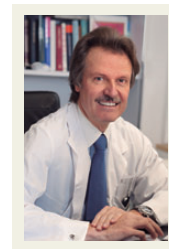**ISSUE @ A GLANCE**

Mitral valve disease, atrial fibrillation, and device therapy

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Transcatheter mitral interventions have been developed to address an unmet need, and as alternatives to surgery in patients at high risk or considered inoperable.[1,2] Beyond MitraClip therapy, alternative repair technologies are being developed to expand the armamentarium of transcatheter intervention. Recently, the feasibility of transcatheter mitral valve implantation in native non-calcified valves was reported in patients at very high operative risk. These issues are critically discussed in a timely *Clinical Review* article entitled '**The future of transcatheter mitral valve interventions: competitive or complementary role of repair vs replacement?**' by Francesco Maisano from the University Hospital Zurich in Switzerland.[3] The authors review the current state-of-the-art of mitral valve intervention, and identify potential future scenarios that might benefit most from the transcatheter repair and replacement devices under development. He also acknowledges the small body of scientific evidence[4,5] on hard outcomes during long-term follow-up of these novel procedures.

Atrial tachyarrhythmias are often associated with mitral valve disease, but are also frequent in elderly patients without it. As both arrhythmias are associated with a risk of stroke, anticoagulation is considered mandatory in those with a high CHA_2DS_2VASC score.[6,7] In the first research paper entitled '**Randomized trial of atrial arrhythmia monitoring to guide anticoagulation in patients with implanted defibrillator and cardiac resynchronization devices**', Jonathan L. Halperin from Mount Sinai School of Medicine in New York[8] hypothesized that the introduction and termination of anticoagulation based upon arrhythmia monitoring would reduce both stroke and bleeding.

To that end, they randomized 2718 patients with dual-chamber and biventricular defibrillators to start and stop anticoagulation based on remote rhythm monitoring vs. usual office-based follow-up with anticoagulation. The primary composite endpoint was stroke, embolism, and major bleeding. The trial was stopped after 2 years for futility. About one-third of the patients (34.8%) developed atrial tachycardia, 264 meeting study anticoagulation criteria. Adjudicated atrial electrograms confirmed atrial fibrillation in 91%. Primary events did not differ between groups, with a hazard ratio of 1.06. Major bleeding had a hazard ratio of 1.39. In patients with atrial tachyarrhythmias, similar thrombo-embolism rates of 1.0 and 1.6 per 100 patient-years, respectively, were noted. Although atrial tachyarrhythmia burden was associated with thrombo-embolism, there was no temporal relationship between arrythmias and stroke. The authors conclude that in patients with implanted defibrillators, the strategy of early initiation and interruption of anticoagulation based on remotely detected atrial tachyarrhythmias did not prevent thrombo-embolism or bleeding. Jeffrey S. Healey from McMaster University in Hamilton, Canada discusses this conclusion critically in an **Editorial**.[9]

Coronary artery disease is an important cause of sudden death.[10] In addition, genetic diseases of the conduction system are known triggers of fatal arrhythmias.[11–13] Furthermore, genome-wide association studies have identified variants associated with coronary disease. In the second clinical research paper '**Predicting sudden cardiac death using common genetic risk variants for coronary artery disease**', Jussi Aleksi Hernesniemi et al. from the North Karelia Central Hospital in Joensuu, Finland studied the association between these variants and sudden cardiac death.[14] The authors developed a weighted genetic risk score from variants most strongly associated with coronary artery disease identified by the CARDIoGRAMplusC4D Consortium, explaining 11% of the heritability of coronary disease. The association between genetic risk score for coronary disease and the occurrence of sudden death was studied in three independent autopsy series of consecutive cases combining altogether 1035 autopsies with 306 sudden deaths due to coronary artery disease. The results were replicated in a prospective study of 2321 patients. In a meta-analysis of the autopsy series, the genetic risk score for coronary disease associated significantly with the risk of sudden death due to coronary disease even after adjusting for age, body mass index, and sex, with an odds ratio of 1.042 for one allele increase in the genetic risk score for coronary disease. The genetic risk score for coronary disease also predicted the risk of sudden death due to coronary disease in a prospective study, with a hazard ratio of 1.049. In the meta-analysis of all cohorts, the association was highly significant, with an odds ratio of 1.045. The authors conclude that genetic risk estimates for coronary disease may also be used to predict sudden cardiac death. An **Editorial** by Birgit Stallmeyer from the Institute for Genetics of Heart Disease in Münster, Germany puts these findings into context.[15]

