Medicom International Conference Series in Cardiology

EHRA 2022 Congress

European Heart Rhythm Association

03 – 05 APRIL 2022 • COPENHAGEN • DENMARK

PEER-REVIEWED CONFERENCE REPORT

CSP Non-Inferior to BiVP

The randomised-controlled LEVEL-AT trial showed that conduction system pacing may be an alternative to biventricular pacing in patients with HF and wide QRS segments.

read more on PAGE 6

Reassuring Safety Profile of PFA

Real-world data from the MANIFEST-PF survey displayed a reassuring safety profile of pulsed-field ablation in general, and in particular with respect to oesophageal damage.

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Sex Differences Revealed in AF

Results from the RACE V project indicated that progression of AF is more prevalent in men and that the sexes have different determinants driving this progression.

read more on PAGE 13

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ISSN	2468-8762 22:12

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Letter from the Editor

Dear colleagues,

We thank you for your interest in this summary report for the 2022 European Heart Rhythm Association Meeting in Copenhagen, Denmark. It was an exciting return to meet face-to-face again after the pandemic years, and learning, sharing and networking together in-person.

Our editorial team and peer reviewers have worked hard to bring you some of the very best content of the meeting. You will find late-breaking science, new evidence and updates on the following topics: Diagnostics and Prevention, Developments in Devices, Updates on Ablation, News on Atrial Fibrillation, and Other topics. Conduction system pacing and Pulsed field ablation were the new technologies that gained lots of atttention. Techniques in the centre of attention were artificial intelligence, remote monitoring, and screening. And last but not least, better patient characterisation and selection were key topics in numerous scientific sessions.

We hope you find our peer-reviewed summaries informative, balanced, and of help in your clinical practice.

Yours, sincerely
Michiel Rienstra

Biography
Michiel Rienstra, MD, PhD, MHA, is Cardiologist and Professor of Clinical Cardiology and serves as Clinical Director of the Department of Cardiology, and cardiologist at the University Medical Center Groningen, The Netherlands. He is founder of the regional network HeartNet Northern-Netherlands. Prof. Rienstra earned his medical degree at the University of Antwerp, Belgium, his PhD degree at the University of Groningen, the Netherlands, and his Master of Health Administration at Tilburg University, the Netherlands. He combines treatment of patients with arrhythmias and HF with clinic-oriented AF and HF research. His research consists of conducting investigator-initiated clinical studies to improve AF or HF treatment (among others the RACE study group) studying the epidemiology of AF and its risk factors, uncovering the genetics of AF in part with the AFGen international consortium, and applying novel bioinformatics tools to improve AF risk prediction using biobanks of AF patients. He is fellow of the European Society of Cardiology and the American Heart Association.
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Conflict of Interest Statement:
Consultancy fees from Medtronic, Arca Biopharma Inc, and Roche to the institution.

Diagnostics and Prevention

Cardiac magnetic resonance imaging improves prediction of post-MI sudden cardiac death

Cardiac magnetic resonance (CMR) imaging may improve the prediction of sudden cardiac death after myocardial infarction (MI). The first results of the updated PROFID clinical prediction model suggested that core scar and grey zone quantification add predictive value to the model. In future, CMR imaging may be used in conjunction with to left ventricular ejection fracture (LVEF) to predict the risk of sudden cardiac death in post-infarction patients.

The prevailing strategy to predict sudden cardiac death in post-infarction patients is based primarily on LVEF, explained Dr Nikolaos Dagres (Heart Center Leipzig, Germany) [1]. A major shortcoming of this approach is the lack of discriminative ability. A significant number of patients with an LVEF ≤35% may be overtreated, whereas patients who have an LVEF >35% may be undertreated [2]. PROFID aims to improve the predictive performance for sudden cardiac death, facilitating a personalised treatment approach.

Previously, a risk prediction tool was developed and tested based on data from 19 different datasets worldwide including 224,898 participants who had experienced a previous infarction or ischaemic cardiomyopathy with an LVEF <50%. The results showed that LVEF had a predictive value for sudden cardiac death in non-implantable cardioverter defibrillator (ICD) patients (area under the curve [AUC] 0.618), but other clinical characteristics or biomarkers did not improve the predictive performance of the model.

Dr Dagres presented the updated clinical risk prediction model, which included CMR data obtained from 2,049 participants >40 days after the infarction occurred. The first results of the updated model indicate that adding core scar size and grey zone size increased the predictive performance of the model at 12 months post-MI, especially in non-ICD patients (AUC 0.753). In patients with ICD, the 12-month post-MI AUC was 0.535 without CMR data and 0.598 with CMR data.

The PROFID risk model is still under investigation, but these results suggest that core scar size and grey zone size, as assessed by CMR imaging, may help clinicians to predict post-MI sudden cardiac death, particularly in those without traditional indications for prophylactic ICD. Importantly, improving the risk prediction for these patients may enable clinicians to offer a personalised-treatment approach based on this risk score.

1. Dagres N, et al. Cardiac magnetic resonance imaging for prediction of risk for sudden cardiac death after myocardial infarction, the updated PROFID clinical prediction model. Late-breaking science 1, EHRA 2022, 3¬–5 April, Copenhagen, Denmark.
2. Dagres N, et al. Eur Heart J. 2020;41(39):3781‒3782.

AI model accurately predicts sudden cardiac death in overall population

A novel prediction model for sudden cardiac death was able to calculate the risk for sudden cardiac death with high accuracy. The model, based on artificial intelligence (AI), included both cardiac risk factors and non-cardiac risk factors. A subsequent study will aim to enhance the prediction of sudden cardiac death by identifying relevant clinical subgroups.

Prof. Xavier Jouven (Georges-Pompidou European Hospital, France) and co-authors aimed to develop a sudden cardiac death prediction with a particular focus on the low-risk general population since they comprise the highest absolute number of sudden cardiac death and are more difficult to capture than patients with known high-risk factors, such as previous myocardial infarctions [1]. The study group included 12,784 cases of sudden cardiac death from the Paris Sudden Death Expertise Center and 10,000 matched controls. Using AI, an individualised 1-year predicted risk score for sudden cardiac death was calculated.

Selected were 200 variables from 10,000 medical codes. The developed deep-learning model displayed an area under the curve (AUC) of 0.88, a sensitivity of 81%, and a positive predictive value of 88%. Notably, when non-cardiovascular variables were added, the AUC of the model was elevated from 0.81 to 0.88. Furthermore, the model was able to identify participants who had a risk of 90% or more of experiencing sudden cardiac death in the coming year with a positive predictive value of 95%, capturing 43% of the total number of sudden cardiac death cases. The study group will be working

to improve the sudden cardiac death risk prediction model by identifying clinical subgroups of interest in a successive study.

1. Jouven X, et al. Prediction of sudden cardiac death using artificial intelligence. Late-breaking science 1, EHRA 2022, 3–5 April, Copenhagen, Denmark.

Developments in imaging tools for AF

Although echocardiography is still the most widely applied tool to stratify patients in clinical practice, late gadolinium enhancement (LGE)-MRI and electrocardiographic imaging (ECGi) are promising tools that may contribute to a personalised approach in atrial fibrillation (AF) management.

"The severity of atrial cardiomyopathy is related to the success of rhythm control therapies," said Prof. Lluis Mont (University of Barcelona, Spain) [1]. The more precise the extent of atrial cardiomyopathy in patients can be measured, the better the selection of which patients should receive rhythm control therapy and which patients should receive rate control therapy. Prof. Mont discussed the developments in imaging tools that can be applied to discriminate between patients with AF.

Echocardiography

Everything starts by obtaining a good echo. Measuring the left atrium size with echocardiographic imaging is a simple, reproducible, and robust predictor for AF recurrence and stroke. Evidence suggests that more advanced echocardiographic techniques can reveal functional deficits of the atrium [2].

LGE-MRI

Although evidence has been presented on the measurement of atrial cardiomyopathy via LGE-MRI, this tool is still in progress. LGE-MRI images of fibrosis have been shown to correlate with low-voltage areas of the left atrium and the degree of fibrosis on LGE-MRI has been associated with AF recurrence [3,4]. However, the randomised-controlled ALICIA trial (NCT02698631) and DECAAF II trial (NCT02529319) did not show a clinical benefit of MRI-guided pulmonary vein isolation (PVI) versus conventional PVI. LGE-MRI has not yet demonstrated to improve outcomes through MRI-guided ablation but may help in the selection of suitable patients for AF ablation.

