STROKESTOP: Benefits of systematic screening for atrial fibrillation

Presented By

Dr Emma Svennberg, Karolinska Institute, Danderyd Hospital, Sweden

Conference

EHRA 2021

Trial

STROKESTOP

Results from a systematic atrial fibrillation screening study including almost 28,000 elderly individuals showed that population-based screening for atrial fibrillation (AF) reduced the risk of ischaemic and haemorrhagic stroke, systemic embolism, and death, leading to a significant net clinical benefit.

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

The aim of the STROKESTOP study (**NCT01593553**) was 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 (n=13,979) and a control group (n=13,996). The follow-up period was 5 years and the combined primary endpoint was ischaemic stroke or systemic thromboembolism, all-cause mortality, and severe bleeding. Subjects invited for screening were initially examined via single-lead ECG and followed up systematically.

Results showed a small but statistically significant favourable outcome in the screening arm. Evaluation of the pre-defined secondary endpoint, the as-treated analysis, showed a significantly better outcome than controls or non-participants. However, the participants were overall healthier than non-participants and so this result has to be viewed with caution.

Dr Emma Svennberg (Karolinska Institute, Danderyd Hospital, Sweden) concluded that population-based screening for AF provided a net clinical benefit in an elderly population.

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

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Young-onset atrial fibrillation: predictors and clinical profile

Presented By

Prof. Amit Segev, Sheba Medical Centre, Israel

Conference

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

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

The study cohort consisted of 16,432 patients. Clinical, electrocardiographic, and echocardiographic data were collected and compared among patients with and without AF at baseline. Baseline characteristics of patients with AF (n=366) were statistically significantly different from those without AF (n=16,066) in a variety of parameters strongly and independently associated with young-onset AF, such as age, male gender, obesity, and heart failure. A subgroup of patients with no AF at baseline were followed for development of new-onset AF (NOAF).

A subset of 10,691 patients without AF at baseline was followed for a median of 41.5 months, during which 85 patients developed NOAF (equivalent to 0.5%/year). Independent predictors of NOAF were increased age, hypertension, heart failure, and right and left bundle branch block.

In summary, young-onset AF is characterised by a specific clinical profile of comorbidities and ECG abnormalities. Subjects at high risk for the development of NOAF can be identified, and more intense follow up of selected individuals may result in early diagnosis and intervention.

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

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RACE 3: early benefits targeted therapy in AF and HF diminished at 5-year follow-up

Presented By

Prof. Michiel Rienstra, University Medical Center Groningen, the Netherlands

Conference

EHRA 2021

Trial

RACE 3

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 5-year follow-up did not show superior efficacy of combined treatment [1].

Targeted therapies refer to interventions that aim to modify the atrial substrate and have a favourable effect on risk factors and diseases underlying AF. The aim of the RACE 3 trial (NCT00877643) was to study the long-term effects of targeted therapies on maintenance of sinus rhythm, cardiovascular (CV) morbidity, and mortality after 5 years.

Patients with early AF and HF were randomly treated with either conventional therapies (n=109) or conventional plus targeted therapies (i.e. mineralocorticoid receptor antagonists, statins, ACE-inhibitors and/or angiotensin-receptor blockers, and cardiac rehabilitation; n=107). After 3 weeks, all patients were electrocardioverted and received rhythm control and HF therapy. The primary endpoint was 1-year sinus rhythm on 7-day Holter, the secondary endpoint was CV morbidity and mortality. Prof. Michiel Rienstra (University Medical Center Groningen, the Netherlands) presented the 5-year follow-up results.

After 1 year, 75% of participants receiving targeted therapy were in sinus rhythm versus 63% of participants receiving only conventional therapy (P=0.042), showing superiority of targeted therapy. The recent 5-year outcomes show that 46% versus 39% of participants were in sinus rhythm (P=0.346), showing no statistically significant difference in efficacy. Evaluation of the secondary endpoint at 5 years showed that only 16% of patients suffered from CV morbidity or mortality and there was no difference between the treatment arms.

