ESC Congress 2017 In Review

Official peer-reviewed highlights

Focus on
Arrhythmias

In This Issue

Evolving Treatments for Atrial Fibrillation

An examination of the current use of antiarrhythmic drugs for atrial fibrillation and what the future may hold, as well as a look at new tools and hybrid approaches for ablation, and whether or not real world data supports our expectations for NOACs.

Also

- Anticoagulation for Cardioversion of AF
- Clinical Trial Highlights
- ICDs: Four Decades of Evidence

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ESC European Society of Cardiology

Dear Colleagues,

We are delighted to present this issue of *ESC Congress 2017 in Review*, focused on the topic of arrhythmias. The peer-reviewed highlights in this issue are based on presentations at the European Society of Cardiology (ESC) Congress 2017 held in Barcelona, Spain.

The feature article takes a closer look at evolving treatments for atrial fibrillation, including the use of antiarrhythmic drugs, ablation, and whether the cumulative evidence on oral anticoagulation in the general population is comparable to the results from large randomised controlled trials. Additional articles look back on 4 decades of development and experiences with implantable cardioverter defibrillators (ICDs) to treat patients with cardiomyopathies, areas of uncertainty in the use of anticoagulation for cardioversion, and highlights of new trials that may guide future developments in ICD and cardiac resynchronisation therapy.

The Hot Line trials covered in this issue include RE-DUAL PCI and IMPACT-AF. Data from RE-DUAL PCI showed that dual antithrombotic therapy with dabigatran and a $P2Y_{12}$ inhibitor was superior to triple therapy with warfarin at preventing bleeding after percutaneous coronary intervention among AF patients. Results from IMPACT-AF indicated that a customised, multilevel educational intervention, with appropriate monitoring and follow-up, increases the use of oral anticoagulants in patients with AF, compared with usual care.

We are confident that the articles and practical perspectives presented in *ESC Congress 2017 in Review - Focus on Arrhythmias* will provide you with new insights into several areas of treatment of patients with AF. Please be reminded that in order to access ESC Congress content (videos, slides, abstracts, reports, and ESC TV interviews) all year long, you can visit us any time online at www.escardio.org/365.

We hope to see you in Munich for ESC Congress 2018. For more information, please visit www.escardio.org/ESC2018.

Professor Stephan Achenbach, FESC
ESC Congress Programme Committee Chair 2016-2018

Dear Practitioner,

We are pleased to share with you this special issue of *ESC Congress in Review 2017* with a focus on arrhythmias from presentations at the European Society of Cardiology (ESC) Congress 2017 held in Barcelona, Spain.

The featured article takes a closer look at current and evolving treatments for atrial fibrillation (AF): catheter ablation, including a hybrid approach that combines the strengths and minimises the limitations of either surgical or catheter ablation alone, pulmonary vein isolation, and antiarrhythmic drug therapy.

Some of the interesting highlights in this special report include results from the CASTLE-AF trial, the first trial designed to study the effectiveness of catheter ablation in improving mortality as well as heart failure (HF) progression in patients with HF and AF compared with standard care according to the ACC/AHA/ESC 2006 Guidelines for the Management of Patients with AF. Catheter ablation of AF significantly reduced the primary endpoint of mortality and HF hospitalisation compared with conventional treatment; patients receiving catheter ablation were 38% less likely to experience the primary endpoint, 47% less likely to die, and 44% less likely to be hospitalised with worsening HF.

Results of the IMPACT-AF study indicated that a customised, multilevel educational intervention program, with appropriate monitoring and follow-up, can increase the use of oral anticoagulants (OAC) in patients with AF. The educational component of the study targeted the patient and their family as well as healthcare providers, monitoring and feedback identified patients not being treated with OAC and reviewed opportunities for them to start/restart medication and identified patients who were at high risk for not staying on medications and intervened to prevent discontinuation —the result was a 9.1% absolute greater increase in OAC use in the intervention group at 12 months.

In addition to the results from clinical trials and registry updates, you will also find articles that reflect on 4 decades of ICD therapy and indications for 2017, as well as the use of anticoagulant therapy for cardioversion of AF.

We hope that you find the articles and practical perspectives that are contained in this special focused edition of *ESC Congress 2017 in Review – Focus on Arrhythmias* helpful in integrating this new information into your clinical practice.

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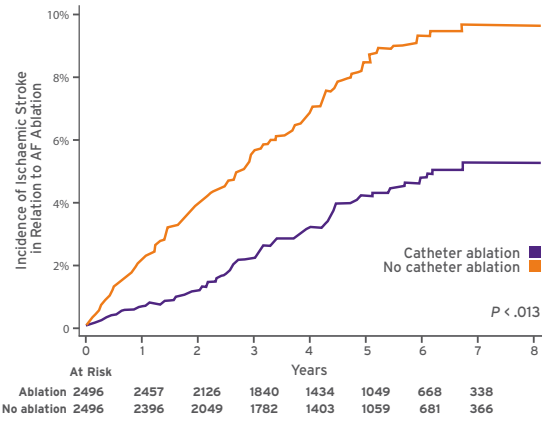
Evolving Treatments for Atrial Fibrillation

Written by **Maria Vinall**

Ablation of AF—Where Do We Stand?

Atrial fibrillation (AF) is the most common arrhythmia; it can be treated by either antiarrhythmic drug therapy (AAD) or catheter ablation and pulmonary vein isolation (PVI). Karl-Heinz Kuck, MD, Asklepios Klinik St. Georg, Hamburg, Germany, believes that mortality and ischaemic stroke outcomes after catheter ablation are better than after AAD. The Swedish health registries support his opinion with recent data showing annualised mortality rates of 0.77% and 1.62% ($P < .001$) for ablated and nonablated patients, respectively (Figure 1). Annualised stroke rates were also significantly ($P = .013$) lower, 0.70% for ablated and 1.01% in nonablated patients [Friberg L et al. *Eur Heart J*. 2016]. However, randomised clinical trials supporting this hypothesis are so far still missing, especially regarding stroke prevention.

Figure 1. Impact of Catheter Ablation on Mortality: Data From Swedish Health Registries



Reprinted from Friberg L et al. Catheter ablation for atrial fibrillation is associated with lower incidence of stroke and death: data from Swedish health registries. *Eur Heart J*. 2016. doi:10.1093/eurheartj/ehw087. By permission of Oxford University Press on behalf of the European Society of Cardiology.

AF is generally considered to progress from paroxysmal through persistent to 'permanent' forms, as a result of atrial electrical and structural remodelling. This process can be interrupted with early and more active approaches to AF detection followed by rhythm-reversion, and maintenance of sinus rhythm (SR), Prof Kuck believes [Nattel S et al. *Eur Heart J*. 2014]. The pulmonary veins (PV) have been identified as a primary initiating source of AF [Haissaguerre M et al. *N Engl J Med*. 1998]. The ESC Guidelines for AF ablation [Kirchhof P et al. *Eur Heart J*. 2016] state that the cornerstone for a successful procedure is to target PVs and/or PV antrum for electrical isolation. Circumferential PVI results in stable SR in a large proportion of patients for up to 5 years [Ouyang F et al. *Circulation*. 2010] and freedom from atrial tachyarrhythmias for up to 10 years [Heeger CH et al. *Circ Arrhythm Electrophysiol*. 2018. In press].

There are 2 approaches to PVI: radiofrequency catheter using heat in a focal point by point delivery guided by electroanatomical mapping and the cryoballoon approach using freezing inside a balloon with single step delivery, guided by fluoroscopy without mapping. Although efficacy outcomes are similar between the 2 approaches, the cryoballoon offers some advantages according to Prof Kuck: shorter procedure times, fewer serious adverse events, fewer cardiovascular rehospitalisations, lower rate of repeated ablations, and overall lower cost [Kuck KH et al. *N Engl J Med*. 2016; Chun JRK et al. *J Am Heart Assoc*. 2017].

Patients with persistent AF may need more than one ablation procedure [Tilz RR et al. *J Am Coll Cardiol*. 2012]. Past strategies included other approaches such as PVI plus linear lesions, PVI plus ablation of complex fractionated atrial electrograms (CFAE), or a combination of PVI plus linear lesions plus CFAE ablation. However, no reduction in the rate of recurrent AF has been demonstrated with PVI plus CFAE or PVI plus linear lesions in a randomised trial of 589 patients with persistent (follow up of 18 months) [Verma A et al. *N Engl J Med*. 2015].

