Arrhythmias, syncopy, and sudden death

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Sudden death is a devastating event for the patient and their family, particularly in children and young adults, as well as the working population.1–4 In spite of all progress in prevention and risk stratification,5 this remains an important health issue. The most important causes are coronary artery disease,6 cardiomyopathies,7 and channolopathies,8,9 as well as lifestyle, in particular ‘recreational’ drug use.10 Together with its US partner societies, the European Society of Cardiology has provided guidelines on ventricular arrhythmias and sudden death,11 as well as on the management of syncope,12 which should help practising cardiologists to deal with these problems.

Nevertheless, there are rare conditions such as arrhythmogenic right ventricular dysplasia or cardiomyopathy (ARVD/C) where we need more evidence for proper management. In this issue, Richard Hauer from the Heart Lung Center Utrecht in The Netherlands reports in a first paper entitled ‘Impact of genotype on clinical course in arrhythmogenic right ventricular dysplasia/ cardiomyopathy-associated mutation carriers’ the effects of the genotype on the clinical course and arrhythmic outcome among 577 patients from 241 families with ARVD/C-associated mutation carriers.13 The authors found that patients with sudden cardiac death or ventricular fibrillation at presentation were younger than those presenting with sustained monomorphic ventricular tachycardia. Over 6 years of follow-up, amongst 541 subjects presenting alive, 2% died, 30% had sustained ventricular tachycardia or fibrillation, 14% had an ejection fraction of <55%, 5% experienced heart failure, and 2% required cardiac transplantation. Of note, 4% of the patients with more than one mutation had earlier occurrence of sustained ventricular tachycardia or fibrillation, lower arrhythmia-free survival, more commonly a reduced ejection fraction or heart failure, and more often underwent cardiac transplantation. DSP mutation carriers experienced a more then four-fold higher occurrence of left ventricular dysfunction and heart failure compared with PKP2 carriers. Missense mutation carriers had similar death or transplant-free survival and ventricular tachycardia or fibrillation compared with those with truncating or splice site mutations. Men were more likely to be symptomatic and had earlier and more severe arrhythmias. The authors conclude that a presentation with sudden cardiac death or ventricular fibrillation occurs at a significantly younger age as compared with sustained monomorphic ventricular tachycardia. Importantly, the genotype of the ARVD/C mutation carriers impacts on the clinical course and disease expression, and male sex negatively modifies the phenotypic expression of the disease.

The second paper ‘The TMEM43 Newfoundland mutation p.S358L causing ARVC-5 was imported from Europe and increases the stiffness of the cell nucleus’ by Hendrik Milting from the Herz- und Diabeteszentrum NRW Universitätsklinik of the Ruhr-University in Bochum complements the first paper of this issue nicely and provides additional information on the genetics of ARVC.14 The authors noted that the mutation causing ARVC-5 was recently identified on the island of Newfoundland and is caused by the fully penetrant missense mutation p.S358L in TMEM43. Although TMEM43-p.S358L mutations carriers were found in Germany and Denmark, their genetic relationship to the Canadian and European patients and the disease mechanism of this mutation remained to be clarified. Their German family shared a common haplotype with those from Newfoundland, the USA, and Denmark, providing evidence that the mutation appears to have a founder. Skin fibroblasts from a female mutation carrier were then analysed in cell culture by atomic force microscopy and it was revealed that the cell nuclei provide an increased stiffness compared with TMEM43 wild-type controls. The authors conclude that they identified a German family not affected by a spontaneous TMEM43 mutation. It therefore has to be expected that an unknown number of European families are affected by the TMEM43-p.S358L mutation. They recommend that due to its deleterious clinical phenotype, this mutation should be checked in any case of ARVC-related genotyping. It appears that the reduced elasticity of the cell nucleus might be related to the massive loss of cardiomyocytes, which is typically found in ventricles of ARVC hearts.

