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EDITOR'S PAGE


Advances in Clinical Electrophysiology

2015 in Review

David J. Wilber, MD, FACC, *Editor-in-Chief, JACC: Clinical Electrophysiology*
Jagmeet P. Singh, MD, DPHIL, *Deputy Editor, JACC: Clinical Electrophysiology*

Over the past year, there was considerable progress and innovation in heart rhythm therapy. In this overview, we touch upon just a few of the major publications over the past year that are most likely to significantly impact clinical practice and set the tone for 2016.

Optimal strategies for ablation of atrial fibrillation (AF) continued to be an intense focus of clinical investigation. The multicenter randomized trial STAR AF II (Substrate and Trigger Ablation for Reduction of Atrial Fibrillation Trial Part II) compared the outcomes of 3 ablation strategies (pulmonary vein isolation [PVI] alone, PVI plus ablation of electrograms showing complex fractionated activity, and PVI plus additional left atrial linear ablation) in 589 patients with persistent AF (1). Over a follow-up of 18 months, additional left atrial ablation beyond PVI was not associated with a significant reduction in recurrences of AF. However, freedom from recurrent AF without antiarrhythmic drugs at 1 year with PVI alone remains suboptimal (41%), suggesting the need for alternative approaches in this subset of patients. The STAR AF II trial was conducted without contact-force guidance. Previous data indicate that optimized contact force may improve the durability of PVI following radiofrequency (RF) ablation. This year, the TOCCASTAR (TactiCath Contact Force Ablation Catheter Study for Atrial Fibrillation) study provided additional evidence of the benefit of force sensing during ablation (2). In this study, 300 patients with paroxysmal atrial fibrillation (PAF) were randomized to ablation using a force-sensing irrigation catheter or one without force sensing. Although there was no overall difference between the 2 groups with respect to 1-year freedom from recurrent AF, outcomes were significantly better when force was >10 g for more than 90% of applications.

An additional approach to improving the outcome of PV isolation has been the use of adenosine to assess the completeness of PVI, and unmask dormant conduction that can be targeted for additional ablation during the initial procedure. This endpoint was evaluated in 2 different randomized trials. In the ADVICE (ADenosine following pulmonary Vein Isolation to target dormant Conduction Elimination) trial, 284 of 534 patients (53%) had dormant conduction unmasked after PV isolation (3). These patients were then randomized to additional adenosine-guided ablation or no further ablation. There was a significant reduction in the 1-year risk of recurrent AF (hazard ratio: 0.44) associated with the adenosine approach. By contrast, in the UNDER-ATP (UNmasking Dormant Electrical Reconduction by Adenosine TriPhosphate) trial, 2,113 patients undergoing PVI for PAF were randomized to an adenosine-guided or conventional endpoints for ablation (4). There was no difference between the 2 strategies with respect to 1 year AF recurrence (hazard ratio: 0.89). However, in this study, adenosine unmasked dormant conduction in only 28% of patients. The ultimate role of the adenosine-guided endpoint remains controversial.

The results of the first of several ongoing randomized comparative trials of RF catheter ablation and cryoballoon (CB) ablation was published in 2015. In FreezeAF (PV-Isolation With the Cryoballoon Versus RF: a Randomized Controlled Prospective Non-Inferiority Trial), designed as a noninferiority study, 315 patients with PAF were assigned to either RF or CB therapy (5). The primary endpoint of the study (freedom from recurrent atrial arrhythmia and

persistent complications) was similar between the 2 groups at 1 year (RF 71%, CB 74%). For the index procedure, the periprocedural complication rate was significantly higher in the CB compared to RF group (12% vs. 5%). The trial confirmed noninferiority of CB therapy for treatment of PAF. However, the study was conducted using first generation CB technology and without force sensing RF catheters. Subsequent technological advances in both forms of ablation therapy are likely to impact the outcomes of future comparative trials.

