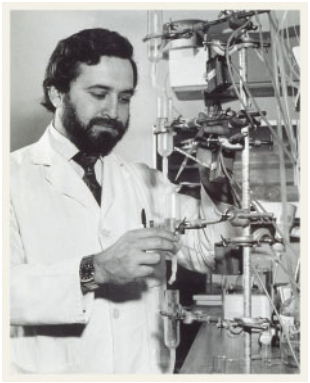

by endothelial cells and its enzymatic origin. 'Soon, with the discovery of several isoforms of NO synthases, NO escaped from the intercellular space between endothelial and vascular smooth muscle cells and, from memory to erection, became a major player throughout the body as a freely diffusible, short-lasting neurohumoral signal'.

Professor Vanhoutte from the Department of Pharmacology and Pharmacy, Li Ka Shing Faculty of Medicine, The University of Hong Kong, said the incredible explosion of knowledge that followed had peaked at the time that the Nobel prize was awarded in 1998. He pointed out that from the cardiovascular point of view, it was then already established that the endothelial release of NO plays a key role in moment-to-moment changes in local vasomotor tone in response to changes in shear stress and presence of certain neurohumoral mediators (e.g. catecholamines, serotonin, vasopressin).

'It also was obvious', he continued, 'that absence of sufficient NO-release by endothelial cells is setting the stage for the occurrence of the inflammatory response leading to atherosclerosis, and, hence, so-called 'endothelial dysfunction' became a biomarker of diseases such as hypertension and diabetes, and a precursor of coronary artery occlusions, to name but a few.

'Thus, the Nobel prize in 1998 was one of recognition, but no longer one of illumination. It rightfully acknowledged the initial contribution of three distinguished contributors to a field that kept on growing. As always in modern biological research, thanks to the dedication of many others, some of whom (including ourselves) today still try to unravel the details of the ways by which endothelial cells exert their overall important protective role against cardiovascular diseases and their complications, as well as to define the ways this protection can be optimized'.

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# What was hot at the EHRA2019 Congress

With more than 5500 participants attending the EHRA2019 Congress held from 17 to 19 March in Lisbon, the turnout exceeded our expectations. We were also fortunate to receive a record number of abstracts (>1600) and late-breaking trial submissions (>40). Many sessions had standing room only (see *Figure 1*) and it was great to feel the general buzz and energy which prevailed during the 3 days of the meeting. Innovations were the theme of the congress, which was also reflected in our programme.

The innovation award went to Dr Francesco Robotti (Zurich, Switzerland). Based on the observation that body reaction may cause complications after implantation of medical implants, his group has developed a protective hydrogel membrane, comprising micro-engineered biosynthesized cellulose called Hylomate. The membrane can be deployed at the interface between implantable electronic devices and the surrounding tissue. The protective effect is based on the combination of the physic-chemical properties of biosynthesized cellulose and the unique micro-engineered surface, together minimizing fibrotic tissue deposition. The technology was validated in a large animal model by histopathological analysis 12 months after implantation of coated and non-coated devices. When compared with standard of care procedures of pacemaker implantation, Hylomate dramatically reduces fibrotic tissue formation showing no sign of chemical or mechanical degradation.

The Basic Science Young Investigator Award (YIA) went to Felix Wiedman (Heidelberg, Germany) who presented a study to establish a selective atrial fibrillation (AF) therapy by targeting TASK-1 channels. The TASK-1 ($hK_{2P}3.1$) two-pore-domain potassium channel displays atrial specific expression in the human heart. TASK-1 currents were recently shown to regulate atrial action potential duration. Furthermore, up-regulation of atrial TASK-1 currents was described in patients suffering from AF. Therefore, these channels may represent a promising new drug target for atrial specific AF therapy. Dr Wiedman from Constanze Schmidt's laboratory could show that specific pharmacological inhibition of the TASK-1 channel can be used for acute cardioversion of paroxysmal AF as well as rhythm control of persistent AF in a new porcine model of AF. A first clinical study, translating the concept of atrial-specific TASK-1 inhibition into clinics, was started in January 2019 at the Heidelberg University Hospital.