Prof. Rienstra concluded that the RACE 3 study demonstrated that targeted therapies on top of conventional studies do not improve maintenance of sinus rhythm at 5-year follow-up in patients with persistent AF and HF.

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. 2021 EHRA Congress, 23-25 April.

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Personalised pulmonary vein isolation procedure feasible and effective

Presented By

Dr Cheryl Terés, Teknon Medical Centre, Spain

Conference

EHRA 2021

Trial

Ablate-by-LAW

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.

The main reason for the recurrence of paroxysmal atrial fibrillation (AF) is pulmonary vein (PV) reconnection. The creation of more efficient lesion creation and durable PV isolation was aided by the development of the ablation index. The left atrium is a thin structure with only 1-5mm wall thickness, and wall thickness is an independent predictor for PV reconnection. The aim of the Ablate-by-LAW study (NCT04218604) was to determine the efficacy, safety, and feasibility of adapting the ablation index to the left atrial wall thickness (LAWT).

The Ablate-by LAW study included multi-detector spiral computed tomography (MDCT)-derived LAWT, the MDCT-derived 3D 'fingerprinted' oesophagus image, a single-catheter strategy, and general anaesthesia with high-rate low-volume ventilation. Power settings and targeted ablation index were adapted to LAWT, which was categorised into 5 different thickness ranges. Furthermore, the distance between the oesophagus and the left atrial posterior wall was mapped and the lesion personalised by trying to avoid ablation through the closest part.

Dr Cheryl Terés (Teknon Medical Centre, Spain) presented results from 90 patients included in this study after a follow-up period of 11 months:

- 4 out of 90 patients (4.5%) had recurrences documented by ECG or self-reported symptoms;
- median procedural time was 1 hour;
- median radiofrequency time was 14 minutes;
- median fluoroscopy time was 0.75 minutes; and
- median fluoroscopy dose area product was 1 mGy/m².

Dr Terés concluded that the feasibility of incorporating 3D LAWT maps was demonstrated and that it 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, the recurrence rate was similar to previously reported protocols with lower procedural requirements.

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

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Components of AF management and early rhythm-control therapy in EAST-AFNET 4

Presented By

Dr Andreas Metzner, University Heart & Vascular Center Hamburg, Germany

Conference

EHRA 2021

Trial

Phase 4, EAST-AFNET 4

The EAST-AFNET 4 study showed that an early, structured rhythm control therapy based on antiarrhythmic drugs and catheter ablation can prevent atrial fibrillation (AF)-related complications when compared with usual care. This approach is feasible and clinical benefit can be achieved without many additional visits, using regionally different treatment choices.

Dr Andreas Metzner (University Heart & Vascular Center Hamburg, Germany) presented an analysis of the EAST-AFNET 4 study (**NCT01288352**) focussing on components of AF management and early rhythm control in patients with AF. The EAST-AFNET 4 study evaluated the effects of early rhythm control in patients with AF on the composite primary endpoint of cardiovascular death, stroke, hospitalisation for heart failure or acute coronary syndrome. 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.

Over 90% of patients received oral anticoagulation therapy, with more than 54% of patients receiving a direct oral anticoagulant (DOAC). There was no difference in the treatment of heart failure, hypertension, or diabetes. Rate control therapy was used in 4 out of 5 patients in both study arms. The number of in-person follow-up visits was low in both study arms: 1.94 visits/patients in controls versus 2.13 visits/patient in the treatment arm, with the higher number in the second study population being derived from more frequent visits after randomisation to adjust rhythm control therapy.

In usual care, rhythm control remained the exception. Antiarrhythmic drug (AAD) therapy in the treatment arm was initially given to 84% of patients, with 45% of patients still receiving AAD after 2 years. Random group was by far the strongest predictor of receiving therapy at any time.

Results showed a 21% risk reduction for cardiovascular death, stroke, hospitalisation for heart failure or acute coronary syndrome in patients receiving early rhythm control.

