in the treatment of ventricular tachycardia, including noninvasive cardiac radiation. Catheter ablation and implantable devices continue to demonstrate effectiveness in patients with congenital heart disease.

In the past year, there have been numerous ground-breaking discoveries and observations that illustrate the vibrancy and promise of our field. In this review, we have tried to capture articles published in the year 2017 of particular interest to cardiac electrophysiologists. Although we have focused on articles from our journal, we have captured many of the most impactful articles in numerous other journals. We apologize for omitting a large number of other important articles that cannot be included in this review because of space limitations. We have placed some of these in our Data Supplement.

BASIC ELECTROPHYSIOLOGY

Bradyarrhythmias

The search for new biological therapies for bradycardia met with recent progress as human keratinocytes genetically reprogrammed into electrically unstable cardiomyocytes were shown to persist and provide continued catecholaminergic-responsive pacing for 13 weeks after subepicardial injection into immunosuppressed dogs at the time of atrioventricular (AV) node ablation.[1] Although only 40% to 80% of the beats matched the site of cell injection, this is first study to test a human induced pluripotent stem cell–based biological pacemaker in a large animal model of heart block and represents an important step forward in biological pacing.

Key Words: atrial fibrillation ■ cardiac electrophysiology ■ catheter ablation ■ long QT syndrome ■ tachycardia, ventricular

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Atrial Arrhythmias

The past year also provided several interesting studies exploring new translational means of treating AF. Pharmacological inhibition of SK channels was shown to promote conversion of vernakalant-resistant AF in a porcine model.[2] Given atrial-selectivity of SK channels, this work positions SK blockade as a promising novel pharmacotherapeutic for AF. Cellular modeling provided important insight into the mechanisms underlying successful rotor-guided ablation of AF. Using a reductionist cell monolayer approach, termination was found to require a line of conduction block reaching from the rotor core to at least 1 unexcitable boundary.[3] In contrast, incomplete conduction block merely provides a stable anchor for rotors to circulate about and perpetuate AF (Figure 1). Thus, providing critical insights into the mechanism(s) underlying procedural success for a novel ablation strategy that, to date, has met with variable outcomes.

Ventricular Arrhythmias

Mechanisms of Altered Repolarization

Ventricular fibrillation (VF) is dominated by stable, nonmeandering spiral waves or focal activity.[4] Yin et al[5] recently showed that stable rotor dynamics colocalize with regional repolarization heterogeneities created by differential expression of apamin-sensitive SK currents in a rabbit model of ischemic cardiomyopathy. Pharmacological SK blockers disrupted this colocalization and decreased vulnerability to fibrillation, positioning pharmacotherapeutic SK blockade as a promising new antiarrhythmic agent for VF in patients with heart failure. In complementary work, Klein et al[6] showed that prolongation of terminal repolarization seen in swine models of ischemic cardiomyopathy was largely attributable to reductions in the inward rectifier potassium current (I_{K1}), which, in turn, promotes fibrillation through increasing triggered activity and decreases in postrepolarization refractoriness, with the latter promoting myocyte re-excitation before complete recovery of the resting membrane potential to markedly enhance functional reentrant states.

Despite ≈50% of patients experiencing heart failure with preserved ejection fraction (EF) dying an arrhythmic death, the mechanisms governing this proarrhythmic state remain poorly defined. To address this question and lay the foundation for future therapeutic approaches, Cho et al[7] recently showed reduction in the potassium currents (I_{to}, I_{Kr}, and I_{K1}) in a high-salt diet-induced heart failure with preserved EF rat model led to increased susceptibility to ventricular arrhythmias via QT prolongation and delayed repolarization.

Finally, chronic stressors (such as high angiotensin or catecholaminergic states) impact on electrophysiological function; however, the mechanism(s) underpinning this effect remain elusive. Jiang et al[8] recently found that KCNQ1 and KCNE1 (the 2 components that generate the slow delayed rectifier current I_{Ks}) are differentially trafficked such that KCNE1 resides at the cell surface while KCNQ1 is mainly sequestered in the junctional sarcoplasmic reticulum until exposed to stress

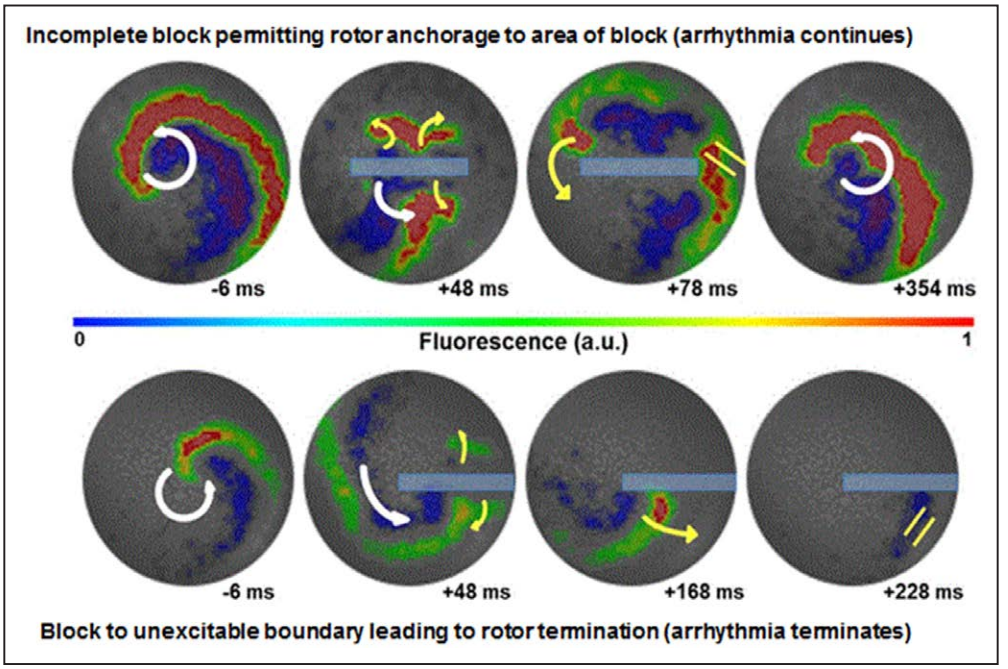

Figure 1. Effect of core region targeting with linear conduction block.
Representative optical signal images of before and after light exposure to induce block not reaching any unexcitable boundaries (**top**) or reaching only 1 unexcitable boundary (**bottom**). White arrows indicate the original rotor while the new wave (yellow arrows) denotes the new wave that anchors to the incomplete area of block (arrhythmia continues; **top**) or collides with the unexcitable boundary of the culture (arrhythmia terminates; **bottom**). Adapted from Feola et al[3] with permission. Copyright © 2017, American Heart Association, Inc.

whereupon it then traffics to the cell surface boosting I_{Ks} amplitude and dispersion of refractoriness.

CLINICAL MANAGEMENT OF ATRIAL ARRHYTHMIAS

Genetics of AF

Increasing insight into AF pathogenesis has been derived from genetic analyses and may improve prognostication for AF and its complications. By combining 5 study cohorts of 18 191 individuals, Lubitz et al[9] analyzed predictors of incident AF, as well as subsequent complications, such as stroke. They found that while a genetic risk score was associated with incident AF (maximum C statistic, 0.629–0.811), it added only marginally to clinical risk prediction (maximum ΔC statistic from clinical score alone, 0.009–0.017). However, the genetic risk score did predict thromboembolic stroke and may prove useful among patients of low clinical risk and subclinical AF.

In a Mendelian randomization analysis of genetic alleles associated with obesity, Chatterjee et al[10] explored the relationship between obesity and AF in 51 646 patients of European decent. They found strong support for a causal link between obesity and AF and a basis for public health interventions.

