Godina 2019. u kardiologiji: aritmije i elektrostimulacija

The year in cardiology: arrhythmias and pacing
The year in cardiology 2019

A. John Camm[1]*, Gregory Y.H. Lip[2,3], Richard Schilling[4], Hugh Calkins[5], Jan Steffel[6]

[1]St. George's University of London, Cardiology Clinical Academic Group, Molecular & Clinical Sciences Institute, London, UK
[2]Liverpool Centre for Cardiovascular Science, University of Liverpool, Liverpool Heart & Chest Hospital, Liverpool, UK
[3]Aalborg Thrombosis Research Unit, Department of Clinical Medicine, Aalborg University, Aalborg, Denmark
[4]Barts Heart Centre, London, UK
[5]Johns Hopkins Medical Institutions, Baltimore, MD, USA
[6]Department of Cardiology, Division of Electrophysiology, University Hospital Zurich, Switzerland

RECEIVED:
January 9, 2020
ACCEPTED:
January 21, 2020

CITATION: Cardiol Croat. 2020;15(5-6):132-45. | https://doi.org/10.15836/ccar2020.132

***ADDRESS FOR CORRESPONDENCE**: A. John Camm, Molecular & Clinical Sciences Institute, Cranmer Terrace, London, SW19 0RE, London, UK. / Phone: +44 208 725 3414, Fax: +44 208 725 3416 / E-mail: jcamm@sgul.ac.uk

ORCID: A. John Camm, https://orcid.org/0000-0002-2536-2871 • Gregory Y.H. Lip, https://orcid.org/0000-0002-7566-1626 Richard Schilling, https://orcid.org/0000-0002-0621-8241 • Hugh Calkins, https://orcid.org/0000-0002-9262-9433

TO CITE THIS ARTICLE: Schilling R, Calkins H, Steffel J. The year in cardiology: arrhythmias and pacing. Cardiol Croat. 2020;15(5-6):132-45. https://doi.org/10.15836/ccar2020.132

TO LINK TO THIS ARTICLE: https://doi.org/10.15836/ccar2020.132

Reproduced from: Camm AJ, Lip GYH, Schilling R, Calkins H, Steffel J. The year in cardiology: arrhythmias and pacing. Eur Heart J. 2020 Feb 1;41(5):619-625c. https://doi.org/10.1093/eurheartj/ehz931, by permission of Oxford University Press on behalf of the European Society of Cardiology.

Uvod

Tijekom protekle godine postignut je velik napredak u pogledu antikoagulantne i ablacijske terapije fibrilacije atrija (FA).

Osim nedavno objavljenih smjernica Europskoga kardiološkog društva (ESC) o liječenju bolesnika sa supraventrikulskim aritmijama, postignuti su samo manji napredci u istraživanju na tom području. Ventrikulske aritmije i terapija uređajima doživjeli su skroman napredak.

Supraventrikulske aritmije

Ove je godine objavljeno nekoliko publikacija o elektrokardiografskoj dijagnozi supraventrikulskih tahikardija (SVT)[1–4] i povećalo se zanimanje bolesnika za novo otkrivanje supraventrikulskih aritmija.[5] Tehnologija elektrofiziološkog mapiranja omogućila je napredak u mapiranju SVT-a.[6] Pojavio se iznenađujuće veliki interes za primjenu novih antiaritmijskih lijekove pri SVT-u, u rasponu od intranazalnog etripamila (L-tip kalcijeva antagonista) koji se uporabljuje za prekid

Preamble

During this last year, there has been much progress with regard to anticoagulant and ablation therapy for atrial fibrillation (AF).

Apart from recently issued European Society of Cardiology Guidelines for the management of patients with supraventricular arrhythmias, there has been little progress in research in this field. Ventricular arrhythmias and device therapy have seen modest progress.

Supraventricular tachycardias

This year has seen several publications on the ECG diagnosis of supraventricular tachycardia (SVT)[1–4] and interest in new consumer-led discovery of supraventricular arrhythmias.[5] EP mapping technology has provided better mapping of SVT.[6] There has been a surprising interest in new antiarrhythmic drugs for SVT, ranging for intranasal etripamil (an L-type calcium antagonist) for termination of SVT[7,8] and nifekalant to increase the refractoriness of

SVT-a[7,8] i nifekalanta koji se rabi za povišenje_refraktornosti akcesornih puteva i smanjenja učestalosti preekcscitiranih supraventrikulskih aritmija.[9]

Smjernice

U 2019. godini objavljene su nove smjernice Europskoga kardiološkog društva za liječenje bolesnika sa SVT-om[10] koje su prethodno izašle tijekom 2003. Međutim, malo je onoga što je novo. Spomenute smjernice inzistiraju na ablaciji kao najboljem obliku liječenja za većinu kružnih atrijskih i *AV junctional*/ovisnih tahikardija. Međutim, atrijska tahikardija koja se pojavi nakon ablacije FA ne bi se trebala razmatrati za ablaciju najmanje 3 mjeseca nakon postupka ablacije FA Smjernice ističu da bi ablacija AV nodalnih kružnih aritmija trebala biti uspješna u gotovo svih, bez rizika od nastupa AV bloka. Preporučena je invazivna elektrofiziološka procjena rizika kod Wolff–Parkinson–Whiteova sindroma čak i u bolesnika koji su asimptomatski, ali imaju visokorizična zanimanja ili se bave natjecateljskim sportom. Smjernice preporučuju ablaciju kod visokorizičnih ili simptomatskih bolesnika s WPW-om, ali ništa ne govore o ablaciji više akcesornih puteva. Istaknuto je da SVT mogu uzrokovati tahikardijom posredovanu kardiomiopatiju i da se ablacijom ne uklanja samo tahikardija već i postiže oporavak ventrikulske funkcije.

Postoje snažne preporuke klase III. „što ne treba činiti", uglavnom vezane za terapiju antiaritmicima (**slika 1**).

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 in 2003. However, there was little which 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**).

Recommendations for the acute management of wide QRS tachycardia in the absence of an established diagnosis		
Verapamil is not recommended in wide QRS-complex tachycardia of unknown aetiology.	III	B
Recommendations for the therapy of MRATs		
Acute therapy		
Propafenone and flecainide are not recommended for conversion to sinus rhythm.	III	B
Recommendations for the therapy of AVRT due to manifest or concealed APs		
Chronic therapy		
Digoxin, beta-blockers, diltiazem, verapamil, and amiodarone are not recommended and are potentially harmful in patients with pre-excited AF.	III	B
Recommendations for the acute therapy of pre-excited AF		
Haemodynamically stable patients		
Amiodarone (i.v.) is not recommended.	III	B
Recommendations for the therapy of SVTs in congenital heart disease in adults		
Chronic therapy		
Sotalol is not recommended as a first-line antiarrhythmic drug as it is related to an increased risk of pro-arrhythmias and mortality.	III	C
Flecainide and propafenone are not recommended as first-line antiarrhythmic drugs in patients with ventricular dysfunction and severe fibrosis.	III	C

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 from Brugada et al.[10]

Stratifikacija rizika i odluka o liječenju fibrilacije atrija

Mnoga su istraživanja istaknula nova dostignuća u procjeni rizika za razvoj FA i njezinih komplikacija, kao i uporabu lijekova iz skupine novih oralnih antikoagulantnih lijekova (NOAC) za tromboprofilaksu.

Procjena rizika

Brojni se klinički čimbenici povezuju s povećanim rizikom od razvoja FA[11], međutim, potreban je jednostavan, praktičan i pouzdan pristup za identifikaciju bolesnika s povećanim rizikom od razvoja FA.

Klinički čimbenici kao što su promjene u indeksu tjelesne mase[12] i poremećaj spavanja[13] povezani su s povećanim rizikom od razvoja FA. Opisani su različiti klinički bodovni sustavi za procjenu rizika u otkrivanju incidencije FA, ali kao što obično bude s većinom kliničkih bodovnih sustava, svi imaju skromnu prediktivnu vrijednost za identifikaciju visokorizičnih bolesnika sve dok nedavno nisu izvedeni složeni modeli iz multivarijatnih analiza.