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. 2021 EHRA Congress, 23-25 April.

Posted on **24 April, 2021**

Added but limited value of ECG-based mortality prediction in COVID-19 patients using machine learning

Presented By

Dr Hidde Bleijendaal, Amsterdam University Medical Center, the Netherlands

Conference

EHRA 2021

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 are able to 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: a logistic regression model using manually annotated ECG features, and a pre-trained deep neural network (DNN) using the raw ECG waveforms. Data from 2 other centres (n=248) were used for external validation. Furthermore, a baseline model was created using only age and sex to evaluate the added value of ECG.

The performance of both prediction models was similar, with a mean area under the receiver operating curve of 0.76 for the logistic regression model and 0.77 for the DNN in the external validation cohort versus 0.76 in the baseline model. After adjustment for age and sex, the following ECG features remained as significant predictors for mortality in COVID-19 patients:

- increased ventricular rate,
- right bundle branch block,
- ST-depression, and
- low QRS voltages.

Dr Bleijendaal concluded: "predication of mortality in this dataset in COVID-19 patients is mostly based on age and sex. The added value of the ECG seems to be present, but limited."

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

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

Presented By

Prof. Thomas Vanassche, University Hospitals Leuven, Belgium

Conference

EHRA 2021

Prof. Thomas Vanassche (University Hospitals Leuven, Belgium) presented the new 2021 EHRA practical guide on the use of non-vitamin K antagonist oral anticoagulant (NOAC) in patients with atrial fibrillation with a strong focus on peri-operative and bleeding patients [1,2].

Management of bleeding under NOAC, also called direct oral anticoagulant (DOAC), therapy follows the EHRA practical guideline on atrial fibrillation [3]. The guideline was updated with regards to the use of specific DOAC reversal agents and availability in Europe. Post-bleeding management even in minor bleeds is considered important. The impact of bleeding on the patient's consideration of risks and benefits of anticoagulation, the risk of repeat bleeding, modifiable bleeding risk factors and choice, and dosing of DOAC should be discussed. Anticoagulation should be re-initiated in the absence of absolute contraindication.

Periprocedural management of DOACs is a frequent clinical problem. The rapid onset and offset of DOAC effect simplifies periprocedural management and preoperative treatment with low molecular weight heparin is not needed. Surgical factors and patient's characteristics determine the time of last preoperative DOAC intake. The full dose of DOAC should be resumed 24 hours after low-risk interventions and 48-72 hours after high-risk interventions.

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

- The importance of post-bleeding management even in minor bleeds, and an integrated management of bleeds is recommended 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: NOACs in pre-operative and bleeding patients. 2021 EHRA Congress, 23-25 April.
2. **Steffel J, et al. Europace 2021;00:1–65.**
3. Govender K. Oral anticoagulant and bleeding: role of antidotes. 2021 EHRA Congress, 23-25 April.

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DOACs and bleeding: the role of antidotes

Presented By

Dr Kaveshree Govender, Milpark Hospital, South Africa

Conference

EHRA 2021

The use of direct oral anticoagulants (DOACs) in patients with atrial fibrillation 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.

Major bleeding in patients with atrial fibrillation medicated with factor Xa (FXa) and factor IIa (FIIa) inhibitors is still 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) presented their role in managing bleeding complications [1].

The 2018 EHRA practical guideline on atrial fibrillation provided guidance on managing bleeding episodes in DOAC-treated patients: delay or discontinuation of DOAC treatment in mild bleeding, symptomatic treatment in non-life-threatening major bleeding with or without antidote-treatment, and finally antidote-treatment in life-threatening bleeding events.

Available antidotes for DOACs have been introduced:

- Anti-fibrinolytic agents, which are readily available at low costs, show low thrombogenicity and were recommended by the 2018 EHRA guideline.
- Off-label use of haemostatic agents (i.e. activated prothrombin complex concentrate for dabigatran-associated bleeding and 4-factor prothrombin complex concentrate for FXa inhibitor-associated bleeding).
- Non-specific agents, which currently lack the support of good-quality clinical studies.
- Andexanet alpha, a specific antidote for FXa inhibitor-associated bleeding.
- Idarucizumab, a specific antidote for dabigatran-associated bleeding.

