The refractoriness of accessory pathways and reduce the rate of pre-excited supraventricular arrhythmias. (9)

Guidelines
2019 saw new European Society of Cardiology guidelines for the management of patients with SVT(10) which had previously been updated in 2003. However, there was little that was very new. The guidelines insisted that ablation was the best initial management for most re-entrant atrial and AV junctional tachycardia. However, atrial tachycardia occurring after ablation for AF should not be considered for ablation until at least 3 months after the AF ablation procedure. The guidelines stressed that ablation for AV nodal re-entrant tachycardia could be achieved in almost all without risk of AV block. An invasive EP risk assessment of Wolff-Parkinson-White syndrome was recommended, even in patients who are asymptomatic but have high-risk occupations or are competitive athletes. The guidelines recommend ablation in high risk or symptomatic WPW patients, but stop short of recommending ablation of all accessory pathways. It is pointed out that SVT may cause tachycardia-mediated cardiomyopathy and that ablation may not only eliminate the tachycardia but restore ventricular function.

There are strong Class III recommendations – “what not to do”, mostly related to antiarrhythmic drug therapy (Figure 1).

**ATRIAL FIBRILLATION RISK ASSESSMENT AND TREATMENT DECISIONS**

Various studies have highlighted new developments in the risk assessment for the development of AF and its complications, as well as the use of the non-vitamin K antagonist oral anticoagulants (NOACs) as thromboprophylaxis.

**Risk assessment**
Numerous clinical factors associated with incident AF have been described(11) but a simple, practical and reliable approach to identifying patients at risk of incident AF is needed.

Clinical factors such as change in body mass index have been associated with an increased risk of AF(12) as has disordered sleep pattern.(13) Various clinical risk scores for identifying incident AF have been described, and as with most clinical
scores, all have modest predictive value for identifying high-risk patients, and, until recently, there have been complex models derived from multivariate analyses. The C2HEST score was derived and validated in Asia and has recently been externally validated in a French post-stroke cohort and the Danish nationwide registries. This would facilitate targeted intensive screening for AF, for example, in the post-stroke population with AF, where oral anticoagulation (OAC) as secondary prevention is well established. In contrast, two randomised trials in embolic stroke of unknown source (ESUS) using NOACs failed to show a significant reduction in recurrent stroke, while one trial (NAVIGATE-ESUS) showed an excess of bleeds.

Screening for AF has attracted much attention, with population-based approaches and new technologies. The Apple Watch study investigated if a smartwatch-based irregular pulse notification algorithm identified possible AF, and reported that among participants who received notification of an irregular pulse, 34% had atrial fibrillation AF on subsequent ECG patch readings and 84% of notifications were concordant with AF. The Huawei Heart Study also showed the usefulness of photoplethysmographic (PPG)-based technology in population screening for AF, with the positive predictive value of PPG signals being 91.6% and leading to improved anticoagulation use (>80%).

Risk assessment continues to evolve, with availability of new data showing stroke risks associated with AF patients with hypertrophic cardiomyopathy and imaging-documented significant coronary artery lesions. There has been much interest in the use of sophisticated methods such as machine-learning, even predicting incident AF from a simple 12-lead ECG. More complex risk assessment approaches improve AF stroke risk prediction (at least statistically), but need to be balanced against simplicity and practical application. For now, an independent Patient Centered Outcome Research Institute (PCORI)-sponsored systematic review and evidence appraisal identified that among the commonly used risk stratification schemes in patients with AF, the CHA2DS2-VASc and HAS-BLED scores were the best predictors for stroke and bleeding risks, respectively. Bleeding risk prediction only focused on modifiable bleeding risk factors is an inferior strategy to a formal risk assessment using the HAS-BLED score.

