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European Heart Rhythm Association

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PEER-REVIEWED CONFERENCE REPORT

Atrial Fibrillation

Cryoballoon ablation in patients with paroxysmal atrial fibrillation was more effective with lower recurrence rates and increased quality of life compared with anti-arrhythmic drugs treatment in the Cryo-FIRST study.

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Diagnostics

Novel ECG-based predictors help to differentiate between cardiac sarcoidosis and ARVC and a novel echocardiographic score helps to differentiate between athlete's heart and ARVC. Further, ECG-parameters can help predict mortality in COVID-19 patients.

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Devices

Long-term outcomes of the EFFORTLESS S-ICD Registry show a high level of efficacy over 5 years. Burden of inappropriate shocks was relatively low and could be further decreased by early reprogramming.

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Editor Prof. Marc Peter Bonaca, University of Colorado, USA

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Letter from the Editor

Prof. Marc P. Bonaca

Dear colleagues,

Thank you for your interest in this summary report for the 2021 European Heart Rhythm Association Virtual Meeting. Our hope is that you find the summaries enclosed to be informative and balanced but also succinct. Our editorial team and peer reviewers have worked hard to bring you some of the very best content of the meeting.

There are important new data on atrial fibrillation including the long-term results from RACE 3 and the results of STROKESTOP. A summary of the 2021 EHRA practical guide to DOACs in the pre-operative setting and management in the context of bleeding may be helpful in the management of these situations. In addition, there are data on ablation, devices, and diagnostic tools. Finally, there are key topics regarding antiarrhythmic drugs in children and imaging for patients with congenital heart disease.

We found the meeting to be rich, engaging, and informative and we hope the following summaries accurately represent this dynamic meeting.

Sincerely,
Marc Bonaca

Biography

Marc P. Bonaca, MD, MPH, is a Cardiologist and Vascular Medicine Specialist who serves as the Executive Director of CPC Clinical Research and CPC Community Health at the University of Colorado Anschutz Medical Campus. He is the Director of Vascular Research and an Associate Professor of Medicine at the University of Colorado School of Medicine and the inaugural holder of the William R. Hiatt Endowed Chair in Cardiovascular Research.

Dr Bonaca earned his medical degree from the University of Connecticut School of Medicine and his Masters in Public Health at Harvard University. He served as a Medical House Officer at Brigham and Women's Hospital and Harvard Medical School. After completion of his training he joined the faculty of the Cardiovascular Division and Vascular Medicine section of Brigham and Women's Hospital and Harvard Medical School and became an Investigator at the TIMI Study Group.

Dr Bonaca's research focus is on ischemic risk in patients with atherosclerotic vascular disease, risk prediction, and risk modification through the use of pharmacologic and biologic therapies. His key areas of interest include patients with peripheral artery disease, polyvascular disease and diabetes with a focus on the breadth of risk including ischemic limb outcomes, microvascular complications and major adverse cardiovascular events.

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Atrial Fibrillation and Direct Oral Anticoagulant

Predictors of young-onset atrial fibrillation

Atrial fibrillation (AF) in the young is uncommon and not well studied. A recent retrospective study in a large cohort evaluated the presence of predictors for new-onset AF in individuals ≤45 years and identified a profile of comorbidities and ECG abnormalities associated with early-onset AF [1].

Dr Amitai Segev (Sheba Medical Centre, Israel) presented a study that retrospectively evaluated 16,432 patients aged ≤45 years who were admitted to the internal and cardiology wards at a large tertiary centre between January 2009 and December 2019 [1]. The purpose of the study was to identify the determinants of AF in this population to facilitate timely diagnosis, follow-up, and management.

Clinical, electrocardiographic (ECG), and echocardiographic data were collected and compared between participants with AF (n=366) and without AF (n=16,066) at baseline. A subgroup of participants without AF at baseline and a subsequent hospital visit were followed for the development of new-onset AF. Baseline characteristics of patients with AF were statistically significantly different from those without AF in a variety of parameters strongly and independently associated with young-onset AF, including age, male gender, obesity, and heart failure (see Table).

Table: Independent predictors of new-onset AF. Adapted from [1]

Multivariable			
	Hazard ratio	95% CI	P
Age, per year	1.12	1.06-1.17	<0.001
Hypertension	1.84	1.03-3.28	0.037
CHF	9.37	3.88-22.62	<0.001
LBBB	4.85	1.16-20.29	0.031
RBBB	2.88	1.03-8.08	0.045
Univariable			
	Hazard ratio	95% CI	P
CHARGE-AF	2.53	1.83-3.49	<0.001
CHA_2DS_2-VASc	1.29	1.01-1.66	0.044

AF, atrial fibrillation; CHF, congestive heart failure; CI, confidence interval; LBBB, left bundle branch block; RBBB, right bundle branch block
Cox proportional hazards regression on determinants associated with new-onset AF.

A total of 10,691 participants were followed for a median of 41.5 (16.6-78.6) months, during which 85 patients developed new-onset AF (equivalent to 0.5%/year). Independent predictors of new-onset AF were increased age, hypertension, heart failure, and right and left bundle branch block (P≤0.045).

The analysis also compared 2 clinical scores in their ability to predict new-onset AF. The CHARGE-AF score is a validated clinical score incorporating readily available variables, such as age, ethnicity, lifestyle parameters, and cardiovascular comorbidities. The CHA_2DS_2-VASc score has originally been developed to predict the risk of stroke in AF. In this study, the CHARGE-AF score outperformed the CHA_2DS_2-VASc score in new-onset AF prediction (area under the ROC curve 0.75 [0.7-0.8] vs 0.56 [0.48-0.65], respectively).

In summary, young-onset AF is characterised by a specific clinical profile of comorbidities and ECG abnormalities. The incidence of new-onset AF in individuals admitted to hospital was 0.5%/year. Outcomes of this retrospective cohort study suggest that patients at high risk for the development of new-onset AF can be identified by clinical parameters and that more intense follow-up of selected individuals may result in early diagnosis, followed by early intervention.

1. Segev A. Atrial fibrillation in the young: clinical characteristics, predictors of new onset and outcomes. EHRA 2021 Congress, 23-25 April.

RACE 3 long-term results show fading benefit of targeted therapies in AF and HF

In the RACE 3 trial, patients with early persistent atrial fibrillation (AF) and heart failure (HF) received either conventional plus targeted therapies or conventional therapies alone. While results were promising at 1 year, results from the 5-year extension study did not show superior efficacy of combined treatment [1].

Targeted therapies aim to modify the atrial substrate and have a favourable effect on risk factors and diseases underlying AF.

Previously, the 1-year results of the RACE 3 trial (NCT00877643) suggested that targeted therapies in addition to conventional therapies improves sinus rhythm maintenance in patients with early persistent AF and mild-to moderate early HF [2]. Prof. Michiel Rienstra (University Medical Center Groningen, the Netherlands) presented the 5-year results from the RACE 3 extension study [1].

The multicentre, randomised RACE 3 trial aimed to evaluate whether the targeted therapy of underlying conditions could benefit sinus rhythm maintenance by reducing cardiovascular risk [2]. Participants with early AF and mild-to-moderate HF were randomly assigned to conventional therapies (n=109) or conventional plus targeted therapies (i.e. mineralocorticoid receptor antagonists, statins, ACE-inhibitors and/or angiotensin-receptor blockers, or cardiac rehabilitation; n=107). After 3 weeks, all patients were electrocardioverted and received rhythm control and HF therapy according to guidelines. Patients in the targeted arm were followed-up every 3 months for 5 years, patients in the conventional arm every 3 months for 1 year and then once yearly. Patient characteristics were similar in both groups; the mean age was 64 and 65 years, respectively, and 21% were women. The primary endpoint was sinus rhythm during 7-day Holter monitoring at 1 year. The presented outcomes were the long-term effects after 5 years of follow-up.

At 1 year, sinus rhythm was achieved by 75% of participants receiving targeted therapy versus 63% of participants receiving conventional therapy only (OR 1.177; 95% CI 1.02-3.05; P=0.042), showing superior efficacy of the targeted therapy [2]. At 5 years, targeted therapy led to sinus rhythm in 46% of participants assigned to intervention versus 39% of participants on conventional therapy (OR 1.297; 95% CI 0.76-2.23; P=0.346); thus, no longer showing a significant difference in efficacy.