Other approaches for treating persistent AF have therefore been evaluated, such as PVI plus ablation of focal sources and rotors, PVI plus isolation of left arterial appendage (LAA), PVI plus ablation of autonomic ganglia, and PVI plus isolation of the area of fibrosis. The latter is of interest as it has been independently associated with likelihood of recurrent arrhythmia [Marrouche NF et al. *JAMA*. 2014]. Finally, fibrotic areas have been successfully targeted with box isolation to reduce AF/atrial tachycardia [Kottkamp H et al. *J Cardiovasc Electrophysiol*. 2016]. However, none of these approaches have consistently proven to be successful in adding benefit over PVI alone, nor have they been shown to reduce hard endpoints in randomised clinical trials.

A logical approach to prevent AF progression may be represented by the maintenance of SR as vigourously and as early as possible. This is under investigation in two trials: CABANA, which compares ablation with AADs; and EAST, which evaluates rhythm control with ablation and AADs against guideline-mandated initial rate control, in patients presenting with their first episode of AF. CABANA is expected to complete in 2018; EAST in 2019.

Hybrid Approaches to Ablation of AF

The ideal AF ablation procedure should be minimally invasive, result in transmural lesions, involve the permanent isolation of the PVs, and offer the possibility of customising the treatment strategy. Laurent Pison, MD, PhD, FESC, Heart and Vascular Center, Maastricht UMC, Maastricht, The Netherlands, feels the hybrid strategy offers the best advantages for successful ablation. This approach combines the strengths and minimises the limitations of either surgical or catheter ablation alone by combining them. Prof Pison reviewed a few of the early procedures that led to the hybrid approach [Vroomen M and Pison L. *J Interv Card Electrophysiol*. 2016].

The improved Cox-Maze-procedure (Cox-Maze IV) has achieved good success rates in both paroxysmal and persistent AF over the long-term while being less invasive [Weimar T et al. *Circ Arrhythm Electrophysiol*. 2012]. A surgical approach involving a complete thoracoscopic PVI with ganglionic plexus ablation and LAA amputation is safe and effective for the treatment of lone AF. Freedom from AF was obtained in 77% of patients during a mean follow-up of 11.6 months [Yilmaz A et al. *Eur J Cardiothorac Surg*. 2010]. Interpretation of most surgical studies, however, is limited by inconsistent methodologies, incomplete follow-up and insufficient methods used for rhythm assessment (eg, telephone interviews).

Hybrid AF ablation is minimally invasive and results in durable lesions and high rates of chronic PVI even after long-term follow-up [Velagic V et al. *J Cardiovasc Electrophysiol*. 2016]. Only recently, practical guides to perform this procedure have been developed. Surgical and catheter ablation may be performed at the same time or as a 2-stage procedure, (electrophysiology study after surgery either during the same or a later hospital admission). Surgery involves a thoracoscopic approach (monolateral or bilateral thoracic, subxiphoidal, transabdominal transdiaphragmatic). Surgical epicardial ablation can be performed with cryoenergy or unipolar / bipolar radiofrequency energy. Compared with standard minimally invasive surgical approaches, the hybrid approach yields better results in long-standing persistent AF [La Meir M et al. *Int J Cardiol*. 2013]. Indeed, the hybrid procedure appears to offer the best of 2 techniques but more randomised trials will be needed like the HARTCAP-AF study, an ongoing prospective trial comparing hybrid ablation to catheter ablation alone.

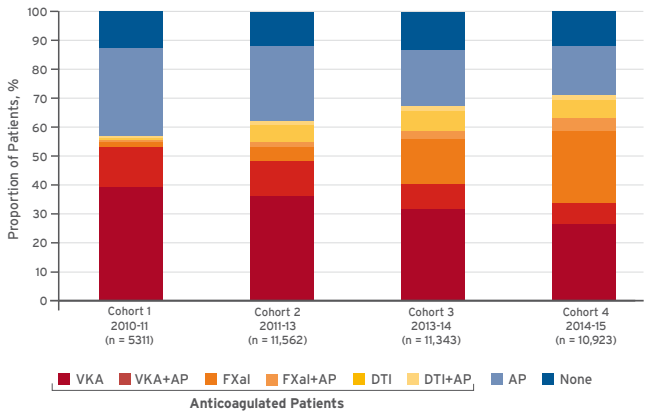
New Oral Anticoagulants

Reza Wakili, MD, West-German Heart and Vascular Center Essen, University Duisburg-Essen, Germany, believes there is strong cumulative evidence in the general population supporting the use of non-vitamin K antagonist (VKA) oral anticoagulants (NOAC) to treat AF that is comparable to the results from large randomised controlled trials (RCT).

Between 20% and 30% of all strokes are due to AF [Kirchhof P et al. *Eur Heart J*. 2016]. Between 1992 and 2010, ischaemic stroke rates among Medicare patients with AF decreased significantly in all demographic subpopulations in all age categories, coincident with increasing use of anticoagulation [Shroff GR et al. *J Am Heart Assoc*. 2014]. However, VKAs, such as warfarin, carry a high risk of bleeding, require routine monitoring of the INR, and present many food and drug interactions. More recently, NOACs targeting a single factor of the coagulation cascade (IIa: dabigatran, Xa: rivaroxaban, apixaban and edoxaban) have been developed, showing an overall favourable risk-benefit profile, with significant reductions in stroke, intracranial haemorrhage, and mortality with a similar risk of major bleeding as with warfarin, but with an increased risk of gastrointestinal (GI) bleeding [Ruff CT et al. *Lancet*. 2014; Ntaios G et al. *Stroke*. 2017].

If the benefits of NOACs are so evident, why do we need general population data? In clinical practice the patient populations and settings vary and those differences may affect observed benefits and risks. In the GARFIELD-AF observational study of general population data in 17,162 individuals, the use of rivaroxaban, dabigatran, and apixaban were associated with similar outcomes to those reported in RCTs [Bassand JP et al. *Eur Heart J*. 2016]. Most importantly, intracranial haemorrhage is significantly decreased with NOACs compared with VKAs in both RCTs and registry data. As a consequence of generally more favourable results with NOACs compared with VKAs, the pattern of OAC use is changed since the introduction of NOACs. Data from the registry showed that the use of VKAs and antiplatelet monotherapy declined and the use of factor Xa inhibitors and direct thrombin inhibitors for AF treatment increased (absolute increase ~15%) between 2010 and 2015 (Figure 2) [Camm AJ et al. *Heart*. 2017]. This was observed across all the CHA_2DS_2-VASc score subgroups.

Figure 2. Evolution of Antithrombotic Treatment in AF



AF, atrial fibrillation; AP, antiplatelet; DTI, direct thrombin inhibitors; FXaI, factor Xa inhibitors; VKA, vitamin K antagonists.

Patients at high risk of bleeding remain undertreated, however, and Prof Wakili believes there is a need for RCTs with NOACs for this cohort, as the evidence suggests that they benefit from NOAC treatment [Ruff CT et al. *Lancet*. 2014].

If bleeding risks are too high for anticoagulants to be used safely, another option is available to prevent thromboembolism related to AF. ESC guidelines state that LAA occlusion may be used for stroke prevention in patients with AF and contraindications for long-term OAC (eg, those with a previous life-threatening bleed without a reversible cause (class IIb, level of evidence B) [Kirchhof P et al. *Eur Heart J*. 2016]. However, the level of evidence for this recommendation remains low owing to the paucity of RCT data. In contrast, new data recently emerged for NOACs in the setting of AF and CAD, and more specifically after PCI [Cannon CP et al. *N Engl J Med*. 2017; Gibson CM et al. *N Engl J Med*. 2017]. Guidelines are being rewritten to recommend NOAC treatment for this patient group.

In conclusion, there is strong cumulative evidence from general population data and RCTs that NOACs are safer than and at least as effective as warfarin. However, GI bleeding remains an issue and more data is needed regarding elderly patients with end-stage kidney failure and AF-CAD patients.