Obesity has emerged as an important risk factor for the development of AF, and a major contributor to the increasing incidence of AF. Previous studies demonstrated that aggressive risk factor modification, including weight loss, can significantly reduce the risk of recurrent AF following ablation. The LEGACY (Long-Term Effect of Goal directed weight management on Atrial Fibrillation Cohort: A five year follow-up study) demonstrated that in a group of 355 patients with AF enrolled prospectively in an outpatient weight control program, sustained weight loss ≥10% resulted in a 6-fold greater probability of AF-free survival, and significantly reduced AF burden and the need for rhythm control therapies (ablation or antiarrhythmic drugs) (6). Sustained weight loss was also associated with significant improvements in other AF-associated risk factors, including hypertension, hyperglycemia, elevated lipids, and indices of systemic inflammation. This study underscores the potential central role of a physician directed dedicated weight management clinic in treating overweight and obese patients with AF.

Important new observations regarding ablation of ventricular tachycardia (VT) were also published in 2015. In the VISTA study, 118 patients with well tolerated ischemic VT were randomized to 2 different ablation strategies (7). The first was a "clinical" approach, targeting specific VT morphologies with activation and entrainment mapping during VT, or pacemapping to identify exit sites from critical isthmuses. The second was extensive substrate mapping with targeting of all abnormal late and fractionated potentials identified within the scar during sinus rhythm and without respect to specific VT morphology (7). At 1 year follow-up, the substrate approach was associated with a significant reduction in VT recurrence (16% vs. 48%), lower use of antiarrhythmic drugs (12% vs. 58%), and a lower incidence of the combined endpoint of death or rehospitalization (21% vs. 47%). The trend toward reduced mortality alone was not statistically significant. While in clinical practice, VT ablation often consists of a hybrid of the 2 strategies, the findings of this study strongly support the concept that more extensive substrate-based ablation is associated with improved clinical outcomes. The question of whether attempts to target specific VT morphologies should be abandoned altogether, particularly in combination with or after failure of a substrate approach, cannot be answered by the data in this study. The impact of VT ablation on long-term survival remains uncertain. The results of multicenter retrospective study of ablation outcomes in 2,061 patients who had VT ablation in the setting of structural heart disease were recently published (8). Overall, the 1 year incidence of death or heart transplant was 15%. Patients without VT recurrence had significantly better survival rates, independent of functional class, ejection fraction, and other comorbidities. While these findings do not establish that VT ablation per se improves survival, they suggest that recurrent VT post-ablation is an important marker of mortality risk. Whether better ablation strategies and tools, with concomitant reductions in recurrent VT, can improve survival remains to be established by clinical trials.

Over the course of 2015, much has happened in the arena of device therapy, that is, leadless pacing, a relook at defibrillator testing, magnetic resonance imaging (MRI)-safe technology, remote monitoring, and sensor strategies. Pacing therapy in 2015 was dominated by the advent of leadless therapy (9,10). Two new device strategies on this front include the Nanostim (St. Jude Medical, St. Paul, Minnesota) and the Micra (Medtronic, Dublin, Ireland) leadless pacemakers. Both devices have fared well in terms of safety and efficacy in early and intermediate follow-up. There were no significant unforeseen events with respect to device migration, dislodgements, device telemetry issues, infections, nor reoperations or device-related deaths. All the pacing and sensing parameters for these technologies remained stable throughout the follow-up. Notably, a longer follow-up will be of interest to gauge the durability of these findings and the need for device retrieval, replacement, or upgrade. It is unclear as to which of these 2 has the better sensor, the more superior fixation strategy, and what is the most appropriate way of managing these patients in the setting of systemic infections. Another recurring question that comes up is whether these will be niche products for a small set of indications (i.e., AF with slow ventricular rate), or will it have a wider market appeal. The natural advancement of the leadless single-chamber device will be to a dual-chamber and then to a 3-chamber resynchronization device with left ventricular pacing. The technology will need to mature a fair bit more before this becomes a reality.