After 5 years, the rate of cardiovascular morbidity or mortality was similar between the treatment arms (log-rank P=0.353). Changes in the underlying conditions were statistically significant in systolic blood pressure, total cholesterol, and LDL-cholesterol, with more favourable outcomes for the targeted treatment group. Prof. Rienstra concluded that these long-term outcomes showed that targeted therapies on top of conventional studies did not improve maintenance of sinus rhythm in patients with persistent AF and HF at 5-year follow-up. However, the study may have limited power due to the small number of participants (n=109).

1. Rienstra M. Targeted therapy of underlying conditions in patients with persistent atrial fibrillation and mild to moderate stable heart failure: long-term outcome of the RACE 3 Trial. EHRA 2021 Congress, 23-25 April.
2. Rienstra M, et al. Eur Heart J 2018;39(32):2987-2996.

STROKESTOP: Benefits of systematic screening for atrial fibrillation

Population-based screening of over 28,000 elderly Swedish individuals for atrial fibrillation (AF) reduced the risk of ischaemic and haemorrhagic stroke, systemic embolism, and death, leading to a net clinical benefit in this population [1].

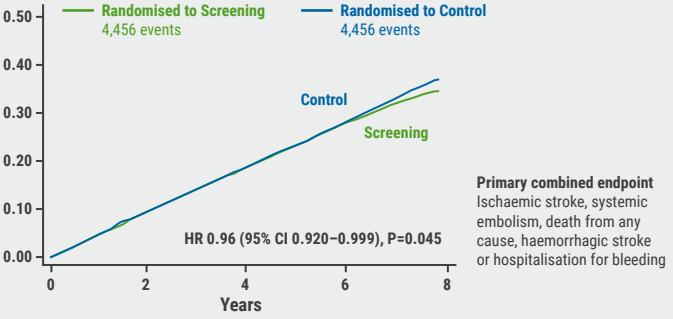
Patients with AF have a 5-fold increased risk of ischaemic stroke, and 10% of stroke patients have undetected AF, leading to a 1.5-3-fold increased risk of death. The risk of stroke and death can be reduced by 65% and 26%, respectively, when AF is diagnosed and patients receive treatment with oral anticoagulants [1].

The STROKESTOP study (NCT01593553) aimed to evaluate whether early detection and treatment of AF can reduce the risk of ischaemic stroke and death without an excess risk of bleeding. All residents aged 75 and 76 years in two Swedish regions were identified and randomised 1:1 into a screening group (n=13,979) and a control group (n=13,996), without any applicable exclusion criteria. Screening intervention was single ECG twice daily for 14 days in individuals without history of AF. If AF was detected or there was prior AF without anticoagulant treatment, a systematic follow-up was initiated. From the 13,979 subjects invited to screening, 7,165 (51.3%) participated in the study. The control group was followed-up for a minimum of 5.6 years without any loss. Patient characteristics with regards to age, gender, and medical history (e.g. diabetes, cardiovascular diseases) were well balanced between screening and control groups. However, there were significant differences between participants and non-participants in screening, with subjects participating in the screening having significantly fewer comorbidities (e.g. heart failure 4.8% vs 10.3%, stroke, or embolism 8.8% vs 13.5%, hypertension 31.6% vs 39.6%, diabetes 11.6% vs 18.9%; all P<0.001) [1].

Subjects without a history of AF who were invited for screening were examined via single lead ECG twice a day for 14 days. Subjects in which AF was detected and subjects with prior AF but without anticoagulant treatment were followed-up systematically.

AF was significantly more often diagnosed in subjects participating in the screening than in controls (P=0.005). Final results from the primary endpoint showed a small but statistically significantly favourable outcome in the screening arm with 4,456 incidences compared with 4,616 in the control arm (P=0.045; see Figure). Ninety-one invited individuals were required to prevent 1 event.

Figure: AF screening resulted in a lower risk of death and benefits of screening slowly increased over time [1]



Dr Emma Svennberg (Karolinska Institute, Denderyd Hospital, Sweden) concluded that population-based screening for AF provided a net clinical benefit in an elderly population. The presented study was one of the first to evaluate the benefits of systematic screening. Efforts must be made to increase participation in AF screening as non-participants were at highest risk of adverse events. STROKESTOP 2 will look further into potential socio-economic factors influencing participation in screening examinations.

1. Svennberg E, et al. Benefits of systematic screening for atrial fibrillation – the STROKESTOP study. EHRA 2021 Congress, 23-25 April.

Deep dive into EAST-AFNET 4 results on early rhythm-control in atrial fibrillation

Results from the EAST-AFNET 4 suggested that early, structured rhythm control therapy based on antiarrhythmic drugs and catheter ablation reduced atrial fibrillation (AF)-related complications when compared with usual care. A clear explanation for this benefit did not emerge from a closer look at the data [1].

Dr Andreas Metzner (University Heart & Vascular Centre Hamburg, Germany) presented an analysis of the EAST-AFNET 4 study (NCT01288352) focussing on the components of AF management and treatment patterns. The EAST-AFNET 4 study was designed to evaluate the effects of early rhythm control on the composite primary endpoint of cardiovascular death, stroke, hospitalisation for heart failure or acute coronary syndrome [2]. Participants (n=2,789) were randomised into 2 study arms: one receiving usual care (n=1,394) and the other receiving early rhythm-control therapy (n=1,395). Mean follow-up time was 5.1 years/patient.

Results showed a 21% risk reduction for cardiovascular death, stroke, hospitalisation for heart failure or acute coronary syndrome in patients receiving early rhythm control. To derive treatment recommendations from this important finding and to evaluate the impact of clinical benefit or additional disease management, treatment patterns were further analysed [1].

Over 90% of patients received oral anticoagulation therapy, with more than 54% of patients receiving direct oral anticoagulants (DOACs) in both groups. Furthermore, there was no difference in treatment of heart failure, hypertension (~70% of patients), or diabetes. Rate control therapy was used in 4 out of 5 patients in both study arms, with a larger proportion of patients receiving beta blocker-monotherapy in the control group. The use of rate control therapy slightly decreased over time in both groups.

The number of in-person follow-up visits was low in both study arms: 1.94 versus 2.13 visits/patient, with the higher number in the treatment arm being derived from more frequent visits after randomisation to adjust rhythm-control therapy.

In usual care, rhythm control remained the exception. Antiarrhythmic drug therapy in the treatment arm was initially given to 84% of patients, with 45% of patients still receiving antiarrhythmic drugs after 2 years. AF ablation was typically performed on patients on antiarrhythmic drugs, likely reflecting recurrent AF. While the proportion of patients receiving ablation was higher in the treatment arm, the numbers increased over time in both groups in a parallel manner. Predictors for AF ablation therapy were country of enrolment and enrolment to an ablation-site, indicating that local availability played an important role.

Dr Metzner concluded: "Systematic and early rhythm control results in clinical benefit when added to evidence-based oral anticoagulation, therapy of concomitant cardiovascular conditions, and rate control therapy. The clinical benefit of early rhythm control was achieved without many additional visits and with regionally different treatment choices within guideline recommendations."

1. Metzner A. Components of AF management and early rhythm control in patients with atrial fibrillation: a detailed analysis of the EAST-AFNET 4 dataset. EHRA 2021 Congress, 23-25 April.
2. Kirchhof P, et al. N Engl J Med 2020;383:1305-16.

Cryo-FIRST study: improved AF and QoL outcomes with cryoballoon versus drug therapy

The phase 4 Cryo-FIRST trial assessed the efficacy and safety of first-line cryoballoon ablation versus antiarrhythmic drugs in patients with paroxysmal atrial fibrillation (AF). The presented secondary efficacy outcomes of the trial suggest superiority of cryoballoon ablation in freedom of AF recurrence and quality of life (QoL) over 12 months compared with antiarrhythmic drugs [1,2].

The phase 4, international, multicentre Cryo-FIRST study (NCT01803438) evaluated the safety and efficacy of pulmonary vein isolation using a cryoballoon as first-line therapy in comparison with antiarrhythmic drugs (class I or II) in rhythm control-naïve patients with paroxysmal AF [2]. The main results, previously presented at the AHA Scientific Session 2020, demonstrated that first-line cryoballoon ablation is superior to antiarrhythmic drugs in the prevention of atrial arrhythmia recurrence over 12 months [3]. At the EHRA 2021, Dr Nikola Pavlović (University Hospital Sestre Milosrdnice, Croatia) focused on the secondary efficacy outcomes of AF recurrence and QoL [1].