Specific agents are less readily available and are costly and should primarily be used for life-threatening bleeding and for urgent invasive procedures in DOAC-treated patients.

Dr Govender concluded that DOAC-associated bleeding should be risk-stratified to determine burden management. Moderate or life-threatening bleeding requires temporary discontinuation of the drug and supportive care. Specific antidotes are less readily available and are costly but show good efficacy and should be used for life-threatening bleeding and for urgent invasive procedures in DOAC-treated patients. 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. 2021 EHRA Congress, 23-25 April.

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EHRA practical guide on cardiac imaging in electrophysiology

Presented By

Prof. Thomas Deneke, Heart Centre Bad Neustadt, Germany

Conference

EHRA 2021

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 an overview of a manuscript currently being finalised, which gives practical advice on the usage of CT and MRI for different scenarios in patients planned for or after AF and VT ablation and patients with complications after ablation procedures. The presented data should help electrophysiologists decide on which technology (i.e. CT, MRI, or both) and specific techniques to use in which clinical setting.

A standardised protocol for the inclusion of CT and MRI 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 (automatic, semi-automatic), and finally image integration and registration. Prof. Deneke further discussed which modality (CT or MRI) is ideal in AF and VT ablation:

- MRI can be used for the majority of workflow procedures, except for the detection of intramural fat and calcification prior to VT ablation, for which CT is more suitable.
- MRI imaging at 3 months post-procedure best indicates the long-term ablation lesion scar in patients with AF ablation.
- CT is the modality of choice for the diagnosis of ablation-related complications (incl. fistula, perforation, bleeding, stenosis, and ischaemic events).

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

Posted on **25 April, 2021**

Subcutaneous implantable cardioverter-defibrillator maintains efficacy over 5 years

Presented By

Prof. Pier Lambiase, University College London, UK

Conference

EHRA 2021

Trial

EFFORTLESS S-ICD

The EFFORTLESS S-ICD Registry evaluated the 5-year safety and efficacy of the subcutaneous implantable cardioverter-defibrillator (S-ICD). The system was shown to maintain high shock efficacy over time. The burden of inappropriate shocks was relatively low and it could be shown that re-programming after early incidents could reduce inappropriate shocks in years 2-5 [1].

The objective of the EFFORTLESS S-ICD Registry (NCT01085435) was to evaluate the long-term outcomes of patients implanted with an S-ICD. Prof. Pier Lambiase (University College London, United Kingdom) presented on the spontaneous efficacy throughout the 5-year study and predictors of later outcomes. Enrolled were 984 patients with diverse underlying aetiologies, of which 703 patients completed the study. Mean study follow-up was 4.44 years. In only 2% of the patients, S-ICD was replaced with a transvenous device for pacing.

Prof. Lambiase presented the 5-year efficacy outcomes:

- No definite electrode failures occurred, and 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 whose S-ICD was re-programmed for causes of inappropriate shocks in year 1 had fewer inappropriate shocks in years 2-5, but this reduction was not statistically significantly different from patients without re-programming after inappropriate shocks.
- Evaluation of late appropriate shocks showed that 10% of participants had untreated episodes which self-terminated, 6% had monomorphic ventricular tachycardia, 3% a combination of monomorphic and polymorphic ventricular tachycardia/ventricular fibrillation, and 6% had ventricular fibrillation alone. The main predictor for appropriate shocks was appropriate shocks in the first year ($P<0.0001$).
- 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, the results of this 5-year follow-up of S-ICD in a large cohort showed that S-ICD maintained a high level of cardioversion efficacy over 5 years. Prof. Lambiase also emphasised: "Importantly, untreated inappropriate sensing episode 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. 2021 EHRA Congress, 23-25 April.

Posted on **25 April, 2021**