Stroke and bleeding risk assessments incorporating biomarkers have been proposed based on highly selected anticoagulated

---

**FIGURE 1: Some “What not to do” recommendations from the 2019 ESC Guidelines on the management of patients with supraventricular tachycardia.**

MRAT, macro re-entrant atrial tachycardia. Reproduced with permission from ref. (20).
clinical trial cohorts, but “real-world” studies have not shown the usefulness of such schemes. One study showing sequential addition of biomarkers did not improve the usefulness of stroke and bleeding risk prediction.\(^{(27)}\) Also, there are no data across the patient pathway, when first diagnosed and non-anticoagulated, or on aspirin – and following the initiation of OAC. Of note, many risk factors are based on baseline risk assessment, but do not remain static and change with age and incident risk factors.\(^{(21,28)}\) Thus, AF assessment is not a “one off” item and needs to be reassessed at regular intervals, e.g., every 4 - 6 months.\(^{(29)}\)

**Non-vitamin K antagonist oral anticoagulants and atrial fibrillation management in clinical practice**

The NOACs have changed the landscape of stroke prevention in AF. These drugs are now the preferred OAC option in most guidelines, but challenges remain in their use among high-risk subgroups that were under-represented in clinical trials, as well as adherence and persistence.

Clinical trial cohorts are selected populations and may be at lower risk compared to “real-world” clinical practice data.\(^{(30)}\) The year also saw the first publications of real-world data for edoxaban, which was the fourth NOAC to enter the market.\(^{(31)}\) Increasing data for the NOACs in the elderly have been published,\(^{(32,33)}\) clearly showing their effectiveness and safety even in very elderly subjects, aged ≥80. Additional data emphasise the importance of using the appropriate label-adherent dosing to ensure best outcomes, as well as persistence data with the NOACs, for example, with dabigatran.\(^{(34)}\) One trial, AEGEAN, showed high adherence and persistence with apixaban (~90%), but did not show additional benefit from interventions to improve adherence/persistence.\(^{(35)}\)

Also, studies of NOAC use in extremes of renal function, both severe renal impairment and supranormal renal function are important. The latter is pertinent given that all 3 Factor Xa inhibitors showed numerically more ischaemic strokes in the subgroup with CrCl >95mL/min when compared with warfarin in their pivotal trials, although this is not apparent in real-world observational data.\(^{(36)}\) In end-stage renal failure, observational data show better safety for apixaban over warfarin.\(^{(37)}\)

The last year has seen new trials with NOACs in catheter ablation (CA) for AF, and in the setting of AF patients presenting with an ACS or undergoing PCI/stenting. For CA, an interrupted NOAC-based strategy appears to be a safer option compared to a warfarin-based strategy.\(^{(38-40)}\) In AF/ACS/PCI patients, the publication to AUGUSTUS and ENTRUST-AF PCI completes the trials of NOACs in this clinical setting.\(^{(41,42)}\) These trials suggest that when OAC is used, a NOAC-based regime or a dual therapy (i.e. OAC plus a P2Y12 inhibitor) is associated with less major bleeding.\(^{(43)}\) Of the overall thrombotic or ischaemic outcomes, there is little difference between a triple therapy or dual therapy approach, or a NOAC-based strategy compared to a warfarin-based strategy. However, a dual therapy approach may be associated with an excess of stent thrombosis and myocardial ischaemic events, and thus patients who are at high risk of such outcomes may merit a short period of triple therapy at the start. In stable coronary disease, OAC alone is associated with better outcomes compared to dual therapy, in the AFIRE trial.\(^{(44)}\)

While the concept of integrated AF management has been proposed, its application and implementation in a simple, user-friendly manner have not been previously validated. Integrated care has been associated with reduced mortality and hospitalisation.\(^{(45)}\) One integrated and holistic approach to AF management, streamlining the decision-making management approaches that would be uniformly applicable across the whole AF patient pathway, starting with primary care and linking with secondary care (including cardiologist/non-cardiologists), and understandable for the AF patients per se, is the ABC (Atrial fibrillation Better Care) pathway: Avoid stroke; Better symptom management with patient-centred symptom directed decisions on rate or rhythm control; and Cardiovascular and risk factor optimisation, including lifestyle changes\(^{(46)}\) (Figure 2). The ABC pathway approach has now been shown in independent studies to be associated with a reduction in mortality, hospitalisation and adverse outcomes, as well as reduced healthcare costs, when compared to “non-ABC” adherent management.\(^{(47,48)}\) The ABC pathway was tested in a cluster randomised trial showing improved clinical outcomes with an ABC pathway management based on an interactive App that included risk assessments, patient decision aids, educational materials and dynamic tracking of risk (mAFA-II trial;\(^{(49)}\) presented as Late Breaking Science at the ESC congress, September 2019).