The Cryo-FIRST study enrolled 218 treatment-naïve participants with paroxysmal AF (aged 18-75 years; 32% women) from 18 sites in 9 countries. The participants were randomised 1:1 to pulmonary vein isolation with a cryoballoon or antiarrhythmic drugs treatment. The primary endpoint of the study was ≥1 episode of recurrent atrial arrhythmia and the secondary endpoints included freedom from AF recurrence and QoL at 12 months. Participants were monitored by 7-day Holter at 1, 3, 6, 9, and 12 months of follow-up, and QoL was assessed using AFEQT and SF-36V2 questionnaires at baseline and at each follow-up.

Out of the 218 participants, 187 completed the 12-month follow-up. At 1 year, freedom from AF recurrence was significantly higher in participants treated with cryoballoon ablation (86.6%) than in antiarrhythmic drug-treated participants (75.5%; P=0.023). Similarly, the AFEQT summary score was 9.9 points higher in the cryoballoon ablation group compared with the drug-therapy group (95% CI 5.5-14.2; P<0.001). The SF-36 health domain scores were similar between the groups. However, Dr Pavlović pointed out that QoL assessment may have been impaired because the study was not blinded.

In conclusion, the efficacy of cryoballoon ablation showed superior results to antiarrhythmic drug-treatment in both presented endpoints, i.e. AF recurrence and QoL. The safety profile of both treatment regimens was similar.

1. Pavlović N. Impact of initial rhythm control with cryoballoon ablation versus drug therapy on atrial fibrillation recurrence and quality of life: results from the Cryo-FIRST study. EHRA 2021 Congress, 23-25 April.
2. Kuniss M, et al. N Europace 2021.
3. Velagic V, et al. Circulation. 2020;142:A13915.

2021 EHRA practical guide: DOACs in pre-operative and bleeding patients

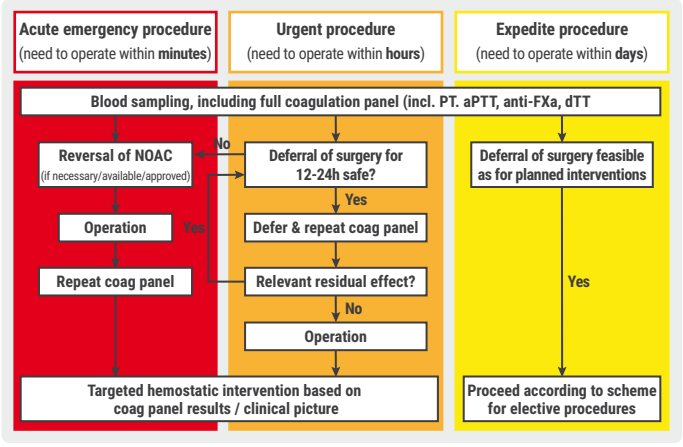
The new and updated 2021 EHRA practical guide on the use of non-vitamin K antagonist oral anticoagulant in patients with atrial fibrillation highlights the importance of post-bleeding management, as well as personalised, peri-procedural oral anticoagulation management by adjusting treatment to the expected bleeding risk [1,2].

Prof. Thomas Vanassche (University Hospitals Leuven, Belgium) presented the new 2021 EHRA practical guide, focussing on pre-operative and bleeding patients [1]. Direct oral anticoagulants (DOACs) have shown to be safer and more effective than vitamin K antagonists, and as a result are recommend by most international guidelines [2]. They also cause fewer bleedings compared with vitamin K antagonists. The guideline was updated with regards to the use of specific DOAC reversal agents. Idarucizumab, a specific reversal for dabigatran, is administered by intravenous bolus injection in 2 consecutive doses of 2.5 g each. It acts immediately and for up to 24 hours without effects on other anticoagulants. It is available in all European countries. Andexanet alfa is a specific reversal for rivaroxaban and apixaban and is administered as an intravenous bolus followed by continued infusion. The dose is dependent on the type and timing of last use of DOAC [3]. The effect lasts throughout the infusion time and may affect post-reversal anticoagulation. It is currently available in Germany, Austria, UK, the Netherlands, Sweden, Denmark, and Finland.

The guidelines further emphasised the importance of post-bleeding management even in minor bleeds. The impact of bleeding on the patient's compliance should be re-evaluated, as well as the risk of repeat bleeding, modifiable risk factors, and choice and dosing of DOAC. Anticoagulation should be re-initiated in the absence of absolute contraindication.

Peri-procedural management of DOACs is a frequent clinical problem. Stopping and restarting anticoagulation increases risk of complications, both in bleeding and thrombosis. The rapid onset and offset of DOAC effect simplify peri-procedural management, eliminating the need for pre-operative heparin bridging. Surgical factors (e.g. bleeding risk of procedure) and patient characteristics (e.g. comorbidities) determine the time of last pre-operative DOAC intake. The full dose of DOAC should be resumed 24 hours after low-risk and 48-72 hours after high-risk interventions. For patients requiring an urgent surgical intervention, a decision tree is available (see Figure).

Figure: Decision tree of DOAC management for patients requiring urgent surgical intervention. Modified from [1,2].



aPTT, activated partial thromboplastin time; dTT, diluted thrombin time; FXa, factor Xa; PT, prothrombin time.

To summarise, Prof. Vanassche highlighted the following updates in the 2021 EHRA practical guide:

- updated information on reversal agents;
- the importance of post-bleeding management and an integrated management of bleeds, including the treatment of modifiable risk factors;
- for elective procedures, a unified, simplified, and practical approach is feasible without drug level measurement and without heparin treatment.

1. Vannasche T. Focus on special situations: DOACs in pre-operative and bleeding patients. EHRA 2021 Congress, 23-25 April.
2. Steffel J, et al. EP Europace 2021;00:1-65.
3. Govender K. Oral anticoagulant and bleeding: role of antidotes. EHRA 2021 Congress, 23-25 April.

DOACs and bleeding: the role of antidotes

The use of direct oral anticoagulants (DOACs) in patients with atrial fibrillation (AF) is associated with the risk of bleeding complications. To manage severe and life-threatening bleeding, specific antidotes have become available that can effectively restore haemostasis [1].

Major bleeding in patients with AF medicated with factor Xa (FXa) and factor IIa (FIIa) inhibitors remained a concern. The major limitation was the lack of specific reversal agents. However, antidotes have now become available and Dr Kaveshree Govender (Milpark Hospital, South Africa) reviewed their role in managing bleeding complications [1].

The 2018 EHRA practical guideline on AF provides guidance on managing bleeding episodes in DOAC-treated patients [2]. Andexanet alfa was approved as a reversal agent for rivaroxaban and apixaban, while idarucizumab is used as a specific reversal for dabigatran.

Andexanet alfa is a recombinant modified FXa. FXa inhibitors bind to andexanet alfa with the same affinity as to endogenous FXa. Consequently, endogenous FXa is partially freed to contribute to effective haemostasis. The efficacy of 400-800 mg bolus and 480-960 mg infusion dose andexanet alfa in patients with acute major bleeding was shown by Connolly et al. in 2019 [3].

Idarucizumab is a monoclonal antibody fragment developed to reverse the anticoagulant effect of dabigatran. Its efficacy was shown in the RE-VERSE AD study (NCT02104947). Idarucizumab rapidly reversed anticoagulation in 98% of patients after a single dose of 5 g, as assessed by activated partial thromboplastin time, thrombin time, ecarin clotting time, and activated clotting time.

Specific agents are recommended for life-threatening bleeding, bleeding into critical organs, and other uncontrolled major bleeding, as well as for urgent invasive procedures in DOAC-treated patients. The limitations of the use of these specific agents are cost, availability, and possible thrombogenicity [1,2].

Also recommended by the 2018 EHRA guideline to help control bleeding are non-specific agents [2]. Anti-fibrinolytic agents are readily available at lower costs and have shown a low risk of thrombosis. However, their use is not well supported by good-quality clinical studies.