AF Screening

There is increasing emphasis on subclinical AF, with a variety of consumer and medical diagnostic devices on the market. Among 1001 older patients in the REHEARSE-AF study (Assessment of Remote Heart Rhythm Sampling Using the AliveCor Heart Monitor to Screen for Atrial Fibrillation), patients randomized to self-screening using a consumer, hand-held ECG device 1× to 2× weekly (and prn symptoms) demonstrated a hazard ratio of 3.9 for the detection of AF at 12 months, compared with patients receiving routine care.[11] And in the ASSERT-II study (Prevalence of Subclinical Atrial Fibrillation Using an Implantable Cardiac Monitor in Patient With Cardiovascular Risk Factors), the authors used implantable loop recorders to assess the prevalence of subclinical AF among 256 patients at increased risk of AF.[12] The investigators identified at least 5 minutes of subclinical AF among 34.4% of patients per year over mean follow-up of 16 months. These data, among others, contributed to a summary statement from the AF-SCREEN group, which reviewed the protocols and devices studied, as well as the rates of AF detection in various populations.[13] Although the group endorsed the use of routine screening in at-risk populations, they acknowledge the need for outcomes studies to understand the impact of treatment in the setting of earlier AF detection.

Antiarrhythmic Therapy

There continue to be emerging data on the management of patients initiating or chronically receiving dofetilide. Among 138 patients hospitalized for dofetilide reinitiation, Cho et al[7] demonstrated that roughly one third of these patients required dofetilide dose modification or discontinuation, among both groups that were restarting a previously tolerated dose or receiving an increased dose.[14] There were 2 patients with torades de pointes, both admitted for dose increases.

ATRIAL ARRHYTHMIA ABLATION AND SURGERY

Atrial Arrhythmia Ablation

AF Ablation in Heart Failure

During the past year, strong evidence has emerged supporting the role of AF ablation in patients with left ventricular (LV) systolic dysfunction.

The CAMERA-MRI multicenter trial (Catheter Ablation Versus Medical Rate Control in Atrial Fibrillation and Systolic Dysfunction)[15] showed that catheter ablation of AF was associated with an improvement in EF when compared with medical rate control (18% versus 4% improvement in EF) with a higher likelihood of normalization to ≥50% (58% versus 9%). The absence of LV late gadolinium enhancement by magnetic resonance imaging (MRI) predicted greater improvements in LV EF.

Similarly, CASTLE-AF trial (Catheter Ablation vs Standard Conventional Treatment in Patients With LV Dysfunction and AF)[16] presented at the European Society of Cardiology Sessions 2017 and subsequently published in 2018 showed a benefit of catheter ablation of AF in patients with heart failure. CASTLE-AF included 397 patients with LV EF <35%, New York Heart Association class >II, and AF which had failed antiarrhythmics. Patients were randomized to either routine AF medical management or catheter ablation. The primary end point was a composite of death from any cause or hospitalization for worsening heart failure, which was observed in 28.5% of the ablation group and in 44.6% of the control group after a mean follow-up of 37.8 months (relative risk reduction, 38%). Catheter ablation also resulted in improvement of EF by ≈8%.

Ablation for Persistent AF

Both the understanding and management of persistent AF continue to be challenging. During the past year, multiple studies have assessed mapping and catheter ablation strategies in persistent AF.

In the STABLE-SR multicenter trial (Electrophysiological Substrate Ablation in the Left Atrium During Sinus Rhythm),[17] 229 patients with nonparoxysmal AF were randomized to undergo pulmonary vein isolation (PVI) with (1) cavotricuspid isthmus ablation, high-density left

atrial mapping in sinus rhythm with homogenization of areas with low-voltage, and elimination of areas with complex electrograms or (2) additional linear lesions and defragmentation. In the substrate-based approach, ≈50% of patients did not require ablation beyond PVI. Freedom from arrhythmia rates was comparable in the groups but with shorter procedures and shorter energy delivery times in the substrate-based strategy.

The value of atrial substrate ablation in addition to PVI versus PVI alone was assessed in a clinical trial,[18] which randomized 118 patients with persistent and longstanding persistent AF to undergo PVI alone or PVI with substrate modification targeting complex fractionated atrial electrograms and linear ablation. The 1-year freedom from atrial arrhythmia rates was comparable between the groups (54% in PVI alone versus 57% in PVI+substrate).

Cryoablation and Laser Balloon Ablation

Balloon-based ablation has been introduced to improve efficiency and shorten AF ablation procedures. After becoming a widely accepted technology, cryoballoon ablation continues to be refined. In a prospective study,[19] 140 patients with paroxysmal AF undergoing cryoablation were randomized to a conventional strategy of 180-second cryoapplications per vein with a bonus freeze or to a shorter-time application protocol, with 1 application that lasted the time required for conduction block (time-to-effect) plus 60 seconds and a 120-second bonus freeze. The time-to-effect–based cryotherapy dosage led to shorter cryotherapy and procedure times, with comparable safety, and 1-year freedom from arrhythmia recurrences, compared with the conventional approach.

Although initial applications for balloon-based ablations targeted paroxysmal AF, there has been growing interest in balloon-based ablation in persistent AF. In a multicenter trial published last year,[20] 134 patients with persistent AF were randomized to undergo either laser balloon ablation or wide area circumferential PVI using radiofrequency. The freedom from AF rates was comparable between the groups (Figure 2).

Surgical and Hybrid AF Ablation

In recent years, hybrid AF ablation procedures have become increasingly popular. Minimally invasive surgical ablation techniques have been developed, but their efficacy has yet to be systematically tested.

In a study published last year,[21] 70 patients with persistent AF underwent minimally invasive epicardial surgery for AF followed by catheter-based electroanatomic mapping and ablation 2 to 3 months later. The majority of patients after epicardial ablation were found to require additional endocardial catheter ablation to complete the ablation sets. The arrhythmia-free survival off antiarrhythmic agents at 12 months was 77%.

The outcomes of on-pump, minimally invasive, stand-alone Cox maze procedure up to 5 years after surgery were examined[22] in 133 patients with persistent and longstanding persistent AF. At 5 years, 73% were in sinus rhythm off antiarrhythmics after single surgical intervention, and 13 patients required catheter-based reinterventions for atrial arrhythmias.

VENTRICULAR ARRHYTHMIAS

In this section, we will review a series of high impact articles centered around sudden cardiac death risk associated with underlying mechanisms of ventricular tachycardia (VT)/VF, as well as that because of inherited disorders, such as the long-QT syndrome.

Predictors of Ventricular Arrhythmias

Das et al[23] looked at 97 patients with either ischemic or nonischemic cardiomyopathy with a mean LV EF of 27%±7% who were undergoing primary prevention implantable cardioverter-defibrillator (ICD) implantation. They used high resolution (1024 Hz) digital 12-lead ECGs during intrinsic rhythm to record QRS peaks (abnormal intra-QRS low amplitude deflections that deviated from their respective QRS templates). They found that QRS peaks was an independent predictor of future VT/VF.

Resuscitation and Response to Cardiac Arrest

There has been keen interest in determining how to improve treatment of out-of-hospital cardiac arrest, and to this end, Bækgaard et al[24] investigated the impact of public access defibrillation via an automated external defibrillator (AED) on survival after out-of-hospital cardiac arrest in their systematic review. The overall survival to hospital discharge after out-of-hospital cardiac arrest treated by public access defibrillation showed median survival of 40%, but the highest survival was seen in the group who received public access defibrillation from nondispatched lay first responders. Still the figure of 53% for this highest survival group remains less than ideal. Determining where to place AEDs in strategic downtown locations can be challenging. Sun et al[25] sought to identify locations in the city of Toronto for potential AED placement by assessing spatiotemporal cardiac arrest risk at these locations. By using the Toronto Regional RescuNET Epistry cardiac arrest database, they found that coffee shops and bank machines from the 5 largest Canadian banks occupied 8 of the top 10 locations in Toronto. These data will aid policy makers to determine where to deploy AEDs effectively and may be extrapolated to other large metros as well.