The Clinical Cardiology YIA honoured Claire Glashan (Leiden, Netherlands), who could validate *in vivo* intracardiac electrogram recordings from infarcted myocardium by *ex vivo* whole heart histology. Different catheters with various electrode spacing and sizes are currently used with the aim to identify the complex three-dimensional substrate for ventricular tachycardias. The capability to identify layers of viable myocardium by simultaneous recordings from multiple size electrodes has not been validated. Claire Glashan from the group of Katja Zeppenfeld could integrate *in vivo* three-dimensional mapping data with the whole heart histology with high accuracy. Nine swine with early-reperfusion myocardial infarction were mapped using a catheter incorporating three micro-electrodes at the tip of the standard 3.5-mm electrode (Qdot, Biosense-Webster). She could demonstrate that all recordings are affected by changes in viable myocardium occurring throughout the myocardial wall suggesting a larger field-of-view of (micro) electrodes than hypothesized. The simultaneous use of the micro-electrodes allowed for the identification of small near-field components and for the identification of multiple viable layers. These findings are of particular interest for mapping in patients with early-reperfusion infarctions.

The best e-cardiology abstract was presented by Erik Willemen (Maastricht, Netherlands) from the group of Joost Lumens. He combined canine experimental data with computer simulations of whole heart function to investigate the effect of afterload on left and right ventricular response to pacing delay optimization. Interestingly, the animal experiments revealed that both ventricles respond opposingly to variations in interventricular pacing delay. Most notably, left ventricular (LV) pre-excitation increased LV contractility ($dP/dt$max), while it decreased right ventricular (RV) contractility at low LV afterload (i.e. MAP 55 mmHg). Computer simulations of whole heart mechanics and haemodynamics (www.circadapt.org) were performed using invasively measured electrical mapping data as input. The model reproduced the opposing effects of pacing delay optimization on LV and RV response, showing its validity as an *in silico* platform for future (pre-)clinical research in pacing therapy. Simulations extended the experimental findings by demonstrating that changes of LV afterload mostly affect RV rather than LV response, raising the question of whether afterload should be accounted for during pacing delay optimization.

We also introduced for the first time, championships where participants could compete in interpreting ECGs, device electrograms and electrophysiology tracings. Another novelty was giving the stage to patients, who presented their testimonials regarding their perceptions of device and ablation therapy.

Honorary lectures were given by Dr Francis Marchlinski (Philadelphia, USA) on ventricular tachycardia ablation, followed by the Einthoven lectures by Dr Marc Zimmermann (Geneva, Switzerland) and Carsten Israel (Bielefeld, Germany) on electrophysiology and pacing in a humanitarian context.

Here are a few picks from the late-breaking science sessions:

- The RACE7-ACWAS study, presented by Dr Harry Crijns (Maastricht, Netherlands) and published simultaneously in the New England Journal of Medicine. A total of 427 patients with recent-onset (<36 h) AF presenting to the emergency room, were randomized to early cardioversion or a 'wait and see' approach with rate-control medication and delayed cardioversion, if AF did not resolve within 48 h. The primary endpoint was the presence of sinus rhythm at 4 weeks and was non-inferior at 94% in the 'wait and see' group (in whom 69% had cardioverted spontaneously) compared to 91% with early cardioversion.

