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Managing arrhythmias: diagnosis and modern treatment

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Arrhythmias are one of the most common symptoms of heart disease and are associated with considerable morbidity such as stroke,[1] and mortality.[2] Fortunately, with the introduction of ablation techniques and device therapy,[3] their management has considerably improved over the last two decades and again more recently. Thus, the '**The year in cardiology 2015: arrhythmias and device therapy**' by Gerhard Hindricks from the University of Leipzig in Germany[4] is a timely review of the most important and clinically relevant recent developments in arrhythmias and invasive electrophysiology, and new devices in particular.

Ventricular tachycardias are the most feared arrhythmias. Hugh Calkins from the John Hopkins Hospital in Baltimore, USA discusses in more depth '**The role of catheter ablation in the management of ventricular tachycardia**'.[5] As he points out, the treatment strategy for ventricular tachycardia must be guided by patient symptoms, the risk of sudden death, and the underlying cardiac structure. Over the last decades, catheter ablation has emerged as the primary treatment of idiopathic ventricular tachycardia and has become an important management strategy in reducing ventricular tachycardia burden in patients with structural heart disease and an implanted device.[6]

The most common arrhythmia is probably atrial fibrillation (AF), which increases in frequency with age[7] and particularly in those with hypertension[8] and/or heart failure.[9] Here too, catheter ablation has become a valuable treatment option.[10,11] However, a significant number of patients have recurrences after catheter ablation,[12] which could be due to irritability in the left atrium caused by the ablation procedure. In the FAST TRACK entitled '**Efficacy of Antiarrhythmic drugs Short-Term use after catheter ablation for Atrial Fibrillation (EAST-AF) trial**',[13] Satoshi Shizuta and colleagues from the Kyoto University Graduate School of Medicine in Japan sought to evaluate whether 90 days use of an antiarrhythmic drug following AF ablation could reduce the incidence of early recurrence and thereby promote reverse remodelling of the left atrium, leading to improved long-term clinical outcomes. In the largest trial so far, a total of 2038 patients who had undergone radiofrequency catheter ablation for paroxysmal, persistent, or long-lasting AF were randomized to either 90 days use of Vaughan Williams class I or III antiarrhythmic drugs or not. The primary endpoint was recurrent atrial tachyarrhythmias lasting for >30 s or those requiring repeat ablation, hospital admission, or usage of a class I or III antiarrhythmic drug at 1 year. At 90 days, patients on antiarrhythmic drugs had significantly less recurrent atrial tachyarrhythmias compared with controls, with a hazard ratio of 0.84, but not at 1 year. The authors conclude that short-term use of an antiarrhythmic drug for 90 days following ablation of AF reduced recurrent atrial tachyarrhythmias during the treatment period, but it did not improve clinical outcomes later on. The manuscript is accompanied by an **Editorial** by Luis R. Scott from the Mayo Clinic in Arizona, USA.[14]

Congenital heart defects affect ~1% of newborn children.[15] Today, most of them undergo corrective or palliative surgery and can survive into adulthood,[16] also thanks to improved long-term care.[17] However, they are prone to arrhythmias and sudden death. The fear of sudden death has led to restrictions of physical activity and competitive sports. In their paper, '**Sudden unexpected death in children with congenital heart defects**', Jarle Jortveit and colleagues from the Sørlandet Hospital Arendal in Norway[18] investigated whether the rate of sudden deaths in children with congenital heart defects was related to cardiac disease, co-morbidities, and/or physical activity. To that end, they analysed data of 943 871 live births in Norway from 1994 to 2009. Among 11 272 children with congenital heart defects, they identified 19 or 0.2% who experienced sudden deaths. A cardiac cause of death was identified in seven of these cases. None of the children died during physical activity, but two survived cardiac arrest during sports. The authors conclude that sudden death is infrequent in children with congenital heart defects who survived beyond 2 years of age. Co-morbidity was common among children who died; physical activity is rarely associated with sudden death, challenging certain recommendations for such patients. The manuscript is accompanied by a thought-provoking **Editorial** by Gerhard-Paul Diller from the University Hopital Münster in Germany.[19]

The ECG remains the most important tool in the diagnosis of arrhythmias. Until recently, the inferolateral early repolarization syndrome possibly included patients with Brugada-like ECG recorded only in the high intercostal spaces.[20,21] In their paper entitled '**Significance of electrocardiogram recording in high intercostal spaces in patients with early repolarization syndrome**',[22] Shiro Kamakura and colleagues from the National Cerebral and Cardiovascular Center investigated ECG recordings

in the second to fourth intercostal spaces in 56 patients with early repolarization syndrome and spontaneous ventricular fibrillation not linked to structural heart disease. They underwent drug provocation by sodium channel blockade. Eighteen patients with type 1 Brugada-like ECG were excluded. Thirty-eight patients were classified into four groups: (A) those with early repolarization and type 1 Brugada-like ECG only in high intercostal spaces; (B) those with early repolarization syndrome with non-type 1 Brugada-like ECG only in in high intercostal spaces; (C) those with early repolarization syndrome with non-type 1 Brugada-like ECG in the standard ECG; and (D) those with early repolarization syndrome only, spontaneously or after drug testing. During almost 10 years of follow-up, the rate of ventricular fibrillation including electrical storm was significantly higher in groups A (67%), B (80%), and C (50%) than in group D (11%). Thus, in about a third of patients with early repolarization syndrome who showed a Brugada-like ECG in the high intercostal spaces, ventricular fibrillation recurred, specifically in those with Brugada-like ECG in any pre-cordial lead including high intercostal spaces. Such patients comprised about half of the entire early repolarization cohort. The manuscript is accompanied by an interesting **Editorial** by Josep Brugada from the Hospital Clinic of Barcelona in Spain.[23]

An important risk factor of ventricular arrhythmias is a long[24] or short QT-interval[25] in the ECG. In their basic science paper entitled '**Oestradiol regulates human QT-interval: acceleration of cardiac repolarization by enhanced KCNH2 membrane trafficking**', Lars Anneken from the Universitätsklinikum Erlangen in Germany assessed the relationship between QTc duration and gonadal hormones as well as the underlying mechanisms.[26] They measured hormone levels and QTc intervals in women during clomiphene stimulation for infertility and those before, during, and after pregnancy. Three heterozygous LQT-2 patients with the KCNH2-p.Arg752Pro missense mutation and unaffected family members were studied during their menstrual cycles. High oestradiol levels, but neither progesterone nor the oestradiol/progesterone ratio, inversely correlated with QTc. Consistent with clinical data, *in vitro* oestradiol stimulation enhanced IKCNH2 via oestradiol receptor-α-dependent promotion of KCNH2 channel trafficking. Of note, the heat shock protein 90 inhibitor geldanamycin abolished the oestradiol-induced increase in IKCNH2 currents, but had no effect on KCNH2 transcription, translation, or the expression of oestradiol receptors and chaperones. Oestradiol enhanced the physical interaction of KCNH2 channel subunits with heat shock proteins and augmented ion channel trafficking to the membrane. The authors conclude that elevated oestradiol levels were associated with shorter QTc intervals in healthy women and female LQT-2 patients. Oestradiol acts on KCNH2 channels via enhanced oestradiol receptor-α-mediated heat shock protein 90 interaction, augments membrane trafficking, and thereby increases repolarizing current. These results provide mechanistic insights into hormonal control of human ventricular repolarization and open up novel therapeutic avenues, as critically discussed in an **Editorial** by Katja E. Odening from the Heart Center University of Freiburg, Germany.[27]

The editors hope that this issue of the *European Heart Journal* will be of interest to its readers.

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