**ABLATION**

**Clinical outcomes**

A number of publications have described AF CA outcomes and impact on prognosis. Probably the most eagerly awaited was the CABANA study.\(^{(51)}\) This multicentre study randomised 2,204 patients to CA or drug therapy. As designed, intention to treat, the study was neutral for CA impacting on the primary composite endpoint of death, disabling stroke, serious bleeding, or cardiac arrest. This type of study is incredibly difficult to recruit for because the clinicians most likely to recruit are seeing a patient referred for a CA, so even if they are prepared to enter the study, the cross-over rate is likely to be high from drug to ablation, as it was in this study (27.5%). When analysing by treatment, there was a prognostic benefit, but this subverts the principle of randomisation and increases bias.
The cerebral micro-emboli associated with AF CA do not appear to have much impact and CA itself may improve cognitive impairment as in the 308 patients studied and followed for 1 year.(52) Most electrophysiologists continue to tell patients that the primary goal of AF ablation is quality of life (QOL). The first randomised controlled trials (RCT) of AF CA vs. drugs to examine QOL as the primary endpoint were published in 2019 and favoured CA.(53) While this was a small study, with 155 patients, it does open the way for double-blind RCTs of AF CA with QOL as the primary outcome.

The use of cryoablation for AF has accumulated more evidence this year: it is faster than RF CA,(54) associated with lower risk of pericardial effusion,(55,56) and has superior outcomes(54,55) regardless of centre volume.(57) Several large registries have published this year. The Swedish registry reveals CA procedure complications and death were low and that AF, ventricular tachycardia (VT), and premature ventricular complex (PVC) CA numbers increased, with AF having the highest repeat procedure rate (41%).(58) A European registry demonstrated that cryoablation is as effective for female patients, but is associated with higher complication rates.(59) The Danish registry confirmed that success rates for AFL ablation were 90%, but that AF is a common presentation (13%) within the 2 years after.(60) The German Helios registry showed that pericardial effusion rates were 0.9% in 21 141 AF CA, and were more likely in low volume centres, but only if RF was used rather than cryo.(55)

CA of VF storm after myocardial infarction was reported in a multicentre study of 110 patients.(61) In-hospital mortality (27%) and 2-year follow-up mortality (36%) were high and associated with the time taken to perform CA.

A retrospective study of 110 patients demonstrated CA of recurrent VT in patients with arrhythmogenic ventricular cardiomyopathy, is no more effective than drugs, but is more likely to be successful if both epicardial and endocardial approaches are used.(62)

New mapping technologies
It is recognised that the primary reasons for failure of CA in complex arrhythmia are a lack of understanding of the mechanism. There continues to be huge effort to solve this. This year ripple mapping has been used successfully in persistent AF (18 months 53% vs. 39% conventional),(63) atrial tachycardia,(64) and VT in arrhythmogenic right ventricular cardiomyopathy (ARVC).(64) Non-contact mapping is returning to clinical practice with an observational trial showed good outcomes for persis-
tent AF CA at 12 months (59%). The STAR mapping system (Figure 3) presented its feasibility clinical trial of 35 patients showing freedom from AF after persistent AF CA guided by STAR of 80% at 18 months. It remains to be seen whether any of these make it to widespread clinical use.

Energy sources
High power short-duration RF may make point-by-point AF CA faster and, at least so far, not being associated with worse outcomes. Electroporation is also showing promise as a novel energy source that is highly effective with low complication rates. The use of radiotherapy to treat intractable VT is an exciting innovation, showing promising results in a small prospective study of 19 patients.