Alternatively, off-label use of haemostatic agents could be considered: activated prothrombin complex concentrate (APCC) for dabigatran-associated bleeding and 4-factor prothrombin complex concentrate (4FPCC) for FXa inhibitor-associated bleeding [1].

Dr Govender concluded that specific antidotes have shown efficacy in DOAC-associated bleeding and are recommended in patients with severe bleeding. If unavailable, non-specific agents are best considered in severe bleeding, but there is a lack of evidence for both safety and efficacy.

1. Govender K. Oral anticoagulant and bleeding: role of antidotes. EHRA 2021 Congress, 23–25 April.
2. Steffel J, et al. Eur. Heart J. 2018;39(16):1330–1393.
3. Connolly S, et al. N Eng J Med 2019;380:1326–1335.

Atrial Ablation

Early rhythm-control ablation: insight from the CHARISMA registry

Early ablation therapy (<1 year after the first arrhythmic event) significantly reduced the risk of atrial fibrillation (AF) recurrence compared with delayed ablation [1]. Besides the timing of ablation, hypertension was an important predictor of recurrence.

An early rhythm-control therapy in patients with AF has been associated with improved cardiovascular outcomes and a lower rate of recurrences, for example in the recent EAST-AFNET 4 trial [2,3]. Dr Luca Segreti (Azienda Ospedaliero, Universitaria Pisana, Italy) and colleagues aimed to investigate the importance of timing of ablation in preventing AF recurrences.

The study enrolled 153 consecutive patients from the CHARISMA registry (NCT03793998), who underwent AF ablation at 8 Italian centres. Ablations were guided by a novel radiofrequency ablation catheter with local impedance (LI)-sensing capability through a dedicated algorithm. Patients were grouped as early treated (n=80), if the procedure was performed within 1 year after the first AF episode, and as delayed treated (n=73), if admitted for ablation after more than 1 year. The study's endpoint was pulmonary vein isolation (PVI) as assessed by entrance and exit block. Long-term endpoints were AF and atrial tachycardia (AT) recurrences. Follow-up took place at 3, 6, and 12 months post-ablation.

Patient and arrhythmia characteristics were similar between the groups. According to current ESC AF guideline classification, 123 (80.4%) of the participants met Class I indications, 23 (15%) met Class IIa indications, and 7 (4.6%) Class IIb indications. The mean time to ablation procedure from the first arrhythmic episode was 202 days in early treated patients and 1,945 in patients receiving delayed treatment. No differences were found between AF type in terms of ablation strategy. At the end of the procedures, pulmonary veins had been successfully isolated in all participants.

Mean follow-up period was 366 days, during which 18 patients (11.8%) suffered an AF/AT recurrence after the 90-day blanking period. Recurrences occurred mostly in the delayed treatment group compared with the early treatment group (17.8% vs 6.3%, respectively; P=0.042) and the time to AT/AF recurrence was longer in the early treatment group (HR 0.2876; 95% CI 0.10–0.80; P=0.0181). Multivariate logistic analysis adjusted for baseline confounders showed that only hypertension was independently associated with recurrences (HR 4.66; 95% CI 1.5–14.48; P=0.0081). An early rhythm-control therapy was associated with a low risk of recurrences beyond the hypertension risk factor, ranging from 2% (no hypertension and an early ablation therapy) to 30.3% (with hypertension and a delayed procedure).

Dr Segreti concluded that patients with AF without common risk factors undergoing early ablation have a lower risk of recurrences compared with delayed treatment and that LI-guided ablation of AF is a safe and efficacious procedure.

1. Segreti L. Early rhythm control ablation therapy in preventing AF recurrences: insight from the CHARISMA registry. EHRA 2021 Congress, 23-25 April.
2. Lycke M, et al. Europace 2020;euaa383.
3. Kirchhof P, et al. N Engl J Med 2020;383(14):1305-1316.

Personalised pulmonary vein isolation procedure feasible and effective

The Ablate-by-LAW study evaluated a personalised pulmonary vein isolation procedure adapting the ablation index to the left atrial wall thickness. The method was shown to be feasible and effective while posing a less demanding ablation protocol [1].

The main reason for recurrence of paroxysmal atrial fibrillation (AF) is pulmonary vein (PV) reconnection. The left atrium is a thin structure with only 1-5 mm wall thickness and wall thickness is a determinant of transmural lesion formation during AF ablation and an independent predictor for PV reconnection. The utility of the ablation index to dose radiofrequency delivery for the reduction of AF recurrences has already been proven at the posterior and anterior wall. The aim of the presented study was to determine the efficacy, safety, and feasibility of adapting the ablation index to the left atrium wall thickness (LAWT).

In the single-centre Ablate-by-LAW study (NCT04218604), the multi-detector computed tomography-derived LAWT was assessed and integrated into the CARTO navigation system. Left atrial wall thickness maps were computed and categorised into 1 mm-layers and ablation index was titrated to the LAWT (ablation index 300-500 in steps of 50/mm wall thickness). The 3D 'fingerprinted' oesophagus images were also computed, the distance between the oesophagus and the left atrial posterior wall was mapped and the lesion personalised by avoiding ablation through the closest part. The primary endpoint was freedom from AF recurrences. Follow-up was scheduled at 1, 3 and 6 months, and every 6 months thereafter.

Dr Cheryl Terés (Teknon Medical Centre, Spain) presented first results from 90 patients included in this study after a follow-up period of 11 months. Mean LAWT was 1.25 mm. Mean ablation index was 366 on the right PVs with a first-pass isolation in 84 (93%) patients and 380 on the left PVs with first-pass in 87 (97%) [1].

Median procedural time was 59 minutes (49-66 min), with 14 minutes (12.5-16 min) radiofrequency time, 0.75 minutes (0.5-1.4 min) fluoroscopy time and 1 mGy/m² fluoroscopy dose area product, thus using a relatively low ablation index compared with previously recorded ablation index protocols. No major complications occurred. First results of the primary endpoint show that, so far, only 4 out of 90 patients (4.5%) had recurrences documented by ECG or self-reported symptoms.

Dr Terés concluded that the feasibility of incorporating 3D LAWT maps was demonstrated, and that they can be successfully used for PV isolation. Tailoring of delivered radiofrequency energy and ablation line design depending on wall thickness increased efficacy and showed a high rate of first-pass isolation. Furthermore, recurrence rate was similar to previously reported protocols with lower procedural requirements.

1. Teres C. Personalized atrial fibrillation ablation by tailoring ablation index to the left atrial wall thickness. The ablate by-law single center study. EHRA 2021 Congress, 23-25 April.

Pulmonary vein isolation: cryoballoon non-inferior to radiofrequency ablation

A prospective, randomised study evaluated the efficacy of cryoballoon ablation in comparison with the standard radiofrequency ablation in patients undergoing pulmonary vein isolation (PVI) for paroxysmal atrial fibrillation (AF) [1]. Both protocols were equally efficient in achieving PVI. However, cryoballoon ablation was associated with higher rates of recurrence in the first 3 months.

The single procedure success rates of durable PVI for paroxysmal AF varies between 80% and 90%. This prospective, randomised controlled, non-inferiority study (NCT-00774566), presented by Dr Bastian Kaiser (Robert-Bosch-Hospital Bad Cannstatt, Germany), investigated the efficacy of cryoballoon PVI versus PVI with radiofrequency energy following the CLOSE protocol in terms of single-procedure, arrhythmia-free outcome, safety, and procedural time.

The study enrolled and randomised 150 patients undergoing *de novo* PVI for paroxysmal AF. In group A (n=75), PVI was performed using a 23 or 28 mm cryoballoon. In group B (n=75), ablation was performed with radiofrequency energy according to the CLOSE protocol. Follow-up was after 3 months and at the end of the study period (mean 14±2 months). The primary endpoint was arrhythmia-free survival.

The procedural time in group A was statistically significantly shorter than in group B (70.53 min vs 115.35 min; P<0.01), while fluorescence time and dose area product did not differ between groups. Both procedures were performed with a low number of complications.

Results showed that cryoballoon PVI and PVI using ablation index following the CLOSE protocol are equally efficient in achieving durable PVI (PV recovery in 2.67% vs 4%; P=ns). Cryoballoon ablation led to significantly more AF recurrence during the blanking period of 3 months (P=0.048), most likely due to the higher myocardial damage by the cryoballoon, a theory supported by higher corresponding troponin levels. At

the end of the 14-month follow-up, the difference between treatment group was not detectable anymore (P=0.110).