C2HEST bodovni sustav izveden je i testiran u Aziji, a nedavno je bio eksterno validiran u Francuskoj u skupini ispitanika s preboljenim moždanim udarom i u Danskom nacionalnom registru.[14,15] Ovo bi trebalo olakšati ciljani intenzivan probir za FA, npr. u skupini bolesnika nakon preboljenoga moždanog udara s FA u kojih je primjena oralnih antikoagulantnih lijekova (OAC) u sekundarnoj prevenciji dobro utemeljena. Suprotno tomu, dva randomizirana ispitivanja primjene NOAC-a kod embolijskog moždanog udara nepoznata izvora (ESUS) pokazala su znatno smanjenje rekurentnoga moždanog udara, dok je u jednom ispitivanju (NAVIGATE-ESUS) utvrđena povećana učestalost krvarenja.[16,17]

Probir FA, temeljen na pristupu populaciji i novim tehnologijama, privukao je mnogo pozornosti.[18] U istraživanju *Apple Watch* ispitivano je mogu li algoritmi za prepoznavanje nepravilnog ritma na pametnim telefonima identificirati FA. Objavljeno je da je u 34 % ispitanika koji su primili obavijest o nepravilnom pulsu na zapisu EKG-a registrirana FA te da je 84 % zapisa bilo u skladu s FA.[19] *Huawei Heart Study* također je pokazala korisnost od tehnologije temeljene na fotopletizmografiji (PPG) u probiru populacije s FA s pozitivnom prediktivnom vrijednošću PPG signala od 91,6 %, što dovodi do poboljšane uporabe antikoagulantnih lijekova (>80 %).[20]

Dostupnošću novih podataka koji upućuju na rizik od moždanog udara u bolesnika s FA i hipertrofijskom kardiomiopatijom[21] i značajnim lezijama u koronarnim arterijama utvrđenima oslikavenjem[22], stratifikacija rizika dalje se razvija. Postoji velik interes za uporabu sofisticiranih metoda, poput strojnog učenja, radi predviđanja učestalosti FA na temelju učinjenog 12-kanalnog EKG-a.[23] Složeniji pristupi procjene rizika dovode do boljeg (barem statistički) predviđanja rizika od pojave moždanog udara u bolesnika s FA, ali ih treba uravnotežiti s jednostavnijom i praktičnijom primjenom. Za sada su pod pokroviteljstvom neovisnog *Patient-Centered Outcome Research Institute* (PCORI) provedeni sustavan pregled i procjena dokaza te je utvrđeno da su među najčešće primjenjivanim shemama stratifikacije rizika za bolesnike s FA upravo CHA_2DS_2VASc i HAS-BLED najbolji pokazatelji rizika od moždanog udara i krvarenja.[24] Procjenjivanje rizika od krvarenja temeljeno samo na promjenjivim čimbenicima rizika

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, 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.[14,15] 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 randomized 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.[16,17]

Screening for AF has attracted much attention, with population-based approaches and new technologies.[18] 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.[19] 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%).[20]

Risk assessment continues to evolve, with availability of new data showing stroke risks associated with AF patients with hypertrophic cardiomyopathy[21] and imaging-documented significant coronary artery lesions.[22] There has been much interest into use of sophisticated methods such as machine-learning, even predicting incident AF from a simple 12-lead ECG.[23] 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 Cantered Outcome Research Institute (PCORI)-sponsored systematic review and evidence appraisal identified that amongst the commonly used risk stratification schemes in patients with AF, the CHA_2DS_2VASc and HAS-BLED scores were the best predictors for stroke and bleeding risks, respectively.[24] Bleeding risk prediction only focused on modifiable bleeding risk factors is an inferior strategy to a formal risk assessment using the HAS-BLED score.[25,26]

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

od krvarenje inferiorna je strategija u odnosu prema službenoj procjeni rizika s pomoću HAS-BLED bodovne ljestvice.[25,26]

Procjene rizika od moždanog udara i krvarenja primjenom biomarkera temeljene na rezultatima visoko selektivnih kliničkih istraživanja s antikoagulantnim lijekovima koja su iz kliničke prakse, nisu pokazale veću korisnost. Istraživanje koje se koristilo sekvencijalnim dodavanjem biomarkera nije dokazalo njihovu korisnost u predviđanju rizika od moždanog udara i krvarenja.[27] Također nema podataka o situacijama kada je u bolesnika prvo postavljena dijagnoza, a da do tada nisu bili antikoagulirani ili su bili prvo na acetilsalicilatnoj kiselini te potom na OAC-u. Napominjemo, da su mnogi čimbenici rizika temeljeni na temeljnim vrijednostima pri procjeni, ali oni ne ostaju statični te se mijenjaju sa životnom dobi i vezanim rizičnim čimbenicima.[25,28] Zaključno, stratifikacija u bolesnika s FA nije jednokratno pitanje te zahtijeva novu procjenu u redovitim intervalima, npr. svakih 4 – 6 mjeseci.[29]

Novi oralni antikoagulantni lijekovi i liječenje fibrilacije atrija u kliničkoj praksi

Novi oralni antikoagulantni lijekovi promijenili su razmišljanje o prevenciji moždanog udara kod FA. Oralni antikoagulantni lijekovi postali su terapija izbora u većini smjernica, ali ostaje izazov njihove primjene u visokorizičnih podskupina bolesnika koji su bili nedovoljno zastupljeni u kliničkim istraživanjima, kao i njihova ustrajnost i upornost u uzimanju terapije.

Kohorte kliničkog istraživanja sastoje se od odabrane skupine bolesnika koji mogu i imati niži rizik u usporedbi s onima iz stvarne kliničke prakse.[30] Tijekom godine također su objavljene prve publikacije iz stvarne kliničke prakse o edoksbanu koji je četvrti NOAC na tržištu.[31] U porastu je bio broj objavljenih podataka o primjeni NOAC-a u osoba starije životne dobi[32,33] koji jasno upućuju na učinkovitost i sigurnost ovih lijekova i u veoma starih osoba (životne dobi >80 godina). Dodatni podatci ističu važnost uporabe odgovarajuće obilježenih i označenih doza kako bi se osigurali najbolji rezultati, kao i dosljednost u podatcima o NOAC-ima, npr. kod dabigatrana.[34] Istraživanje AEGEAN pokazalo je visoku dosljednost i upornost s apiksabanom (oko 90 %), no nije pokazala dodatnu dobrobit od intervencije na poboljšanje dosljednosti i upornosti.[35]

Također postoje istraživanja o primjeni NOAC-a kod različitog stupnja bubrežne funkcije, kao što su značajna renalna insuficijencija i supernormalna bubrežna funkcija. Posljednja je situacija važna s obzirom na to da su sva tri inhibitora faktora Xa pokazala višu učestalost ishemijskih udara u podskupini s CrCl >95 mL/min u usporedbi s varfarinom, iako to nije bilo vidljivo u stvarnim kliničkim opservacijskim podatcima.[36] Kod posljednjeg stadija bubrežnog zatajenja opservacijski podatci pokazuju veću sigurnost u primjeni apiksabana u usporedbi s varfarinom.[37]

Prošle godine objavljena su nova istraživanja primjene NOAC-a pri kateterskoj ablaciji (CA) zbog FA i u bolesnika s FA u kojih se razvio akutni koronarni sindrom (ACS) ili su bili podvrgnuti perkutanoj koronarnoj intervenciji/implantaciji stenta. Za CA strategija temeljena na neprekinutom uzimanja NOAC-a čini se sigurnija opcija u usporedbi sa strategijom temeljenom na uzimanju varfarina.[38-40] U bolesnika s FA / ACS / PCI studije AUGUSTUS i ENTRUST-AF PCI upotpunjuju ispitivanja o NOAC-ima u kliničkoj praksi.[41,42] Ta ispitivanja upućuju na to da, kada se uporabljuje OAC, onda su režimi temeljeni

agulated 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 changes with age and incident risk factors.[25,28] 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 its use amongst high-risk subgroups that were under-represented in clinical trials, as well as its 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 emphasize 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 supra-normal renal function. The latter is pertinent given that all three Factor Xa inhibitors showed numerically more ischaemic strokes in the subgroup with CrCl >95 mL/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 uninterrupted 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, 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]

na NOAC-u ili dualna terapija (npr. OAC zajedno s inhibitorom P2Y12) povezani s manje velikih krvarenja.[43] Uzimajući u obzir sve trombotske ili ishemijske događaje, ne postoji velika razlika u primjeni trojne ili dvojne terapije ili u liječenju temeljenom na NOAC-ima u odnosu na varfarin. Međutim, dvojna terapija može biti povezana s većom učestalošću tromboze stenta i ishemijskih događaja, tako da bolesnici koji su pod povećanim rizikom od razvoja takvih događaja mogu imati koristi od početne, kratkotrajne primjene trojne terapije. Pri stabilnoj koronarnoj bolesti srca primjena samo OAC-a u terapiji povezana je s boljim ishodima u usporedbi s dvojnom terapijom, sukladno rezultatima studije AFIRE.[44]

Iako je predložen koncept integriranog pristupa FA, njegova primjena i provedba na jednostavan način prilagođen korisniku nisu za sada testirane. Integrirano zbrinjavanje povezano je sa smanjenjem hospitalizacije i smrtnosti.[46] Integrirani i holistički pristup zbrinjavanju usmjeruje na ujednačeno donošenje odluka koje bi bilo primjenjivo na cjelokupni put bolesnika s FA, počevši od primarne te nadovezujući se na sekundarnu skrb (uključujući kardiologe i druge specijalnosti). Tako je ABC (Atrial fibrillation Better Care) pristup za bolesnike s FA razumljiv sam po sebi: Avoid stroke – sprječavanje moždanog udara; Better symptom management – bolja kontrola simptoma s usmjerivanjem prema bolesniku te odlukom o kontroli frekvencije ili ritma; Cardiovascular and risk factor optimisation – kontrola kardiovaskularnih i rizičnih čimbenika, uključujući i promjenu stila života[45] (**slika 2**). U neovisnim istraživanjima primjena ABC pristupa dovela je do smanjenja smrtnosti, hospitalizacije i nepovoljnih ishoda, kao i do smanjenja troškova zdravstvene skrbi u usporedbi s „ne-ABC" pridruženim pristupom.[47-50] ABC pristup testiran je u skupini randomiziranih studija upućujući na poboljšane kliničke ishode pri primjeni ovakvoga pristupa na interaktivnim aplikacijama koji uključuju procjenu rizika, upute za zbrinjavanje, edukacijske materijalne i dinamičko praćenje rizika (mAFA-II trial[20], prikazan kao *Late Breaking Science* na Kongresu ESC-a u rujnu 2019.).