Guidelines and consensus statements
A number of guidelines have been published this year and while these are useful reviews of the literature, the temptation to accept them as dogma has to be resisted, given that they are often drive by consensus of a well-intentioned writing group rather than hard data. The CA of ventricular arrhythmia (VA) guideline suggests that programmed electrical stimulation may come back into fashion as a method for prognostic prediction, this time in patients with frequent PVCs and structural heart disease, and also recommends use of ICE for VA ablation, although much of the world does not use ICE without any apparent compromise to their outcomes. The sex differences in arrhythmia consensus highlighted that although outcomes may be different, this should not influence provision of CA for females.

VENTRICULAR ARRHYTHMIAS
Arrhythmogenic cardiomyopathy
This has been an exciting year in arrhythmogenic cardiomyopathy (ACM). There are major publications to be aware of. The first is the Heart Rhythm Society Consensus Document on Arrhythmogenic Cardiomyopathy. This document, which was led by McKenna and Towbin, redefines ACM as a condition that presents with symptomatic and/or asymptomatic arrhythmias in association with some degree of cardiac dysfunction. This “big tent” approach includes classic ARVC, the more recently described arrhythmogenic left ventricular cardiomyopathy, as well as other subgroups of patients. Included within ACM are sarcoidosis, Chagas disease, myocarditis, and a large number of inherited cardiomyopathies. This is a comprehensive and provocative article that is important to be aware of. One of the writing group’s goals was to encourage having patients present with arrhythmias and a cardiomyopathy to a specialised centre that performs comprehensive

---

**FIGURE 3:** Ai - STAR map in an anterior-posterior view that shows an ESA (highlighted by the number (1)) mapped to the anterior wall at the base of the LA appendage. Aii - Ablation here as demonstrated on a CARTO map in an anterior-posterior view resulted in Aiii - AF cycle length slowing from 152ms - 193ms, as measured from the LA appendage electrograms. Further cluster lesions at this ESA also intermittently organised CS activation. Bi - STAR map in a tilted posterior-anterior view that shows a further ESA (highlighted by the number (2)) mapped to the posterior-inferior wall. Bii - Ablation here as shown on the CARTO maps in a similar view resulted in Biii - AF termination to AT as shown on the intracardiac electrograms. The AT was mapped to a mitral isthmus dependent flutter, which was successfully ablated to sinus rhythm.
evaluation, arranges for genetic testing, and determines a patient’s arrhythmic risk and need for an ICD. (74)

Another important publication was authored by Cadrin-Tourigny, et al. (74) Through the combined efforts of 5 international ARVC registries, an ARVC risk calculator was developed to help estimate arrhythmic risk and inform decisions regarding ICD implantation (www.ARVCrisk.com). More than 500 ARVC patients from 5 registries in North America and Europe were enrolled. During 5 years of follow-up, 28% experienced sustained VT, sudden death, or received an appropriate ICD therapy. A prediction model to estimate annual arrhythmic risk was developed (Figure 4). The variables at baseline included in the model are recent syncope, age, gender, non-sustained VT, the number of PVCs in 24 hours, and right ventricular ejection fraction. Furthermore, a final paper by Chatterjee, et al. (75) investigated the diagnostic value of an anti-Desmoglein-2 antibody in diagnosing ARVC. An antibody to DSG-2 was identified in 12/12 and 25/25 ARVC cohorts and 7/8 borderline subjects. The antibody was absent in 11/12 and 20/20 control cohorts. The authors concluded that anti-DSG-2 antibodies are a sensitive and specific marker for ARVC. Before this test can be used clinically, it will need to be tested in more controlled populations, including those with cardiac sarcoidosis.

Cardiac arrest
Sondergaard, et al. (76) examined the use of bystander CPR among patients who experienced out of hospital cardiac arrest in Denmark. More than three-fourths of cardiac arrests occurred in residential locations. Bystander CPR increased between 2001 and 2004 from 36% - 84% in public locations and from 16% - 61% in residential locations. Not surprisingly, the increased use of CPR resulted in an increased 30-day survival from 6% - 25% for arrests in public locations and from 3% - 10% in residential locations.