1. Kaiser B. Pulmonary vein isolation using cryoballoon ablation versus RF ablation using ablation index following the CLOSE protocol: a prospective randomised trial. EHRA 2021 Congress, 23-25 April.

Pulmonary vein isolation lesions plus personalised methods shows promising results

PVI+ strategies, which use pulmonary vein isolation (PVI) with additional personalised methods, showed promising results in first single-centre studies for some of these methods [1]. Confirmation from randomised, multicentre studies is pending.

PVI is the standard of care for paroxysmal atrial fibrillation (AF). The innovation in this field mainly focuses on lesion durability and improved energy sources. Recent clinical trials have shown an >80% success rate at 1 year [2-4]. However, in persistent AF, PVI is not particularly effective and non-PV drivers as mechanisms for persistent AF are postulated.

To approach these non-PV targets, several PVI+ ablation strategies have been developed: an anatomical approach including linear lesions, ganglionic plexi ablation, and non-PV trigger ablation or isolation, and, with significant overlap, a targeted approach including ganglionic plexi ablation, non-PV trigger ablation or isolation, and locally-guided ablation. Dr Tom De Potter (Cardiovascular Research Center Aalst, Belgium) provided an overview of the clinical evidence of these approaches [1].

Linear lesions are the most well studied of these approaches and most of the related single-centre studies show a trend towards benefit. However, a recent, large, multicentre, randomised study showed that PVI alone was not inferior to PVI plus linear lesions [5]. More recently, ablation shifted towards posterior wall isolation, which is achievable in most cases with a low procedural risk and good 12-month outcomes as shown by a retrospective meta-analysis. However, statistical analysis of randomised clinical trials did not show superiority of PVI+ posterior wall isolation [6].

Percutaneous linear cryoablation is another strategy to facilitate Cox-maze-like lesions. To evaluate the safety and efficacy of this method, a first-in-man study (NCT02839304) has been conducted. Results showed an 84% success rate after 12 months in patients with paroxysmal AF and a similarly good efficacy of 82% success rate with a good safety profile in patients with persistent AF (n=60). Dr De Potter also introduced anatomical alcohol ablation, for which benefit over PVI has been suggested, and left atrial appendage isolation, for which no results are available yet [7-9].

Targeted ablation focuses on a leading circle concept with multiple or random re-entrant wavelets, which can be observed in real-time. Different approaches have been published for targeted ablation. For example, using atrial mapping, panoramic non-invasive and invasive mapping. Several mapping systems are currently being researched [10], confirmation of efficacy in a randomised trial is not available yet.

Dr De Potter emphasised the inter-patient variability in AF and significant inter-observer variability in target identification. Machine learning could be of high potential to enhance target identification, i.e. pattern recognition algorithms may overcome interpretation issues [11].

In conclusion, non-PV ablation targets are of significant interest not only for the very large persistent AF population, but also for the heart failure population and in patients with recurrent AF after PVI. Randomised clinical trials are available, ongoing, or planned for anatomical and targeted PVI+ strategies [11].

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Diagnostic Tools

EHRA Practical Guide on cardiac imaging in electrophysiology

In patients planned for atrial fibrillation (AF) or ventricular tachycardia (VT) ablation and diagnosis of complications, electrophysiologists are recommended to use MRI for most procedures but to opt for CT for the detection of intramural fat and calcification prior to VT ablation, and for the diagnosis of ablation-related complications [1].

Prof. Thomas Deneke (Heart Centre Bad Neustadt, Germany) presented practical advice on the usage of CT and MR for different scenarios in clinical electrophysiology, such as monitoring implanted active devices, before or after AF and VT ablation, and monitoring complications after electrophysiology procedures. This overview aimed to inform electrophysiologists' decisions on which technology (CT, MR, or both) and specific techniques to use in which clinical setting [1].

A standardised protocol for the inclusion of CT and MR in the planning of catheter ablation procedures was presented: pre-procedural imaging for the acquisition of imaging data, optional post-processing of imaging data, followed by integration in the mapping system by segmentation of imaging data (i.e. automatic, semi-automatic), and finally image integration and registration.

Prof. Deneke further discussed which modality (CT or MR) is ideal for which scenario in AF and VT ablation (see summary in Tables).

To aid diagnosis of ablation-related complications, CT is suitable for the detection of atrio-oesophageal fistula, oesophageal perforation (i.v. + p.o. water soluble contrast material), vascular complications, and active bleeding. Both CT and MR are suitable for diagnosis of stroke, cerebral ischaemia, and pulmonary vein stenosis.

In summary, MRI is recommended for most workflow procedures and to indicate long-term ablation lesion scars, while CT is the modality of choice in ablation-related complications.

1. Deneke T. EHRA practical guide on pre- and postprocedural cardiac imaging in electrophysiology. EHRA 2021 Congress, 23-25 April.

Tables: CT and MR imaging for AF ablation and VT ablation [1]

AF ablation			
		CT	MR
Pre-procedural imaging	document anatomy	++	++
	document LAA morphology (thrombembolic risk)	++	++
	rule out left atrial appendage thrombus	++	++
	determine left atrial fibrosis		+
Post-processing	determine amount and location of intramural fat and calcification		√
	delineate ablation lesions		√ (imaging at 3 mo indicates best long-term ablation lesion scar)
Integration	of anatomy	√ (may reduce AF recurrences)	√
	of left atrial fibrosis		√

VT ablation			
		CT	MR
Pre-procedural imaging	to rule out intracavitary thrombus (as alternative to contrast echo)	+++	+++
	determine scar location	++	+++
	determine scar transmurality	+	++
	determine core borderzone transition		+
	determine amount and location of intramural fat and calcification	++	
Post-processing	VT substrate (scar)	√ (channels, scar transmurality >75%, scar/borderzone transition)	√ (wall thickness channels)
Integration of "scar"		√ (improve focus mapping = shorter procedure, select sites for functional substrate mapping, avoid RF in areas with viable myocardium)	√ (improve focus mapping = shorter procedure)

Novel diagnostic score accurately differentiates between athlete's heart and ARVC

Patients with arrhythmogenic right ventricular cardiomyopathy (ARVC) often present with atrial asymmetry which is not seen in athlete's heart. Thus, the proportion

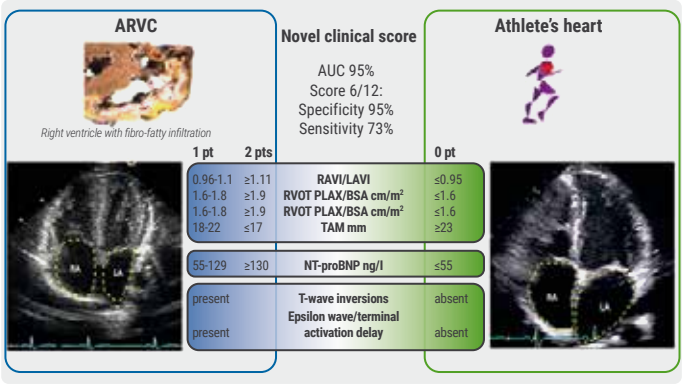
of atrial dimensions could be used to differentiate between both entities. A novel diagnostic score including readily available clinical parameters demonstrated high diagnostic accuracy [1].

The 2010 Task Force Criteria are the current gold standard to diagnose ARVC [2]. However, these criteria have not been tested to differentiate ARVC from athlete's heart. In addition, they are not easy to assess in clinical practice as they require myocardial biopsy, genetic testing, morphology of ventricular tachycardia, and right-ventricular regional wall-motion abnormalities.

Dr Valentina Rossi (University Hospital Zurich, Switzerland) and colleagues evaluated whether atrial dimensions could be used to differentiate between both conditions, since the right atrium is often larger than the left atrium in patients with ARVC, even at an early stage, while atria enlargement follows a more symmetrical pattern in athlete's heart [1].