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Two new implantable cardioverter-defibrillators (ICDs) were shown to be safe and effective during and after an MRI. The Evera MRI study (Evera MRI ICD, Medtronic) (11) examined 275 patients receiving a de novo single- or a dual-chamber device with pre-specified leads. Patients were randomized on a 2:1 basis to either an MRI at 1.5-T of the cardiac, thoracic, cervical, and head, or a 1-h waiting period without MRI. The primary efficacy endpoints of no significant change in the ventricular pacing capture threshold and change in R-wave amplitude in the study group at 30 days post-MRI were observed. Importantly, in a subgroup of patients who went on to have ventricular tachycardia/ventricular fibrillation (VF), there was no negative impact on sensing, detection, or treatment from the device. The ProMRI study was a similar evaluation of single- and dual-chamber ICDs (Iforia ProMRI system, Biotronik, Berlin, Germany) in a single-arm non-randomized study of 175 patients (12). Again, no adverse events related to the ICD and MRI exposure were observed, without any change in pacing and sensing parameters. MRI-safe technology is here to stay and will be increasingly used over the coming years.

Since the dawn of ICDs in the early 1980s, routine defibrillation threshold testing (DFT) has been a recognized part of the implantation strategy. Because DFT testing could potentially be harmful because of the procedural anesthesia, induction of VF, and/or the delivered shock, it remains unclear whether regular peri-implant testing is justified in the current era of ICDs with a high reliability. The SIMPLE (Shockless Implant Evaluation) trial, the largest multicenter clinical trial addressing this issue, randomized 2,500 eligible ICD recipients: 1,253 to the DFT arm and 1,247 to no testing (13). The investigators examined the composite outcome of arrhythmic death or failed appropriate shock. The results of the study are compelling and clearly demonstrate that ICD implantation without DFT testing did not reduce the long-term efficacy of the ICD. The non-DFT approach was not inferior for the primary endpoint of ineffective shock or arrhythmic death (7%) versus the DFT testing group (8%). Even though the overarching message may be directed to avoiding "routine" DFT testing, there still needs to be some individualization for unique clinical circumstances (e.g., right-sided devices).

The recently published WEARIT-II (Prospective Registry of Patients Using the Wearable Defibrillator) registry (14), which followed 2,000 recipients of the wearable cardioverter defibrillator (WCD) for a median wear time of 90 days, helped influence the new 2015 guidelines for sudden cardiac death prevention. WCDs can be considered (as a Class IIa indication) for a limited time period for patients with a high risk for sudden cardiac death, but do not meet the current indications for an ICD. This subset of patients also includes patients in the post-myocardial infarction period with arrhythmias, those with active myocarditis, and those that have had an ICD explanted secondary to infection. In this registry, there were a total of 120 sustained ventricular tachyarrhythmic (ventricular tachycardia/VF) events observed in 41 patients, one-half of which received appropriate WCD therapy, with only 10 patients (0.5%) receiving inappropriate WCD shocks. Notably, a substantial proportion of the patients improved their left ventricular ejection fraction and subsequently did not need an ICD beyond the use of the WCD.

Other important areas of investigation and advances in 2015 have been in the realm of remote monitoring and sensor strategies. The emphasis here has been on the reduction of heart failure hospitalization, which has become an increasingly difficult problem. Important work examining the use of big data in 269,471 consecutive U.S. patients implanted with pacemakers, ICDs, or cardiac resynchronization therapy devices was able to show that the benefit of remote monitoring extends across all devices, improving clinical outcomes and decreasing health care expenses (15). With respect to sensor strategies, an extension of the CHAMPION (CardioMEMS Heart Sensor Allows Monitoring of Pressure to Improve Outcomes in NYHA Class III Heart Failure Patients) trial using pulmonary artery pressure-guided management showed an extended efficacy of this approach over an 18-month follow-up (16). Management of New York Heart Association functional class III heart failure based on home transmission of pulmonary artery pressure with an implanted pressure sensor was able to significantly lower hospital admission rates for heart failure.

ADDRESS CORRESPONDENCE TO: Dr. David J. Wilber, Editor-in-Chief, *JACC: Clinical Electrophysiology*, American College of Cardiology, Heart House, 2400 N Street NW, Washington, DC 20037. E-mail: dwilber@lumc.edu.

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