CARDIAC DEVICES
What is the evidence behind current guideline recommendations for primary prevention ICD implantation in our present day and age? Can patient populations, background therapies and treatment algorithms, particular in heart failure, and underlying trials conducted well over a decade ago be extrapolated to current daily clinical practice? (Figure 5). (77) According to a large analysis from the French-British-Swedish-Czech CRT Network, death due to progressive heart failure remains the leading cause of death for most patients. (78) Moreover, increasing evidence indicates left ventricular (LV) remodelling as a main driver or arrhythmogenic events leading to sudden cardiac death (SCD), which may be reduced by modalities aimed at preventing (or even reversing) these processes, i.e. neuro-hormonal blockade and cardiac resynchronisation therapy.

![Figure 4: Prediction of sustained ventricular arrhythmia in ARVC](image)

**Model for 5-year risk prediction**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Coefficient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td>0.49</td>
</tr>
<tr>
<td>Age</td>
<td>-0.022</td>
</tr>
<tr>
<td>Recent syncope</td>
<td>0.66</td>
</tr>
<tr>
<td>Non-sustained VT</td>
<td>0.81</td>
</tr>
<tr>
<td>Ln (24h PVC count)</td>
<td>0.17</td>
</tr>
<tr>
<td>Leads with T-wave inv.</td>
<td>0.11</td>
</tr>
<tr>
<td>RVEF</td>
<td>-0.025</td>
</tr>
</tbody>
</table>

\[
1 - 0.8022^{\text{exp}(-0.025t)} = 5\text{-year risk}
\]

FIGURE 4: Prediction of sustained ventricular arrhythmia in arrhythmogenic right ventricular dysplasia/cardiomyopathy.

ARVC = arrhythmogenic right ventricular dysplasia/cardiomyopathy, inv. = inversion, PVC = premature ventricular complex, RVEF = right ventricular ejection fraction, VT = ventricular tachycardia. (74)
These concepts and findings call into question the validity of the available randomised clinical trial evidence underlying current recommendations for primary prevention ICD implantation in heart failure patients. On a conceptual level, they additionally raise the question if trials should generally come with a “due date”, after which they would require re-validation. On the flipside, however, device therapies have advanced over the last decades, including better algorithms to detect ventricular arrhythmias and to prevent inadequate shocks, as well as the development of extravascular systems such as the S-ICD and the extravascular (EV-) ICD. Indeed, even entirely leadless CRT systems appear to be feasible. If proven safe and effective in the (ongoing) large RCTs, these novel modalities will come with a substantially reduced system-related morbidity, which may again tip the scale towards device-based SCD prevention. Indeed, inadequate shocks, as well as infections, remain the most devastating complications of current ICD systems, which come along with a substantial impact on quality of life, morbidity, and mortality.

In addition, better means of risk prediction for SCD above and beyond left ventricular ejection fraction (LVEF) are desperately needed in order to better protect those patients who need it (and prevent those who do not from unnecessary device implantation). One such risk prediction model for patients post-myocardial infarction with preserved LVEF has recently been put forward using electrocardiographic non-invasive risk factors (PVCs, non-sustained VT, late potentials, prolonged QTc, increased T-wave alternans, reduced heart rate variability, and abnormal deceleration capacity with abnormal turbulence).

**ARRHYTHMIAS AND PACING**

![Figure 5: Two-year cause-specific mortality and non-fatal vascular events for patients with cardiovascular disease according to New York Heart Association (NYHA) class.](image-url)

<table>
<thead>
<tr>
<th>NYHA 0/1</th>
<th>NYHA 2</th>
<th>NYHA 3</th>
<th>NYHA 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Absolute rate (%)</td>
<td>% of Deaths</td>
<td>Absolute rate (%)</td>
<td>% of Deaths</td>
</tr>
<tr>
<td>CRD</td>
<td>0</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>TSAD</td>
<td>&lt;1</td>
<td>&lt;1</td>
<td>1</td>
</tr>
<tr>
<td>RSAD</td>
<td>2</td>
<td>17</td>
<td>5</td>
</tr>
<tr>
<td>SVD</td>
<td>2</td>
<td>17</td>
<td>3</td>
</tr>
<tr>
<td>NFVE</td>
<td>4</td>
<td>33</td>
<td>3</td>
</tr>
<tr>
<td>Non-CVD</td>
<td>4</td>
<td>33</td>
<td>4</td>
</tr>
</tbody>
</table>