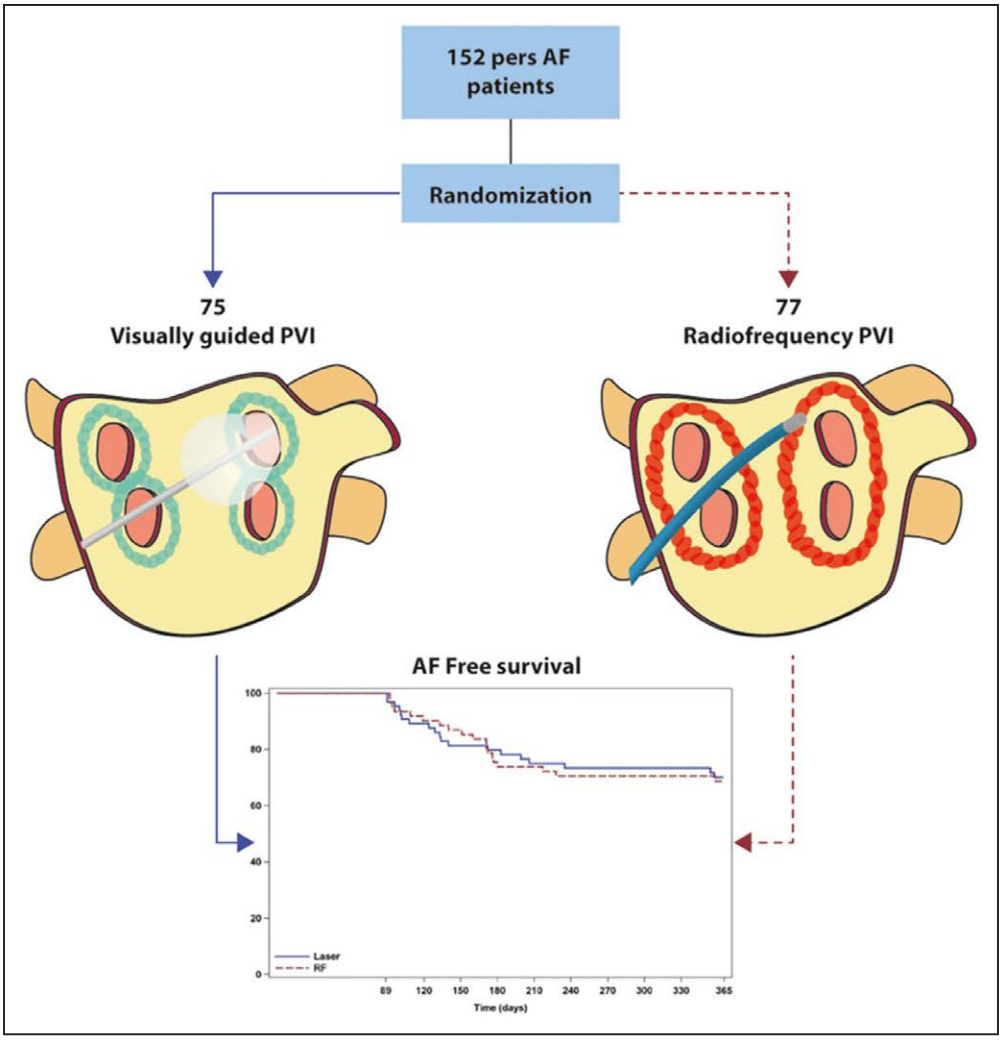

Figure 2. Freedom from atrial fibrillation (AF): laser vs radiofrequency ablation.
A total of 152 patients with persistent atrial fibrillation were randomized to laser balloon or radiofrequency (RF) ablation. Freedom from atrial fibrillation or atrial tachyarrhythmias was similar in the 2 groups (*P*=0.40). Kaplan-Meier analysis depicting the AF-free survival after a single ablation (blue line, laser balloon group; red dotted line, RF current group). PVI indicates pulmonary vein isolation. Reprinted from Schmidt et al[20] with permission. Copyright © 2017, American Heart Association, Inc.

Along these lines, Boutilier et al[26] investigated the possibility of using a drone network to optimize AED delivery to sites of out-of-hospital cardiac arrests efficiently to improve AED utilization ahead of historical 911 response times in Toronto. Using mathematical modeling, their primary analysis quantified the drone network size required to deliver an AED 1, 2, or 3 minutes faster than historical median 911 response times. They found that a drone network of ≈100 drones can perform at least 3 minutes faster to deliver an AED to the cardiac arrest site.

Inherited Arrhythmic Disorders

Long-QT Syndrome

This year also saw several investigations into inherited disorders that predispose to sudden cardiac arrest and VT/VF. Sugrue et al[27] looked at cases of genetically confirmed cases of long-QT syndrome types 1 and 2 and found that left slope of the surface T wave in lead V6 and the T-wave center of gravity *x* axis (last 25% of the wave) in lead 1 were predictors of future long-QT syndrome–associated cardiac events, especially in long-QT syndrome type 2. Greer-Short et al[28] were interested in revealing the concealed nature of long-QT syndrome type 3 syndrome and looked at gain of function mutations in the voltage-gated Na channel (Nav1.5), which is associated with the long-QT syndrome type 3 syndrome. The authors showed that by increasing intercellular cleft width at cell-cell connections, this resulted in action potential duration prolongation and produced early after depolarizations, possibly triggering arrhythmogenesis.

Catecholaminergic Polymorphic VT

Landstrom et al[29] demonstrated in whole-exome sequencing, incidentally identified catecholaminergic polymorphic VT–associated variants showed a 9%

prevalence, but these variants were of undetermined significance, and in the absence of a clinical suspicion of catecholaminergic polymorphic VT, are unlikely to represent markers of true catecholaminergic polymorphic VT pathogenicity.

Brugada Syndrome

Milman et al[30] undertook a study of Brugada syndrome patients to identify the age of the first arrhythmic event in these patients and found arrhythmic events occurred between the ages of 16 and 70 years and the peak arrhythmic event rate occurred between 38 and 48 years of age. It was striking that at all ages, arrhythmic event rates were significantly higher in Asians compared with non-Asians.

VT ABLATION

In the area of VT research, notable preclinical and clinical advances were reported in 2017.

Procedural Safety

Whitman et al[31] alerted us to the fact that stroke risk for patients undergoing endocardial VT ablation deserves further study and probably more definitive recommendations on postprocedural anticoagulation and antithrombotic management. In their small patient series, 7 (58%) of the 12 patients undergoing LV ablation (mostly for premature ventricular contractions) had multiple new cerebral emboli detected on head MRI, compared with 0 of the 6 who underwent right ventricular ablation (again mostly premature ventricular contractions); 63% of those undergoing retrograde LV approach had >1 new brain lesion. Further study is underway to better assess risk and preventive management options.[31]

Kusa et al[32] demonstrated potential clinical benefit of percutaneous LV assist devices during VT ablation in a retrospective, single-center analysis of 194 patients (109 percutaneous LV assist devices). The percutaneous LV assist device patients were more likely to have dilated cardiomyopathy, New York Heart Association ≥III, lower LV EF, and electrical storm; their procedures were longer and were more likely to have persistently inducible VT post-ablation, and their hospital stays were longer than the non–percutaneous LV assist devices group. However, despite these marked differences, no differences were seen between groups for both acute procedural outcomes and the primary end point (recurrent VT, heart transplantation, or death).