Ablacija

Klinički ishodi

U brojnim su istraživanjima opisani rezultati kateterske ablacije FA i njezin utjecaj na prognozu. Vjerojatno je najočekivanija bila studija CABANA.[51] Ona je uključila 2204 ispitanika randomiziranih na CA ili farmakološko liječenje. Kako je dizajnirana u svrhu liječenja, studija je bila neutralna glede ispitivanja utjecaja CA na primarni složeni ishod koji se sastojao od smrtnog ishoda, teškoga moždanog udara ili srčanog zastoja. Kod ovakvih tipova istraživanja nevjerojatno je teško prikupiti ispitanike. Naime, iako većina liječnika susreće bolesnike koji trebaju CA, pa čak i ako su oni pripremljeni ući u istraživanje, postoji velika učestalost prelazaka iz skupine s

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 hospitalization.[46] 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; Cardiovascular and risk factor optimisation, including lifestyle changes[45] (**Figure 2**). The ABC pathway approach has now been shown in independent studies to be associated with a reduction in mortality, hospitalization and adverse outcomes, as well as reduced healthcare costs, when compared to 'non-ABC' adherent management.[47–50] The ABC pathway was tested in a cluster randomized 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[20]; 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 randomized 2204 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 randomization 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 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 randomized controlled trials (RCT) of AF CA vs drugs to examine QOL as the primary endpoint was published in 2019

FIGURE 2. Please see the original article (Eur Heart J. 2020 Feb 1;41(5):619-625c.).

lijekovima u skupinu s ablacijama, kao što je to bilo u ovoj studiji (27,5 %). Kada su se analizirali rezultati liječenja, postojala je prognostička korist, ali to pokopava princip randomizacije i povećava pristranost.

Moždani mikroembolizmi povezani uz FA i CA čini se da nemaju veću važnost te CA sama može poboljšati kognitivne sposobnosti, kao što je to u jednoj studiji kroz jednu godinu proučavano i praćeno u 308 ispitanika.[52]

Većina elektrofizioloģa i dalje govori svojim bolesnicima da je primarni cilj ablacije FA poboljšanje kvalitete života (QOL). Prvo randomizirano kontrolirano istraživanje (RCT) utjecaja ablacije FA u usporedbi s primjenom lijekova na kvalitetu života kao primarnim ishodom, objavljeno je 2019. te daje prednost primjeni CA.[53] Iako je to bilo malo istraživanje koje je obuhvatilo 155 ispitanika, ono otvara put za dvostruko slijepe RCT o utjecaju ablacije FA na QOL.

Uporaba krioablacije kod FA tijekom ove godine sakupila je više podataka: ona je brža od kateterske ablacije FA[54], povezana je s manjim rizikom od razvoja perikardijalnog izljeva[55,56] i ima superiorne ishode[54,55] bez obzira na volumen centra.[57]

Ove su godine objavljeni rezultati nekoliko velikih registara. Švedski registar CA prikazuje da su kateterske procedure povezane s vrlo niskom stopom komplikacija i smrti, a kako se povećava učestalost kateterskih ablacija, tako se od komplikacija najčešće ponavlja FA (41 %) u odnosu na ventrikulsku tahikardiju (VT) i ventrikulske ekstrasistole (VES).[58] Prema europskom registru, krioablacije su jednako učinkovite u žena, ali su povezane s višom učestalosti komplikacija.[59] Danski je registar potvrdio da je stopa uspjeha ablacije undulacije atrija 90 %, ali da je FA uobičajena pojava (13 %) unutar 2 godine od postupka.[60] Njemački registar Helios pokazao je da je učestalost perikardijalnog izljeva iznosila 0,9 % na temelju praćenja 21 141 bolesnika s kateterskom ablacijom FA te da je veća vjerojatnost pojave navedenog u centrima s malim volumenom pri uporabi radiofrekventne ablacije (RF), ali ne i krioablacije.[55]

Objavljeni su rezultati multicentričnog istraživanja koje je obuhvatilo 110 ispitanika podvrgnutih kateterskoj ablaciji zbog električke oluje.[61] Unutarbolnički mortalitet (27 %) i smrtnost tijekom dvije godine praćenja (36 %) bili su veliki i povezani s vremenom učinjene kateterske ablacije.

Retrospektivna studija koja je obuhvatila 110 ispitanika s rekurentnim VT-om kod aritmogene ventrikulske kardiomiopatije pokazala je da CA nije djelotvornija od lijekova, ali je vjerojatnije da će biti uspješnija ako se primjenjuju epikardijalni i endokardijalni pristup.[62]

Nove tehnologije mapiranja

Uviđa se da je osnovni razlog neuspjeha kateterskih ablacija kompleksnih aritmija nedostatak nerazumijevanja mehanizma aritmije. Ulažu se veliki napori u pokušaj njegova rješenja. Ove godine uspješno je primijenjeno *ripple* mapiranje kod perzistentne FA (18 mjeseci 53 % nasuprot 39 % konvencionalnog mapiranja)[64], atrijske tahikardije[65] i VT-u u aritmogenoj desnostranoj ventrikulskoj kardiomiopatiji (ARCV).[66] Nekontaktno mapiranje vratilo se u kliničku praksu te u opservacijskim ispitivanjima pokazuje dobre ishode u bolesnika podvrgnutih kateterskoj ablaciji perzistentne FA tijekom 12-mjesečnog razdoblja (59 %).[67] Predočeno je kliničko ispitivanje primjenom STAR maping sustava (**slika 3**) u 35 bolesnika u kojemu se u 80 % bolesnika nije pojavila ponovna FA

and favoured CA.[53] While this was a small study, 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 2 years after.[60] The German Helios registry showed that pericardial effusion rates were 0.9% in 21 141 AF CA, and was 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 recognized 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 used in persistent AF (18 months 53% vs. 39% conventional),[64] atrial tachycardia,[65] and VT in arrhythmogenic right ventricular cardiomyopathy (ARVC).[66] Non-contact mapping is returning to clinical practice with an observational trial showed good outcomes for persistent AF CA at 12 months (59%).[67] 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.[68] 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.[63] Electroporation is also showing promise as a novel energy source that is highly effective with low complication rates.[69] The use of radiotherapy to treat intractable VT is an exciting innovation, showing promising results in a small prospective study of 19 patients.[70]

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. CA of ventricular arrhythmia (VA) guideline suggests that programmed electrical stimulation

FIGURE 3. Please see the original article (Eur Heart J. 2020 Feb 1;41(5):619-625c.).

nakon STAR vođene kateterske ablacije perzistentne FA tijekom 18-mjesečnog razdoblja praćenja.[68] Ostaje vidjeti hoće li se neki od njih početi primjenjivati u širokoj kliničkoj praksi.

Izvori energije

Primjena visoke radiofrekventne (RF) energije u kratkom razdoblju čini point-by-point katetersku ablaciju FA bržom i za sada nije povezana s lošijim ishodom.[63] Elektroporacija također obećava kao novi izvor energije te je visoko učinkovita s niskom učestalošću komplikacija.[69] Primjena radioterapije u liječenju postojane VT uzbudljiva je inovacija koja obećava dobre rezultate u malom prospektivnom istraživanju u 19 bolesnika.[70]

Smjernice i usuglašena stajališta

Ove su godine objavljene brojne smjernice i one su koristan pregled literature. Međutim, treba se oduprijeti iskušenju da se smjernice prihvate kao dogma jer su one često temelje na usuglašenim stajalištima autora, a ne na čvrstim dokazima. Smjernice o kateterskoj ablaciji ventrikulskih aritmija upućuju na povratak programirane električne stimulacije kao metodu prognostičkog predviđanja u bolesnika s učestalim VES-om i strukturnom bolesti srca, a također preporučuju primjenu ICE-a kod ablacija ventrikulskih aritmija (VA), iako velik dio ne rabi ICE bez uočljivih posljedica na ishode liječenja.[71] Zajednički dokument upozorava na razlike u ishodima liječenja aritmija koje ovise o spolu, međutim, to ne bi trebalo utjecati na primjenu kateterske ablacije u žena.[72]

Ventrikulske aritmije

Aritmogena kardiomiopatija

Ovo je bila važna godina za aritmogenu kardiomiopatiju (ACM). Velik je broj publikacija koje treba spomenuti. Prva je Heart Rhythm Society Consensus Document on Arrhythmogenic Cardiomyopathy.[73] Ovaj dokument, čiji su glavni autori McKenna i Towbin, redefinira ACM kao stanje srčane disfunkcije koje se pojavljuje uz simptomatske i/ili asimptomatske aritmije. Ovaj prošireni pristup definicije uključuje klasičnu aritmogenu kardiomiopatiju lijeve klijetke (ARVC), ali i druge podskupine bolesnika (sarkoidoza, Chagasova bolest, miokarditis i velik broj nasljednih kardiomiopatija). Ovo je opsežan i provokativan članak koji treba imati na umu. Jedan od ciljeva grupe autora jest poticanje da se bolesnici s aritmijama i kardiomiopatijama liječe u specijaliziranim centrima koji provode sveobuhvatnu obradu, organiziraju gensko testiranje te utvrđuju rizik od aritmije i potrebu za ICD-om.[74]