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The editors would like to thank the many members of the ESC Congress 2017 presenting faculty who generously gave their time to ensure the accuracy and quality of the articles in this publication

Catheter Ablation of Atrial Fibrillation Improves Mortality and Disease Progression in Patients With Heart Failure

Written by **Maria Vinall**

Nassir F. Marrouche, MD, University of Utah, Salt Lake City, Utah, USA, presented the CASTLE-AF trial [NCT00643188], which showed that catheter ablation of atrial fibrillation (AF) in patients with heart failure (HF) is associated with improved all-cause mortality, cardiovascular mortality, and fewer admissions for worsening HF and hospitalisation, compared with conventional standard of care treatment.

Patients with HF and AF have an increased risk of morbidity and mortality, compared with HF patients with no AF. The CASTLE-AF trial was designed to study the effectiveness of catheter ablation in improving mortality as well as HF progression in patients with HF and AF compared with standard care.

CASTLE-AF was a prospective, multicentre (31 sites; 9 countries), randomised, controlled trial. A total of 363 patients were enrolled (179 received ablation; 184 conventional therapy). The study included patients with symptomatic paroxysmal or persistent AF, left ventricular ejection fraction (LVEF) ≤ 35%, and NYHA class ≥ II who had failed or shown intolerance to ≥ 1 antiarrhythmic drug (AAD) or were unwilling to take an AAD, and who had a cardioverter defibrillator with automatic daily home-monitoring capabilities already implanted. The primary endpoint was the composite of all-cause mortality and unplanned hospitalisation for worsening HF. Conventional treatment was according to the ACC/AHA/ESC 2006 Guidelines for the Management of Patients With Atrial Fibrillation [Fuster V et al. *Circulation*. 2006]. Efforts were made to maintain sinus rhythm. Anticoagulation was initiated and maintained throughout the study. An INR between 2.0 and 3.0 was maintained. The ablation protocol consisted of pulmonary vein isolation with additional lesions at the discretion of operator and repeat ablation after a blanking period.

Participants were a mean age of 64 years; median LVEF was about 32%; 86.1% were men. Most subjects had persistent AF (70% in the ablation group; 65% in the conventional group). More than half of the subjects were NYHA class II (58% vs 61%, ablation and conventional group), about 28% were class III, and 1% to 2% were class IV. Implantable cardioverter defibrillators (ICD) were present in 73% of patients in the ablation group and 72% in the conventional group. The remaining patients had a cardiac resynchronisation therapy defibrillator (CRT-D) device. More than 90% of patients were being treated with either an angiotensin-converting enzyme inhibitor or angiotensin II receptor blocker, β-blocker, diuretic, or oral anticoagulant.

The absolute change in LVEF from baseline was significantly higher in the ablation arm versus conventional care at 12, 36, and 60 months. The primary endpoint, a composite of all-cause mortality and unplanned hospitalisation for worsening HF, was significantly improved for the ablation group (risk reduction [RR] compared with conventional treatment, 38%; $P = .007$). All-cause mortality was significantly reduced in the ablation group (RR, 47%; $P = .011$), as were admissions for worsening HF (RR, 44%; $P = .004$), cardiovascular mortality risk (RR, 51%; $P = .009$), and cardiovascular hospitalisation (RR, 28%; $P = .041$).

In this study, catheter ablation of AF was associated with improved mortality and HF hospitalisation when compared with conventional treatment in patients with HF and AF.

Multilevel Educational Intervention Significantly Increases the Proportion of Atrial Fibrillation Patients Treated With Anticoagulation

Written by **Phil Vinall**

Oral anticoagulation (OAC) is underused in patients with atrial fibrillation (AF). Christopher B. Granger, MD, Duke University Medical Center, Durham, North Carolina, USA, presented data from the IMPACT-AF trial

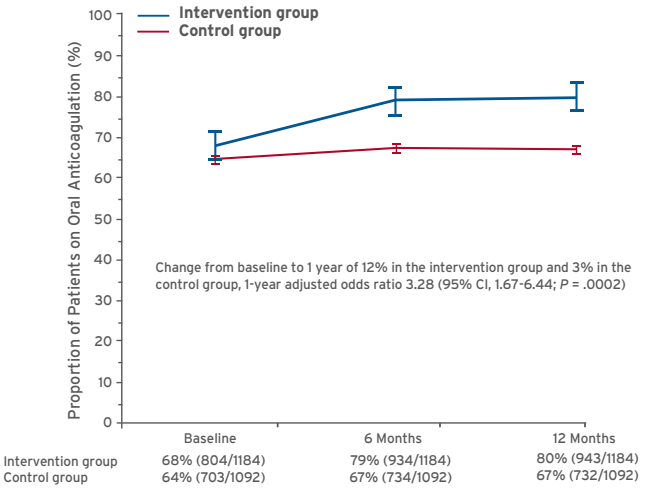
[NCT02082548] indicating that a customised, multilevel educational intervention, with appropriate monitoring and follow-up, increases the use of OAC in patients with AF, compared with usual care.

IMPACT-AF [Vinereanu D et al. *Lancet*. 2017] is a prospective, cluster-randomised, controlled trial in adult patients with AF, a CHA_2DS_2-VASc score ≥ 2, and no absolute contraindication for OAC. Clusters (48 sites; 5 middle-income countries) were randomised in a 1:1 ratio to receive a quality-improvement educational intervention (interventional group) or usual care (control group). The educational component targeted the patient and their family as well as health care providers. A monitoring and feedback component was developed to identify patients not being treated with OAC and review opportunities for them to start/restart medication and to identify patients were are at high risk for not staying on medications and intervene to prevent discontinuation.

The diagnosis of AF was confirmed by a 12-lead ECG and/or rhythm strip, or reports of 2 ECGs 2 weeks apart showing AF. Patients with a mechanical prosthetic valve were excluded as were those who were clinically unstable, had a life expectancy of < 6 months, were unable to provide consent or to have 1 year of follow-up, or had an absolute contraindication to OAC. The primary outcome was the change in the proportion of patients treated with OAC from baseline to 1 year. Secondary clinical outcomes were death, stroke, and bleeding.

A total of 2,281 participants (1,187 in the intervention group; 1,094 controls) were enrolled. Patients were a mean age of 70 years, 47% were women, and the mean CHA_2DS_2-VASc score was 3.6. At baseline, 34% of patients were not on an OAC; 78% of these were on antiplatelet agents. The 3 main reasons for not being on baseline anticoagulants were patient preference or refusal (26%), physician determination that the risks outweighed the benefits (15%), and concomitant antiplatelet therapy (13%). At 12 months there was a 9.1% absolute greater increase in OAC use in the intervention group (Figure 1).

Figure 1. Primary Outcome: OAC Status Over 1 Year



Reprinted from *Lancet*. Vinereanu D et al. A multifaceted intervention to improve treatment with oral anticoagulants in atrial fibrillation (IMPACT-AF): an international, cluster-randomised trial. doi: 10.1016/S0140-6736(17)32165-7. Copyright 2017. With permission from Elsevier.

The results were consistent across subgroups and particularly important for patients who were on aspirin at baseline (OR, 5.07; 95% CI, 2.09 to 12.28; *P* = .01). Among patients who were not on OAC at baseline, 48% of those in the intervention group were on OAC at 1 year, compared with 18% in the control group (OR, 4.60; 95% CI, 2.20 to 9.63; *P* < .0001). There were no differences in the secondary outcomes of mortality, major bleeding, clinical relevant nonmajor bleeding, or the composite of stroke, systemic embolism, and major bleeding. A nominally significant decrease was noted in stroke (HR/OR, 0.48; 95% CI, 0.23 to 0.99; *P* = .043); however, the study was not powered for this outcome.

In this study, a customised, multifaceted, and multilevel intervention involving education of patients with AF and their providers, with regular monitoring and feedback, resulted in a significant increase in the proportion of patients treated with OACs and a favourable trend in stroke reduction.

Atrial Fibrillation Screening Using a Smartphone App: Results of the AFinder Program

Written by **Brian Hoyle**

A study of over 10,000 people in Hong Kong has indicated the feasibility of a smartphone application (app) that screens for atrial fibrillation (AF) in the general community. However, the app's diagnostic performance needs improvement before routine use is possible.

The AFinder program results were presented by Ngai-Yin Chan, MD, Princess Margaret Hospital, Hong Kong.