Electrocardiographic imaging

ECGi is a non-invasive tool that can measure the activation and local conduction velocities of the heart. Also, ECGi allows for single beat mapping to detect individual AF patterns. ECGi-derived activation times have shown useful in diagnosing atrial cardiomyopathy and are predictive of AF recurrence after PVI [5]. "Currently, our study group is linking MRI fibrosis to conduction velocities to see whether accurate prognosis and personalised ablation decisions can be made based on this imaging tool."

"All in all, imaged-based phenotyping has great potential to move us towards personalised AF management," concluded Prof. Mont.

1. Mont L. Imaging tools for atrial phenotyping to tailor rate vs. rhythm control. Precision medicine approach to AF, EHRA 2022, 3–5 April, Copenhagen, Denmark.
2. Papadopoulos CH, et al. Hellenic J Cardiol. 2018;59(3):140–149.
3. Oakes RS, et al. Circulation. 2009;119(13):1758–1767.
4. Marrouche NF, et al. JAMA. 2014;311(5):498–506.
5. Eichenlaub M, et al. Europace. 2021;23(12):2010–2019.

Large impact of remote screening tool on sleep apnoea diagnoses in AF

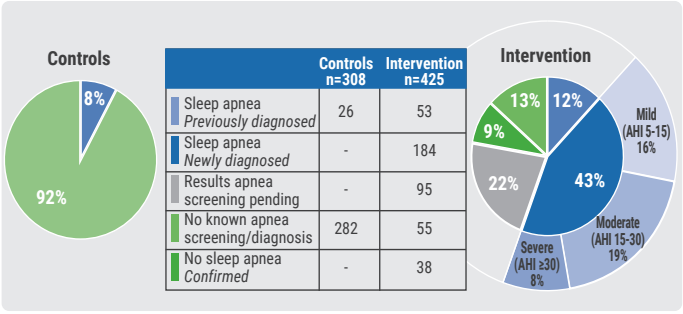
A structured polygraphy screening incorporated in a novel, remote, mobile, health pathway revealed that a high proportion of patients with atrial fibrillation (AF) who were set for catheter ablation had underlying sleep apnoea (SA). Diagnosing SA in patients with AF is important since this information can be used to counsel patients on the success rates of ablation and other AF therapies. Moreover, targeted SA therapies can be initiated.

E-health is increasingly applied in heart rhythm control strategies and in screening for comorbidities such as SA. In addition, SA is difficult to diagnose in patients with AF but may contribute to AF progression. Dr Dominique Verhaert (Maastricht University Medical Center, Netherlands) and colleagues aimed to assess a structured remote polygraphy screening tool for SA in patients who were scheduled for AF ablation [1]. In total, 733 patients with paroxysmal or persistent AF were randomised to an at-home sleep test to screen for SA (n=425) or standard-of-care (n=308). In the control group, 8% of the participants had been previously diagnosed with SA while SA status was unknown in the remaining 92%. In the intervention group, 12% of the participants had been previously diagnosed with SA.

The screening intervention identified 184 new cases of SA (43%). Following the apnea-hypopnea Index (AHI), these new diagnoses included mild (16%), moderate (19%), and severe cases (8%) of SA. Furthermore, SA had been ruled out in 9% of the participants and the results were still pending at the time of the analysis for 22% of the participants. Therefore, the number of newly identified cases of SA may be even

higher than the current analysis suggests. In 13% of the participants in the intervention group, SA status was still unknown because these participants preferred not to be screened (see Figure).

Figure: The impact of screening on diagnosed apnoea [1]



	Controls n=308	Intervention n=425
Sleep apnea *Previously diagnosed*	26	53
Sleep apnea *Newly diagnosed*	-	184
Results apnea screening pending	-	95
No known apnea screening/diagnosis	282	55
No sleep apnea *Confirmed*	-	38

AHI, apnea-hypopnea Index.

"This study showed that SA is highly prevalent in patients with AF who are set for catheter ablation. The knowledge of SA status is important because it provides the opportunity to initiate targeted treatments, such as continuous positive airway pressure (CPAP) therapy. The follow-up study will reveal whether these results will have an impact on AF ablation outcomes."

1. Verhaert DVM, et al. The impact of a structured polygraphy screening incorporated in a novel remote mobile health pathway on sleep apnoea prevalence in patients with atrial fibrillation. E-Cardiology award session, EHRA 2022, 3–5 April, Copenhagen, Denmark.

AI model accurately discriminates between arrhythmias

An artificial intelligence (AI) model was able to successfully distinguish between patients with cavotricuspid isthmus (CTI)-dependent atrial flutter and non-CTI dependent atrial tachycardia, based on patient ECGs. Since the model performed well in this proof-of-concept study, future studies will explore the diagnostic capacities of AI with regard to other arrhythmias.

It would be helpful for clinicians and patients if the mechanism of arrhythmias could be identified via ECGs with a high degree of certainty, according to Dr Arunashis Sau (Imperial College London, UK) [1]. Two main categories of atrial arrhythmias are CTI-dependent atrial flutter and non-CTI dependent atrial tachycardia. The current study aimed to train a convolutional neural network to discriminate between these 2 categories of arrhythmias. The model was compared with expert assessments, using an invasive electrophysiology study as the source of truth. Collected were 13,557 ECGs from 288 patients. The training data set consisted of 13,500 ECGs from 231 patients and the test set included 57 ECGs from 57 patients.

The model achieved an accuracy of 86%, which was a significantly higher accuracy than the electrophysiologist assessment (79%) and a numerically higher accuracy than the electrophysiologist consensus (81%). The area under the curve of the model was 0.94. Notably, experts were more likely to incorrectly diagnose an atrial flutter case as being atrial tachycardia than the AI model (34.5% vs 10.3%). According to Dr Sau, this finding could have significant implications, given that CTI-dependent atrial flutter is more amendable to catheter ablation. Furthermore, when the model and electrophysiologist consensus agreed, the prediction accuracy was 100%. "This result indicates that the use of this model with human-in-the-loop provides powerful results," argued Dr Sau.

"We successfully trained a neural network to distinguish CTI-dependent atrial flutter from atrial tachycardia, with a performance that is at least equivalent to human expert performance," concluded Dr Sau. "Other studies will be conducted to further analyse the use of AI in ECG-based diagnosing of patients with arrhythmias."

1. Sau A, et al. Classification of organised atrial arrythmias using explainable artificial intelligence. E-cardiology award session, EHRA 2022, 3–5 April, Copenhagen, Denmark.

Impact of AF screening on stroke prevention influenced by systolic blood pressure

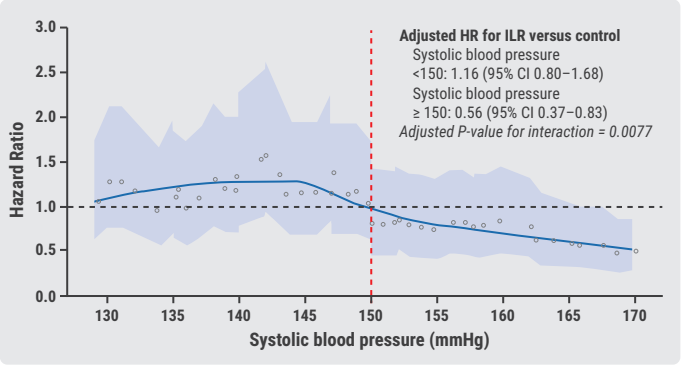
Screening for atrial fibrillation (AF) via continuous monitoring with an implantable loop recorder (ILR) was more efficacious in terms of stroke prevention for participants with higher systolic blood pressure (BP). In addition, higher systolic BP was related to an increased risk of longer AF episodes, which may partially explain the association between systolic BP and stroke prevention via AF screening.

Hypertension is a known risk factor for both clinical AF and AF-related stroke. However, it remains unclear whether continuous screening for AF can prevent strokes in individuals with high systolic BP. To address this, Dr Lucas Yixi Xing (Copenhagen University Hospital, Denmark) and colleagues conducted a post-hoc analysis of the LOOP study (NCT02036450) [1]. The previously published LOOP study included 6,004 participants ≥70 years old without AF but with

≥1 of the following stroke risk factors: hypertension, diabetes mellitus, heart failure, or previous stroke [2]. The participants were randomised to continuous monitoring with ILR and subsequent anticoagulation therapy if AF was detected (n=4,503) or standard therapy (n=1,501) to assess whether the intervention was able to prevent strokes. Although ILR screening was associated with a 3-fold increase in the detection of AF and subsequent initiation of anticoagulation therapy, no significant risk reduction in stroke or systemic arterial embolism was observed (HR 0.80; P=0.11). The current post-hoc analysis assessed the relation between AF screening and hypertension in stroke prevention [1]. In addition, the research group investigated how systolic BP affected AF occurrence and AF burden.