Mapping Insights

Komatsu et al[33] described features consistent with a distinct entity and variant of reentrant verapamil-sensitive fascicular VT involving the Purkinje network around papillary muscles. Among 13 patients with papillary muscle VT, verapamil had impact on VT but terminated it in only 6 (slowed in 7). Successful ablation was not achieved with ablation at mid-diastolic Purkinje potentials recorded around the papillary muscles during VT.

Noninvasive Ablation: A New Frontier

In 5 patients with refractory VT and comorbidities, 3 of whom had undergone prior catheter ablation, Cuculich et al[34] demonstrated that noninvasive ablation using stereotactic body radiation therapy was effective in dramatically reducing VT burden by 99.9% with average, on-table procedure time of 14 minutes; subsequent VT treatment was still required in 2 of the patients, and 1 patient died. Noninvasive stereotactic body radiation therapy may truly revolutionize our ability to manage VT patients for whom invasive ablation might otherwise be deferred. However, the long-term safety and efficacy are unclear; results from ongoing study of this technique in a larger number of patients and with longer follow-up are highly anticipated.

CARDIAC IMPLANTABLE ELECTRONIC DEVICES

The year 2017 saw important advances in the field of cardiac implantable electronic device management. Several studies that have advanced our understanding of arrhythmogenesis, patient selection for and management of patients with cardiac implantable electronic device have been highlighted.

Implantable Cardioverter Defibrillator

Analysis of RAFT (Resynchronization in Ambulatory Heart Failure Trial) showed significantly longer time to appropriate ICD therapy in patients with a primary prevention cardiac resynchronization defibrillation compared with ICD, with no such difference in patients with a secondary prevention device. Cardiac resynchronization defibrillation was not associated with significant difference in the burden of ventricular arrhythmia in both groups. A meta-analysis showed a 55% increased incidence of appropriate ICD therapies in heart failure patients with sleep disordered breathing (both central and obstructive sleep apnea) compared with patients without sleep disordered breathing.[35]

Interesting temporal climatic temperature trends in the incidence of electrical storm was reported from the TEMPEST multicenter study (Trial to Evaluate the Management of Paroxysmal Supraventricular Tachycardia During Electrophysiologic Study With Tecad-

enoson) of patients with ICD.[36] Electrical storm was more likely to occur during working days, early in the morning between 8 and 10 AM, and during months that register an increased temperature variation compared with the previous month.

Optimization of ICD Programming

With recent advances focused on reducing unnecessary ICD shocks, Thogersen et al[37] question the appropriateness of generic programming recommendations for all ICD manufacturers. They report 10 individuals whose ICD failed to treat VF despite otherwise normal function due predominantly to interaction between programming of fast detection rates and manufacturer-specific detection algorithms.

CARDIAC RESYNCHRONIZATION THERAPY

Derval et al[38] sought to characterize LV activation in patients with narrow QRS, intraventricular conduction delay, and left bundle branch block using high density mapping. Patients with normal QRS and intraventricular conduction delay had LV activation through the Purkinje network resulting in multiple sites of breakthrough. In comparison, left bundle branch block demonstrated a single site of breakthrough on the septum with delayed transseptal conduction and homogenous activation of the LV. Patients with intraventricular conduction delay had slower and more heterogenous propagation compared with those with normal QRS. These findings help explain the lack of benefit from cardiac resynchronization therapy in patients with intraventricular conduction delay and normal QRS.

Rodríguez Muñoz et al[39] described the use of echocardiography to optimize AV delay in cardiac resynchronization therapy using analysis of flow dynamics of blood entering the mitral inflow getting immediately redirected to the outflow tract without reaching the LV apex, that is, the mitral-aortic flow reversal. Optimal AV delay achieves perfect coupling between the inflow and outflow patterns, whereas long AV delays desynchronize the 2 flows and short AV delays reduce the flow reversal. They also report a formula to calculate the optimal AV delay and show improvement in acute hemodynamics in a resynchronization cohort.

PACEMAKER FOR TREATMENT OF VASO-VAGAL SYNCOPE

The optimal programming of pacemaker for treating vaso-vagal syncope with cardioinhibitory response on tilt table testing was reported in the SPAIN (Closed Loop Stimulation for Neuromediated Syncope) double blind randomized controlled trial. The DDD-closed loop stimulation algorithm resulted in significantly reduced syncope burden and time to first recurrence by 7-fold compared with DDI sham programming.[40]

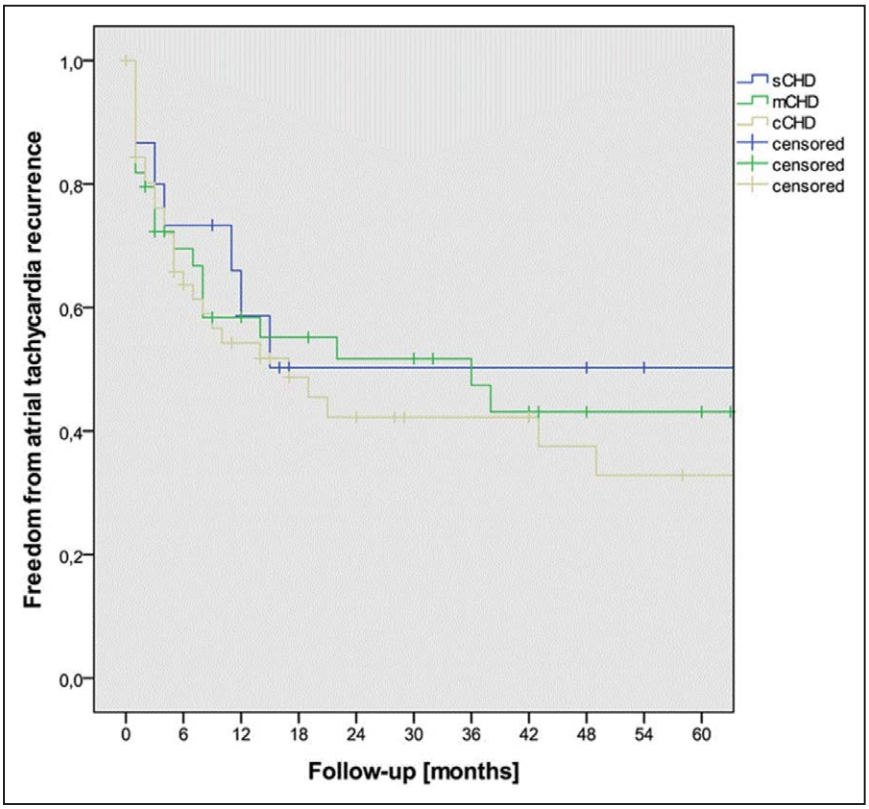

Figure 3. Freedom from atrial tachycardia post-ablation in congenital heart disease (CHD).
Four years after catheter ablation, there is similar recurrence rate in groups with simple CHD (sCHD), moderate CHD (mCHD), or severe CHD (sCHD). *P*=NS. Reprinted from Klehs et al[44] with permission. Copyright © 2017, American Heart Association, Inc.