AF is a disease that is suitable for screening, and conventional medical screening is recommended for people aged ≥ 65 years. Recent studies have indicated the potential value of a smartphone app that provides electrocardiogram data in the broader community screening of AF [Lowres N et al. *Thromb Haemost*. 2014; Svennberg E et al. *Circulation*. 2015; Chan PH et al. *J Am Health Assoc*. 2016; Chan NY et al. *Heart*. 2017].

The AFinder program investigated the feasibility of a community-based screening program in over 10,000 citizens of Hong Kong aged ≥ 50 years. The primary outcomes were the number needed to screen (NNS) to diagnose one case of AF and the NNS for one appropriately treated, newly diagnosed AF. Secondary outcomes were the prevalence of previously known but undertreated AF and the diagnostic performance of the smartphone app.

Trained layperson volunteers assisted in 118 community AF screening sessions held at 108 community centres in Hong Kong from November 2015 to September 2016. Information concerning AF history and symptoms, subsequent medical treatments, compliance, and medical conditions were sought through base-line questionnaires completed at the time of screening and follow-up 9 months later.

Of the 11,574 Hong Kong residents who were screened, interpretable data were available for 10,735 (92.8%). Of these, 244 (2.3%) had AF, with 74 cases (0.69%) being newly diagnosed. The NNS for one newly diagnosed AF was 145.

Of the 74 newly diagnosed cases, oral anticoagulation treatment was indicated in 72. Forty-seven of the 74 newly diagnosed people sought medical treatment. Of these, 17 participants received oral anticoagulation and 30 participants did not (among this latter group, 17 were prescribed aspirin, 1 was given clopidogrel and 12 nothing). The NNS for one case of newly diagnosed AF who subsequently received oral anticoagulation was 671.

People with newly diagnosed AF were older, less likely to have had a stroke, and less likely to have peripheral artery disease (Table 1). Forty-eight percent of the newly diagnosed cases were asymptomatic.

Table 1. Characteristics of Newly Diagnosed AF

	All Participants With AF (n = 244)	Newly Diagnosed AF (n = 74)	Known AF (n = 133)	*P* value
Age	79.5±7.9	81.1±7.3	78.1±8.1	.007
Sex (F), n(%)	172 (70.5)	51 (68.9)	97 (72.9)	.542
Medical conditions				
Heart failure, n(%)	17 (7.0)	6 (8.1)	9 (6.8)	.738
Hypertension, n(%)	172 (70.5)	50 (67.6)	95 (71.4)	.569
Diabetes, n(%)	63 (25.8)	19 (25.7)	34 (25.6)	.973
Stroke, n(%)	40 (16.4)	9 (12.2)	22 (16.5)	.0004
Coronary artery disease, n(%)	25 (10.2)	7 (9.5)	12 (9.0)	.920
Peripheral artery disease, n(%)	8 (3.3)	0	7 (5.3)	.045

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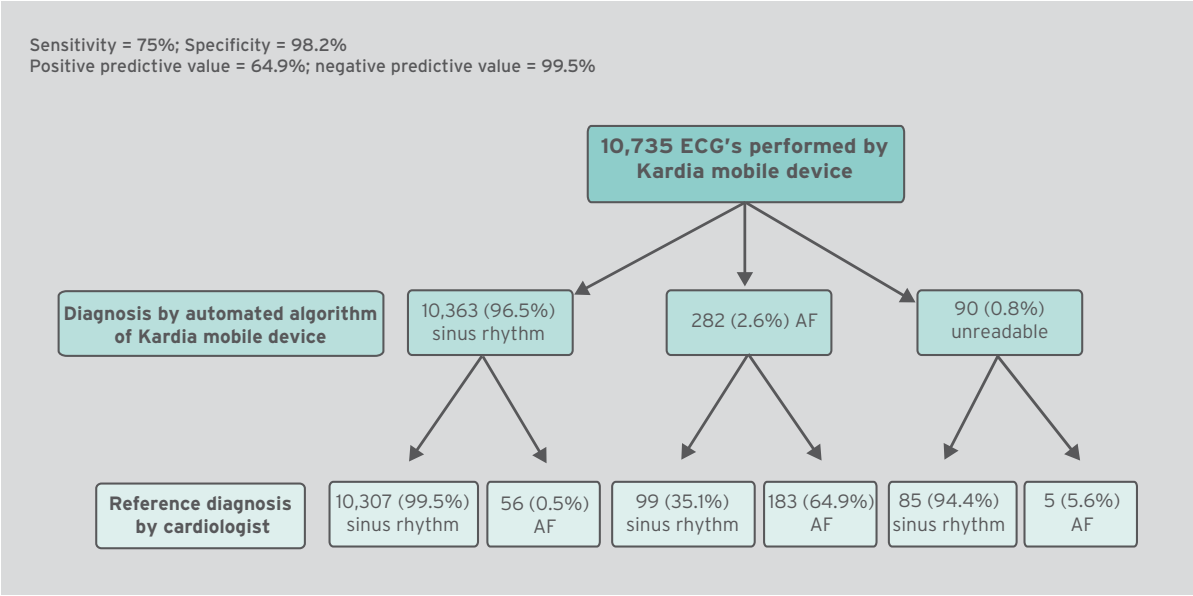
Appropriate treatment with oral anticoagulation therapies of newly diagnosed and known AF patients was unsatisfactory, according to Dr. Chan, with respective rates of 22.2% and 33.8%. Among the 133 patients with known AF, the comparative analysis of those who were appropriately treated and undertreated revealed significant differences in the prevalence of stroke (31.1% vs 9.1%; *P* = .001) and peripheral artery disease (11.1% vs 2.3%; *P* = .033). Of the 88 patients with known AF, not receiving oral anticoagulation, one-quarter was taking an antiplatelet drug (which was aspirin in all but one patient).

Article continued on page 10.

The diagnostic performance of the smartphone app was mixed. Specificity and negative predictive value were excellent, while sensitivity and positive predictive value were suboptimal (Figure 1).

While the smartphone app seems feasible for AF screening in the general community with a newly diagnosed NNS similar to other programs, deficiencies that need to be corrected include aspects of the diagnostic performance (sensitivity and positive predictive value) and post-screening efforts to increase the rates of delivery of the appropriate treatment for those with newly diagnosed AF or existing AF that is undertreated.

Figure 1. Diagnostic Performance of the Automated Detection Algorithm for AF



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Results From RE-DUAL PCI

Written by **Nicola Parry**

Christopher P. Cannon, MD, Harvard Medical School, Baim Institute for Clinical Research, Boston, Massachusetts, USA, reported data from the RE-DUAL PCI trial, showing that dual antithrombotic therapy with dabigatran and a $P2Y_{12}$ inhibitor reduced bleeding when compared to triple therapy with warfarin in patients with atrial fibrillation (AF) undergoing percutaneous coronary intervention (PCI).

According to Dr Cannon, although triple antithrombotic therapy comprising warfarin plus dual antiplatelet therapy is standard care after PCI for patients with AF, this triple combination leaves these individuals at high risk for bleeding events. The WOEST trial suggested that removing aspirin from the triple-therapy regimen could be done safely [Dewilde WJ et al. *Lancet*. 2013]. Dr Cannon and colleagues conducted the RE-DUAL PCI trial to investigate the efficacy and safety of dual therapy with dabigatran and a $P2Y_{12}$ inhibitor in AF patients after PCI [Cannon CP et al. *N Engl J Med*. 2017].

This multicentre, open-label trial randomised 2,725 patients with AF who had undergone PCI to receive either triple therapy (warfarin, plus a $P2Y_{12}$ inhibitor [clopidogrel or ticagrelor] and aspirin) or dual therapy (dabigatran [110 mg or 150 mg BID] plus a $P2Y_{12}$ inhibitor [clopidogrel or ticagrelor]).

The study's primary endpoint was time to first ISTH major or clinically relevant nonmajor bleeding (CRNM).