Participants with a higher systolic BP (≥150 mmHg) benefitted significantly more from ILR screening for AF in terms of stroke prevention than participants with a systolic BP <150 mmHg (HR 0.56 vs HR 1.16; P for interaction=0.0077; see Figure). Although systolic BP did not significantly influence the occurrence of new-onset AF in the intervention arm (HR 1.10; 95% CI 0.92–1.33), participants with a systolic BP ≥150 mmHg displayed significantly higher rates of AF episodes that lasted ≥24 hours (HR 1.69; 95% CI 1.07–2.66).

Figure: Interaction between systolic BP and the effect of ILR screening on stroke or systemic arterial embolism [1]



CI, confidence interval; ILR, implantable loop recorder.

"The current analysis showed that the benefit of ILR screening for AF on stroke prevention increased with increasing systolic BP. This effect may be partially explained by the finding that high systolic BP was associated with an increased risk for longer AF episodes. However, these results should be interpreted with caution since this was a post-hoc analysis, and BP measurement was only taken at a single point," concluded Dr Xing.

1. Xing LY, et al. Systolic blood pressure and effects of screening for atrial fibrillation with long-term continuous monitoring. What is new on stroke prevention, EHRA 2022, 3–5 April, Copenhagen, Denmark.
2. Svendsen JH, et al. Lancet. 2021;398(10310):1507–1516.

Developments in Devices

Conduction system pacing potential alternative for biventricular pacing in HF

Conduction system pacing (CSP) demonstrated non-inferiority to biventricular pacing (BiVP) in terms of cardiac resynchronisation and ventricular remodelling in patients with heart failure and wide QRS segments. Evidence from the randomised-controlled LEVEL-AT trial suggests that CSP may be an alternative to BiVP in these patients, but additional studies are warranted before changing guidelines.

CSP is an emerging technique to treat patients with an indication for cardiac resynchronisation therapy (CRT), but only a few randomised studies have compared the BiVP therapy with CSP. Dr Margarida Pujol-López (Institut Clínic Cardiovascular, Spain) and colleagues designed the non-inferiority LEVEL-AT trial (NCT04054895), in which patients with heart failure (a left ventricular ejection fracture ≤35%) and a wide QRS segment (≥130 ms in left bundle branch block/≥150 ms in non-left bundle branch block), or patients with atrioventricular block and cardiac dysfunction were randomised 1:1 to CSP or BiVP (n=35 per group) [1]. The primary endpoint was a change in left ventricular activation time (LVAT), assessed by electrocardiographic imaging at day 45.

In the CSP arm, 11% of the participants received His bundle pacing, and 89% received left bundle branch area pacing. The primary endpoint displayed that CSP (LVAT -28 ms) was non-inferior to BiVP (LVAT -21 ms; $P_{non\text{-}inferiority}<0.001$). The mean left ventricular end-systolic volume change was -37 mL for patients in the CSP arm and -30 mL for patients in the BiVP

arm ($P_{non\text{-}inferiority}$=0.04). The mean QRS shortening times for patients in the CSP arm and patients in the BiVP arm were -53 ms and -48 ms, respectively ($P_{non\text{-}inferiority}$<0.001). Finally, the total procedure time (mean 125 vs 129 minutes) and the number of complications requiring re-intervention (11.4% for both) were comparable for the 2 treatment conditions.

Although CSP is a promising technique, study discussant Prof. Christophe Leclercq (University Hospital Rennes, France) argued that this study is not able to deliver solid conclusions on the safety, efficacy, and long-term results of CSP. "The results of the LEVEL-AT trial are encouraging. However, the assessed population was small, the inclusion criteria were wide and the crossover rate of CSP to BiVP was rather high (23%). Larger, randomised-controlled trials are needed before guideline recommendations should be considered regarding the application of CSP as a tool for left bundle branch pacing in patients with heart failure."

1. Pujol-López M, et al. Conduction system pacing vs. biventricular pacing in Heart Failure and wide QRS patients: a randomized study. Late-breaking science 1, EHRA 2022, 3–5 April, Copenhagen, Denmark.

Left bundle branch area pacing is a feasible technique for HF and bradyarrhythmia

Left bundle branch area pacing (LBBAP) is a feasible primary pacing technique for patients with heart failure (HF) or bradyarrhythmia. The MELOS study is the largest multicentre, observational study to report on the efficacy and safety of this emerging pacing technique. Left bundle fascicular pacing (LBFP) and left ventricular septal pacing (LVSP) may result in better outcomes than proximal LBBP.

LBBAP includes LVSP, LBBP, and LBFP. Prof. Marek Jastrzębski (Jagiellonian University, Poland) and colleagues conducted the large observational MELOS study to assess the safety and efficacy of these pacing techniques in patients with HF or bradyarrhythmia (n=2,533) [1]. The mean age of the study population was 73.9 years, 57.6% were women, 27.5% had a history of HF, 22.4% had a left bundle branch block, and 87.9% were assessed prospectively. The main study outcomes were feasibility, success rate, and learning curve of the implantation procedure.

The learning curve suggested that approximately 150 to 200 procedures (any LBBAP procedure) needed to be performed to obtain the optimal success rate. In addition, the success rate of LBBAP techniques was 91.6% in patients with bradyarrhythmia and 76.8% in patients with HF. Predictors of failure were broad baseline QRS segments, low left ventricular ejection fractures, and HF. Prof. Jastrzębski added that these results indicate that patients who could benefit the most from the procedure are also the ones in whom the implantation is most difficult to be conducted successfully. Nonetheless, the capture threshold (0.77 V) and sensing (10.6 mV) suggest that the technique is adequate.

The obtained paced QRS segments (137–145 ms) and paced V6 R-wave peak time (77–83 ms) pointed to a physiological activation of the left ventricle. Furthermore, Prof. Jastrzębski mentioned that LBFP and LVSP are the dominant real-world techniques with 69.5% and 25.1% of the total LBBAP procedures and that these procedures lead to significantly better results than LBBP.

Complications were observed in 8.2% of the participants, most commonly being intraprocedural perforation of the interventricular septum (3.7%). Other complications included acute chest pain (1%), acute coronary syndrome (0.43%), coronary artery fistula (0.28%), and ST elevation in multiple leads (0.24%). According to Prof. Jastrzębski, complications were resolved without long-lasting sequelae.

Invited discussant Dr Angelo Auricchio (Cardiocentro Ticino, Switzerland) argued that LBBAP is promising, but that the success rate and complication rate need to be improved. "More training, better tools, more experience and consistency across centres are needed to evolve this technique. Next to that, guiding technology needs to be improved to support the implantation. Finally, large randomised-controlled trials should provide evidence on the safety and efficacy of LBBAP."

1. Jastrzęvski M, et al. Multicentre European left bundle branch area pacing outcomes study: MELOS. Late-breaking science 1, EHRA 2022, 3–5 April, Copenhagen, Denmark.

Focus on the efficacy of cardiac resynchronisation therapy in HF plus concomitant AF

No significant association between the presence of atrial fibrillation (AF) in patients with heart failure (HF) and the efficacy of cardiac resynchronisation therapy (CRT) was observed in an analysis including 5 major clinical trials. However, the results were not conclusive, and further studies are warranted to address this issue.

Although the efficacy of CRT in patients with HF has been established in landmark trials, it has been suggested that

the efficacy of CRT may be reduced in patients with HF and concomitant AF. This issue has not been thoroughly investigated, since patients with HF plus AF were limited in the conducted CRT trials. However, approximately 25% of the patients who receive CRT in the real world have AF. Dr Frederik Dalgaard (Herlev and Gentofte Hospital, Denmark) investigated the association between CRT and AF status in patients who were included in 5 landmark CRT trials (i.e. MIRACLE, MADIT-CRT, BLOCK-HF, RESERVE, and COMPANION) [1]. In total, 4,062 patients were analysed, of whom 661 had a history of paroxysmal AF. The clinical outcomes of this study were a combination of HF hospitalisation and all-cause mortality, and all-cause mortality alone.