MRI IN PATIENTS WITH CARDIAC IMPLANTABLE ELECTRONIC DEVICE

Two large prospective registries, MagnaSafe and Nazarian et al,[41] established the safety of 1.5 Tesla MRI in 3009 patients with non-MRI conditional devices.[42] Both studies used similar protocols, with the notable exception of exclusion of ICD patients who are pacemaker dependent and those undergoing thoracic MRI in the MagnaSafe study. Tachycardia therapies were programmed off, and pacemaker-dependent patients were programmed to pace asynchronously. Death, lead, or device failure and need for immediate device revision were not observed. Device reset was infrequently noted along with small changes in lead sensing and pacing parameters that did not reach clinical significance. These data will make MRI more widely available to patients with cardiac implantable electronic device.

Dalouk et al[43] report that telemedicine video-conferencing clinics are noninferior to in-person clinics in determining ICD outcomes, useful in remote areas without subspecialty care.

PEDIATRIC AND CONGENITAL HEART DISEASE

Atrial Arrhythmias

Atrial arrhythmias are a common problem in adults and children with congenital heart disease (CHD). Acute success rates with ablation and long-term recurrence risks after ablation have been an ongoing problem. Klehs et al[44] describe their experience with radiofrequency ablation in 144 patients with congenital heart disease and report an overall acute success rate of 81%. The acute success rates were not influenced by the complexity of the congenital heart disease (Figure 3), and acute success rates were notably lower in left atrial tachycardias. Although the acute success rates were good, tachycardia recurrences occurred in 54% of patients at a mean follow-up of 7.4 years, with higher rates of recurrence noted on those patients with complex atrial repairs or palliation (ie, Fontan, Mustard, and Senning patients).

Avila et al[45] sought to identify factors associated with the development of atrial tachycardia in adults with CHD. In a cohort of 3311 patients presenting with atrial tachycardia, they identified 8 factors independently associated with atrial tachycardia, including univentricular physiology, previous intracardiac repair, systemic right ventricle, pulmonary hypertension, pulmonary regurgitation, pulmonary atrioventricular valve regurgitation, and pulmonary and systemic ventricular dysfunction. With the presence of ≥3 of these factors, atrial tachycardia–free survival after 40 years of age was only 50%, and the factor most commonly associated with development of atrial tachycardia was univentricular physiology with an odds ratio of 13.2.

Labombarda et al[46] also looked to assess the types of atrial arrhythmias and factors associated with arrhythmia development in adults with CHD. The authors evaluated a multicenter cohort of 482 CHD patients and found that intraatrial reentrant tachycardia was the most common atrial arrhythmia identified (62%), but in patients >50 years of age, AF became the most common atrial arrhythmia. The authors found that older age and hypertension were factors associated with AF, and 23% of patients >50 years of age developed permanent atrial arrhythmias.

Sudden Cardiac Death

Adults with CHD are at risk for malignant ventricular arrhythmias and sudden cardiac death. Identifying patients at risk remains problematic, and evidence-based guidelines in CHD patients are limited. Vehmeijer et al[47] evaluated the predictive ability of the 2014 Consensus Statement on Arrhythmias in Adult Congenital Heart Disease Patients and the 2015 European Society of Cardiology Guidelines recommendation for ICD placement in ACHD patients. The authors assessed 25 790 adult congenital heart disease patients from an international multicenter registry and noted that the Consensus Statement would have recommended ICD placement in only 41% of patients who experienced sudden death while the European Guidelines would have identified only 35%. The authors highlight the current limitations and challenges in identifying those adults with CHD at risk for sudden death.

ARTICLE INFORMATION

The Data Supplement is available at http://circep.ahajournals.org/lookup/suppl/doi:10.1161/CIRCEP.118.006648/-/DC1.

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Year in Review in Cardiac Electrophysiology

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SUPPLEMENTAL MATERIALS

Basic Electrophysiology

Bradyarrhythmias

New research into the causes of bradyarrhythmias recently revealed an intriguing association between sick sinus syndrome, atrial fibrillation and left ventricular noncompaction.[1] While SCN5A mutation carriers presented at a much younger age (20±18 versus 39±22 years, p=0.03), HCN4 mutation carriers were more likely to have atrial fibrillation (44% versus 9% in SCN5A patients) and left ventricular non-compaction (50% versus 0% in SCN5A patients). It follows that, although mechanistic proof is wanting, HCN4 mutations within first heart field progenitor cells during cardiac development could disrupt the formation of electrically/structurally abnormal tissue in the atria or left ventricle.

Atrial Fibrillation

Recent work has also shed light on the drivers of atrial fibrillation. Using a cardiac-restricted transgenic over-expression model, cAMP-responsive elements located in the promoter region of target genes promoted adverse metabolic and structural remodelling through re-expression of the fetal gene program even before onset of atrial fibrillation. [2] Given electrophysiological similarities to human atrial fibrillation, this mouse model opens new avenues to dissect transcriptional elements responsible for the generation of atrial fibrillation.

Mechanisms of Altered Depolarization

The mechanisms driving electrophysiological remodeling of cardiomyopathy remain an area of active research. To address these questions, Liu et al.[3] recently found that increases in the reduced form of nicotinamide adenine dinucleotide seen within cardiomyopathic states activates

protein kinase C delta to boost mitochondrial ROS and directly inhibit the cardiac sodium channel. Interestingly, Salvarani et al.[4] found that TGFβ1 signaling drastically alters the electrophysiological function of bystander cardiac myofibroblasts through changes in membrane channels and connexin expression which, in turn, modifies myocyte electrophysiology through cell-cell coupling. The relative contribution of these novel mechanisms remains to be define but represent intriguing avenues for future study.

Mechanisms of Altered Late Sodium Current

Successful defibrillation is inherently dependent on prevention of re-fibrillation. Azam et al.[5] studied the role of late sodium current (I_{NaL}) blockade using ranolazine or GS-967 on ventricular re-fibrillation in rabbit hearts. Treatment with either drug lowered susceptibility to sustained re-fibrillation after initial defibrillation of long-duration fibrillation (6 min), pointing to a novel therapeutic strategy to improve resuscitation rates. Given that Purkinje cells are more susceptible to arrhythmia than ventricular myocytes, Li et al.[6] compared I_{NaL} activity in both cell types and found that Purkinje cells have a significantly larger I_{NaL} rate dependence that matched a steeper action potential duration rate adaptation rendering Purkinje cells more prone to rate dependent electrical instability, which was exacerbated by enhanced I_{NaL} (anemone toxin, ATX-II) and inhibited by I_{NaL} blockade (ranolazine).

Mechanisms of Mechanically Induced Fibrillation (Commotio Cordis)

Quinn et al.[7] studied the mechanisms underlying the not uncommon clinical scenario whereby subcontusional mechanical stimuli elicit premature ventricular excitation to induce fibrillation. Interestingly, this work showed that premature ventricular excitation was dependent on stretch activated, non-selective cation channels and fibrillation required premature ventricular excitation

overlap with the trailing edge of normal repolarization thus defining the critical window of vulnerability for commotio cordis-induced fibrillation.

Atrial Arrhythmia Management

Left Atrial Appendage Closure

Left atrial appendage closure has emerged as an alternative to oral anticoagulation for stroke prevention in AF, yet is largely unproven in the surgical literature. In a propensity-matched analysis of 10,633 adult cardiac surgery patients, Melduni, et al studied the impact of left atrial appendage closure during routine cardiac surgery on subsequent outcomes. [8] In the matched analysis, patients who underwent LAA closure had a higher rate of post-operative AF (adjusted odds ratio, 3.88; 95% confidence interval, 2.89–5.20), with no effect on the risk of stroke (adjusted HR, 1.07; 95% confidence interval, 0.72–1.58) or mortality (adjusted HR, 0.92; 95% confidence interval, 0.75–1.13).