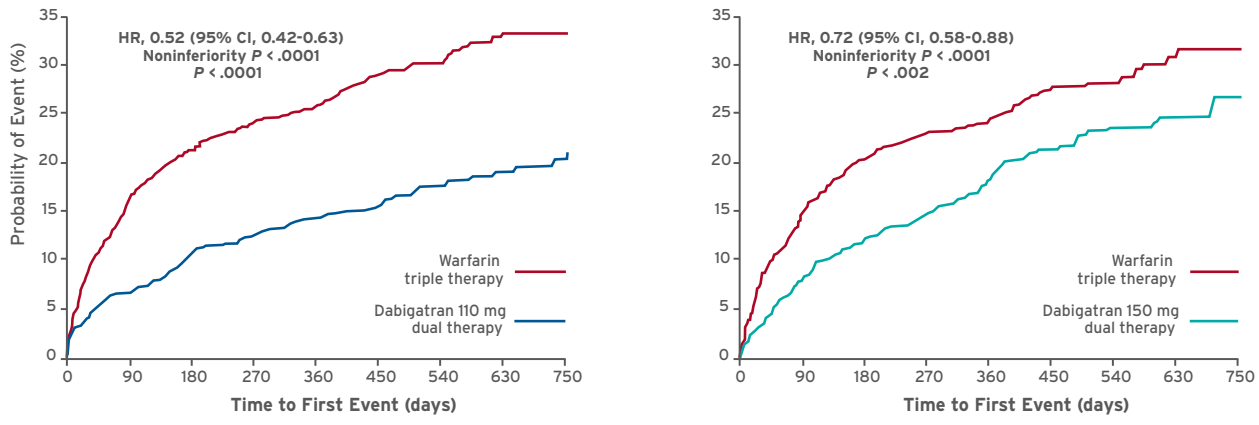
Compared with the triple-therapy regimen, treatment with dabigatran 110 mg with a $P2Y_{12}$ inhibitor reduced by almost 50% the incidence of major or CRNM bleeds at 14 months (15.4% vs 26.9%; HR, 0.52; 95% CI, 0.42 to 0.63, $P < .001$ for noninferiority, $P < .001$ for superiority; Figure 1). Dr Cannon noted that this was consistent with an absolute risk reduction (ARR) of 11.5%. Dual therapy using dabigatran 150 mg was also associated with fewer bleeds (20.2% vs 25.7%; HR, 0.72; 95% CI, 0.58 to 0.88; $P < .001$ for noninferiority, $P = .002$ for superiority; Figure 1), representing a 5.5% ARR.

Compared with the triple-therapy regimen, both dual-therapy groups also had lower rates of intracranial haemorrhage, with a 0.7% ARR (HR, 0.3; 95% CI, 0.08 to 1.07; $P = .064$) using dabigatran 110 mg, and a 0.9% ARR (HR, 0.12; 95% CI, 0.02 to 0.98; $P = .047$) using dabigatran 150 mg.

The investigators also performed a prespecified analysis of thrombotic events that occurred during the trial, evaluating the effect of dual versus triple therapy on the incidence of a composite of death, thromboembolic events (myocardial infarction, stroke, or systemic embolism), or unplanned revascularisation. Combining the 2 dabigatran dose groups, they found that dual therapy met the threshold for noninferiority for the composite endpoint (incidence, 13.7% vs 13.4%; HR, 1.04; 95% CI, 0.84 to 1.29; $P = .005$ for noninferiority). In the patients treated with 110-mg dual therapy, the incidence of death, thromboembolic events, or unplanned revascularisation was 15.2% versus 13.4% in the triple-therapy group (HR, 1.13; 95% CI, 0.90 to 1.43; $P = .30$). In the patients treated with 150-mg dual therapy, the incidence was 11.8% versus 12.8% in the triple-therapy group (HR, 0.89; 95% CI, 0.67 to 1.19; $P = .44$).

Dr Cannon concluded that these dabigatran dual-therapy regimens, using doses approved worldwide for stroke prevention, offer clinicians 2 additional options for managing AF patients following PCI.

Figure 1. Rates of Major Bleeding or Clinically Relevant Nonmajor Bleeding in RE-DUAL



Anticoagulation for Cardioversion of Atrial Fibrillation

Written by **Maria Vinall**

During this special update session, experts in the field discussed some of the areas of uncertainty in the use of anticoagulation for cardioversion of atrial fibrillation (AF).

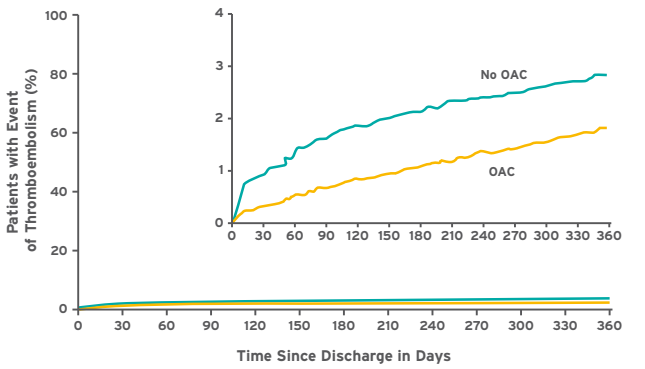
Paulus Kirchhof, MD, Institute of Cardiovascular Sciences, University of Birmingham, Birmingham, United Kingdom, opened by suggesting that there is growing evidence to support early cardioversion with novel oral anticoagulants, including in anticoagulation-naïve patients. This includes the results of the X-VeRT [Cappato R et al. *Eur Heart J*. 2014] and ENSURE [Goette A et al. *Lancet*. 2016] studies, as well as data from the EMANATE study, which was presented at the 2017 ESC Congress.

The aim of cardioversion, similar to other rhythm-control therapy options, is to improve symptoms. Whether early rhythm-control therapy has benefits beyond earlier restoration of sinus rhythm and improvement of symptoms is currently being tested [Kirchoff P et al. *Am Heart J*. 2013], but recent reports are encouraging. Cardioversion can be performed electrically or pharmacologically. Electrical cardioversion is more effective, but requires sedation. A combination of biphasic shocks, paddle electrodes, and an anterior-posterior electrode position promotes success [Kirchoff P et al. *Lancet*. 2002; Kirchhof P et al. *Eur Heart J*. 2005]. While quicker and more effective, electrical conversion is also accompanied by an increased risk of stroke. This can be offset with oral anticoagulation.

Pharmacological cardioversion with antiarrhythmic drugs (AADs), although less effective (from ~50% to ~20% depending on duration of AF) and slower than electrical cardioversion, offers a therapeutic alternative especially in patients with shorter a duration of AF. Short-term treatment with AADs after cardioversion is less effective than is long-term treatment, but can prevent most recurrences of AF [Kirchhof P et al. *Lancet*. 2012].

Patients undergoing cardioversion without anticoagulation are at high risk of stroke [Hansen ML. *Europace*. 2015]. Oral anticoagulation with vitamin K antagonists or non-vitamin K antagonist (VKA) oral anticoagulants (NOACs) result in a marked reduction of ischaemic strokes in patients undergoing cardioversion [Hansen ML et al. *Europace*. 2015].

Figure 1. Thromboembolism After Discharge for DC Cardioversion of AF



AF, atrial fibrillation; DC, direct current; OAC, oral anticoagulation.

Reprinted from Hansen ML et al. Thromboembolic risk in 16,274 atrial fibrillation patients undergoing direct current cardioversion with and without oral anticoagulant therapy. *Europace*. 2015; https://doi.org/10.1093/europace/euu189. By permission of Oxford University Press on behalf of the European Society of Cardiology.

The ESC recommends the use anticoagulants for at least 3 weeks before cardioversion, in patients with a transoesophageal echocardiography (TOE) detected thrombus, and long-term after cardioversion to reduce stroke risk. NOACs are at least as safe as VKA for stroke prevention in patients undergoing cardioversion, and may even reduce stroke risk relative to VKA therapy based on recent randomised trials.

Riccardo Cappato, MD, Humanitas University, Electrophysiology & Arrhythmia Center, Humanitas Research Institute, Milan, Italy, discussed some of the practical issues when anticoagulating AF patients undergoing cardioversion.