After a median follow-up of 21 months, 837 patients had been hospitalised for HF, and 555 patients had deceased. The results showed that the ratio of hazard ratios between patients with and without AF was not significant (HR 1.24; P=0.16). Similarly, the secondary outcome of all-cause mortality did not display a significant interaction effect of CRT efficacy for those with and without AF (HR 1.34; P=0.19). Results did confirm that the overall population benefitted from CRT compared with no-CRT in terms of HF hospitalisation plus all-cause mortality (HR 0.74; 95% CI 0.62–0.87; P=0.005). The effect was smaller and non-significant in patients with concomitant AF (HR 0.87; P=0.37).

Including data from 5 landmark trials did not unambiguously confirm the efficacy of CRT in patients with HF and concomitant AF. Larger trials, focusing specifically on this sub-population of patients, are needed to address the efficacy of CRT in this group of patients.

1. Dalgaard F, et al. Cardiac resynchronization therapy in patients with a history of atrial fibrillation: insights from five major clinical trials. CRT News, EHRA 2022, 3–5 April, Copenhagen, Denmark.

RESET: No survival benefit of CRT-defibrillator over CRT-pacemaker in HF

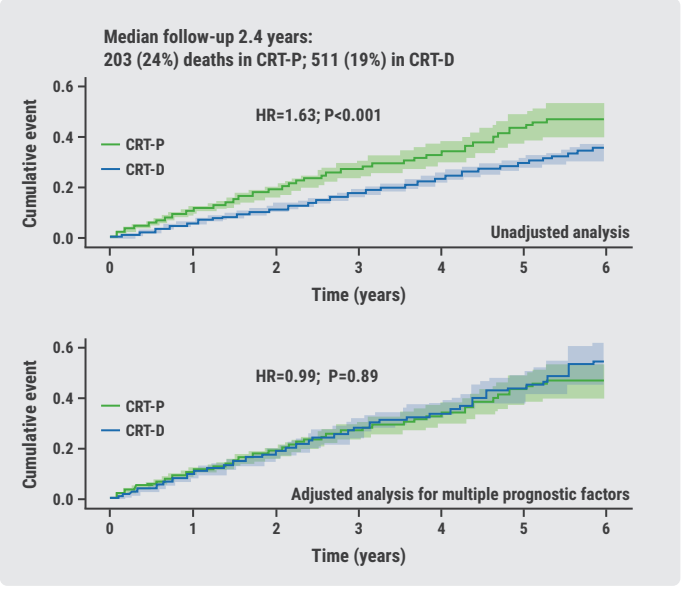
In patients with heart failure (HF) and an indication for cardiac resynchronisation therapy (CRT), patients who had a CRT-defibrillator (D) device did not show a survival benefit over patients who had a CRT-pacemaker (P) device. The results of the observational part of the RESET-CRT project further warrant the ongoing randomised part of the RESET-CRT project comparing CRT-D and CRT-P devices in patients with HF.

"Should patients with HF and an indication for CRT receive a defibrillator?" asked Prof. Nikolaos Dagres (Heart Center Leipzig, Germany) [1,2]. Since the risk of sudden cardiac death in this population has decreased in recent years due to improved medication, this issue has come into question [2]. The existing evidence on this topic is conflicting. A post-hoc analysis of the COMPANION trial (NCT00180258) suggested that CRT-D reduced all-cause mortality compared with CRT-P in patients with non-ischaemic cardiomyopathy (NICM) [3]. In contrast, a subgroup analysis of the DANISH trial (NCT00542945) did not display a benefit of CRT-D over CRT-P in patients with NICM [4]. A head-to-head trial comparing these devices was needed.

The RESET-CRT project includes a randomised clinical trial comparing CRT-D and CRT-P in patients with HF and an indication for CRT, and a retrospective observational part, mimicking the randomised trial. Prof. Dagres presented the results of the observational part, in which 847 patients with a CRT-P device and 2,722 patients with a CRT-D device were analysed [1,5]. All-cause mortality was the primary outcome of the study.

Baseline characteristics revealed a mean age difference of approximately 7 years between participants with CRT-P devices (76.7 years) and participants with CRT-D devices (69.9 years). Furthermore, patients with CRT-P devices were less often men (52% vs 65%) and were more likely to have atrial fibrillation (59% vs 41%), reflecting the situation in clinical practice.

Figure: Difference in all-cause death between CRT-P and CRT-D: unadjusted and adjusted results [1,2]



After a median follow-up of 2.4 years, the non-adjusted analysis showed a reduced mortality rate in patients with CRT-D devices compared with those with CRT-P devices (24% vs 19%; HR 1.63; P<0.001) (see Figure on previous page). However, the age-adjusted analysis demonstrated no survival benefit of CRT-D over CRT-P (HR 1.13; P=0.165). Further adjustment for prognostic factors and comorbidities established that CRT-D did not outperform CRT-P in this population (HR 0.99; P=0.89).

"After adjustment for age and comorbidities, we observed no survival difference between CRT-D and CRT-P, justifying the need for the randomised part of the RESET-CRT trial, which will provide a head-to-head comparison between the 2 devices," concluded Dr Dagres.

1. Dagres N, et al. Survival of cardiac resynchronization therapy patients with and without defibrillator: Real-world evidence from the observational part of the RESET-CRT project. Late-breaking science 1, EHRA 2022, 3–5 April, Copenhagen, Denmark.
2. Barra S, et al. Eur Heart J. 2020;41:1976–1986.
3. Doran B, et al. JACC: Heart Failure. 2021;9(6):439–449.
4. Kober L, et al. N Engl J Med 2016;375:1221–1230.
5. Hadwiger M, et al. Eur Heart J. Apr 3, 2022. DOI: 10.1093/eurheartj/ehac053.

Insertable cardiac monitors effective for AF detection in cryptogenic stroke

Insertable cardiac monitors (ICMs) demonstrated to be an effective tool for the identification of atrial fibrillation (AF) in patients who experienced a cryptogenic stroke or cryptogenic transient ischaemic attack (TIA) in the NOR-FIB trial. The early start-up of ICMs was accessible to and manageable for clinicians.

For the prevention of secondary stroke, detection of the underlying cause is crucial. Prolonged cardiac rhythm monitoring and ≥72 hours of ECG monitoring are guideline-recommended for ruling out underlying AF in patients who experienced a cryptogenic stroke since 2014 and 2020, respectively. However, ICMs are still not implemented in stroke guidelines as the preferred option to perform this task. The NOR-FIB trial (NCT02937077) was designed to identify AF and quantify AF burden in patients who had had a cryptogenic stroke or cryptogenic TIA and were under continuous monitoring of an ICM for a year [1]. Included were 259 patients from 18 Scandinavian centres. Patients in whom AF episodes ≥2 minutes were registered, received a recommendation for oral anticoagulant treatment. Dr Barbara Ratajczak-Tretel (University of Oslo, Norway) presented the results.

After 12 months, AF was identified in 29% of the patients. Most (87%) of the detected AF cases at 12 months were already detected at 6 months after ICM insertion. Associated with the occurrence of AF were a higher age (P<0.001), an elevated pre-stroke CHA_2DS_2-VASc score (P<0.001), and an increased National Institutes of Health Stroke Scale (NIHSS) score (P=0.002). AF was also associated with hypertension and dyslipidaemia in the study population. Participants with detected AF were asymptomatic in 93% of the cases and 92% of the identified AF cases displayed recurrence of AF. Moreover, stroke recurrence was observed in 3% of the patients with AF and in 5% of the patients in whom AF was not detected.

According to Dr Ratajczak-Tretel, the NOR-FIB trial demonstrated that ICM was an effective tool for detecting underlying AF in patients who experienced a cryptogenic stroke or cryptogenic TIA. "Importantly, the use of ICMs was manageable for the attending neurologists or stroke physicians. Therefore, the use of ICMs appears feasible to be implemented in the assessment of patients who experienced a cryptogenic stroke or TIA."

1. Ratajczak-Tretel B, et al. Atrial fibrillation in cryptogenic stroke and TIA patients in the Nordic atrial fibrillation and stroke (NOR-FIB) study: Topline results. What is new on stroke prevention, EHRA 2022, 3–5 April, Copenhagen, Denmark.

Updates on Ablation

First results of the POWER FAST III trial

The first results of the POWER FAST III trial showed that the number of oesophageal lesions was similar in patients who received high-power short duration (HPSD) radio-frequency (RF) pulmonary vein isolation (PVI) ablation and in patients who were treated with a conventional low-power long duration (LPLD) radio-frequency (RF) PVI ablation.