Hospitalization and AF

Among patients with AF, hospitalization is the most common adverse event with roughly 30 events per 100 patient-years. Among Medicare beneficiaries with AF, Freeman, et al found that while hospitalization rates and healthcare utilization increased from 1999 to 2013, these changes were associated with improved outcomes and reduced mortality.[9]

A sub-analysis of the PIONEER study explored hospitalization rates among AF patients undergoing intracoronary stenting. [10] The patients randomized to either rivaroxaban 15 mg daily plus P2Y12 inhibitor monotherapy (HR = 0.79) or 2.5 mg rivaroxaban twice daily plus dual antiplatelet therapy (HR=0.75) had a lower risk of all-cause mortality or adverse events compared with standard triple therapy (vitamin K antagonism and dual antiplatelet therapy).

Stroke Prevention

Despite the use of well-known stroke risk scores (e.g., CHA_2DS_2-VASc) in many pivotal trials, they have significant limitations. Across 34 AF studies, Quinn, et al studied the variability in stroke rates at each CHA_2DS_2-VASc risk score level. [11] They found substantial variation in both overall and score-based stroke rates – 27% of cohorts reported a stroke risk of <1% for patients with a CHA_2DS_2-VASc score of 2, while 18% of cohorts reported a stroke risk of >2% for patients with a CHA_2DS_2-VASc score of 1. These rates vary dramatically from those upon which the recommendations of oral anticoagulation are based.

AF Risk and Medical Comorbidity

The BiomarCaRE consortium explored the impact of cardiovascular risk factors on sex-specific incident of AF among 79,793 individuals from 4 European community studies with an overall mean age of 50. [12] They demonstrated significant lifetime risk of AF with important differences between men and women, which were modified by cardiovascular risk factors of body mass index and total cholesterol.

While significant hyperthyroidism is associated with AF, the impact of subclinical thyroid disease on development of AF has been unclear. In a systematic review of 30,085 individual participant data in 11 cohorts, Baumgautner, and colleagues studied the relationship between thyroid hormone levels and incident AF among euthyroid patients. [13] In 278,955 person-years of follow-up, they found that free thyroxine, but not thyroid stimulating hormone, was associated with incident AF.

Atrial Arrhythmia Mapping and Ablation

High density mapping of atrial tachycardias

High density mapping technologies with algorithms for automated annotation of signals were introduced in recent years, aiming to improve mapping and ablation outcomes of complex arrhythmias. Relying fully on automated algorithms for annotation and activation maps could be, however, misleading especially in cases with areas of scar or diseased tissue with slow conduction. This was emphasized with findings from a study which employed high density mapping in patients who had previously undergone AF ablation[14] and showed that the majority of suggested microreentries (86%) were pseudo-reentry in areas of wavefront collision or as artifact because of annotation of noise or interpolation in areas of incomplete mapping. It is therefore important to be aware of this caveat with high density mapping and still rely on interpretation of electrograms in the candidate circuit and activation in the wider surrounding region or origin.

Atrial Fibrillation Ablation

A clinical trial[15] included 113 patients with persistent AF which had converted to paroxysmal AF on antiarrhythmic drugs and were randomized to PVI alone vs PVI with linear ablations. The procedures were shorter with PVI alone but freedom from arrhythmia recurrences was comparable between the groups.

Rotor mapping and ablation in persistent AF continues to be a topic of interest but the controversy continues and no real clinical benefit has been proven to date. In 2017, the novel noninvasive epicardial and endocardial electrophysiology system (NEEES) was used to identify rotors in 10 patients undergoing AF ablation. [16] A total of 410 electrical rotors we identified but

rotor presence based on the NEEES analysis did not directly correlate with the extent and anatomic location of scar by MRI.

In a study examining the contribution of the endocardial portion of the hybrid surgical catheter ablation procedure,[17] 70 patients with persistent AF underwent minimally invasive epicardial surgery for AF followed by catheter-based electroanatomic mapping and ablation 2 to 3 months later. The majority of patients after epicardial ablation were found to require additional endocardial catheter ablation to complete the ablation sets. The arrhythmia free survival off antiarrhytmics at 12 months was 77%.

Ventricular Arrhythmias

Ventricular Arrhythmia Mechanisms

There has been growing interest in the role of the autonomic nervous system in arrhythmogenesis. Hamon and colleagues employed a porcine model to record neuronal activity from a ventricular ganglion and evaluated dynamic changes in this activity in response to right ventricular outflow tract (RVOT) PVCs [18]. Compared with fixed short and fixed long coupling interval PVCs, variable coupling interval PVCs had a greater impact on neuronal response, including those receiving sympathetic and parasympathetic input. These changes, the authors argue, may be critical for arrhythmogenesis and remodeling and may play a role in the development of cardiomyopathy.

Others have investigated clues in the surface QRS complex that may inform on arrhythmic risk. Aizawa and colleagues sought to understand the underlying mechanisms of J waves by recording

the J wave response to rapid atrial pacing in patients with idiopathic VF (IVF) compared to non-IVF patients without history of cardiac arrest [19]. The IVF patients had larger J waves than the non-IVF patients and showed J wave reduction when RR intervals were shortened whereas J waves were augmented or unchanged in the non-IVF patients. This variant response suggests possibly different mechanisms to explain J wave responses, early repolarization in IVF patients and conduction delay in the non-IVF patients. Mikami and colleagues investigated the utility of including RVEF to LVEF for prediction of future arrhythmic events in patients with systolic dysfunction [20]. They found that in fact RV dysfunction was independently predictive of future arrhythmic events in this population.

Long QT Syndrome

Vink and colleagues sought to identify the effect of age and sex on the QTc interval in children and adolescents with LQT1 and LQT2 syndromes and found that in both genotypes, male patients showed QTc shortening after the onset of puberty, but in LQT2, male patients under the age of 14 years, had a significantly longer QTc [21]. The age of 12-14 years may signify an important transitional period in these patients.

Roberts, et al, were interested in the true arrhythmic risk conferred by loss of function KCNE2 variants as associated with the LQT6 syndrome [22]. Due in part to lack of genotype-phenotype segregation, their findings suggest that many KCNE2 variants and perhaps all, have been erroneously designated as LQTS-causative mutations, but perhaps these variants may confer proarrhythmic risk when provoked by additional environmental/acquired or genetic factors or both.

Eleclazine, a novel cardiac late sodium channel inhibitor, which is currently undergoing clinical development for treatment of long QT (ClinicalTrials.gov identifier: NCT01849003), was demonstrated to be superior to flecainide in suppressing catecholamine-induced non-sustained VT as well as T-wave alternans, in an intact porcine model.[23]Findings suggest potential utility of this drug, which has been relatively well-tolerated in ongoing clinical studies, for treatment of catecholaminergic polymorphic VT patients as well as for long QT.

Hypertrophic Cardiomyopathy

Wang and co-authors aimed to understand the prognostic significance of NSVT in hypertrophic cardiomyopathy [24]. They found the incidence of NSVT was significantly associated with ICD-treated VT/VF and a faster rate (>200 bpm), longer duration (>7 beats), and repetitive runs of NSVT were more highly predictive of ICD-treated VT/VF.

Ventricular Tachycardia Mapping and Ablation

Fascicular Tachycardia

Further insights gleaned from our most fundamental electrophysiologic mapping tool, the surface 12-lead ECG, were reported to facilitate management of fascicular VT.

ECG and intraprocedural criteria were identified by Ma and colleagues [25]to predict proximal, para-Hisian exit of LPF-VT based on 41 cases of successful RFA of LPF-VT at their institution. QRS duration ≤120 ms, R/S ≥0.6 in V6, and R/S ≤1.0 in lead I each predicted proximal LPF-VT exit with high sensitivity and specificity and could be potentially used in pre-procedural

preparation. Intraprocedurally, a higher ratio of the presystolic potential time during VT potential to the HV in sinus rhythm was also more often found in proximal LPF-VT.