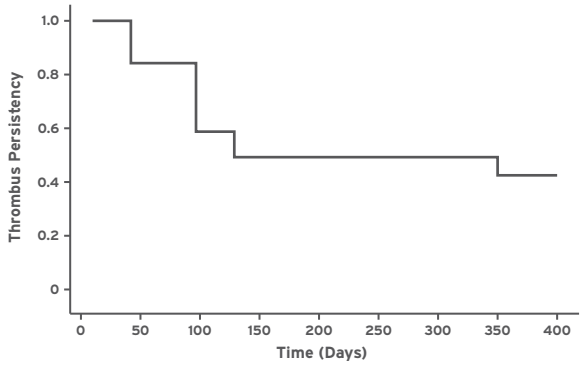
When deciding to perform acute or elective cardioversion, the decision is guided by the timing or symptoms of AF. The choice of early or delayed elective cardioversion will impact the number of patients effectively cardioverted and the probability of restoration and maintenance of sinus rhythm. Data regarding the choice of pharmacological or electrical cardioversion is not clear cut. The decision is based on the natural course of AF and comorbidities of the patient, as well as logistics (availability of direct current shock system, tradition, costs, setting, early vs delayed). The earlier the decision the better.

Acute or early delayed cardioversion AF patients may be pretreated with either intravenous or oral AADs. Pretreatment with AADs is believed to increase the likelihood of restoration of sinus rhythm and helps prevent recurrent AF although this is not supported by available systematic data. Post-treatment AADs may improve maintenance of sinus rhythm, but studies are not definitive due to potential confounding.

Anticoagulation therapy in acute cardioversion may reduce the risk of thromboembolic events in patients with stroke risk factors (heart failure, hypertension, diabetes, prior stroke, female sex, or age above 65 to 75 years) [Airaksinen KJ et al. *J Atr Fibrillation*. 2013]. However, this therapy is normally not required in low-risk patients. In elective cardioversion, although the data is not clear, it may be beneficial. Selection of the type of cardioversion (acute vs elective; pharmacological vs electrical; early vs delayed) is subject to various factors and may influence acute and long-term success rates.

Francisco Marín, MD, Department of Cardiology, Hospital Universitario Virgen de la Arrixaca, Murcia, Spain, discussed how to deal with left atrial appendage (LAA) clots when performing nonvalvular AF, which occurs in between 0.5% to 14% of patients. Patients with LA thrombus are at an increased risk for embolic stroke or death (Figure 2) [Bernhardt P et al. *Am J Cardiol*. 2004].

Figure 2. Thrombus Persistence Over 12-Months



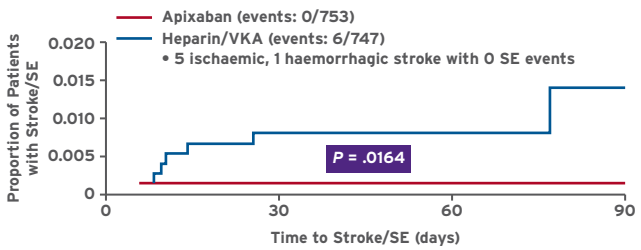
Reprinted from Bernhardt P et al. Fate of left atrial thrombi in patients with atrial fibrillation determined by transesophageal echocardiography and cerebral magnetic resonance imaging. *Am J Cardiol*. 2004;doi: 10.1016/J.AMJCARD.2004.06.010. Reproduced with permission from Excerpta Medica.

ESC Guidelines [Kirchhof P et al. *Europace*. 2016] recommend performing a TOE prior to cardioversion and anticoagulation when a thrombus is detected, with subsequent delay of cardioversion for 3 to 4 weeks. A follow-up TOE is warranted. Anticoagulation is associated with thrombus resolution in > 80% of patients [Collins LJ et al. *Circulation*. 1995; Jaber WA et al. *Am Heart J*. 2000]. In a recently published study, prevalence of TOE-detected LAA thrombus was similar with NOACs and VKAs and thrombus resolution was obtained in 50% of cases with anticoagulation. Age, LAA hypocontractility and left ventricular ejection fraction were found to be independently associated with the occurrence of LAA thrombus [Da Costa A et al. *Am Heart J*. 2017].

Michael D. Ezekowitz, MBChB, DPhil, MA, Sidney Kimmel Medical School, Thomas Jefferson University, Lankenau and Bryn Mawr hospitals, Philadelphia, PA, USA, spoke about cardioversion in the modern era. The availability of NOACs which have a rapid onset of action, (hours) is changing medical practice. Post hoc analyses of cardioversions in all the pivotal trials that lead to the approval of the NOACs found low event rates; for example the first and largest, the RE-LY study, showed that dabigatran is a reasonable alternative to warfarin in cardioversion patients with or without TOE guidance [Nagarakanti R et al. *Circulation*. 2011].

In Dr Ezekowitz's opinion, a limitation with RE-LY, and similar studies, is that study subjects were on prolonged periods of anticoagulation therapy prior to cardioversion. An objective of prospective cardioversion clinical trials comparing NOACs and VKAs was to expedite cardioversion and evaluate their efficacy in preventing strokes and systemic embolisms while maintaining an acceptable level of bleeding. These trials suffer from the limitation of being underpowered; low events rates due to effective anticoagulation require a trial size of between 25,000 to 45,000 patients to be adequately powered, which are not feasible, so the studies is generally underpowered. Three recent cardioversion trials (EMANATE, X-VeRt and ENSURE-AF) have similar designs, baseline demographics, outcomes, and endpoints. Results from all 3 show that NOACs are an effective and safe alternative to treatment for patients undergoing electrical cardioversion for nonvalvular AF and they may allow cardioversion to be performed promptly following the start of anticoagulation. The primary outcome from EMANATE is shown in Figure 3.

Figure 3. EMANATE: Stroke/Systemic Embolic Outcomes



VKA, vitamin K antagonist; SE, systemic embolism.

Reproduced with permission from MD Ezekowitz, , MBChB, DPhil, MA.

All the speakers agreed that the use of anti-coagulants, preferably NOACs is necessary in patients undergoing cardioversion, to resolve the risks associated with thrombus and possible stroke.

Implantable Cardioverter Defibrillators: Four Decades of Evidence

Written by **Brian Hoyle**

The first automatic implantable cardioverter defibrillator (ICD), implanted first in the early 1980s, has evolved and has become an indispensable life-saving facet of cardiac care for patients with ischaemic and nonischaemic cardiomyopathy (NICM) and other conditions.

However, the DANISH study [Køber L et al. *N Engl J Med*. 2016] questioned whether ICDs are life-saving in NICM. As explained by Luigi Di Biase MD, PhD, Albert Einstein College of Medicine at Montefiore Hospital, New York, New York, USA. DANISH, a randomised controlled trial, assigned 1116 patients with NICM, symptomatic systolic heart failure with an left ventricular ejection fraction (LVEF) ≤35% to receive an ICD (n = 556) or usual clinical care (n = 560). After about 68 months of follow-up, mortality from any cause was similar in the ICD and control groups (21.6% vs 23.4%).

Dr Di Biase put the DANISH results into the context of decades of data and the number of patients needed to treat. Evidence for benefit from ICD therapy in ICM patients come from the MADIT I trial of 196 patients, MUSTT involving 351 patients with coronary artery disease (CAD), the MADIT II trial of 1,232 patients, and the SCD-HeFT trial of 1,676 patients.

Before DANISH, evidence for the benefit of ICD therapy in NICM was not definitive and had come from CAT involving 104 patients, AMIOVIRT which included 103 patients, the DEFINITE trial involving 458 patients, SCD-HeFT, the COMPANION trial, and two meta analyses [Desai AS. *JAMA*. 2004; Theuns D. *Europace*. 2010].

The total weight of evidence still favours a survival benefit for ICDs in the primary prevention of death in patients with NICM, according to Dr Di Biase. The recent DANISH trial results will likely not change the current guidelines [Romero J, Di Biase L. *Europace*. In press].

Another contemporary issue concerning ICDs is the identification of primary prevention patients who will most benefit from the device. The present class I indication of primary prevention ICD therapy (LVEF ≤35%) is limited in predicting the likelihood of sudden cardiac death (SCD). Furthermore, the majority of SCDs occur in patients with LVEF exceeding 35%. The risk of SCD is highest in the first month following myocardial infarction (MI). This risk is reduced in patients with an ICD. Ischaemic patients with ventricular tachycardia are markedly more likely to experience cardiovascular death or SCD versus those with ischaemia alone or ventricular tachycardia alone [Harkness JR et al. *Am J Cardiol*. 2011].

Individual risk markers cannot identify patients effectively who might benefit more from an ICD. The best solution, according to Alon Barsheshet, MD, Rabin Medical Center and Tel-Aviv University, Tel-Aviv, Israel, is use of risk stratification algorithms.