A recently published meta-analysis favoured HPSD PVI ablation over LPLD PVI ablation in terms of efficacy [1]. "However, this meta-analysis included mostly single-centre, non-randomised studies," argued Prof. José Luis Merino (La Paz University Hospital, Spain) [2]. "Moreover, the rate of oesophageal injuries should be compared for the 2 treatment modalities." The multicentre, randomised POWER FAST III trial (NCT04153747) included 267 patients with paroxysmal or persistent atrial fibrillation (AF), who were randomised 1:1 to receive HPSD-RF PVI (70 Watt for 9–10 seconds) or LPLD-RF PVI (25–40 Watt, guided by ablation lesion indexes). The primary safety outcome was the incidence of acute thermal oesophageal injuries at endoscopy. The primary efficacy endpoint was the incidence of atrial arrhythmias at 1-year follow-up.

After 1 year, the acute PVI efficacy was comparable for the 2 treatments with a 100% success rate for left PVIs and a 99.2% (HPSD arm) and 98.4% (LPLD arm) success rate for right PVIs. In addition, the first pass PVI rate was higher in the LPLD arm than in the HPSD arm (82% vs 66.7%; P=0.007). No significant differences were observed concerning acute spontaneous or adenosine PV reconnections. Also, the mean procedural duration was comparable for participants in the LPLD arm (191.5 minutes) and those in the HPSD arm (186.5 minutes; P=0.74).

The rate of acute oesophageal thermal lesions was similar for the treatment arms, with 6.5% in the LPLD and 7.5% in the HPSD arm (P=0.94). The complication rates were comparable (6.0% vs 7.9%; P=0.64). The rate of pericardial effusions was numerically 4 times higher in the HPSD arm (3.2%) than in the LPLD arm (0.7%) but this was not significant (P=0.2). Furthermore, the rate of systemic embolism trended towards significance in disfavour of the HPSD arm (3.2% vs 0%; P=0.055).

"The identical rates of oesophageal lesions are somewhat disappointing since the lesion sets that we place tend to be broader and more shallow for HPSD PVI ablation. It was expected that this procedure would spare the oesophagus," argued Dr Boris Schmidt (Cardioangiologisches Centrum Bethanien, Germany). "In addition, the rates of pericardial effusions were high in the HPSD arm. The 9 seconds 70 Watt dose that was applied in this study might have been too much for some regions in the left atrium. To avoid oesophageal lesions in HPSD PVI ablation, temperature monitoring could be used as a safety measure."

1. Ravi V, et al. Europace. 2021;23(5):710–721.
2. Castrejon S, et al. High radiofrequency power for faster and safer pulmonary vein ablation trial (POWER FAST III): preliminary safety and short-term results. Late-breaking science 2, EHRA 2022, 3–5 April, Copenhagen, Denmark.

Real-world safety results on pulsed-field ablation with pentaspline catheter

The MANIFEST-PF survey demonstrated that pulsed-field ablation (PFA) with the pentaspline catheter achieved pulmonary vein isolation (PVI) in 99.9% of the investigated real-world cases. The safety profile of this technique was reassuring with regard to oesophageal damage and consistent with that of preferential tissue ablation.

PFA has shown to be safe and efficacious in first-in-human trials, but the sample sizes of these trials were rather limited [1,2]. In the current retrospective study, Dr Vivek Reddy (Mount Sinai Hospital, NY, USA) and colleagues aimed to assess the real-world performance of the pentaspline PFA catheter [3]. More specifically, the objectives were to assess the safety, effectiveness, and usage of this tool in clinical practice. A survey was sent to 24 centres to gather data from 90 operators on 1,758 patients who underwent PFA.

An indication of paroxysmal atrial fibrillation (AF) was detected in 57.5% of the patients and 35.2% had an indication of persistent AF. The average procedure time was 65 minutes and 15.8% of the patients were discharged on the day of the procedure.

The most commonly used pre-procedural imaging techniques were transoesophageal echocardiogram (TEE) and CT imaging. During the procedure, fluoroscopy and intracardiac echocardiography (ICE) were frequently utilised. Notably, MRI was not used as a pre-procedural imaging technique in 70.8% of the cases. The use of electro-anatomical mapping was divided among operators: 35–40% of the operators always used this technique, but a similar amount of surgeons never used this method during PFA ablation with the pentaspline catheter. Besides PVI, roofline and left atrial posterior wall lesion sets were used by 12.5% of the operators.

The mean PVI success rate was 99.9%, ranging between 98.9% and 100% across centres. In terms of safety, major PFA-specific complications were limited. No cases of oesophageal fistulae, dysmotility, pulmonary vein stenosis, or persistent phrenic nerve injury were observed. One case of treatment-related coronary artery spasm was reported. In 8 patients, transient phrenic nerve injury was seen. However, these events were considered to be minor PFA-specific events. Furthermore, pericardial tamponade (0.97%), stroke (0.40%), and vascular complications requiring surgery (0.23%) were the most common major non-PFA specific adverse events. One patient who experienced a stroke died

from this complication. The most frequently reported non-PFA specific minor events were haematoma, which occurred in 2.45% of the patients.

"This study showed us a reassuring safety profile of PFA with the pentaspline catheter, in particular with respect to oesophageal fistulae, the most devastating complication in PVI," concluded discussant Dr Tom De Potter (Cardiovascular Research Center Aalst, Belgium).

1. Verma A, et al. Circ Arrhythm Electrophysiol. 2022;15(1):e010168.
2. Di Monaco A, et al. J Cardiovasc Dev Dis. 2022;9(4):94.
3. Reddy V, et al. MANIFEST-PF: multi-national survey on methods, efficacy and safety on the post-approval clinical use of pulsed field ablation. Late-breaking science 2, EHRA 2022, 3–5 April, Copenhagen, Denmark.

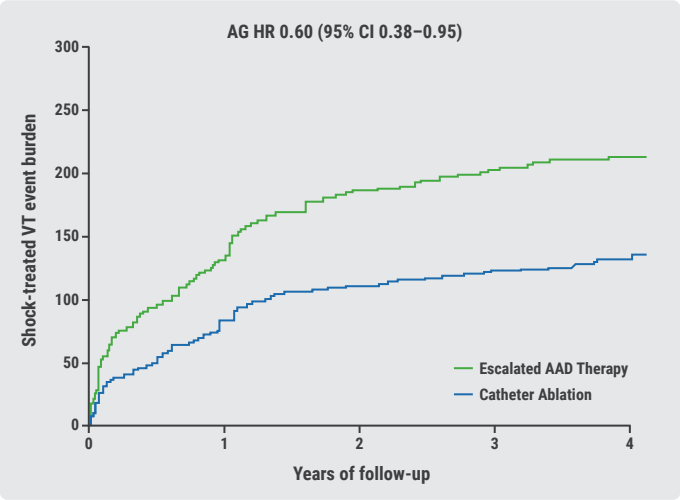
VANISH: Ablation reduces shock burden compared with anti-arrhythmic drug in ventricular tachycardia

Catheter ablation was associated with a reduced shock-treated ventricular tachycardia (VT) event burden and appropriate shock burden compared with escalated anti-arrhythmic drug (AAD) treatment in patients with AAD-refractory VT who experienced a prior myocardial infarction (MI).

The previously published, multicentre, randomised-controlled VANISH trial (NCT00905853) included 259 patients with an implantable cardioverter-defibrillator (ICD) who experienced a prior MI and VT event on AAD treatment in the last 6 months. These patients were randomised to catheter ablation (n=132) or escalated AAD therapy (n=127). After a median follow-up of 23.4 months, the primary composite endpoint of all-cause mortality, VT storm, and appropriate ICD shock favoured ablation over escalated AAD therapy (HR 0.72; P=0.04) [1]. In the current analysis, Prof. Michelle Samuel (University of Montreal, Canada) and colleagues compared shock-treated VT event burden and appropriate shock burden between the 2 study arms [2]. Shock-treated VT event burden was defined as the total number of VT events treated with ≥1 ICD or external shock. Appropriate shock burden was calculated as the total number of appropriate ICD or external shocks, regardless of the number of VT events.

The number of shock-treated VT events per 100 person-years was lower in the catheter ablation arm (39.07) than in the escalated AAD therapy arm (64.60; Anderson-Gill HR 0.60; 95% CI 0.38–0.95; see Figure). Similarly, the number of appropriate shock events favoured the ablation arm (48.35) over the AAD arm (78.23; Anderson-Gill HR 0.61; 95% CI 0.37–0.96).

Figure: Shock-treated ventricular tachycardia event burden [2]



AAD, anti-arrhythmic drug; AG HR, Anderson-Gill hazard ratio; CI, confidence interval; VT, ventricular tachycardia.