**Figure 5:** Two-year cause-specific mortality and non-fatal vascular events for patients with cardiovascular disease according to New York Heart Association (NYHA) class. Numbers and proportions are a conceptual representation of absolute and relative risk and are not strictly evidence-based. Note that for patients in New York Heart Association Class 4, interventions for sudden arrhythmic death may be ineffective or fail to lead to a meaningful prolongation of life because the patient is likely to die soon of worsening heart failure.

CRD = congestion-related death (heart failure, chest infection, multi-organ failure, etc.)
TSAD = terminal sudden arrhythmic death
RSAD = resuscitatable SAD
SVD = sudden vascular death
NFVE = non-fatal vascular event
Non-CVD = non-cardiovascular death

CRD = congestion-related death, otherwise called death due to worsening heart failure, NFVE = non-fatal vascular event (e.g. myocardial infarction and stroke); note that events are more likely to be suddenly fatal as heart failure progresses. Non-CVD = non-cardiovascular death, RSAD = resuscitatable sudden arrhythmic death, SVD = sudden vascular death, TSAD = terminal (non-resuscitatable) sudden arrhythmic death.
Cardiac resynchronisation therapy remains an important treatment modality for heart failure patients to induce reverse LV remodelling and to improve morbidity and mortality. However, the rate of so-called “non-responders” remains in the order of 20% - 30%, depending on definitions and cut-offs. The MORE-CRT MPP trial investigated the effect of stimulating the LV from 2 sites instead of 1 to reduce the number of non-responders. Five hundred and forty-four patients classified as LV from 2 sites instead of 1 to reduce the number of non-responders (defined as an LV end-systolic volume reduction by <15%) 6 months after CRT implantation were randomised to receive the “Multipoint” algorithm turned on (MPP ON) or off (standard of care group). While the conversion rate to “responders” was no different between the 2 groups (31.8% vs. 33.8%), patients in the MPP group programmed to a wide electrode distance were significantly more likely to convert to responders than those programmed to other vector combinations (45.6% vs. 26.2%, p = 0.006). Although interesting and biologically plausible, these findings have to be viewed as hypothesis-generating in view of the negative primary endpoint.

Conflict of interest: A.J.C. has received personal fees and institutional grants from Bayer, Boehringer Ingelheim, Daiichi Sankyo and BMS/ Pfizer, and personal fees from Medtronic, Boston Scientific and Abbott. Professor Lip is a consultant for Bayer/Janssen, BMS/Pfizer, Medtronic, Boehringer Ingelheim, Novartis, Verseon and Daiichi-Sankyo, and a speaker for Bayer, BMS/Pfizer, Medtronic, Boehringer Ingelheim, and Daiichi-Sankyo. No fees are directly received personally. R.S. reports non-financial support from Boston Scientific, during the conduct of the study; in addition personal fees and non-financial support from Daiichi Sankyo, non-financial support from Boehringer-Ingelheim, outside the submitted work. In addition, Dr Schilling has a patent Rhythm AI - STAR mapping pending. J.S. has received consultant and/or speaker fees from Abbott, Amgen, Astra-Zeneca, Atricure, Bayer, Biosense Webster, Biotronik, Boehringer-Ingelheim, Boston Scientific, Bristol-Myers Squibb, Daiichi Sankyo, Medscape, Medtronic, Merck/MSD, Novartis, Pfizer, Sanofi-Aventis, WebMD, and Zoll. He reports ownership of CorXL. H.C. reports personal fees from Abbott Medical, personal fees from Atricure, personal fees from Biosense Webster, personal fees from Boston Scientific, personal fees from Medtronic, outside the submitted work. J.S. has received grant support through his institution from Abbott, Bayer Healthcare, Biosense Webster, Biotronik, Boston Scientific, Daiichi Sankyo, and Medtronic.

REFERENCES

REFERENCES