This observational study included 21 ARVC patients and 42 athletes matched for age, gender, and BMI. The following echocardiographic, laboratory, and electrocardiographic parameters were included in the final score: indexed right/left atrial volumes (RAVI/LAVI ratio), serum NT-proBNP, RVOT measurements (i.e. PLAX and PSAX adjusted for BSA) on TTE, tricuspid annular motion velocity (TAM) on TTE, precordial electrocardiographic T-wave inversions, and depolarisation abnormalities according to the 2010 Task Force Criteria. A score ranging from 0 to 12 to differentiate ARVC and athlete's heart was developed, with higher values suggesting ARVC (see Figure) [1].

Figure: Novel diagnostic score to differentiate between athlete's heart and ARVC [1]



ARVC, arrhythmogenic right ventricular cardiomyopathy; AUC, area under the curve for a ROC curve; BSA, body surface area; LAVI, left atrial volume index; PLAX, parasternal long axis; RAVI, right atrial volume index; RVOT, right ventricular outflow tract; TAM, tricuspid annular motion. Parameters used in 2010 Task Force Criteria used the same cut-off. For newly introduced parameters (RAVI/LAVI, TAM mm, and NT-proBNP), cut-off values were calculated based on the ROC curves.
Figure kindly provided by Dr Rossi.

As per study design, the 2010 Task Force Criteria had the highest specificity (98%) and sensitivity (88%) to diagnose ARVC. However, those 2010 Task Force Criteria that are available in daily clinical practice (i.e. imaging, ECG) alone had a low sensitivity (41%; specificity 98%). In comparison, the proposed novel diagnostic score showed a sensitivity of 67% (specificity 91%) and thus outperformed the 2010 Task Force Criteria available in clinical routine (P<0.001).

The results from this study also showed that ARVC patients had a higher RAVI/LAVI ratio (1.78 vs 0.95; P<0.001), lower right-ventricular function (fractional area change 28 vs 42.18%; P<0.001; TAM 17.9 vs 23.3mm; P<0.001), and higher serum NT-proBNP levels (491 vs 44.8 ng/L; P<0.001).
Dr Rossi concluded: "Our diagnostic score including readily available clinical parameters improves sensitivity and can refine diagnostic work-up in daily clinical practice." Due to the relatively small number of patients included, validation in larger cohorts should be sought.

1. Rossi V. A novel diagnostic score to differentiate between athlete's heart and ARVC. EHRA 2021 Congress, 23-25 April.
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Limited added value of ECG-based mortality prediction in COVID-19 patients using machine learning

ECG-based machine learning models were able to identify predictors of mortality in patients with COVID-19 in the first 72 hours after admission. The added value of prediction models based on ECG features was present but limited [1].

Dr Hidde Bleijendaal (Amsterdam University Medical Center, the Netherlands) presented a study aimed to evaluate whether ECG-based machine learning models can predict all-cause, in-hospital mortality in COVID-19 patients and to identify ECG features associated with mortality [1]. Included were 882 patients admitted with COVID-19 in 7 different Dutch hospitals. Raw-format 12-lead ECGs recorded after admission (<72 hours) were collected, manually assessed, and annotated using pre-defined ECG features. Using data from 5 of the 7 centres (n=634), 2 mortality prediction models were developed. The first prediction model was a multivariate logistic regression (LASSO) model adding manually extracted ECG features and was used to identify ECG features associated with mortality. The second was a deep learning model (DNN) developed using raw-format ECGs, age, and sex.

To implement transfer learning, a pre-trained model (large dataset, different task) fine-tuned for current prediction task was used. A baseline model was created using only age and sex to evaluate the added value of ECG. Data from 2 other centres (n=248) were used for external validation.

Performance of both prediction models was similar, with a mean area under the ROC of 0.76 (95% CI 0.68–0.82) for the LASSO model (sensitivity 0.86, specificity 0.54) and 0.77 (95% CI 0.70-0.83) for the DNN in the external validation cohort (sensitivity 0.86, specificity 0.57). Respective results for the baseline model were slightly lower or similar: AUC was 0.76 (95% CI 0.68–0.82), sensitivity was 0.87, and specificity was 0.49. After adjustment for age and sex, increased ventricular rate, right bundle branch block, ST-depression, and low QRS voltages remained as significant predictors for mortality in COVID-19 patients.

Dr Bleijendaal concluded, "Predication of mortality in this dataset in COVID-19 patients is mostly based on age and sex. However, by adding ECG data we did improve the AUC slightly. The added value of the ECG seems to be present but is limited."

1. Bleijendaal H. Electrocardiogram-based mortality prediction in patients with COVID-19 using machine learning. EHRA 2021 Congress, 23-25 April.

The precordial R-prime wave: a discriminator between cardiac sarcoidosis and ARVC

Cardiac sarcoidosis in the right ventricle may often mimic arrhythmogenic right ventricular cardiomyopathy (ARVC), but the histopathologic differences between the diseases result in different right ventricular activation patterns. A multicentre, retrospective study showed that cardiac sarcoidosis led to a larger precordial R-prime wave, which can be used to differentiate between the conditions [1].

Dr Jarieke Hoogendoorn (Leiden University Medical Centre, the Netherlands) presented the results of a multicentre, retrospective study aimed to discriminate between patients with cardiac sarcoidosis and ARVC using electrocardiogram (ECG) [1]. Cardiac sarcoidosis with right ventricular involvement may mimic ARVC. Thus, Dr Hoogendoorn and colleagues hypothesised that the histopathologic differences between the diseases would result in different specific right ventricular activation patterns detectable on ECG. In ARVC, scar tissue progresses from epicardium to endocardium and may lead to delayed activation of areas with reduced voltages with small amplitude on the ECG. In cardiac sarcoidosis, patchy transmural right ventricular scar tissue leads to conduction block and thus late activated areas with preserved voltages, reflected as preserved R-prime (R')-waves in the right precordial leads.

This retrospective study included patients with cardiac sarcoidosis with right ventricular involvement (n=13) or gene-positive ARVC referred for ventricular tachycardia ablation (n=23). A non-ventricular-paced, 12-lead surface ECG prior to ablation was obtained and analysed using the Leiden ECG Analysis and Decomposition Software. Based on the hypothesis that conduction block in cardiac sarcoidosis leads to late activated areas with preserved voltages, the surface area of the R'-wave in V1-V3 was measured. An R'-wave was defined as any positive deflection from baseline after an S-wave.

An R'-wave in V1-V3 was present in all cardiac sarcoidosis patients compared with 11 (48%) of ARVC patients (P=0.002). The maximum R'-wave surface area in lead V1-V3 was 3.55 mm² in cardiac sarcoidosis (IQR 2.18-5.81) versus 0.00 mm² in ARVC (IQR 0.00-0.43; P<0.001). By ROC analysis, the maximum R'-wave surface area in lead V1-V3 was an excellent discriminator (AUC 0.980; 95% CI 0.945-1.000). A cut-off of ≥1.65 mm² had a sensitivity of 85% and specificity of 96% for diagnosing cardiac sarcoidosis. This was validated in a second cohort including 18 cardiac sarcoidosis and 40 ARVC patients, with 72% sensitivity and 88% specificity [1].

Dr Hoogendoorn concluded that transmural right ventricular scars in cardiac sarcoidosis lead to a localised conduction block and thus to a large R'-wave. An easily applicable algorithm including a terminal S-wave and surface area maximum R'-wave in V1-V3 was shown to be a good discriminator between cardiac sarcoidosis and ARVC. The QRS terminal activation in precordial leads V1-V3 may reflect disease specific scar patterns.

1. Hoogendorn J. The precordial R-prime wave: a novel discriminator between cardiac sarcoidosis and arrhythmogenic right ventricular cardiomyopathy in patients presenting with ventricular tachycardia. EHRA 2021 Congress, 23-25 April.

Devices

EHRA expert statement on pacemakers and intracardial devices: "watch out for the little old lady"

Implantation of pacemakers and intracardial devices lead to a high complication rate. The recently published 2021 EHRA expert consensus statement and practical guide on optimal implantation technique for conventional pacemakers and implantable cardioverter-defibrillators provides guidance on the management of the most important complications, such as lead perforation, pericardial effusion, pocket haematoma, and infection [1,2].

Prof. Thomas Starck (German Heart Centre Berlin, Germany) provided recommendations on the prevention and management of complications in patients who received a pacemaker or intracardial devices, based on the 2021 EHRA expert consensus paper [1]. The rate of complications lies between 5 and 10%. Complications with the highest incidences are pocket haematoma (≤16.0%), pericardial effusion (10.2%), infection (≤3.4%), lead dislodgment (≤3.3%), and pneumothorax (≤2.8%). However, procedure-related mortality is low [2].