"Among patients with AAD-refractory VT and a prior MI, catheter ablation reduced shock-treated VT event burden by 40% and appropriate shock burden by 39%, compared with escalated AAD therapy," concluded Dr Samuel.

1. Sapp JL, et al. N Eng J Med 2016;375:111–121.
2. Samuel M, et al. Reduction in shock burden with catheter ablation versus escalated antiarrhythmic drug therapy: Insights from the VANISH trial. News from ventricular ablation, EHRA 2022, 3–5 April, Copenhagen, Denmark.

Low AF recurrence rates after PVI using pulsed-field ablation

Low atrial fibrillation (AF) recurrence rates were observed in patients with paroxysmal or persistent AF who underwent pulmonary vein isolation (PVI) using pulsed-field ablation (PFA). The results further showed durable isolation of pulmonary veins and no indication of PFA lesion regression in patients who had a recurrence of AF and underwent redo procedures.

PFA is a novel technique for PVI, displaying procedural efficacy and safety. However, limited data is available on AF recurrence after PVI through PFA and PVI durability during redo procedures [1,2]. Mr Thomas Kueffer (University of Bern, Switzerland) and colleagues investigated these issues in 41 patients (median age 69 years; 24% women; 56% with persistent AF) who underwent a first PVI with PFA [3]. PVI was verified by 3D-electroanatomical mapping. The duration of the post-procedural blanking period was 3 months. After

this blanking period, episodes of AF or atrial tachycardia were considered as a recurrence of AF when lasting >30 seconds. Seven-day Holter ECGs were conducted to assess AF-recurrence rates at 3 and 6 months.

All performed PVIs using a multipolar PFA catheter were successful. The median total procedure time was 104 minutes, including the time spent on 3D-electroanatomical mapping. A case of cardiac tamponade that required drainage was the only acute complication. During the blanking period, 3 patients displayed early recurrence of AF. After the blanking period, 5 cases of AF recurrence were reported. These cases occurred in 1 patient with paroxysmal AF and 4 patients with persistent AF. In total, 3 redo procedures were performed in patients with AF recurrence, confirming the durable isolation of PVs (12/12; 100%). Furthermore, no evidence of PFA lesion regression was observed.

"AF recurrence rates after PVI by PFA are low," concluded Mr Kueffer. "In patients with recurrence of AF, redo procedures demonstrated the durable isolation of pulmonary veins and did not show signs of PFA lesion regression."

1. Reddy VY, et al. JACC Clin Electrophysiol. 2021;7(5):614–627.
2. Reddy VY, et al. J Am Coll Cardiol. 2019;74(3):315–326.
3. Kueffer T, et al. Pulsed field ablation of atrial fibrillation: Recurrence rate after first pulmonary vein isolation and first insights into durability and redo procedures. Poster Session, EHRA 2022, 3–5 April, Copenhagen, Denmark.

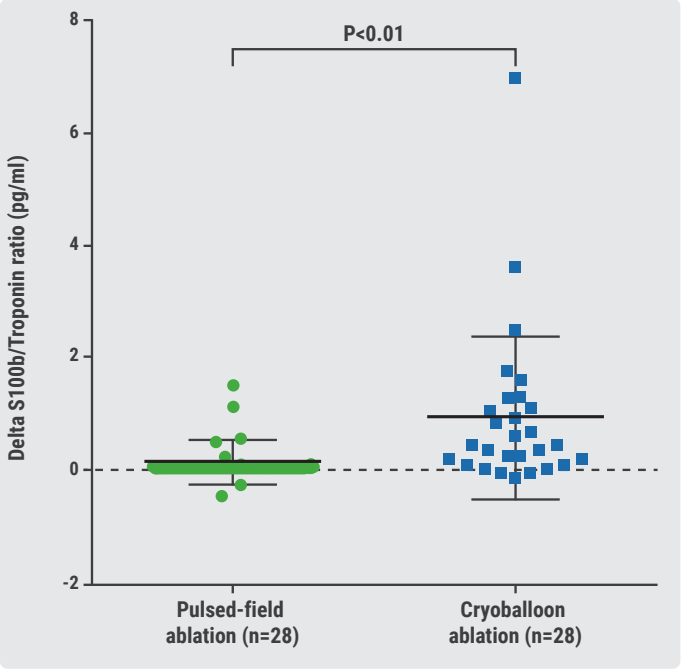
Pulsed-field ablation reduces neurocardiac damage versus cryoballoon ablation

Pulsed-field ablation (PFA) was associated with less neurocardiac damage than cryoballoon ablation as a method for pulmonary vein isolation (PVI). The post-interventional increase in heart rate was significantly lower in patients who were randomised to PFA. In contrast, damage to cardiomyocytes was higher in the PFA arm.

PFA is a novel, non-thermal energy source for PVI. Although it is known that thermal energy sources affect the entire atrial tissue during PVI, including nerves and ganglia, the specific impact of PFA on neurocardiac tissue has not yet been investigated [1]. The current study randomised patients undergoing their first PVI (n=56) 1:1 to PFA or cryoballoon ablation. High-sensitive troponin I levels, indicative of myocardial damage, were assessed as well as S100b levels, a measure for neurocardiac damage. The postinterventional increase in heart rate, which is associated with neurocardiac damage, was also analysed. Dr Marc Lemoine (University Heart & Vascular Center Hamburg, Germany) presented the results [2].

S100b levels were 2.9 times lower in the PFA arm than in the cryoballoon ablation arm (P<0.001), suggesting that neurocardiac damage was reduced in the PFA arm. High-sensitive troponin I levels were 3.3 times higher in the PFA arm than in the cryoballoon ablation arm (P<0.01), which indicates that the damage to cardiomyocytes is increased with PFA compared with cryoballoon ablation for PVI. In addition, the ratio of S100b/troponin was reduced for PFA compared with cryoballoon ablation (P<0.01), suggesting that less neurocardiac damage was inflicted per lesion size (see Figure). Furthermore, a post-interventional increase in heart rate was not observed in patients who received PFA, whereas patients who were subjected to cryoballoon ablation showed a significant increase in post-interventional heart rate compared with patients who received PFA (P<0.01).

Figure: S100b/Troponin ratio for PFA and cryoballoon ablation [2]



"This study validates the experimental concept that PVI by PFA leads to more specific damage to cardiomyocytes than to cardiac ganglia. We observed the loss of post-interventional increase in heart rate in patients who underwent PFA for PVI compared with those who underwent cryoballoon ablation for PVI," concluded Dr Lemoine.

1. Di Monaco A, et al. J Cardiovasc Dev Dis. 2022;9(4):94.
2. Lemoine M, et al. Pulmonary vein isolation by pulsed-field ablation induces smaller neurocardiac damage than cryoballoon ablation. Atrial fibrillation and ablation, EHRA 2022, 3–5 April, Copenhagen, Denmark.

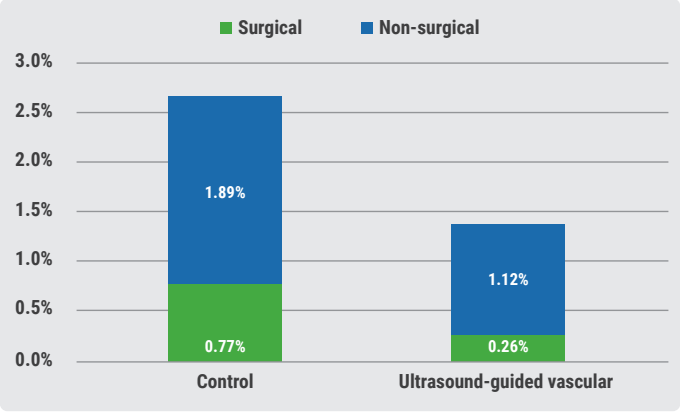
Ultrasound-guided femoral venipuncture reduces complications in catheter ablation

Fewer major vascular complications after catheter ablation were reported in patients with atrial fibrillation (AF) when surgeons had used an ultrasound-guided vascular access strategy. Also, the number of surgical interventions for vascular complications was reduced in the ultrasound-guided patients compared with the non-ultrasound guided patients.

Dr Jana Haskova (Institute for Clinical and Experimental Medicine, Czechia) and colleagues conducted a retrospective study to analyse major vascular complications due to catheter ablation in patients with AF [1]. Included were 4,646 participants who underwent catheter ablation (mean age 61; 33% women), of whom 2,330 were operated on with an ultrasound-guided vascular access strategy. The other 2,316 participants were non-ultrasound guided historic controls. The primary outcome was the number of major complications, defined as complications that required surgery, led to prolonged hospital duration, resulted in re-hospitalisation, or were complications that consisted of significant haematoma/bleeding with a haemoglobin drop >30 g/L.