Various markers to identify high risk of SCD are still under evaluation including: biomarkers; LVEF; electrocardiogram data on depolarisation, repolarisation, autonomic measurement, and nonsustained ventricular tachycardia; electrophysiologic testing; myocardial scar burden; and genetic testing.

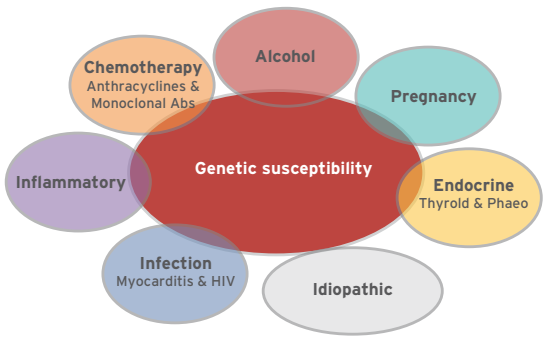
The wearable cardioverter defibrillator, may help protect patients in the vulnerable period soon after MI before an ICD is indicated [Epstein AE et al. *J Am Coll Cardiol*. 2013; Kutyifa V et al. *Circulation*. 2015]; it can be used to identify patients who could benefit from implantation of a permanent ICD [Kutyifa V et al. *Circulation*. 2015].

Scoring-related evaluation must consider time from MI. The scoring needs to consider that many of these patients are older and have other comorbidities contributing to death by other mechanisms. The competing risks of nonarrhythmia comorbidities can affect the benefit of ICD. One developed risk stratification score features 5 risk factors: NYHA functional status > II, atrial fibrillation, QRS complex > 120 ms, age > 70 years, and blood urea nitrogen level > 26 mg/dL. The scoring system allows patients at higher risk to be identified up to 8 years after ICD implantation [Barsheshet A et al. *J Am Coll Cardiol*. 2012]. The number needed to treat to save one life is 6 in patients with low- and intermediate-risk of death as classified by this score.

In NICM, the presence in an electrocardiogram of additional spikes in the QRS complex fragmented QRS and of beat-to-beat variation in T-wave amplitude can identify patients at high risk [Goldberger JJ et al. *J Am Coll Cardiol*. 2014; Halliday BP et al. *Circulation*. May 2017]. Another potentially useful target is myocardial fibrosis, a strong predictor of death [Gulati A et al. *JAMA*. 2013; Halliday BP et al. *Circulation*. July 2017].

Mutations in specific genes appear to heighten the risk of SCD however, more data are required before DNA variants can be used by clinicians as reliable risk indicators for SCD. This genetic susceptibility is likely influenced by a variety of factors (Figure 1) [Halliday BP et al. *Circulation*. July 2017].

Figure 1. Influences on Genetic Susceptibility to Cardiomyopathy and Sudden Cardiac Death



Source: Halliday BP et al. *Circulation*. 2017;136:215-231.

So, while LVEF remains the only predictor of SCD that has been validated in RCTs, it has some limitations. Improved methodologies to target the highest risk patients for ICD implant is a must and should be a dynamic process.

Identifying the benefits and risks of ICD therapy is necessary, but, according to Brian Olshansky, MD, University of Iowa, Des Moines, Iowa, USA, critically important is quality of life (QOL). ICD implantation both improves, and challenges, the QOL of an ICD recipient (Table 1). Concerns about poor QOL could deter recommendations for or use of an ICD implant.

Table 1. Quality of Life Components Related to ICD Implantation

Positives of ICDs	Negatives of ICDs
Lifesaving	Bodily image
Protection	Restrictions
	Unexpected, painful shocks
	Tied to the healthcare system

QOL covers a broad range of subjectively evaluated mental and physical aspects of life. Several dozen tools to measure QOL exist and the best to use for ICD patients is uncertain. The widely used 36-Item Short Form Survey (SF-36) questionnaire, a good benchmark of QOL, can vary by pre-implant personality, anxiety, depression, age, comorbidities, sex, social support, cultural beliefs and ICD indication among other issues. QOL can change with age and with life circumstances. A patient's attitude towards their ICD can change for better or worse [Mark DB et al. *N Engl J Med*. 2008; Perini AP et al. *Am Heart J*. 2017].

Data from primary prevention and secondary prevention trials have shown that for most ICD patients, QOL is on par with those who do not receive ICDs. Most data, however, show that frequent ICD shocks adversely affect QOL (especially if there 5 or more) [Sears SF Jr, Conti JB. *Heart*. 2002].

From the INTRINSIC RV Trial [Gopinathannair R. *J Interv Card Electrophysiol*. 2017], researchers found: 1) QOL improves over time post-ICD implant; 2) women started with lower QOL but improved more over time than men; 3) no difference in QOL with or without ICD shocks; and 4) those under age 50 scored worse at baseline but improved the most over time.

Implantation of an ICD in paediatric age patients is a concern; QOL scores are lower than even chronically ill children. An ICD can be a big blow to a child leading to avoidance of activities in up to 85%, especially for females [Sears SF et al. *Am J Cardiol*. 2011]. However, children may deal with their new ICD reality better than parents think. ICD implantation now does not necessarily mean restriction as even competitive athletes can and are now participating in sports [Lampert R et al. *Circulation*. 2013].

QOL may also depend on the type of ICD implanted (subcutaneous vs transvenous and single chamber vs resynchronization). It is also important to recognize that the ICD can affect more than just the patient; it can affect the patient's partner as well [Dougherty CM *J. Behav Med*. 2016].

European Guidelines recommend a discussion of QOL issues before ICD implant and during disease progression in all patients. Additionally, after ICD implantation, assessment of psychological status and treatment of distress is recommended in patients with recurrent inappropriate shocks [Priori SG. *Eur Heart J*. 2015].

For some, ICD implantation leads to diminished QOL. Discussions between patients and their doctor before, and at select times after implantation is strongly recommended to assuage future concerns. This can give patients, their partners, and their family a proper perspective and provides realistic expectations to ensure the happiest outcomes.

Advances in Heart Failure Devices

Written by **Nicola Parry**

Sudden cardiac death (SCD) is responsible for the deaths of 325,000 individuals each year, said Valentina Kutyifa, MD, PhD, University of Rochester Medical Center, Rochester, New York, USA. However, since the 1990s, significant medical advances have led to improved medical therapies, including drugs such as eplerenone and angiotensin receptor-neprilysin inhibitors that have reduced the risk for cardiovascular (CV) death and SCD. The introduction of implantable cardioverter-defibrillators (ICDs) and cardiac resynchronisation therapy devices (CRT-Ds) has further shaped the landscape of SCD prevention. Importantly, CRT-Ds have significantly improved rates of heart failure (HF) hospitalisations and survival, and reduced the risk for ventricular tachycardia (VT) and ventricular fibrillation (VF), thereby contributing to the decline of SCD in HF in recent decades [Shen L et al. *N Engl J Med*. 2017].

In a symposium on ICDs and CRT-Ds, speakers shared data from studies investigating use of these devices in specific patient populations, and highlighted new trials that may guide future developments in this setting.

Device Implantation in DCM

According to Georg Wolff, University Hospital Düsseldorf, Düsseldorf, Germany, although ICD therapy is used for primary prevention in patients with HF due to dilated cardiomyopathy (DCM), the DANISH trial showed that prophylactic ICD implantation was not associated with significant improvement in all-cause mortality compared with usual clinical care in that population [Køber L et al. *N Engl J Med*. 2016].

He reported findings from an updated meta-analysis of 5 randomised controlled trials including 2,992 patients which re-examined the benefit of ICD therapy in this setting [Wolff G et al. *Clin Res Cardiol*. 2017]. The data showed that ICD device therapy significantly reduced patient mortality compared with usual clinical care (OR, 0.77; 95% CI, 0.64 to 0.93; *P* = .006). It also significantly reduced SCD (OR, 0.43; 95% CI, 0.27 to 0.69; *P* = .0004), said Dr Wolff, but had no significant reduction in CV death or noncardiac death compared with usual clinical care.

To rule out any influence of amiodarone therapy on all-cause mortality, Dr Wolff and colleagues performed a stratified analysis to control for any potential confounding effect of the drug. They found that amiodarone therapy did not affect the overall results, and ICD therapy still provided a significant benefit over usual clinical care.