Autori druge važne publikacije su Cadrin-Tourigny *i sur.*[74] Zajedničkim naporom pet međunarodnih registara razvijen je kalkulator za procjenu rizika od ARVC-a kako bi se lakše procijenio rizik i donijela odluka u potrebi ugradnje ICD-a 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.[71] The sex differences in arrhythmia consensus highlighted that although outcomes may be different, this should not influence provision of CA for females.[72]

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.[73] 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 groups goals was to encourage having patients present with arrhythmias and a cardiomyopathy to a specialized centre that perform comprehensive evaluation, arrange for genetic testing, and determine 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 five 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 five 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 h, and right ventricular ejection fraction. And 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

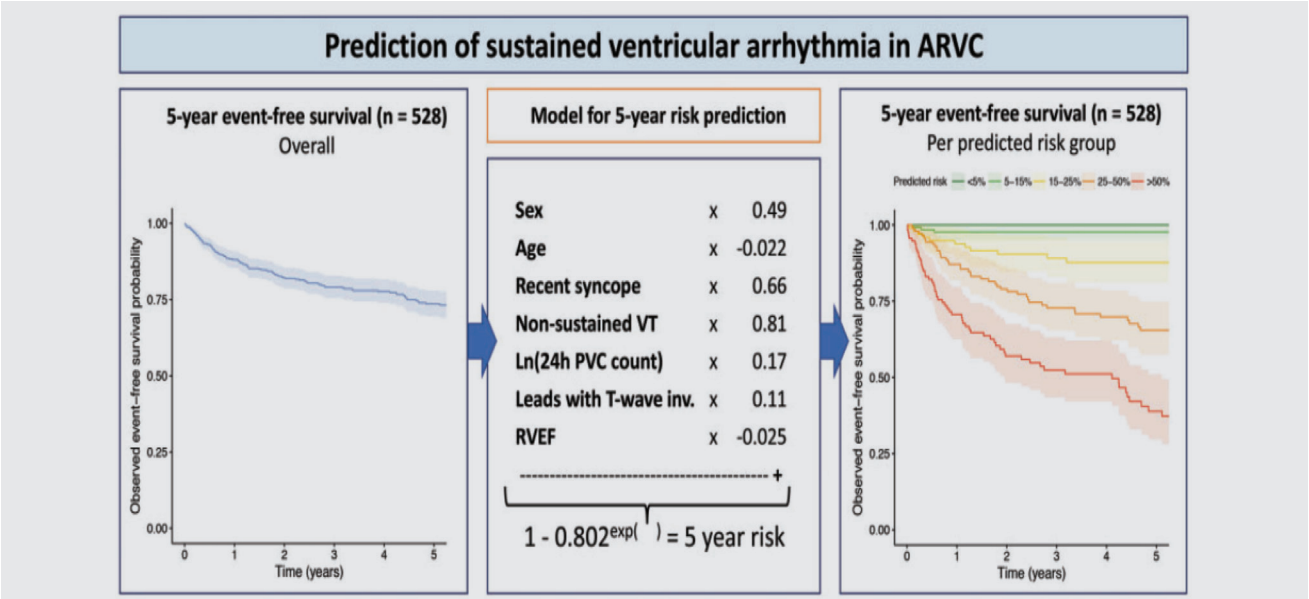


FIGURE 4. Prediction of sustained ventricular arrhythmia in arrhythmogenic right ventricular dysplasia/cardiomyopathy.
ARVC, arrhythmogenic right ventricular dysplasia/cardiomyopathy; inv., inversion; PVC, premature ventricular complex; RVEF, right ventricular ejection fraction; VT, ventricular tachycardia.[74]

(www.ARVCrisk.com). Uključeno je više od 500 bolesnika iz pet američkih i europskih registara. Tijekom razdoblja praćenja od 5 godina 28 % bolesnika doživjelo je postojanu VT, iznenadnu srčanu smrt ili je primilo adekvatnu ICD terapiju. Izrađen je model predviđanja godišnjeg rizika od aritmije (**slika 4**). Osnovne varijable uključene u model jesu nedavna sinkopa, životna dob, spol, nepostojana VT, broj VES-a tijekom 24 sata i ejekcijska frakcija desne klijetke. Chatterjee *i sur.*[75] ispitivali su dijagnostičko značenje anti-Desmoglein-2 protutijela u dijagnozi ARVC-a. Utvrđena je prisutnost protutijela DSG-2 u skupinama 12/12 i 25/25 bolesnika s ARVC-om i 7/8 ispitanika s graničnom dijagnozom. Protutijela nisu bila utvrđena u 11/12 i 20/20 kontrolnim skupinama ispitanika. Autori su zaključili da su anti-Desmoglein-2 protutijela senzitivni i specifični markeri za ARVC. Test treba dodatno testirati u više kontrolnih skupina, uključujući i one sa sarkoidozom srca prije negoli bude dostupan u kliničkoj praksi.

Srčani zastoj

Sondergaard *i sur.*[76] proučavali su u Danskoj laičku CPR u osoba koje su doživjele izvanbolnički srčani zastoj. Više od tri četvrtine srčanih zastoja događa se u stambenim četvrtima. Učestalost laičkog CPR-a između 2001. i 2004. godine porasla je s 36 % na 84 % na javnim mjestima te sa 16 % na 61 % u stambenim četvrtima. Očekivano, povećana učestalost CPR-a rezultirala je povećanjem 30-dnevnog preživljavanja od srčanog zastoja sa 6 % na 25 % na javnim mjestima i s 3 % na 10 % u stambenim četvrtima.

Srčani uređaji

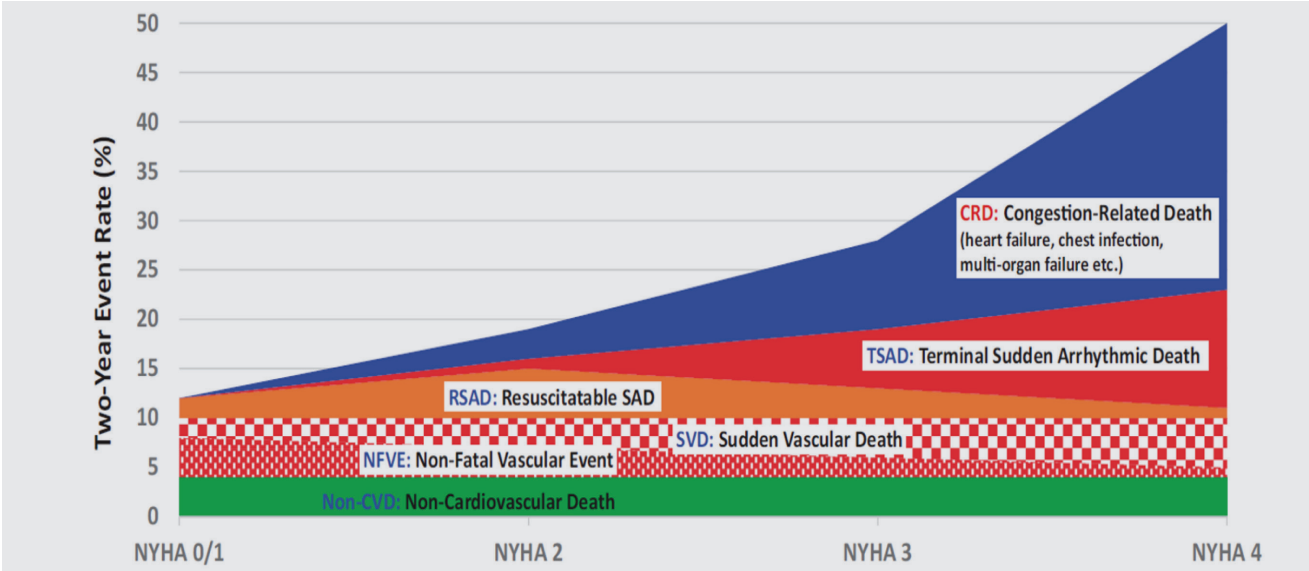
Koji su to dokazi koji stoje iza postojećih smjernica za ugradnju ICD-a u primarnoj prevenciji u današnje doba? Mogu li se populacije bolesnika, terapija, algoritmi liječenja, i to osobito u srčanom zatajivanju, te provedena ispitivanja prije više od in more control populations including those with cardiac sarcoidosis.

Cardiac arrest

Sondergaard *et al.*[76] examined the use of bystander CPR among patients who experience 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% to 84% in public locations and from 16% to 61% in residential locations. Not surprisingly, the increased use of CPR resulted in an increased 30-day survival from 6% to 25% for arrests in public locations and from 3% to 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, 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 the majority of patients.[78] Moreover, increasing evidence indicate 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. neurohormonal blockade and cardiac resynchronization therapy (CRT).[79] These concepts and findings call into question the validity of the available randomized 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



	NYHA 0/1		NYHA 2		NYHA 3		NYHA 4	
	Absolute Rate	% of Deaths	Absolute Rate	% of Deaths	Absolute Rate	% of Deaths	Absolute Rate	% of Deaths
CRD	0%	0%	3%	16%	9%	32%	27%	54%
TSAD	<1%	<1%	1%	5%	6%	21%	12%	24%
RSAD	2%	17%	5%	26%	3%	11%	1%	2%
SVD	2%	17%	3%	16%	4%	14%	5%	10%
NFVE	4%	33%	3%	16%	2%	7%	1%	2%
Non-CVD	4%	33%	4%	21%	4%	14%	4%	8%

FIGURE 5. Two-year cause-specific mortality and non-fatal vascular events for patients with cardiovascular disease according to New York HeartAssociation 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 soon to die of worsening heart failure.