Linear Ablation

Nazer and colleagues[26] demonstrated that radiofrequency ablation (RFA) lesions using a novel, open-irrigated linear, multipolar catheter were significantly more contiguous (0% gaps vs. 53% with gaps of length 2.8±0.9 mm) and of similar or greater length than linear lesion sets applied sequentially using a standard ablation catheter in a swine model. Importantly, irrigation volumes and procedural times were significantly shorter using the multipolar catheter; these findings provide great promise for performing substrate-based VT ablation with greater efficiency and efficacy.

Mapping

Aortic valve closure artifact occurs often when mapping within the aortic root and may lead to erroneous ablation when mistaken for pre-systolic local activation. Among 28 patients undergoing LV outflow tract ablation, Romero and colleagues [27] identified aortic valve closure artifact in 39% of patients, most with the left coronary cusp mapping. Artifact consistently occurred after the terminal portion of the T wave (average 19±37 ms) and was confirmed on correlation with invasive arterial waveforms as well as that seen among patients with mechanical aortic valves.

Epicardial Access

A novel epicardial access needle with embedded pressure sensor at the tip (EpiAccess, EpiEP, Inc., New Haven, CT), to allow for real-time pressure assessment during epicardial access and

possibly avoid RV injury and improve safety, was evaluated in a multicenter effort by Di Biase and colleagues.[28] Successful epicardial access was achieved in all 25 patients enrolled, although one patient presented with a delayed effusion which required drainage (>80mL), but was not felt to be directly related to use of EpiAccess.

Randomized Trial Update

Advances in ablation this year were highlighted by a number of significant collaborations, both between and within ablation centers. Adding to the relatively limited number of randomized clinical controlled trials in VT ablation among patients with ischemic heart disease, the Substrate Modification Study Investigators[29] randomized 111 patients with prior myocardial infarction and unstable VT to ICD+prophylactic RFA or ICD alone. Over a 2.3±1.1 year follow-up, event-free survival did not differ significantly between groups, however catheter ablation was associated with a >50% reduction in ICD therapies throughout follow-up.

Procedural Endpoints

In retrospective analysis of 165 ischemic cardiomyopathy patients undergoing VT ablation at a single center, Fujii et al [30] demonstrated that persistent inducibility of even NSVT (≥5 beats) was associated with significantly increased likelihood of VT recurrence in follow-up, similar to that of patients who had sustained monomorphic VT induced after VT ablation. Inducible NSVT following ablation may suggest continued presence of functional arrhythmia substrate.

International VT Center Collaborative (IVTCC)

IVTCC was an unprecedented collaboration between 12 international ablation centers established several years ago by Drs. Roderick Tung, Kalyanam Shivkumar, and Marmar Vaseghi.[31] In 2017, additional subgroup analyses involving this patient population yielded valuable insights. In elderly patients (age ≥70 years), in-hospital (4.4% versus 2.3%; P=0.01) and 1-year mortality (15% versus 11%; P=0.002) were higher, but 1-year VT recurrence rates were similar (26% versus 25%; P=0.74), and lack of VT recurrence was strongly associated with improved survival. Including only those with clinical heart failure (New York Heart Association (NYHA) Class II-IV), safety and efficacy of ablation even among NYHA-IV patients (N=111) was demonstrated. Despite significantly greater baseline comorbidities, higher rates of recurrent VT, and in-hospital and 1-year mortality in the NYHA-IV vs. NYHA-II-III cohort, [32] those with NYHA-IV free of VT following ablation had similar survival compared with NYHA-II-III patients with recurrent VT (68% versus 73%, respectively). Early VT recurrence (≤30 days), however, was significantly associated with increased mortality, especially in NYHA-IV patients.

Predictors of early mortality (EM) following scar-based VT ablation were also identified. The rate of EM in this cohort was 5% and included lower LVEF (OR per percent decrease: 1.12; 95% CI: 1.05-1.20; p<0.001), chronic kidney disease (OR: 2.73; 95% CI: 1.10-6.80; p=0.030), presentation with VT storm (OR: 3.61; 95% CI: 1.37-9.48; p=0.009), and presence of unmappable VTs (OR: 5.69; 95% CI: 1.37-23.69; p=0.017). [33] Identifying such risk factors prior to ablation should prompt early consideration for hemodynamic support or other care to help mitigate later potential complications.

Finally, safety and outcomes of repeated VT ablation were examined.[34] Those undergoing repeated versus first-time ablation were more likely to have NICM, present with ICD shocks or storm, and been treated with ≥2 antiarrhythmic drugs including amiodarone. Repeat procedures were longer, more complex, had a higher overall complication rate (8% vs 5%, P<0.01), and were associated with increased VT recurrence (29% vs 24%, P<0.001). However, perseverance in the face of poor odds was demonstrated: those without recurrent VT even after repeated ablations, albeit at experienced centers, had survival equivalent to those who undergoing 1st-time ablation (93% vs 92%, P=0.96).

Pacemapping

The spatial resolution of pacemapping of the ventricles was better quantified by Li et al., [35] who showed an essentially linear relationship between distance of sites of pacing (6219 pacing pair combinations acquired from 68 patients) and surface QRS morphology changes, when pacing was restricted to areas with EGM voltage >0.5mV and distance between sites was 10-50 mm. There were differences in resolution depending on the chamber paced, with the greatest differences noted for epicardial pacing sites.

Ablation of Brugada Syndrome Substrate

Among 135 Brugada syndrome patients, Pappone et al [36] found that defining and targeting arrhythmogenic electrophysiologic substrate (AES) with epicardial mapping of the RV outflow tract before and after ajmaline administration was helpful in targeting radiofrequency ablation. Patients with documented spontaneous VT/VF had a wider area of AES compared to those with

inducible VT/VF without ECG documentation of arrhythmias. Radiofrequency ablation eliminated AES leading to ECG normalization and VT/VF noninducibility in all patients.

Cardiac Implantable Electronic Devices

Implantable Defibrillators

ICD therapy for ventricular arrhythmia: Associations and temporal trends

A thorough understanding of risk factors for ICD therapy is vital to improving outcomes. Several cohort studies have reported emerging risk factors for ICD shocks. ICD recipients (excluding CRT-D) who were paced 80 – 98% of the time in the right ventricle (RV) were reported to have approximately 50% increased risk of appropriate ICD shock compared to those who were paced <1%, in a cohort of over 425,000 patients in the ALTITUTDE database.[37] This study highlights the importance of device programming to avoid RV pacing. Surprisingly, those who were paced 98 – 100% of the time in the RV had a lower risk of ICD shocks than those with <1% RV pacing. While intriguing, the later finding should not lead to clinical practice change to maximize RV pacing yet.

Optimization of ICD programming

Yee et al have reported on the safety and efficacy of a new automated anti-tachycardia pacing (AATP) algorithm in terminating VT.[38] AATP uses a dynamic algorithm that adjusts the ATP sequence based on real-time physiologic parameters including: (1) use of a S1-S2/S3 sequence with S1 programmed to reset the VT circuit and S2/S3 programmed to terminate it; (2) programming of a short S1-S2 interval for the first ATP determined by an estimate of the effective refractory period at the pacing site; and (3) analysis of the return cycle length after an

unsuccessful ATP to determine coupling intervals for subsequent ATP sequences (Figure 1). The authors report 80% efficacy in terminating VT and acceleration of VT in 1.3%.