Different factors were identified for lead perforation, including old age, female sex, BMI <20, steroid use, and antiplatelet agent therapy. Prof. Starck said to "watch out for the little old lady." Procedure-related risks include temporary pacing, small diameter intracardial devices leads, longer fluoroscopy time, and several lead locations. Lead revision is indicated in cases of perforation, especially those with additional risk factors, as conservatively treated patients showed a higher risk of tamponade and recurrent symptoms (6 and 1/22 vs 0 and 0/26) [3].

Lead perforation is often associated with pericardial effusion as shown in a prospective evaluation of 968 consecutive patients using a pre-operative and post-operative (within 24h) echocardiography [4]. The incidence of small-to-moderate pericardial effusion was 8.7%, with 94% of the patients being asymptomatic. The incidence of large pericardial effusion with tamponade (>20 mm) was 1.5%. Pericardiocentesis is recommended for large effusions or effusions causing haemodynamic compromise [2]. Pericardiocentesis can be considered in moderate effusions that do not regress quickly, especially if the patient requires anticoagulation. Patients with mild effusions should be monitored closely.

Development of pneumothorax is highly dependent on venous access, and risk factors again include 'the little old lady,' chronic obstructive pulmonary disease, and subclavian vein puncture [5]. Pneumothorax should be drained with a chest tube. The implantation technique of choice is axillary vein puncture or cephalic venous cutdown. Use of intrathoracic subclavian puncture is not advised.

Pocket haematoma is the most common complication after implantation procedures. Heparin-bridging significantly increases risk (P<0.001) and should be avoided, while continued treatment with warfarin or direct oral anticoagulant is recommended [6,7]. Haematoma should be conservatively treated unless there are further complications that require immediate surgical revision. Needle aspiration should not be performed due to a high risk of infection [8].

Further, device infection significantly reduces survival rates in implanted patients (P<0.001) and should be prevented at all costs [9,10]. Risk management includes treatment of modifiable risk factors and adjust medical procedures accordingly.

Prof. Starck emphasised the importance of proper training and implantation technique to avoid or minimise complications and the familiarity of physicians with the management of complications whenever encountered. The presented EHRA consensus statement provides good guidance herein.

1. Starck CT. Prevention and management of complications. EHRA 2021 Congress, 23-25 April.
2. Burri H, et al. EP Europace 2021:euaa367.
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5. Kirkfeldt RE, et al. Europace 2012:14:1132-1138.
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5-Year efficacy of subcutaneous implantable cardioverter-defibrillator

The EFFORTLESS S-ICD Registry showed that a subcutaneous implantable cardioverter-defibrillator (S-ICD) is safe and maintains its high-shock efficacy over 5 years. The burden of inappropriate shocks was low, and re-programming of the device after early inappropriate shocks markedly reduced the incidence of inappropriate shocks in years 2-5 [1].

The objective of the EFFORTLESS S-ICD Registry (NCT01085435) was to report the long-term outcomes of patients implanted with the Boston Scientific S-ICD. In his presentation, Prof. Pier Lambiase (University College London, United Kingdom) focused on spontaneous efficacy throughout the 5-year study and predictors of later outcomes. Enrolled in the study were 984 patients with diverse underlying aetiologies, of whom 703 completed the study. Mean study follow-up was 4.4 years. In only 20 out of 703 patients (2%), S-ICD was replaced for a transvenous device for pacing.

No definite electrode failures occurred. Evaluation of late complications and inappropriate shocks showed that year-1 complications did not predict later complications. Inappropriate shocks were registered in 16.9% of the patients, with the main cause being cardiac oversensing. Patients who were re-programmed for causes of inappropriate shocks in year 1 had fewer IAS in years 2-5, but this was not statistically significantly different from patients without re-programming after inappropriate shocks. Cardiac inappropriate shocks were more likely to occur in years 2-5, due to low amplitude signal and oversensing of ventricular tachycardia (VT)/ventricular fibrillation (VF) (P≤0.033) [1].

An evaluation of late appropriate shocks showed that 10% of patients had untreated episodes that self-terminated, 6% had monomorphic VT, 3% a combination of monomorphic and polymorphic VT/VF, and 6% had VF alone. The main predictor for appropriate shocks was an appropriate shock in the first year (P<0.0001). Other significant predictors were prior cardiac arrest, heart failure, NYHA class I/II, and arrhythmogenic right ventricular dysplasia (ARVD) (P≤0.028). Importantly, ARVD and ischaemic heart diseases were predictors for appropriate shocks for monomorphic VT, potentially identifying a special sub-population.

High-shock efficacy was maintained throughout the entire study period and shock efficacy was not significantly different between rhythm types. Of the 91 (9.2%) deaths reported, none was associated with the S-ICD system or procedure.

In summary, these long-term results on the efficacy of S-ICD in a large cohort showed that S-ICD maintains a high level of cardioversion efficacy over 5 years. Prof. Lambiase added that, "importantly, untreated inappropriate sensing episodes did predict late inappropriate shocks, and this is an opportunity for re-programming and personalising therapy for these patients."

1. Lambiase P. Long-term efficacy and final outcomes of the subcutaneous implantable cardioverter-defibrillator registry. EHRA 2021 Congress, 23-25 April.

Specific Populations

Individualised approaches key to success in resynchronisation therapy non-responders

Non-responsiveness after cardiac resynchronisation therapy (CRT) occurs in 43% of patients, indicating the importance of improved outcomes in the future. A variety of root causes and potential resolution strategies were presented, all of them emphasising the importance of individualised treatment approaches [1].

Prof. Jagmeet Singh (Massachusetts General Hospital, USA) presented treatment strategies for patients not responding to CRT [1]. Response can be assessed using hard measurements, remodelling, soft clinical measurements, and composite scores. As much as 43% of CRT patients are classified as non- or negative-responders after 6 months. However, responding is a continuum and a clear classification is often difficult. For example, 30-40% of patients can be mild responders and non-responsive in some way.

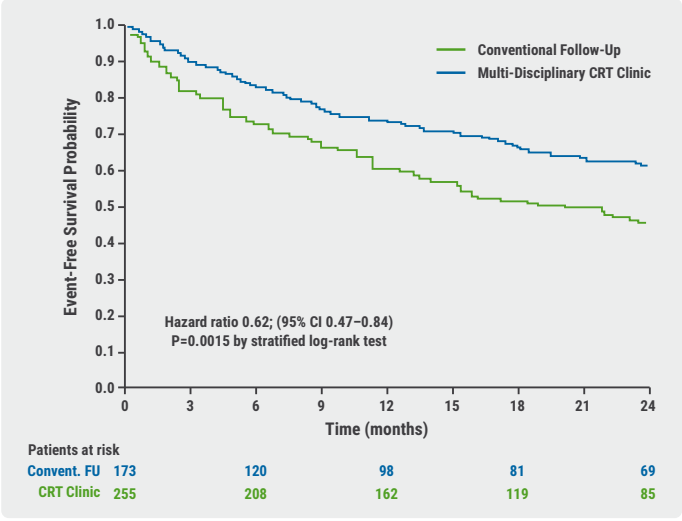
Determinants of CRT response include patient selection, lead implantation, device programming, and follow-up. For example, CRT in heart failure with narrow QRS complex increased mortality [2]. The considerable variability in electrical activation sequence as shown in endocardial maps may explain the variability in CRT response and argue against the one-size-fits-all 'anatomical lead positioning' strategy [3]. Furthermore, non-responsiveness is often multifactorial, with some of the factors not being directly related to CRT (e.g. suboptimal medication, comorbidities).

Individualised care using an integrated approach including heart failure, cardiac arrhythmia, and echocardiography services has been shown to significantly reduce the risk of mortality (see Figure). Optimisation of the devices, such as sound standard programming and use of automatic algorithms (e.g. AdaptivCRT, SMART-CRT, Respond-CRT, Synch-AV), also showed improved outcomes.