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-resucitatable) sudden arrhythmic death.

jednog desetljeća primijeniti na današnju kliničku praksu (**slika 5**)[77]. Prema velikoj analizi Francusko-britansko-švedsko-češke mreže, smrt zbog progresivnoga srčanog zatajivanja ostaje vodeći uzrok smrti za većinu bolesnika.[78] Štoviše, sve je više dokaza koji upućuju na to da je remodeliranje lijeve klijetke (LV) glavni pokretač aritmija koje uzrokuju iznenadnu srčanu smrt (SCD). One se mogu umanjiti primjenom mjera koje su usmjerenje na sprječavanje (ili čak poništavanje) tih procesa, kao što su neurohumoralna blokada ili resinkronizirajuća terapija srca (CRT).[79] Ovi koncepti i zaključci dovode u pitanje valjanost dostupnih dokaza randomiziranih kliničkih ispitivanja koja čine osnovu trenutačnih preporuka za implantaciju ICD-a u primarnoj prevenciji bolesnika sa zatajivanjem srca. Na konceptualnoj razini postavlja se dodatno pitanje treba li rezultate istraživanja prihvaćati s vremenskim ograničenjem nakon čijeg bi isteka zahtijevali reevaluaciju. Međutim, s druge strane, terapija uređajima unaprijeđena je posljednjeg desetljeća, uključujući bolje algoritme za detekci-

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.[80] Indeed, even entirely leadless CRT systems appear to be feasible.[81] 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.[82]

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

ju aritmije i prevenciju neodgovarajuće isporuke šokova, kao i razvoj ekstravaskularnih sustava kao što su S-ICD i ekstravaskularni (EV-) ICD.[80] Čini se da su mogući čak i CRT sustavi bez elektroda.[81] Ako se dokažu da su sigurni i učinkoviti u velikim RCT-ima (koji su u tijeku), ovi, novi uređaji znatno će smanjiti morbiditet povezanog sa sustavom, što ponovno može dovesti do prevage uređaja u prevenciji SCD-a. Doista, neodgovarajuće isporuke šokova i infekcije najznačajnije su razarajuće komplikacije postojećih ICD sustava, što značajno utječe na kvalitetu života, morbiditet i mortalitet.[82]

Dodatno, iznad svega su potrebni bolji čimbenici predikcije SCD-a od ejekcijske frakcije lijeve klijetke (LVEF) kako bi se bolje zaštitili oni bolesnici kojima je uređaj potreban (od onih kojima nije potrebna ugradnja uređaja). Nedavno je predstavljen jedan takav model predviđanja rizika za bolesnike nakon preboljenog infarkta miokarda s očuvanom LVEF koristeći se neinvazivnim elektrokardiografskim čimbenicima rizika (VES, nepostojana VT, kasni potencijali, prolongacija QTc, povećan alternans T-vala, smanjena varijabilnost srčane frekvencije i nenormalni kapacitet usporivanja i turbulencije) u kombinaciji s programiranom ventrikulskom stimulacijom.[83] Algoritam je pokazao izvrsnu senzitivnost i negativnu prediktivnu vrijednost (vjerojatno najvažniji parametar) od 100 %, kao i specifičnost od 83 %, a, s druge strane, pozitivna mu je prediktivna vrijednosti bila samo 22 %. Suvremene slikovne metode, poput MRI-ja, dodatno pridonose u prepoznavanju bolesnika s povećanim rizikom od ventrikulskih aritmija, a koji mogu imati koristi od implantacije ICD-a.[84] Slični su algoritmi također razvijeni za rijetke bolesti kao što je ARVC.[74] Ako pokažu pozitivne učinke u randomiziranim studijima, ovi koncepti mogu dovesti do pomicanja struke iznad postojećih standarda uporabe LVEF kao glavnog čimbenika rizika. Međutim, sve dok takvi rezultati studija nisu dostupni, razložno je pridržavati se trenutačnih dokaza i preporuka smjernica. Istodobno se potiče regrutacija bolesnika u istraživanja koja su u tijeku kako bi se ubrzalo stvaranje dokaza visoke razine koji mogu potencijalno izmijeniti trenutačnu kliničku praksu. Resinkronizirajuća terapija srca ostaje važan modalitet liječenja za bolesnike sa zatajivanjem srca radi indukcije reverzibilnog remodeliranja LV-a i poboljšanja morbiditeta i mortaliteta. Međutim, učestalost takozvanih *non-respondera* (onih koji ne odgovore) ostaje 20 – 30 %, ovisno o definiciji i graničnim vrijednostima.[85] U MORE-CRT MMP studiji ispitivan je učinak stimulacije LV-a s dvaju mjesta, umjesto jednog, kako bi se smanjio broj ispitanika koji ne odgovaraju na liječenje (*non-responders*).[86] Randomizirana su 544 bolesnika klasificirana kao „non-responders" (definirani kao smanjenje endsistoličkog volumena LV-a za <15 %) 6 mjeseci nakon implantacije CRT-a kako bih ušli u grupe u kojima je 'Multipoint'™ algoritam uključen (MPP ON) ili isključen (standardna skrb). Iako se stopa konverzije u onih koji odgovaraju na terapiju („responders") nije razlikovala između dviju grupa (31,8 % u odnosu prema 33,8 %), bolesnici iz MPP grupe programirane na široku elektrodnu udaljenost imali su mnogo veću vjerojatnost konverzije u onih koji odgovaraju na terapiju („respondera") u usporedbi s onima koji su programirani u drugim kombinacijama vektora (45,6 % nasuprot 26,2 %, P = 0.006).[86] Iako su zanimljivi i biološki uvjerljivi, ti se rezultati moraju promatrati u okvirima hipoteze s obzirom na negativan primarni ishod.

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) combined with programmed ventricular stimulation.[83] The algorithm yielded an excellent sensitivity and negative predictive value (arguably the most important parameter) of 100%, as well as a specificity of 93.8%; on the downside, positive predictive value was only 22%. Modern imaging modalities such as MRI may further yield added value in identifying patients at increased risk of ventricular arrhythmias who may benefit from ICD implantation.[84] Similar algorithms are being developed also for rarer disease entities such as arrhythmogenic right ventricular cardiomyopathy (ARVC).[74] If proven positive in randomized clinical outcome trials, these concepts may move the field closer to venturing beyond the current (suboptimal) standard of LVEF for risk stratification. Until such outcome trials are available, however, it may be prudent to stick to the currently available evidence and guideline recommendations; at the same time, recruitment into ongoing trials is encouraged in order to accelerate the generation of high-level evidence which may potentially alter current clinical practice.

Cardiac resynchronization 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.[85] The MORE-CRT MPP trial investigated the effect of stimulating the LV from two sites instead of one to reduce the number of non-responders.[86] Five hundred and forty-four patients classified as non-responders (defined as an LV end-systolic volume reduction by <15%) 6 months after CRT implantation were randomized 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 two 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%, $P = 0.006$).[86] 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. Profesor Lip is a consultant for Bayer/Janssen, BMS/Pfizer, Medtronic, Boehringer Ingelheim, Novartis, Verseon and Daiichi-Sankyo. Speaker for Bayer, BMS/Pfizer, Medtronic, Boehringer Ingelheim, and Daiichi-Sankyo. No fees are directly received personally. R.S. reports other income from Rhythm AI, grants, personal fees and non-financial support from Medtronic, grants, personal fees and non-financial support from Biosense Webster, personal fees and non-financial support from Abbott , personal fees and non-financial support from Boston Scientific, during the conduct of the study; personal fees and non-financial support from Daiichi Sankyo, non-financial support from Boeringher Ingleheim, 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.