These findings demonstrate that ICD therapy confers a survival benefit in the primary prevention setting, reducing SCD, said Dr Wolff. He explained that the results of the DANISH trial suggest an increase in the number-needed-to-treat to prevent any death in patients with ICDs compared with guideline-directed therapy.

Dr Wolff concluded that ICD therapy should therefore remain the standard therapy for primary prevention of SCD in DCM until new data allow clinicians to use risk stratification methods to customise treatment recommendations according to patient characteristics.

Device Implantation in Elderly Patients

ICD and CRT-D implantation is also effective in preventing SCD in elderly patients, and current guidelines recommend that clinicians should consider this treatment in patients with an estimated survival of at least 1 year.

However, Ines Aguiar-Ricardo, MD, University of Lisbon, Lisbon, Portugal, noted that because the guidelines do not specify any age limits for this therapy, clinicians face challenging decisions about whether to implant ICDs in elderly patients, especially because of patients' diminished life expectancy and the frequent presence of associated comorbid conditions.

Because differences in device generator longevity vary according to manufacturer [Alam MB et al. *Europace*. 2014], Dr Aguiar-Ricardo and colleagues conducted a retrospective single-centre study to investigate whether the expected survival rate in elderly patients should influence clinicians' selection of a device based on its longevity [Aguiar-Ricardo I et al. *Eur Heart J*. 2017]. Their study included 249 generator implantations in 210 patients aged ≥ 75 years, from 1995 to 2016.

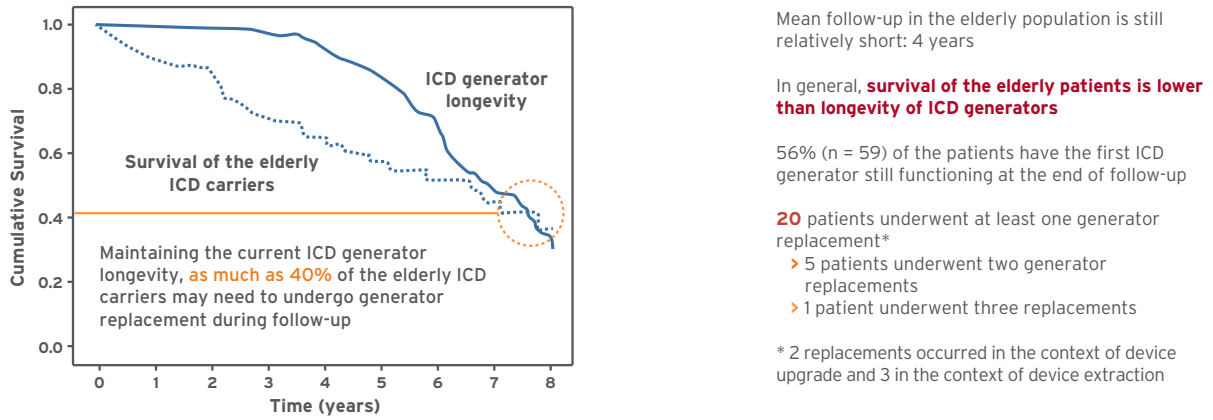
The median long-term survival of these patients was 5.7 years (95% CI, 3.7 to 7.7), said Dr Aguiar-Ricardo. However, there was no significant difference in median survival between patients with ICDs and those with CRT-Ds.

The investigators found that patient median survival time was lower than the longevity of the ICD generators. The first generator was still functioning at the end of follow-up in only 56% of patients, and 20 patients underwent replacement of at least one generator (Figure 1).

And although the longevity of CRT-D generators was also greater than patients' median survival time, the first generator was still functioning at the end of follow-up in only 60% of patients, said Dr Aguiar-Ricardo, and 13 patients underwent at least 1 generator replacement.

This means that as many as 40% of elderly patients with ICDs or CRT-Ds may need to undergo generator replacement during follow-up, she stressed, so it does not make sense to provide generators of shorter longevity for this patient population. It seems most cost-effective to use devices with increased generator longevity for elderly patients to avoid the need for additional replacement, she emphasised.

Figure 1. Patient Survival and ICD Longevity After ICD Implantation



ICD, implantable cardioverter-defibrillator.

Reproduced with permission from I Aguiar-Ricardo, MD.

Device Implantation in CKD

Chronic kidney disease (CKD) is associated with increased CV mortality, especially from SCD, said Mohammed Shurrab, MD, MSc, University of Toronto, Toronto, Canada. The rate of SCD also increases with increased stage of CKD, he added, and SCD accounts for up to 60% of cardiac deaths in dialysis patients. Even mild to moderate renal impairment is a risk factor for CV disease and mortality. However, the efficacy of ICD therapy and CRT in patients with CKD remains controversial despite active use.

Dr Shurrab also reported findings from a meta-analysis of 11 retrospective studies, including 21,136 patients, to investigate the effects of ICD-CRT on survival in CKD patients [Shurrab M et al. *Eur Heart J*. 2017].

Compared with no ICD, use of ICDs was associated with a decrease in all-cause mortality in CKD patients (OR, 0.66; 95% CI, 0.45 to 0.98; P = .04), with a similar protective effect among dialysis-only patients (OR, 0.49; 95% CI, 0.38 to 0.64; P < .001).

CRT use was associated with better survival in CKD patients than ICD use (all-cause mortality OR, 0.73; 95% CI, 0.57 to 0.92; P = .01), but all-cause hospitalisation was similar between the groups (P = .57).

A randomised controlled trial is needed to better define the role of ICD therapy and CRT in CKD patients, concluded Dr Shurrab.

Future Perspectives in Preventing SCD

Dr Kutyifa shared data suggesting that, because of recent medical advances, many clinicians are now changing their practice and no longer systematically implant ICDs for primary prevention in patients with nonischaemic cardiomyopathy [Haguaa KH et al. *Europace*. 2017].

She stressed the need to therefore re-evaluate the use of ICD therapy for patients with ischaemic and nonischaemic cardiac disease, and discussed new studies that are in the pipeline to help accomplish this. For example, RESET SCD is a European Heart Rhythm Association initiative in patients with ischaemic cardiomyopathy. This trial will involve 110 electrophysiology centres in 12 countries, and is estimated to last for 5 years. It will include approximately 2,550 ischaemic cardiomyopathy patients who will receive state of the art treatment with and without ICD implantation; the primary endpoint is all-cause mortality.

Less invasive subcutaneous ICD (S-ICD) technology is now also available, said Dr Kutyifa, and might become more widely used. Emphasising the importance of optimal lead and device selection, she noted that transvenous ICD leads are associated with failures and a 3% to 5% infection risk. However, the S-ICD lead is a novel technology that leaves the heart untouched, and minimises the risk of bloodstream infections. Whether this new technology becomes the primary choice for ICD implantation in the coming decade remains to be seen. However, the PRAETORIAN clinical trial comparing use of the S-ICD with the transvenous ICD with respect to major ICD-related adverse events has recently ended and results will be reported in 1 year [Olde Nordkamp LR et al. *Am Heart J*. 2012].

Although anti-tachycardia pacing (ATP) has been shown to be effective in secondary prevention, its role in treating VT and VF in primary prevention also needs to be re-evaluated, Dr Kutyifa indicated. In this setting, the APPRAISE ATP trial [NCT02923726] is currently recruiting participants, and will investigate ATP in primary prevention patients indicated for ICD therapy and programmed according to current guidance of higher rate cut-offs and therapy delays.

Dr Kutyifa also stressed that the declining incidence of SCD in recent decades does not apply to patients with diabetes and these individuals remain at a high risk for CV death and SCD. After a myocardial infarction (MI), even diabetic patients with relatively preserved left ventricular ejection fraction (LVEF) are at high risk for SCD, and therefore might benefit from the S-ICD. A new trial, MADIT S-CID [NCT02787785], is designed to evaluate whether an S-ICD in patients aged ≥ 65 years with a previous MI, diabetes mellitus, and a relatively preserved LVEF of 36% to 50% will offer a life-saving benefit over conventional medical therapy. The primary endpoint is the reduction in all-cause mortality. The trial will enrol approximately 1,800 patients from the United States, Europe, and Israel, and will involve an interdisciplinary team approach at each site.

Findings from studies such as these will provide important information to help investigators reassess use of ICD therapy for patients with ischaemic and nonischaemic cardiac disease, concluded Dr Kutyifa.