Lead location has also been shown to contribute to clinical benefit. Apical left ventricular lead locations were associated with worse outcome irrespective of QRS morphology and electrical activation sequence, while targeting the most electrically delayed areas improved clinical outcome [5]. A study on multipoint pacing (NCT02006069) was recently stopped for futility, although multisite pacing was shown to be effective in some cases.

Prof. Singh summarised the importance of an individualised approach in CRT. Without selection of the right procedure for the individual at the beginning, non-responsiveness is likely. To gain relevant clinical benefit, treatment of non-responsiveness must also follow an individualised approach including medical optimisation, resolution of rhythm issues, AV optimisation, reassessment of lead location, and alternative pacing approaches.

Figure: Improvement of event-free survival by multi-disciplinary CRT clinic versus conventional follow-up [4]



CRT, cardiac resynchronisation therapy; FU, follow-up.

1. Singh J. How to treat cardiac resynchronisation therapy non-responders? EHRA 2021 Congress, 23-25 April.
2. Ruschitzka F, et al. N Engl J Med 2013;369:1395-1405.
3. Singh JP, et al. J Am Coll Cardiol EP 2020; in press.
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Antiarrhythmic drug treatment in children: evidence-based recommendations

Evidence-based dosing guidance on antiarrhythmic drugs (AAD) treatment is available for several drugs in paediatric subpopulations. Further, intravenous antiarrhythmic therapy may lead to severe adverse events in this population, so caution is recommended [1].

Dr Nico Blom (Leiden University Medical Center, the Netherlands) discussed the available evidence and clinical experience on AAD therapy in children [1]. His overview focussed on supraventricular tachycardia (SVT), as this condition is the most common in children (0.14% incidence). Most SVT events occur in the first year of life, with 90-95% of children having a normal heart. The most common SVT types are atrioventricular re-entrant (AVRT) and atrioventricular nodal re-entry tachycardia (AVNRT). Rare chronic SVT forms include focal (FAT) and multifocal atrial tachycardia (MAT), congenital and postoperative junctional ectopic tachycardia (JET). Postoperative atrial flutter usually occurs in older children and young adults.

Dr Blom further indicated that acute management of SVT by intravenous injection of AAD (after failure of Valsalva and adenosine) could comprise of esmolol (500 µg/kg loading dose over 2 minutes, 50-200 µg/kg/min maintenance), flecainide (1-2 mg/kg over 10 minutes), or amiodarone (5 mg/kg over 30-60 minutes in case of poor cardiac function). Verapamil is never used in infants of <1-2 years, based on case reports in the 1980s.

A randomised, double-blind trial evaluating amiodarone in children enrolled 61 patients (median age 1.6 years) suffering from incessant SVT, postoperative JET or VT and randomised them to either 1, 5, or 10 mg/kg amiodarone followed by 2, 5, or 10 mg/kg/day [2]. Five study patients died (2 possibly

related) and there was a high rate of adverse events, leading to drug withdrawal in 10 patients. The 5 and 10 mg/kg doses were equally effective with 5 mg/kg having less side effects. Dr Blom suggested his institutional ICU-approach for postoperative JET, a slow bolus of 5 mg/kg over 60 minutes followed by continuous infusion of 10-20 mg/kg/day [1].

For maintenance therapy of SVT (AVRT), the most commonly used drugs in newborns and infants are: first-line betablockers or digoxin, second-line Class Ic (i.e. flecainide, propafenone) or sotalol, third-line amiodarone, and fourth-line exotic combinations (e.g. sotalol/flecainide, amiodarone/flecainide) [1,3]. In the first months, SVT in infants can be difficult to control but eventually often resolves. Duration of therapy in symptom- and recurrence-free patients is approximately 6 months, followed by a stop between 6 and 12 months of age (one drug at a time). Maintenance therapy in older children consists of first-line betablockers and second-line sotalol, flecainide, or verapamil. Optimal starting and target oral sotalol dosing for SVT in children was evaluated as 2 and 4 mg/kg/day in neonates (<1 month), 3 and 6 mg/kg/day in infants and children <6 years, and 2 and 4 mg/kg/day in children >6 years [4]. For flecainide, an average dose of 4.5 mg/kg/day was shown to be safe and effective for children <1 year [5].

Focal AT, MAT, and congenital JET in infants are difficult to control with AAD and associated with Takotsubo cardiomyopathy. Ivabradine was introduced as an emerging drug for difficult chronic SVT mechanisms based on abnormal automaticity in infants and young children.

Dr Blom warned, "The most common errors in paediatrics are dosing errors, most likely leading to a 10-fold or greater overdose by calculation errors (commas!), which usually occur when children are admitted to hospital, not when children are dosed by their parents."

In summary, for acute AAD management in infants, amiodarone is mostly used in haemodynamically unstable and postoperative children, but esmolol is a safe alternative. Intravenous AAD must be used with caution and ECMO stand-by is advised. For chronic AAD management in children, propranolol and digoxin were similarly efficacious. In most infants, AAD drugs can be stopped in the first year of life. Solatol and Class Ic drugs are most popular for different SVT forms, while amiodarone is only used as third-line treatment. Ivabradine in emerging for incessant FAT, MAT, and especially JET.

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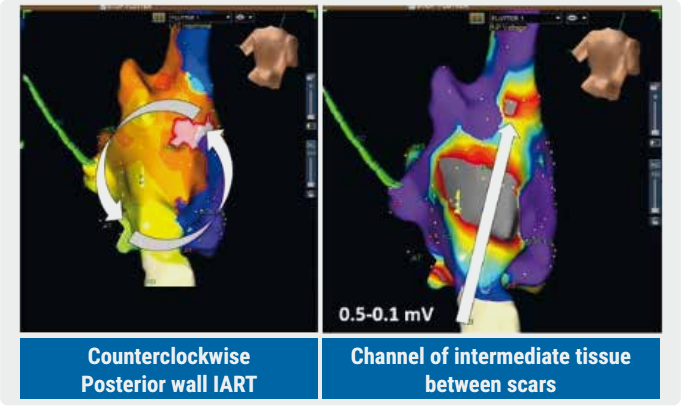
The importance of cardiac imaging in patients with congenital heart disease

Atrial arrhythmia is a common complication in patients with congenital heart disease (CHD). Dr Ivo Roca-Luque's (Hospital Clinic de Barcelona, Spain) focused on the importance of imaging techniques to personalise ablation procedures for cardiac and atrial anatomy and atrial substrate to improve ablation success in this population [1].

In the past decades, surveillance of patients with CHD has improved, leading to a 31% mortality reduction. These patients now grow older, thus increasing the prevalence of intra-atrial re-entrant tachycardia (IART), which is not only associated with severe clinical symptoms but also with cardiac transplant and an approximately 5-fold increased risk of death.

The substrate leading to atrial flutter in patients with CHD were several slow conduction areas and blocking regions (e.g. scars), cavotricuspid isthmus (CTI)-related flutter, or a combination of both. The most frequent circuit is CTI-related IART (51%), followed by non-CTI-related IART (27.7%), and a combination thereof (21.3%). Atrial substrate of arrhythmia can be analysed even without present arrhythmia, as exemplified in the Figure [1].

Figure: Atrial substrate of intra-atrial re-entrant tachycardia (IART). Adapted from [1,2]



Right: imaging from a patient with 2 scars in the posterior wall with scar tissue (grey) and healthy tissue (purple). Left: a counter-clockwise posterior wall IART is shown around the 2 scars. The circuit of arrhythmia could be predicted by electro-anatomical mapping in sinus rhythm.
Figure kindly provided by Dr Roca-Luque.

After ablation, patients with CHD suffer a high rate of IART recurrence. Notably, atypical flutter and complex anatomy are related with higher recurrence rates. Imaging of full cardiac and atrial anatomy using MRI and activation mapping can thus aid the selection of a suitable ablation procedure.

In summary, IART is a severe and frequent complication in patients with CHD and substrate mapping plays a key role in analysing circuits. Imaging and analysis of atrial substrate and cardiac and vascular anatomy before the ablation procedure are important as almost 10% of CHD patients have vascular or anatomic abnormalities. Dr Roca-Luque concluded that "imaging to predict IART substrate can help to improve ablation success."

1. Roca-Luque I. Ablation of atrial arrhythmias in patients with congenital heart disease: does cardiac imaging predict the response to therapy? EHRA 2021 Congress, 23-25 April.
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