LITERATURE

1. Chen Q, Xu J, Gianni C, Trivedi C, Della Rocca DG, Bassiouny M, et al. Simple electrocardiographic criteria for rapid identification of wide QRS complex tachycardia: the new limb lead algorithm. Heart Rhythm. 2020 Mar;17(3):431-438. https://doi.org/10.1016/j.hrthm.2019.09.021
2. May AM, DeSimone CV, Kashou AH, Hodge DO, Lin G, Kapa S, et al. The WCT formula: a novel algorithm designed to automatically differentiate wide-complex tachycardias. J Electrocardiol. 2019;54:61-8. https://doi.org/10.1016/j.jelectrocard.2019.02.008
3. May AM, Brenes-Salazar JA, DeSimone CV, Vaidya VR, Ternus BW, Hodge DO, et al. Electrocardiogram algorithms used to differentiate wide complex tachycardias demonstrate diagnostic limitations when applied by non-cardiologists. J Electrocardiol. 2018;51:1103-9. https://doi.org/10.1016/j.jelectrocard.2018.09.015.
4. Pachón M, Arias MA, Salvador-Montañés Ó, Calvo D, Peñafiel P, Puchol A, et al. A scoring algorithm for the accurate differential diagnosis of regular wide QRS complex tachycardia. Pacing Clin Electrophysiol. 2019;42:625-33. https://doi.org/10.1111/pace.13658
5. Hwang J, Kim J, Choi KJ, Cho MS, Nam GB, Kim YH. Assessing accuracy of wrist-worn wearable devices in measurement of paroxysmal supraventricular tachycardia heart rate. Korean Circ J. 2019;49:437-45. https://doi.org/10.4070/kcj.2018.0323
6. Ernst S, Cazzoli I, Guarguagli S. An initial experience of high-density mapping-guided ablation in a cohort of patients with adult congenital heart disease. Europace. 2019;21:i43-53. https://doi.org/10.1093/europace/euy188
7. Raja JM, Cave B, Jefferies JL, Khouzam RN. Etripamil: intranasal calcium channel blocker: a novel noninvasive modality in the treatment of paroxysmal supraventricular tachycardia. Curr Probl Cardiol. 2019 Jun 22:100430. doi: 10.1016/j.cpcardiol.2019.05.003. [Epub ahead of print]. https://doi.org/10.1016/j.cpcardiol.2019.05.003
8. Faisaluddin M, Ashish K, Hajra A, Mondal S, Bandyopadhyay D. Etripamil: self-management of supraventricular tachycardia is not far away? Int J Cardiol Heart Vasc. 2019;22:82-3. https://doi.org/10.1016/j.ijcha.2018.12.007
9. Hu J, Yu J, Chen Q, Hu J, Huang Q, Xia Z, et al. Efficacy of nifekalant in patients with Wolff-Parkinson-White syndrome and atrial fibrillation: electrophysiological and clinical findings. J Am Heart Assoc. 2019;8:e012511. https://doi.org/10.1161/JAHA.119.012511
10. Brugada J, Katritsis DG, Arbelo E, Arribas F, Bax JJ, Blomström-Lundqvist C, et al.; ESC Scientific Document Group. ESC Guidelines for the management of patients with supraventricular tachycardia. The Task Force for the management of patients with supraventricular tachycardia of the European Society of Cardiology (ESC). Eur Heart J. 2020 Feb 1;41(5):655-720. https://doi.org/10.1093/eurheartj/ehz467
11. Allan V, Honarbakhsh S, Casas JP, Wallace J, Hunter R, Schilling R, et al. Are cardiovascular risk factors also associated with the incidence of atrial fibrillation? A systematic review and field synopsis of 23 factors in 32 population-based cohorts of 20 million participants. Thromb Haemost. 2017;117:837-50. https://doi.org/10.1160/TH16-11-0825
12. Lim YM, Yang PS, Jang E, Yu HT, Kim TH, Uhm JS, et al. Body mass index variability and long-term risk of new-onset atrial fibrillation in the general population: a Korean Nationwide Cohort Study. Mayo Clin Proc. 2019;94:225-35. https://doi.org/10.1016/j.mayocp.2018.10.019
13. Linz D, Brooks AG, Elliott AD, Nalliah CJ, Hendriks JML, Middeldorp ME, et al. Variability of sleep apnea severity and risk of atrial fibrillation: the VARIOSA-AF study. JACC Clin Electrophysiol. 2019;5:692-701. https://doi.org/10.1016/j.jacep.2019.03.005
14. Li YG, Pastori D, Farcomeni A, Yang PS, Jang E, Joung B, et al. A Simple Clinical Risk Score (C2HEST) for predicting incident atrial fibrillation in Asian subjects: derivation in 471,446 Chinese subjects, with internal validation and external application in 451,199 Korean subjects. Chest. 2019;155:510-8. https://doi.org/10.1016/j.chest.2018.09.011
15. Li YG, Bisson A, Bodin A, Herbert J, Grammatico-Guillon L, Joung B, et al. C2HEST Score and prediction of incident atrial fibrillation in poststroke patients: a French Nationwide Study. J Am Heart Assoc. 2019;8:e012546. https://doi.org/10.1161/JAHA.119.012546
16. Hart RG, Sharma M, Mundl H, Kasner SE, Bangdiwala SI, Berkowitz SD, et al. Rivaroxaban for stroke prevention after embolic stroke of undetermined source. N Engl J Med. 2018;378:2191-201. https://doi.org/10.1056/NEJMoa1802686
17. Diener HC, Sacco RL, Easton JD, Granger CB, Bernstein RA, Uchiyama S, et al. Dabigatran for prevention of stroke after embolic stroke of undetermined source. N Engl J Med. 2019;380:1906-17. https://doi.org/10.1056/NEJMoa1813959
18. Mairesse GH, Moran P, Van Gelder IC, Elsner C, Rosenqvist M, Mant J, et al. Screening for atrial fibrillation: a European Heart Rhythm Association (EHRA) consensus document endorsed by the Heart Rhythm Society (HRS), Asia Pacific Heart Rhythm Society (APHRS), and Sociedad Latinoamericana de Estimulacion Cardiaca y Electrofisiologia (SOLAECE). Europace. 2017;19:1589-623. https://doi.org/10.1093/europace/eux177
19. Perez MV, Mahaffey KW, Hedlin H, Rumsfeld JS, Garcia A, Ferris T, et al.; Apple Heart Study Investigators. Large-scale assessment of a smartwatch to identify atrial fibrillation. N Engl J Med. 2019;381:1909-17. https://doi.org/10.1056/NEJMoa1901183
20. Guo Y, Lane DA, Wang L, Chen Y, Lip GYH. mAF-App II Trial Investigators. Mobile Health (mHealth) technology for improved screening, patient involvement and optimising integrated care in atrial fibrillation: the mAFA (mAF-App) II randomised trial. Int J Clin Pract. 2019;73:e13352. https://doi.org/10.1111/ijcp.13352
21. Jung H, Yang PS, Sung JH, Jang E, Yu HT, Kim TH, et al. Hypertrophic cardiomyopathy in patients with atrial fibrillation: prevalence and associated stroke risks in a Nationwide Cohort Study. Thromb Haemost. 2019;119:285-93. https://doi.org/10.1055/s-0038-1676818
22. Steensig K, Olesen KKW, Thim T, Nielsen JC, Jensen SE, Jensen LO, et al. Should the presence or extent of coronary artery disease be quantified in the CHA2DS2-VASc score in atrial fibrillation? A report from the Western Denmark Heart Registry. Thromb Haemost. 2018;118:2162-70. https://doi.org/10.1055/s-0038-1675401