- The CIRCA-DOSE study presented by Dr Jason Andrade (Vancouver, Canada) randomized 346 patients with paroxysmal AF to contact-force-guided radiofrequency ablation vs. cryoablation with 2 × 4 min freezes vs. 2 × 2 min freezes and found no difference in arrhythmia recurrence documented by an implantable loop recorder (and an impressive reduction in median AF burden of around 99% compared to baseline). This study confirms findings of the FIRE and ICE trial, using more recent tools.
- The AVATAR-AF study presented by Dr Prapa Kanagaratnam (London, UK) randomized 321 patients with paroxysmal AF to antiarrhythmics, conventional cryoablation or a protocol with 2 × 3 min freezes (guided by testing of vein occlusion) without pulmonary vein mapping and with same-day discharge. The primary endpoint was time to hospital episodes (including out-patient consultation) related to treatment for atrial arrhythmias. At 1 year from the first intervention, significantly fewer patients had reached the primary endpoint in the AVATAR protocol arm compared to drug therapy [21% vs. 76%, $P < 0.0001$, hazard ratio (HR) 0.156; 95% confidence interval (CI) 0.097–0.250, $P < 0.0001$]. There was

no significant difference between the AVATAR protocol arm and the conventional cryoballoon ablation arm (21% vs. 18%, $P = 0.6$). The study is quite provocative as it dispenses with the need to prove electrical isolation of the pulmonary veins, and also uses a clinical endpoint which relates to healthcare use rather than arrhythmia recurrence *per se*.

- The RAISE CRT trial presented by Michael Glikson (Jerusalem, Israel) randomized 172 patients with ischemic heart disease and a standard indication for cardiac resynchronization therapy (CRT)-D to image-guided (speckle-tracking radial strain echocardiography) left ventricular lead placement vs. usual practice. The primary endpoint was the reduction in left ventricular end-systolic volume, which was similar in both groups as was clinical outcome. This negative study highlights the need to find new strategies to improve response rate with CRT.
- The Electro-CRT trial presented by Dr Charlotte Stephansen (Aarhus, Denmark) randomized 122 patients undergoing CRT implantation to an imaging-guided strategy (targeting latest mechanically activated non-scarred myocardial segment defined by speckle tracking, cardiac computed tomography venography, and positron emission tomography) vs. an electrically guided strategy towards latest activated segment combined with post-implant interventricular pacing delay optimization to achieve narrowest QRS complex. At 6 months' follow-up, the primary endpoint, absolute increase in left ventricular ejection fraction, was greater in the electrical group compared to the imaging group (11 ± 10% vs. 7 ± 11%, $P = 0.03$). This study provides a relatively simple strategy at implantation for improving response to CRT.

'Meet the trialists' sessions were organized for the WRAP-IT trial, published during the congress in the *New England Journal of Medicine*, and discussed by Dr Bruce Wilkoff (Cleveland, USA). This trial randomized 6983 patients undergoing relatively high-risk device intervention (pocket revision, generator replacement, system upgrade, or an implantation of a CRT-D) to receive or not a resorbable antibacterial envelope. The primary endpoint was infection requiring intervention or long-term antibiotic therapy, or death at 12 months and was reduced from 1.2% in the control arm to 0.7% in the envelope group (HR 0.60; 95% CI 0.36–0.98; $P = 0.04$). Therefore, the trial advocates the use of the envelope in selected patients to reduce rates of infection.

Another important trial was the Apple Heart study, presented by Dr Andrea Russo (Moorestown, USA). The study enrolled >400 000 subjects not known for AF, who owned an Apple watch and self-enrolled on the study website to receive an App for detecting AF using photoplethysmography signals recorded by the smartwatch. Subjects who were notified for the presence of arrhythmia were then sent an ECG patch which confirmed the diagnosis in 0.5% of the participants. The positive predictive value of the App was 84%, indicating high specificity. This is a landmark trial which paves the way for future research to better understand the clinical implications of this screening strategy.


Webcasts and slides of the EHRA2019 congress can be found for free on the ESC365 website (https://esc365.escardio.org). Of course, attending a congress offers so much more, and we look forward to welcoming you in Vienna at EHRA2020, to be held on the 29–31 March 2020, where the theme will be 'Joining forces to overcome arrhythmias'. Mark your calendars!


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