The rate of major vascular complications was significantly lower in the ultrasound-guided population than in the historic controls (1.38% vs 2.66%; P=0.003) (see Figure). Moreover, the number of major complications that required surgical intervention was reduced in the ultrasound-guided arm compared with the non-ultrasound-guided arm (0.26% vs 0.77%; P=0.02). Dr Haskova added that older age was associated with a higher complication rate (P=0.0002), whereas male sex was related to a lower complication rate (P=0.003).

Figure: Major vascular complications for ultrasound-guided and control participants [1]



Dr Haskova concluded: "An ultrasound-guided vascular access strategy was associated with a statistically significant reduction of major vascular complications after catheter ablation for AF. Therefore, the routine use of ultrasound guidance is recommended to improve the safety of venous vascular access in patients with AF who undergo ablation."

1. Haskova J, et al. Ultrasound-guided femoral venipuncture for catheter ablation of atrial fibrillation: clinical benefit. Atrial fibrillation and ablation, EHRA 2022, 3–5 April, Copenhagen, Denmark.

News on Atrial Fibrillation

Sex differences revealed in AF determinants and AF progression

The progression of atrial fibrillation (AF) was more prevalent in men than in women, despite the higher average age of the investigated women in the RACE V project. Different AF progression determinants were identified for women and men, indicating that there might be different pathophysiological mechanisms at play.

AF often progresses from the paroxysmal type to the persistent type, which is related to different cardiovascular outcomes [1]. Prior studies revealed sex-specific differences in patients with AF regarding comorbidities, received therapies, and cardiovascular outcomes [2]. The current pre-specified analysis of the RACE V research group investigated sex differences in AF progression and associated comorbidities in 417 patients with paroxysmal AF [3]. The primary endpoint of the study was the AF progression rate. Prof. Michiel Rienstra (University Medical Center Groningen, Netherlands) presented the results.

Baseline characteristics revealed that women were on average 4 years older than men, had a higher symptom burden according to the European Heart Rhythm Association (EHRA) score (68% vs 49%), and were more likely to have a BMI >30

kg/m^2 (32% vs 21%). In contrast, men were more likely to have concomitant coronary artery disease (16% vs 6%), higher volumes of epicardial fat (105 mL vs 89 mL) and pericardial fat (199 mL vs 144 mL), higher mean PR intervals (172 ms vs 672 ms), and larger left atrial volumes (61 ml vs 54 mL).

AF progression was more common in men (15.1%) than in women (8.4%; P=0.032). The corresponding annual AF progression rates were 6.9% in men and 3.8% in women. Interestingly, men and women displayed different determinants of AF progression. In women, AF progression was related to a reduction of tissue factor pathway inhibitor (OR 2.22; P=0.008), PR interval increase (OR 1.72; P=0.034), and an increase of NT-proBNP (OR 2.10; P=0.016). Whereas, in men, significant predictors of AF progression were an increase in PCSK9 (OR 1.60; P=0.011), Factor XIIa C1-esterase inhibitor below the median level (OR 3.06; P=0.009), and an increase in NT-proBNP (OR 2.01; P<0.001). According to Prof. Rienstra, these results indicate that different pathophysiological mechanisms may influence the progression of AF in men and women.

"Further study of differences between men and women regarding the clinical profile and the progression of AF are needed because these differences are of importance when applying personalised management decisions for patients with AF," concluded Prof. Rienstra.

1. Kato T, et al. Circ J. 2004;68(6):568–72.
2. Westerman S & Wenger N. Curr Cardiol Rev. 2019;15(2):136–144.
3. Rienstra M, et al. Prevalence and determinants of atrial fibrillation progression in women and men with paroxysmal atrial fibrillation: RACE V. Late-breaking science 2, EHRA 2022, 3–5 April, Copenhagen, Denmark.

Early rhythm-control therapy efficacious in men and women with AF

Early rhythm control therapy outperformed usual care in both men and women with early atrial fibrillation (AF) and cardiovascular risk factors. No significant interaction effect between treatment and sex was reported. This result is in contrast with other studies, in which rhythm control therapy displayed worse outcomes in women than in men.

Men and women with AF have shown different responses to therapies and rates of cardiovascular complications [1]. The EAST-AFNET 4 trial (NCT01288352) demonstrated significant clinical benefits of early rhythm-control therapy for the included patients with AF (46% women) [2]. In the current pre-specified analysis of this trial, Prof. Isabelle van Gelder (University Medical Center Groningen, Netherlands) assessed the interaction effect of early rhythm-control therapy and sex and investigated sex-specific differences in clinical presentation [3].

Patients with early AF (≤12 months) who were >75 years of age, had a previous transient ischemic attack or stroke, or had at least 1 relevant comorbidity were eligible for this analysis (n=2,789). These patients were randomised to early rhythm-control therapy (i.e. anti-arrhythmic drug or ablation) or usual care. The primary efficacy outcomes were a composite of cardiovascular events and nights spent in hospital. The primary safety outcome was a composite of death, stroke, and rhythm control-related serious adverse events (AEs).

At baseline, a higher percentage of women displayed sinus rhythm compared with men (58% vs 51%; P<0.001), whereas men were more frequently asymptomatic (36% vs 25%; P<0.001). In addition, chronic kidney disease (stage 3 or 4) was more common in women (15% vs 11%; P=0.001) and women had a higher mean CHA2DS2-VASc score at baseline than men (3.73 vs 3.02; P<0.001). In contrast, heart failure (33% vs 23%), diabetes (28% vs 21%), and severe coronary artery disease (24% vs 9.6%) were more frequently reported in men than in women (P<0.001). These results show that the clinical characteristics of men and women with AF are different.

After a median follow-up time of 5.1 years, the composite outcome of cardiovascular events favoured early rhythm-control therapy over usual care significantly in women (HR 0.72; 95% CI 0.55–0.93) and numerically in men (HR 0.83; 95% CI 0.67–1.03). The treatment effect of early rhythm-control therapy did not show a significant interaction with sex (P=0.408), demonstrating that the benefit of early rhythm-control therapy is similar in women and men. The mean nights spent in hospital per year were also similar for women (1.4 days) and men (1.3 days).

The primary safety outcome showed similar event rates for women and men on early rhythm-control therapy (15.8% vs 17.2%). Notably, after 2 years of early rhythm control therapy, women displayed numerically higher rates of sinus rhythm than men (84.6% vs 80.0%), whereas men were more frequently asymptomatic (78.2% vs 69.4%).

As discussant of this study, Prof. Barbara Casadei (University of Oxford, UK) concluded: "This study shows that when we follow the guidelines and detect patients early, we can obtain good results with anti-arrhythmic therapy. However, more

work needs to be done to assess the different components of early rhythm control therapy, ablation, and antiarrhythmic drugs in men and women with AF."

1. Westerman S & Wenger N. Curr Cardiol Rev. 2019;15(2):136–144.
2. Kirchhof P, et al. N Engl J Med 2020;383:1305–1316.
3. Van Gelder IC, et al. Sex Differences in Early Rhythm Control Therapy in Patients with Atrial Fibrillation: data from the EAST trial. Late-breaking science 2, EHRA 2022, 3–5 April, Copenhagen, Denmark.

Progression in remote app-based monitoring of atrial fibrillation

Remote app-based monitoring of atrial fibrillation (AF) has been gaining ground in recent years. Photoplethysmography (PPG)-based devices have been providing data on regularity, frequency, and rate and can aid physicians to analyse symptom/rhythm correlation. App-based monitoring can be both useful for screening of older and younger patients. Finally, the Telecheck-AF study showed how collected app-based data could aid AF management.

The European Heart Rhythm Association (EHRA) has published a practical guide on 'How to use digital devices to detect and manage arrhythmias' during their annual meeting [1]. Prof. Dominik Linz (Maastricht University Medical Center, the Netherlands) reviewed the current state of the art regarding app-based monitoring of AF [2].

Many different wearable devices have been developed in recent years to monitor AF remotely: earlobe sensors, watches, chest belts, armbands, and finger bands. The devices can be divided into electrocardiogram (ECG)-based devices and PPG-based devices. Although PPG-based devices cannot be used to diagnose AF, since this requires ECG-based tools, PPG is a novel technique in cardiology that is highly useful in patients that have already been diagnosed with AF.