23. Attia ZI, Noseworthy PA, Lopez-Jimenez F, Asirvatham SJ, Deshmukh AJ, Gersh BJ, et al. An artificial intelligence-enabled ECG algorithm for the identification of patients with atrial fibrillation during sinus rhythm: a retrospective analysis of outcome prediction. Lancet. 2019;394:861-7. https://doi.org/10.1016/S0140-6736(19)31721-0
24. Borre ED, Goode A, Raitz G, Shah B, Lowenstern A, Chatterjee R, et al. Predicting thromboembolic and bleeding event risk in patients with non-valvular atrial fibrillation: a systematic review. Thromb Haemost. 2018;118:2171-87. https://doi.org/10.1055/s-0038-1675400
25. Chao TF, Lip GYH, Lin YJ, Chang SL, Lo LW, Hu YF, et al. Incident risk factors and major bleeding in patients with atrial fibrillation treated with oral anticoagulants: a comparison of baseline, follow-up and delta HAS-BLED scores with an approach focused on modifiable bleeding risk factors. Thromb Haemost. 2018;118:768-77. https://doi.org/10.1055/s-0038-1636534
26. Guo Y, Zhu H, Chen Y, Lip G. Comparing bleeding risk assessment focused on modifiable risk factors only versus validated bleeding risk scores in atrial fibrillation. Am J Med. 2018;131:185-92. https://doi.org/10.1016/j.amjmed.2017.09.009
27. Rivera-Caravaca JM, Marín F, Vilchez JA, Gálvez J, Esteve-Pastor MA, Vicente V, et al. Refining stroke and bleeding prediction in atrial fibrillation by adding consecutive biomarkers to clinical risk scores. Stroke. 2019;50:1372-9. https://doi.org/10.1161/STROKEAHA.118.024305
28. Chang TY, Lip GYH, Chen SA, Chao TF. Importance of risk reassessment in patients with atrial fibrillation in guidelines: assessing risk as a dynamic process. Can J Cardiol. 2019;35:611-8. https://doi.org/10.1016/j.cjca.2019.01.018
29. Chao TF, Liao JN, Tuan TC, Lin YJ, Chang SL, Lo LW, et al. Incident co-morbidities in patients with atrial fibrillation initially with a CHA2DS2-VASc Score of 0 (Males) or 1 (Females): implications for reassessment of stroke risk in initially 'low-risk' patients. Thromb Haemost. 2019;119:1162-70. https://doi.org/10.1055/s-0039-1683933
30. Fanaroff AC, Steffel J, Alexander JH, Lip GYH, Califf RM, Lopes RD. Stroke prevention in atrial fibrillation: re-defining 'real-world data' within the broader data universe. Eur Heart J. 2018;39:2932-41. https://doi.org/10.1093/eurheartj/ehy236
31. Lee SR, Choi EK, Han KD, Jung JH, Oh S, Lip G. Edoxaban in Asian patients with atrial fibrillation: effectiveness and safety. J Am Coll Cardiol. 2018;72:838-53. https://doi.org/10.1016/j.jacc.2018.05.066
32. Deitelzweig S, Keshishian A, Li X, Kang A, Dhamane AD, Luo X, et al. Comparisons between oral anticoagulants among older nonvalvular atrial fibrillation patients. J Am Geriatr Soc. 2019;67:1662-71. https://doi.org/10.1111/jgs.15956
33. Chao TF, Liu CJ, Lin YJ, Chang SL, Lo LW, Hu YF, et al. Oral anticoagulation in very elderly patients with atrial fibrillation: a Nationwide Cohort Study. Circulation. 2018;138:37-47. https://doi.org/10.1161/CIRCULATIONAHA.117.031658
34. Paquette M, Riou França L, Teutsch C, Diener HC, Lu S, Dubner SJ, et al. Persistence with dabigatran therapy at 2 years in patients with atrial fibrillation. J Am Coll Cardiol. 2017;70:1573-83. https://doi.org/10.1016/j.jacc.2017.07.793
35. Montalescot G, Brotons C, Cosyns B, Crijns HJ, D'Angelo A, Drouet L, et al. Educational impact on apixaban adherence in atrial fibrillation (the AEGEAN STUDY): a randomized clinical trial. Am J Cardiovasc Drugs. 2020 Feb;20(1):61-71. https://doi.org/10.1007/s40256-019-00356-2
36. Lee SR, Choi EK, Han KD, Jung JH, Cha MJ, Oh S, et al. Non-vitamin K antagonist oral anticoagulants in Asian patients with supranormal renal function. Stroke. 2019;50:1480-9. https://doi.org/10.1161/STROKEAHA.118.024264
37. Siontis KC, Zhang X, Eckard A, Bhave N, Schaubel DE, He K, et al. Outcomes associated with apixaban use in patients with end-stage kidney disease and atrial fibrillation in the United States. Circulation. 2018;138:1519-29. https://doi.org/10.1161/CIRCULATIONAHA.118.035418
38. Hohnloser SH, Camm J, Cappato R, Diener HC, Heidbuchel H, Lanz HJ, et al. Uninterrupted administration of edoxaban vs vitamin K antagonists in patients undergoing atrial fibrillation catheter ablation: rationale and design of the ELIMINATE-AF study. Clin Cardiol. 2018;41:440-9. https://doi.org/10.1002/clc.22918
39. Calkins H, Willems S, Gerstenfeld EP, Verma A, Schilling R, Hohnloser SH, et al. Uninterrupted dabigatran versus warfarin for ablation in atrial fibrillation. N Engl J Med. 2017;376:1627-36. https://doi.org/10.1056/NEJMoa1701005
40. Ezekowitz MD. Pollack CVJr, Halperin JL, England RD, VanPelt Nguyen S, et al. Apixaban compared to heparin/vitamin K antagonist in patients with atrial fibrillation scheduled for cardioversion: the EMANATE trial. Eur Heart J. 2018;39:2959-71. https://doi.org/10.1093/eurheartj/ehy148
41. Vranckx P, Valgimigli M, Eckardt L, Tijssen J, Lewalter T, Gargiulo G, et al. Edoxaban-based versus vitamin K antagonist-based antithrombotic regimen after successful coronary stenting in patients with atrial fibrillation (ENTRUST-AF PCI): a randomised, open-label, phase 3b trial. Lancet. 2019;394:1335-43. https://doi.org/10.1016/S0140-6736(19)31872-0
42. Lopes RD, Heizer G, Aronson R, Vora AN, Massaro T, Mehran R, et al. Antithrombotic therapy after acute coronary syndrome or PCI in atrial fibrillation. N Engl J Med. 2019;380:1509-24. https://doi.org/10.1056/NEJMoa1817083
43. Lopes RD, Hong H, Harskamp RE, Bhatt DL, Mehran R, Cannon CP, et al. Safety and efficacy of antithrombotic strategies in patients with atrial fibrillation undergoing percutaneous coronary intervention: a network meta-analysis of randomized controlled trials. JAMA Cardiol. 2019;4:747. https://doi.org/10.1001/jamacardio.2019.1880
44. Yasuda S, Kaikita K, Akao M, Ako J, Matoba T, Nakamura M, et al. Antithrombotic therapy for atrial fibrillation with stable coronary disease. N Engl J Med. 2019;381:1103-13. https://doi.org/10.1056/NEJMoa1904143
45. Lip GY. The ABC pathway: an integrated approach to improve AF management. Nat Rev Cardiol. 2017;14:627-8. https://doi.org/10.1038/nrcardio.2017.153
46. Gallagher C, Elliott AD, Wong CX, Rangnekar G, Middeldorp ME, Mahajan R, et al. Integrated care in atrial fibrillation: a systematic review and meta-analysis. Heart. 2017;103:1947-53. https://doi.org/10.1136/heartjnl-2016-310952
47. Yoon M, Yang PS, Jang E, Yu HT, Kim TH, Uhm JS, et al. Improved population-based clinical outcomes of patients with atrial fibrillation by compliance with the simple ABC (Atrial Fibrillation Better Care) pathway for integrated care management: a nationwide cohort study. Thromb Haemost. 2019;19:1695-703. https://doi.org/10.1055/s-0039-1693516
48. Pastori D, Pignatelli P, Menichelli D, Violi F, Lip G. Integrated care management of patients with atrial fibrillation and risk of cardiovascular events: the ABC (Atrial fibrillation Better Care) pathway in the ATHERO-AF study cohort. Mayo Clin Proc. 2019;94:1261-7. https://doi.org/10.1016/j.mayocp.2018.10.022
49. Pastori D, Farcomeni A, Pignatelli P, Violi F, Lip GY. ABC (Atrial fibrillation Better Care) pathway and healthcare costs in atrial fibrillation: the ATHERO-AF study. Am J Med. 2019;132:856-61. https://doi.org/10.1016/j.amjmed.2019.01.003
50. Proietti M, Romiti GF, Olshansky B, Lane DA, Lip G. Improved outcomes by integrated care of anticoagulated patients with atrial fibrillation using the simple ABC (Atrial Fibrillation Better Care) pathway. Am J Med. 2018;131:1359-1366.e6. https://doi.org/10.1016/j.amjmed.2018.06.012
51. Packer DL, Mark DB, Robb RA, Monahan KH, Bahnson TD, Poole JE, et al. CABANA Investigators. Effect of catheter ablation vs antiarrhythmic drug therapy on mortality, stroke, bleeding, and cardiac arrest among patients with atrial fibrillation. The CABANA Randomized Clinical Trial. JAMA. 2019;321:1261-74. https://doi.org/10.1001/jama.2019.0693
52. Jin MN, Kim TH, Kang KW, Yu HT, Uhm JS, Joung B, et al. Atrial fibrillation catheter ablation improves 1-year follow-up cognitive function, especially in patients with impaired cognitive function. Circ Arrhythm Electrophysiol. 2019;12:e007197. https://doi.org/10.1161/CIRCEP.119.007197