Sudden cardiac death is particularly common in patients with left ventricular dysfunction.[16] In such patients, implantable cardioverter

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defibrillators (ICDs) prolong life and are hence recommended by current guidelines.[17] As a result, ICDs are increasingly implanted for primary prevention and therefore into lower risk patients.

In the third research manuscript entitled '**The effect of duration of follow-up and presence of competing risk on lifespan gain from implantable cardioverter defibrillator therapy: who benefits the most?**', Claire E. Raphael and colleagues from the Imperial College in London[18] noted that estimates of potential lifespan gain are missing. Using data from landmark ICD trials, the authors plotted lifespan gain against baseline annual mortality. Lifespan gain was then extrapolated to a time horizon of >20 years, while adjusting for increasing 'competing' risk from ageing and non-sudden cardiac death, i.e. due to pump failure. At 3 years, directly observed lifespan gain was strongly dependent on baseline event rate. However, projecting beyond the duration of the trial, lifespan gain increased rapidly and non-linearly with time. At 3 years, it averaged 1.7 months, but by 10 years it increased up to nine-fold. Of note, lifespan gain over time horizons of >20 years were greatest in lower risk patients, while competing risks reduced lifespan gain from ICD implantation. The authors conclude that while high-risk patients may show the greatest short-term gain, the dramatic growth of lifespan gain over time suggests that lower risk patients who received an ICD for primary prevention gain most life years. The benefit is underestimated when only trial data are assessed, as trials can only maintain randomization over limited periods of time. Lifespan gain may be further increased through advances in ICD device programming. The implications of this study are explored in a comprehensive Editorial by Kalyanam Shivkumar from the David Geffen School of Medicine at University of California Los Angeles.[19]

In the final paper '**Current worldwide nuclear cardiology practices and radiation exposure: results from the 65 country IAEA Nuclear Cardiology Protocols cross-sectional study (INCAPS)**', Andrew Einstein et al. from the Columbia University College of Physicians and Surgeons in New York aimed to characterize patient radiation doses from nuclear myocardial perfusion imaging.[19] They conducted an observational cross-sectional study of protocols used in 7911 myocardial perfusion studies performed in 308 nuclear cardiology laboratories in 65 countries for a single week. An expert committee identified a priori eight 'best practices' relating to radiation exposure, and a radiation-related quality index. Patient radiation effective dose ranged between 0.8 and 36 mSv. Average laboratory effective dose ranged from 2 to 24 mSv; only 30% of the laboratories achieved the median effective dos of ≤9 mSv as recommended by guidelines. Laboratory quality indexes ranged from 2 to 8. Effective dose and quality index both differed between laboratories, countries, and world regions. The lowest effective dose of 8.0 mSv observed in Europe coincided with high best-practice adherence and a quality index of 6.2. The highest doses of 12.1 mSv and the lowest quality index of 4.9 were noted in Latin America. In hierarchical logistic regression modelling, patients undergoing myocardial perfusion imaging at laboratories following 'best practices' had lower effective dosages. Thus, for myocardial perfusion imaging, marked worldwide variations in radiation safety exist. Targeted effective dosages are achieved in only a minority of laboratories. The practical implications of these findings are discussed in a thought-provoking Editorial by Juhani Knuuti from the Turku University Hospital in Finland.[20]

The editors hope that readers of the European Heart Journal will find this issue of interest.

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