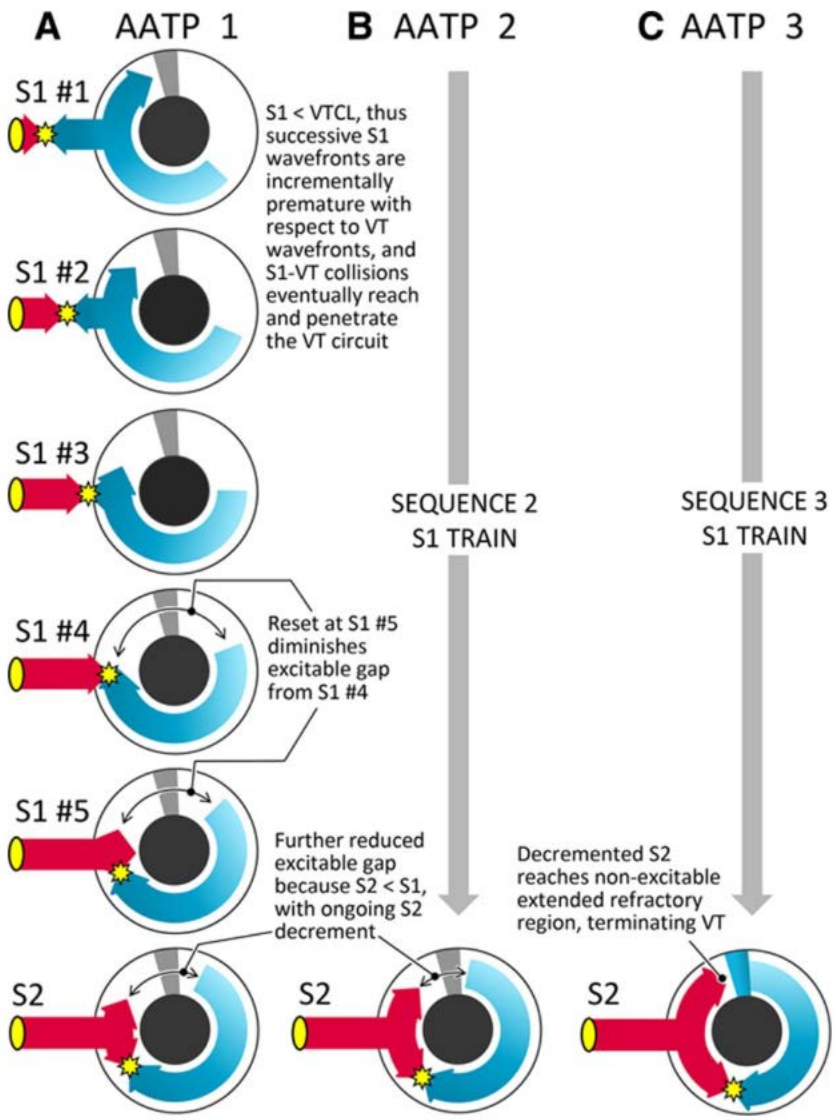

Figure 1. Schematic of antitachycardia pacing (ATP) interaction with myocardium over three successive ATP sequences (AATP 1-3) in a hypothetical sustained monomorphic ventricular tachycardia (SMVT) episode.

Each VT circuit rendering shows the ATP pulse wavefront (red) when it collides with the VT wavefront (blue). The black circle is non-conducting myocardium, and the narrow area projecting radially upward is a region of extended refractoriness or slow conduction (grey, excitable; blue, nonexcitable). Automatic

ATP (AATP) 1 shows S1 and S2 pulse effects. All S1 pulses are 88% of VT cycle length, so AATP 2 and 3 only show S2 effects. **A**, The first four S1-VT collisions approach the VT circuit. The 5th S1 wavefront penetrates the VT circuit before a VT wavefront can exit, propagates orthodromically and antidromically, and advances the timing of the circulating VT wavefront (reset), decreasing the excitable gap. The S2 pulse further reduces the excitable gap without terminating VT. **B**, This S2 is decremented, further reducing the excitable gap, but without terminating VT. **C**, The S2 is decremented again, reaching the region of extended refractoriness when it is non-excitable, blocking VT circuit conduction, and terminating VT.

CIED follow-up and complications

The timing of CIED reimplantation following infection remains a matter of debate. In a cohort of 434 patients with cardiac implantable electronic device (CIED) infection in the MEDIC registry, reinfection of CIED within 6 months occurred in 1.8% of those who underwent device explantation followed by reimplantation (median time to reimplantation 10, interquartile range 6 – 19 days).[39] This contrasted with 11.3% reinfection in those who did not undergo initial device explantation, supporting current recommendation to explant infected CIED when possible. Reimplantation after extraction in general is a safe practice although the study was not designed to identify an ideal time frame to reimplant. Interestingly, only 58% of patients with CIED explantation underwent reimplantation, highlighting the importance of reassessing the need for the device.

Congenital Heart Disease

Ablation of Arrhythmias

Arrhythmia Recurrence after Mustard or Senning Procedures

Patients who have undergone Mustard or Senning procedures are particularly prone to atrial arrhythmias that are difficult to control and ablate. Gallotti et al [40] investigated mechanisms and predictors of recurrent tachycardia after ablation in this challenging patient population. They showed that in 28 patients undergoing 38 ablation procedures, the patients with Senning procedures were more likely to develop recurrent tachycardia. In addition, while CTI flutter was most common, the majority of recurrences after CTI ablation involved the posterior anastomosis after the Senning operation.

A-V Nodal Reentrant Tachycardia

There are limited data on AVNRT development and ablation outcomes in patients with congenital heart disease. Differences in AV nodal location and anatomy makes ablation of AVNRT in the CHD particularly challenging. Papagiannis et al describe 109 pediatric and adult patients with congenital heart disease with inducible AVNRT in the EP laboratory.[41] Patients with complex CHD had lower success rates with ablation (82% vs. 97%, p = 0.008) and higher risk of AV block (14% vs. 0%, p = 0.004) compared to simple congenital heart disease patients.

Anti-arrhythmic Therapy

The use of adenosine use in pediatric heart transplant recipients has been relatively contraindicated due to the presumed risk of prolonged effects on the SA and AV node with cardiac denervation. Flyer et al have challenged this contraindication with a prospective analysis of 80 pediatric heart transplant patients given escalating doses of adenosine during routine cardiac biopsy.[42] The authors demonstrated effective AV block with minimal risk with low dose (25 micrograms/kg or 1.5 mg in patients > 60kg) adenosine administration.

Ventricular Tachycardia

Arrhythmia risk has been attributed to circadian patterns in many arrhythmia syndromes. Miyake at al sought to assess the risk of VT development in multi-center cohort of 80 children with cathecholiminergic polymorphic ventricular tachycardia (CPVT).[43] The authors demonstrated that episodes of ventricular tachycardia were more likely to occur in the afternoon or evening hours, suggesting that there are circadian effects that contribute to arrhythmia development beyond adrenergic stimulation in children with CPVT.

Pacing and Defibrillation

CHD patients will often require pacemakers for sinus node dysfunction and AV block. Patients with single ventricle physiology may be especially prone to problems from chronic ventricular pacing. Bulic et al looked at 23 single ventricle patients that required greater than 50 percent chronic ventricular pacing and compared them to 53 controls patients matched for age, gender, and single ventricle morphology.[44] The authors found that patients requiring pacing were more likely to require heart failure medications, more likely to have moderate to severe atrioventricular valvar regurgitation, and had an almost five-fold higher risk of death or cardiac transplantation (OR 4.9 CI 1.05 – 22.7). The study highlights that the single ventricle population may be particularly prone to pacing inducing cardiomyopathy and the authors posit that new strategies to limit ventricular pacing or improve synchronization may be needed.

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