53. Blomström-Lundqvist C, Gizurarson S, Schwieler J, Jensen SM, Bergfeldt L, Kennebäck G, et al. Effect of catheter ablation vs antiarrhythmic medication on quality of life in patients with atrial fibrillation. The CAPTAF Randomized Clinical Trial. JAMA. 2019;321:1059–68. https://doi.org/10.1001/jama.2019.0335
54. Mörtsell D, Arbelo E, Dagres N, Brugada J, Laroche C, Trines SA, et al.; ESC-EHRA Atrial Fibrillation Ablation Long-Term Registry Investigators. Cryoballoon vs. radiofrequency ablation for atrial fibrillation: a study of outcome and safety based on the ESC-EHRA atrial fibrillation ablation long-term registry and the Swedish catheter ablation registry. Europace. 2019;21:581–9. https://doi.org/10.1093/europace/euy239
55. Bollmann A, Ueberham L, Schuler E, Wiedemann M, Reithmann C, Sause A, et al. Cardiac tamponade in catheter ablation of atrial fibrillation: German-wide analysis of 21 141 procedures in the Helios atrial fibrillation ablation registry (SAFER). Europace. 2018;20:1944–51. https://doi.org/10.1093/europace/euy131
56. Hoffmann E, Straube F, Wegscheider K, Kuniss M, Andresen D, Wu L-Q, et al.; FREEZE Cohort Study Investigators. Outcomes of cryoballoon or radiofrequency ablation in symptomatic paroxysmal or persistent atrial fibrillation. Europace. 2019;21:1313–24. https://doi.org/10.1093/europace/euz155
57. Landolina M, Arena G, Iacopino S, Verlato R, Pieragnoli P, Curnis A, et al. Center experience does not influence long-term outcome and peri-procedural complications after cryoballoon ablation of paroxysmal atrial fibrillation: data on 860 patients from the real-world multicenter observational project. Int J Cardiol. 2018;272:130–6. https://doi.org/10.1016/j.ijcard.2018.07.051
58. Holmqvist F, Kesek M, Englund A, Blomström-Lundqvist C, Karlsson LO, Kennebäck G, et al. A decade of catheter ablation of cardiac arrhythmias in Sweden: ablation practices and outcomes. Eur Heart J. 2019;40:820–30. https://doi.org/10.1093/eurheartj/ehy709
59. Grecu M, Blomström-Lundqvist C, Kautzner J, Laroche C, Van Gelder IC, Jordaens L, et al. In-hospital and 12-month follow-up outcome from the ESC-EORP EHRA atrial fibrillation ablation long-term registry: sex differences. Europace. 2020 Jan 1;22(1):66-73. https://doi.org/10.1093/europace/euz225
60. Giehm-Reese M, Kronborg MB, Lukac P, Kristiansen SB, Nielsen JM, Johannessen A, et al. Recurrent atrial flutter ablation and incidence of atrial fibrillation ablation after first-time ablation for typical atrial flutter: a nation-wide Danish cohort study. Int J Cardiol. 2020 Jan 1;298:44-51. https://doi.org/10.1016/j.ijcard.2019.07.077
61. Komatsu Y, Hocini M, Nogami A, Maury P, Peichl P, Iwasaki YK, et al. Catheter ablation of refractory ventricular fibrillation storm after myocardial infarction: a multicenter study. Circulation. 2019;139:2315–25. https://doi.org/10.1161/CIRCULATIONAHA.118.037997
62. Mahida S, Venlet J, Saguner AM, Kumar S, Baldinger SH, AbdelWahab A, et al. Ablation compared with drug therapy for recurrent ventricular tachycardia in arrhythmogenic right ventricular cardiomyopathy: results from a multicenter study. Heart Rhythm. 2019;16:536–43. https://doi.org/10.1016/j.hrthm.2018.10.016
63. Winkle RA, Mohanty S, Patrawala RA, Mead RH, Kong MH, Engel G, et al. Low complication rates using high power (45–50 W) for short duration for atrial fibrillation ablations. Heart Rhythm. 2019;16:165–9. https://doi.org/10.1016/j.hrthm.2018.11.031
64. Melby DP, Gornick C, Abdelhadi R, Sengupta J, Pai M, Zakaib JS, et al. Outcomes following persistent atrial fibrillation ablation using localized sources identified with Ripple map. J Cardiovasc Electrophysiol. 2019;30:1860–7. https://doi.org/10.1111/jce.14092
65. Luther V, Agarwal S, Chow A, Koa-Wing M, Cortez-Dias N, Carpinteiro L, et al. Kanagaratnam PRipple-AT Study. A multicenter and randomized study comparing 3D mapping techniques during atrial tachycardia ablations. Circ Arrhythm Electrophysiol. 2019;12:e007394. https://doi.org/10.1161/CIRCEP.118.007394
66. Xie S, Kubala M, Liang JJ, Yang J, Desjardins B, Santangeli P, et al. Utility of ripple mapping for identification of slow conduction channels during ventricular tachycardia ablation in the setting of arrhythmogenic right ventricular cardiomyopathy. J Cardiovasc Electrophysiol. 2019;30:366–73. https://doi.org/10.1111/jce.13819
67. Willems S, Verma A, Betts TR, Murray S, Neuzil P, Ince H, et al. Targeting nonpulmonary vein sources in persistent atrial fibrillation identified by noncontact charge density mapping UNCOVER AF Trial. Circ Arrhythm Electrophysiol. 2019;12:e007233. https://doi.org/10.1161/CIRCEP.119.007233
68. Honarbakhsh S, Hunter RJ, Ullah W, Keating E, Finlay M, Schilling RJ. Ablation in persistent atrial fibrillation using stochastic trajectory analysis of ranked signals (STAR) mapping method. JACC Clin Electrophysiol. 2019;5:817–29. https://doi.org/10.1016/j.jacep.2019.04.007
69. Reddy VY, Neuzil P, Koruth JS, Petru J, Funosako M, Cochet H, et al. Pulsed field ablation for pulmonary vein isolation in atrial fibrillation. J Am Coll Cardiol. 2019;74:315–26. https://doi.org/10.1016/j.jacc.2019.04.021
70. Robinson CG, Samson PP, Moore KMS, Hugo GD, Knutson N, Mutic S, et al. Phase I/II Trial of electrophysiology-guided noninvasive cardiac radioablation for ventricular tachycardia. Circulation. 2019;139:313–21. https://doi.org/10.1161/CIRCULATIONAHA.118.038261
71. Cronin EM, Bogun FM, Maury P, Peichl P, Chen M, Namboodiri N, et al. Sapp JLJr, Sarkozy A, Soejima K, Stevenson WG, Tedrow UB, Tzou WS, Varma N, Zeppenfeld K. 2019 HRS/EHRA/APHRS/LAHRS expert consensus statement on catheter ablation of ventricular arrhythmias: executive summary. Europace. 2019 Aug 1;21(8):1143-1144. https://doi.org/10.1093/europace/euz132
72. Linde C, Bongiorni MG, Birgersdotter-Green U, Curtis AB, Deisenhofer I, Furokawa T, et al; ESC Scientific Document Group. Sex differences in cardiac arrhythmia: a consensus document of the European Heart Rhythm Association, endorsed by the Heart Rhythm Society and Asia Pacific Heart Rhythm Society. Europace. 2018 Oct 1;20(10):1565-1565ao. https://doi.org/10.1093/europace/euy067
73. Towbin JA, McKenna WJ, Abrams DJ, Ackerman MJ, Calkins H, Darrieux FCC, et al. Estes NAM3rd, Hua W, Indik JH, Ingles J, James CA, John RM, Judge DP, Keegan R, Krahn AD, Link MS, Marcus FI, McLeod CJ, Mestroni L, Priori SG, Saffitz JE, Sanatani S, Shimizu W, van Tintelen JP, Wilde AAM, Zareba W. 2019 HRS expert consensus statement on evaluation, risk stratification, and management of arrhythmogenic cardiomyopathy. Heart Rhythm. 2019;16:e301–72. https://doi.org/10.1016/j.hrthm.2019.05.007
74. Cadrin-Tourigny J, Bosman LP, Nozza A, Wang W, Tadros R, Bhonsale A, et al. A new prediction model for ventricular arrhythmias in arrhythmogenic right ventricular cardiomyopathy. Eur Heart J. 2019;40:1850–8. https://doi.org/10.1093/eurheartj/ehz103
75. Chatterjee D, Fatah M, Akdis D, Spears DA, Koopmann TT, Mittal K, et al. An autoantibody identifies arrhythmogenic right ventricular cardiomyopathy and participates in its pathogenesis. Eur Heart J. 2018;39:3932–44. https://doi.org/10.1093/eurheartj/ehy567
76. Sondergaard KB, Wissenberg M, Gerds TA, Rajan S, Karlsson L, Kragholm K, et al. Bystander cardiopulmonary resuscitation and long-term outcomes in out-of-hospital cardiac arrest according to location of arrest. Eur Heart J. 2019;40:309–18. https://doi.org/10.1093/eurheartj/ehy687
77. Cleland JGF, Hindricks G, Petrie M. The shocking lack of evidence for implantable cardioverter defibrillators for heart failure; with or without cardiac resynchronization. Eur Heart J. 2019;40:2128–30. https://doi.org/10.1093/eurheartj/ehz409
78. Barra S, Duehmke R, Providencia R, Narayanan K, Reitan C, Roubicek T, et al. Very long-term survival and late sudden cardiac death in cardiac resynchronization therapy patients. Eur Heart J. 2019;40:2121–7. https://doi.org/10.1093/eurheartj/ehz238
79. Packer M. What causes sudden death in patients with chronic heart failure and a reduced ejection fraction? Eur Heart J. 2019 Aug 7. pii: ehz553. doi: 10.1093/eurheartj/ehz553. [Epub ahead of print]. https://doi.org/10.1093/eurheartj/ehz553
80. Steffel J. The subcutaneous implantable cardioverter defibrillator. Eur Heart J. 2017;38:226–8. https://doi.org/10.1093/eurheartj/ehw666

81. Galand V, Polin B, Martins RP, Leclercq C. An entirely leadless cardiac resynchronization therapy. Eur Heart J. 2019;40:858–9. https://doi.org/10.1093/eurheartj/ehy746
82. Olsen T, Jorgensen OD, Nielsen JC, Thogersen AM, Philbert BT, Johansen JB. Incidence of device-related infection in 97 750 patients: clinical data from the complete Danish device-cohort (1982-2018). Eur Heart J. 2019;40:1862–9. https://doi.org/10.1093/eurheartj/ehz316
83. Gatzoulis KA, Tsiachris D, Arsenos P, Antoniou CK, Dilaveris P, Sideris S, et al. Arrhythmic risk stratification in post-myocardial infarction patients with preserved ejection fraction: the PRESERVE EF study. Eur Heart J. 2019;40:2940–9. https://doi.org/10.1093/eurheartj/ehz260
84. Gutman SJ, Costello BT, Papapostolou S, Voskoboinik A, Iles L, Ja J, et al. Reduction in mortality from implantable cardioverter-defibrillators in non-ischaemic cardiomyopathy patients is dependent on the presence of left ventricular scar. Eur Heart J. 2019;40:542–50. https://doi.org/10.1093/eurheartj/ehy437
85. Steffel J, Ruschitzka F. Super response to cardiac resynchronization therapy. Circulation. 2014;130:87–90. https://doi.org/10.1161/CIRCULATIONAHA.113.006124
86. Leclercq C, Burri H, Curnis A, Delnoy PP, Rinaldi CA, Sperzel J, et al. Cardiac resynchronization therapy non-responder to responder conversion rate in the more response to cardiac resynchronization therapy with MultiPoint Pacing (MORE-CRT MPP) study: results from Phase I. Eur Heart J. 2019;40:2979–87. https://doi.org/10.1093/eurheartj/ehz109