Advantages of PPG

Recently, a step-by-step approach to interpret PPG data was published [3]. Prof. Linz explained that PPG is very useful to assess the time spent in AF in patients who have already been diagnosed with AF. The output in waveform, tachogram, and Poincaré plot, which we know from implantable devices, provides data on regularity, frequency, and rate. For example, AF, atrial tachycardia, AV-nodal re-entrant tachycardia, and atrial flutter can be assessed through PPG-based monitoring. Furthermore, PPG recordings may aid physicians to analyse symptom/rhythm correlations. If electrical cardioversion is performed in a patient, PPG-based monitoring can be used to assess rhythm and symptoms before and after the procedure to objectively analyse rhythm/symptoms correlations.

Screening

App-based monitoring can also be useful for screening. Systematic screening through ECG-based devices is recommended in high-risk, older patients, in whom AF is more common. In younger patients without comorbidities, PPG-based devices can be used to exclude AF. Prof. Linz added that digital literacy should be taken into account when wearable devices are considered for AF screening.

Integration in practice

"Physicians need to integrate mobile health data in their clinical workflow," stated Prof. Linz. For this purpose, companies have been investing in the identification of meaningful, actionable data, which clinicians can use for their patient management. The Telecheck-AF study collected data on heart rhythm and heart rate on-demand for a pre-specified period before patients received a teleconsultation. This way, physicians could use the collected data directly in their approach for AF management. The study showed that fewer ECGs, Holters, and face-to-face consultations were needed, without increasing the number of emergency department visitations [4].

"App-based monitoring of AF has been evolving in recent years," concluded Prof. Linz. "Importantly, patient education and engagement are key, since the patient must actively monitor its condition."

1. Svennberg E, et al. EP Europace. 2022;euac038.
2. Linz D. Remote app-based monitoring of AF. Atrial fibrillation (AF) and heart failure (HF) in the digital era, EHRA 2022, 3–5 April, Copenhagen, Denmark.
3. Van der Velden RMJ, et al. EHJ Digital Health. 2021;2(3):363–373.
4. Gawalko M, et al. Europace. 2021;23(7):1003–1015.

Other Topics

Benefits of SGLT2 inhibitors may extend beyond HF-associated outcomes

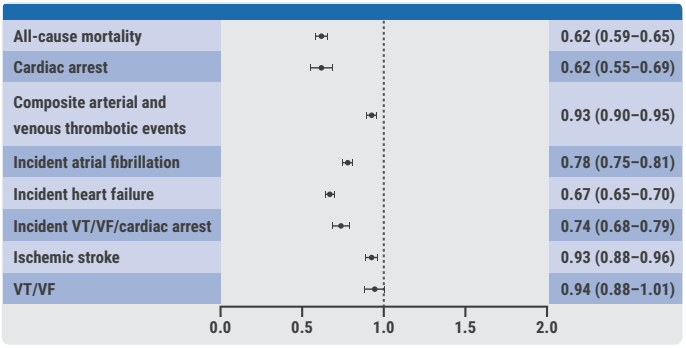
Diabetic patients demonstrated to benefit from sodium-glucose cotransporter-2 (SGLT2) inhibitors beyond the scope of heart failure (HF)-associated outcomes. The risk of HF, overall mortality, cardiac arrest, atrial fibrillation (AF), and ischaemic stroke were reduced in diabetic patients on SGLT2 inhibitors compared with diabetic patients who were not on SGLT2 inhibitors.

The use of SGLT2 inhibitors has been associated with improved outcomes in patients with prevalent HF, regardless of the diabetic status of the patient [1]. Moreover, SGLT2 inhibitors have been shown to exert their effect through various cardiometabolic and cardio-renal pathways [2]. The current study aimed to assess the impact of SGLT2 inhibitors on the risk of HF and cardiovascular events in patients with diabetes [3]. Data from the TriNetX database was used to compare 115,749 patients with diabetes who were treated with SGLT2 inhibitors with 11,749 matched participants who were not treated with SGLT2 inhibitors. The primary outcome was the rate of HF incident. Dr Ameenathul Fawzy (Liverpool Heart and Chest Hospital, UK) presented the results.

After 2 years of follow-up, the rate of HF was significantly lower in patients who were treated with SGLT2 inhibitors (HR 0.67; 95% CI 0.65–0.70). Most secondary outcomes displayed a significant benefit of SGLT2 inhibitors: all-cause mortality (HR 0.62), cardiac arrest (HR 0.62), composite arterial and venous thrombotic events (HR 0.93), AF (HR 0.78), ventricular tachycardia/ventricular fibrillation/cardiac arrest (HR 0.74), and ischaemic stroke (HR 0.93). The number of ventricular tachycardia/ventricular fibrillation events was the only secondary outcome that did not significantly favour patients who were treated with SGLT2 inhibitors over those who were not (HR 0.94; 95% CI 0.88–1.01; see Figure).

"These outcomes show that the benefits of SGLT2 inhibitors appear to extend beyond HF-associated outcomes," argued Dr Fawzy. "Although we observed that SGLT2 inhibitors mediate their effects through multiple pathways, further research is required to evaluate the effects of these agents on specific patient populations, such as post-MI patients."

Figure: Incident HF and other outcomes in diabetic patients with or without SGLT2 inhibitors [3]



VT, ventricular tachycardia; VF, ventricular fibrillation.

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Updates on anti-arrhythmic agents

The INSTANT study showed that oral inhalation of flecainide restored sinus rhythm in patients with recent-onset atrial fibrillation. In the NODE-301 trial, etripamil nasal spray showed to significantly improve paroxysmal supraventricular tachycardia-related symptoms. Small-conductance calcium-activated potassium channel inhibitors showed to delay the cardiac action potential and seem to be atrial selective. Sulcardine reduced the J-Tp interval, a feature only seen for this agent. The GENETIC-AF trial showed a preventive effect of bucindolol on new-onset atrial fibrillation (AF), and, finally, botulinum toxin A delayed postoperative AF after injection.

Prof. John Camm (St George's University of London, UK) discussed the latest evidence concerning the development of novel anti-arrhythmic drugs (AAD) and corresponding administration methods [1].

Inhaled flecainide for AF is currently being tested in the phase 2 INSTANT study (NCT03539302) [2]. Although preliminary results showed only approximately 50% AF conversion in 90 minutes for patients with the highest plasma concentration, a large variation in inhaled drugs between participants was observed. Adding saccharin to the inhaled product appeared to be more successful and may increase the success rate of inhaled flecainide.

Another agent with an alternative administration method is etripamil currently undergoing testing in the NODE-301 trial (NCT03464019). This is a novel, short-acting, calcium channel antagonist, which has demonstrated to reach a maximum plasma concentration in 5 minutes through intranasal administration and showed corresponding PR interval prolongation. An analysis of the NODE-301 results showed that after 30 minutes, 54% of the patients on etripamil achieved conversion compared with 35% of the patients on placebo (HR 1.87; P<0.02) [3].

Small-conductance calcium-activated potassium channels are an interesting group of novel agents as well. These agents were able to delay cardiac action potentials up to 75 ms at top dosage. They appear to be highly atrial selective, since animal studies have shown that the atrial effective refractory period is significantly prolonged with this agent, whereas QT intervals are not prolonged [4]. Clinical studies need to be conducted to assess these agents in human participants.

The next discussed agent was sulcardine, a multiple ion-channel inhibitor. It acts on late-sodium and late-calcium channels, thereby inducing a reduction of J-Tp, the interval between the QRS complex and the peak of the T-wave. This feature has not been observed in other agents. Moreover, almost all intervals were significantly prolonged on the top dosage. Two phase 1 trials have been completed successfully, and a phase 2 trial (NCT01235156) assessing this agent is underway [5,6].

A preventive effect of bucindolol on new-onset AF has been observed in the GENETIC-AF trial [7,8]. This effect was largely confined to the genotype of the β1 adrenergic receptor with 389 Arginine/arginine homozygous genotype. The effect was not observed in the corresponding heterozygous genotype. Furthermore, bucindolol was significantly favoured over metoprolol regarding AF burden in patients with the aforementioned homozygous genotype.

Finally, the Task1 inhibitor doxapram is currently being investigated for AF in the DOCTOS trial (EudraCT 2018-002979-17), and botulinum toxin A is being assessed in the large phase 2 NOVA trial (NCT03779841) for the prevention of postoperative AF. This agent has demonstrated to delay postoperative AF after injection in a previous phase 2 study [9].

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