Atrioventricular (AV) block is an important cause of syncope and commonly treated with the implantation of a device for right ventricular pacing.15 In the third manuscript, ‘Effect of right ventricular pacing lead site on left ventricular function in patients with high-grade atrioventricular block: results of the Protect-Pace study’ Gerald Kaye and colleagues from Princess Alexandra Hospital in Brisbane Australia focus on the effects of pacemaker therapy on left ventricular function.15 It is known primarily from registry data that right ventricular pacing may lead to a deterioration in left ventricular function and cause heart failure in some patients,16–18 while upgrading to biventricular pacing may improve function and symptoms.19 As not all patients are suitable for biventricular pacing (indeed, it may negatively affect outcome in those without left bundle branch block20), novel right ventricular pacing sites have been looked for. The aim of this randomized, prospective, multicentre trial was therefore to compare the change in left
ventricular ejection fraction between the right ventricular apical and high septal pacing over 2 years in 240 patients with high-grade AV block requiring >90% ventricular pacing and with preserved baseline left ventricular function. Patients received either right ventricular apical or high septal pacing. At 2 years, left ventricular ejection fraction slightly decreased both in those receiving apical (from 57% to 55%) and in those receiving high septal pacing (from 56% to 54%). However, there was no difference in intrapatient change in ejection fraction between the two lead positions. Also, there were no differences in heart failure hospitalizations, mortality, or the burden of atrial fibrillation or plasma brain natriuretic peptide (BNP) levels between the two groups. Of note, the procedure time to place the lead into the high septal position increased from 56 to 70 min, and fluoroscopy time increased from 5 to 11 min. The authors conclude that in patients with high-grade AV block and preserved left ventricular function requiring a high percentage of ventricular pacing, high septal right ventricular pacing does not provide a protective effect on left ventricular function over apical pacing in the first 2 years.

Although cardiopulmonary resuscitation was proposed by James Elam as early as 1954 based on experimental studies and introduced into clinical medicine by Peter Safar a few years later,21 many patients with sudden cardiac death die on site or after referral to the hospital in spite of all measures. In the fourth paper, ‘Improved outcome in Sweden after out-of-hospital cardiac arrest and possible association with improvements in every link in the chain of survival’, Anneli Strömös and colleagues from the School of Health and Social Sciences in Sweden analysed the outcome of 59 926 out-of-hospital cardiac arrests in Sweden over an observation period of 19 years recorded in the Swedish Cardiac Arrest Registry.22

From 1992 to 2011, the number of cases reported increased from 27 to 52/100 000 person-years. Crew-witnessed cases, cardiopulmonary resuscitation prior to the arrival of the emergency medical service, and their response time increased. On the other hand, the time delays from collapse to calling for the emergency medical service decreased, as did the time from collapse to defibrillation among patients found in ventricular fibrillation. However, the proportion of patients found in ventricular fibrillation decreased from 35% to 25%. On the other hand, 30-day survival increased from 4.8% to 10.7%, particularly among patients found in a shockable rhythm and in those with return of spontaneous circulation at hospital admission. Among patients hospitalized with return of spontaneous circulation, 41% underwent therapeutic hypothermia and 28% percutaneous coronary intervention. Among 30-day survivors, 94% had a cerebral performance category score of 1 or 2 at discharge from hospital, and the results were even better if patients were found in a shockable rhythm. The authors conclude that over the last decades, 30-day survival after out-of-hospital cardiac arrest in Sweden more than doubled. The increase in survival was most marked among patients found in a shockable rhythm and those hospitalized with return of spontaneous circulation. There were improvements in all four links in the chain of survival, which might explain the improved outcome. These are very encouraging data suggesting that improvements in recognition of out-of-hospital cardiac arrests in the general population, rapid availability of defibrillators, as well as improved logistics of the emergency medical service can have an important impact for this patient population at greatest risk.

Finally, this issue also contains a Clinical Review complementing the first two articles, entitled ‘The research venture in arrhythmogenic right ventricular cardiomyopathy: a paradigm of translational medicine’ by Gaetano Thiene from the University of Padua Medical School in Italy.23

The editors hope that this issue of the European Heart Journal will be received with interest by its readers.

References


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