Cardiac imaging has made enormous progress over the last decades, particularly in the field of magnetic resonance imaging (MRI) and computed tomography. Implied electronic devices such as cardiac pacemakers or implantable cardioverter defibrillators (ICDs) have long been considered a contraindication for MRI examinations due to the risk of complications and even deaths. A better understanding of the underlying mechanisms responsible for such potentially life-threatening complications as well as technical advances have led to the development of devices that are MRI compatible. In a timely Clinical Review article entitled ‘Magnetic resonance imaging safety in pacemaker and implantable cardioverter defibrillator patients: how far have we come?’, Oliver Ritter from the University of Würzburg in Germany addresses this issue. Of note, with ‘MR-conditional’ devices being the new standard of care, MRI in pacemaker and ICD patients has been adopted in clinical routine today. However, specific precautions and specifications of these devices should be carefully followed, to avoid patient risks, which might appear with evolving MRI technologies.

The issue continues with a Clinical Review article on ‘Haem oxygenase signalling pathway: implications for cardiovascular disease’ by Susan Cheng from Brigham and Women’s Hospital in Boston, USA. Interestingly, haem oxygenase appears to modulate cardiovascular risk. In particular, the haem oxygenase pathway is a key endogenous regulator of oxidative, inflammatory, and cytotoxic stress, while also exhibiting vasoregulatory properties. The current review summarizes the accumulating experimental and emerging clinical data indicating how the activity of the haem oxygenase pathway and its products may play a role in mechanisms underlying the development of cardiovascular disease. As the activity of the haem oxygenase pathway is influenced not only by genetic traits and environmental stimuli, but also by pharmacological interventions, the pathway could serve as a prime target for reducing the overall cardiovascular disease burden. However, further work is needed to determine its role as possible prognostic markers and as a therapeutic target.

Secondary prevention as well as cardiac rehabilitation is an important component of the management of patients with cardiovascular disease. However, the true value and the use of the latter continue to be debated. Thus, in the research paper entitled ‘Cardiac rehabilitation and survival in a large representative community cohort of Dutch patients’, Niels Peek from the Academic Medical Center and the University of Amsterdam in the Netherlands assessed the effects of multidisciplinary cardiac rehabilitation on survival in patients with acute coronary syndromes (ACS) and patients that underwent coronary revascularization and/or heart valve surgery. The authors studied a population-based cohort covering ~3.3 million persons. The primary outcome was survival up to 4 years. Among 35,919 patients with an ACS and/or coronary revascularization or valve surgery, 30.7% received cardiac rehabilitation. After propensity score weighting, the adjusted hazard ratio associated with receiving cardiac rehabilitation was 0.65. The largest benefit was observed for patients who underwent coronary artery bypass grafting and/or valve surgery, with an adjusted hazard ratio of 0.55. The authors conclude that in a large and representative community cohort of Dutch patients with an ACS and/or intervention, cardiac rehabilitation was associated with a substantial survival benefit regardless of age, type of diagnosis, and intervention. The manuscript is accompanied by a comprehensive Editorial by Jari Antero Laukkanen from the University of Eastern Finland in Kuopio, Finland.

Besides cardiac rehabilitation, pharmacological interventions, in particular statins, are a cornerstone of cardiovascular prevention. However, the effect of statins on the risk of heart failure hospitalization and death due to this condition remains uncertain. In the second clinical research paper, ‘The effect of statin therapy on heart failure events: a collaborative meta-analysis of unpublished data from major randomized trials’, David Preiss et al. from the University of Glasgow in Scotland, UK aimed to establish whether statins reduce major heart failure events. To that end, the authors searched Medline, EMBASE, and the Cochrane Central Register of Controlled Trials for randomized controlled endpoint statin trials from 1994 to 2014. Furthermore, collaborating with trialists provided unpublished data. Primary and secondary prevention statin trials with >1000 participants followed for >1 year were included. Outcomes consisted of first non-fatal heart failure hospitalization, heart failure death, and a composite of first non-fatal heart failure hospitalization or death due to heart failure. In 132,538 subjects, statin therapy reduced LDL-cholesterol by 0.97 mmol/L. Statins reduced the numbers of patients experiencing non-fatal heart failure hospitalization by 10% and the composite heart failure outcome by 8%, but not death due to heart failure. The effect of statins on the first non-fatal heart failure hospitalization was similar regardless of whether this was preceded by a myocardial infarction or not. The authors conclude that in primary and secondary prevention trials, statins modestly reduced the risks of non-fatal heart failure hospitalization and the composite of non-fatal heart failure hospitalization and death, with no demonstrable difference in risk reduction between those with ischaemic or non-ischaemic causes. This interesting paper is accompanied by a thought-provoking Editorial.
by John Kjekshus from the Faculty Division Rikshospitalet in Oslo, Norway.

Hypertrophic cardiomyopathy remains the most common cause of sudden cardiac death in the young, with an excess of exercise-related deaths.\(^6,17\) The sarcomere mutations causing hypertrophic cardiomyopathy increase the energy cost of contraction. Impaired resting cardiac energetics has been documented by measurement of the phosphocreatine/ATP ratio (PCr/ATP) using \(^{31}\)P MR spectroscopy. In the third clinical research paper, entitled \textit{Exacerbation of cardiac energetic impairment during exercise in hypertrophic cardiomyopathy: a potential mechanism for diastolic dysfunction}, Hugh Watkins et al. from the Frederiksborg Hospital in Denmark hypothesized that cardiac energetics might be further impaired acutely during exercise in such patients, and that this would have important functional consequences.\(^8\) The authors performed \(^{31}\)P MR spectroscopy in 35 patients with hypertrophic cardiomyopathy and 20 age- and gender-matched controls at rest and during leg exercise. Peak left ventricular filling rates and myocardial perfusion reserve were calculated during adenosine stress. Resting PCr/ATP was significantly reduced in hypertrophic cardiomyopathy, with a further reduction during exercise, while this was not the case in normal subjects. There was no correlation between PCr/ATP reduction and cardiac mass, wall thickness, myocardial perfusion reserve, or late gadolinium enhancement. Peak left ventricular filling rates and PCr/ATP were significantly correlated at rest and during stress. The authors conclude that in patients with hypertrophic cardiomyopathy, during exercise the pre-existing energetic deficit is further exacerbated independently of hypertrophy, perfusion reserve, or the degree of fibrosis. This is in keeping with the change at the myofilament level.

Syncope may occur not only due to hypertrophic cardiomyopathy or arrhythmias, but also due to an over-reactivity of physiological cardiovascular reflexes.\(^9\) In the fourth clinical research paper, \textit{Assessment of a standardized algorithm for cardiac pacing in older patients affected by severe unpredictable reflex syncopes}, Michele Brignole and colleagues from the Ospedali del Tiglio in Livagno, Italy tried to resolve the controversy of the effectiveness of cardiac pacing in patients with reflex syncope. To that end, they assessed a standardized guideline-based algorithm in different forms of reflex syncope.\(^{10}\) In their prospective, multicentre, observational study, patients over 40 years of age affected by severe unpredictable and recurrent reflex syncopes underwent carotid sinus massage, followed by tilt testing if the former was negative. Further, this was followed by implantation of an implantable loop recorder if tilt table testing was negative. Those who had an asymptotic response to one of these tests received a dual-chamber pacemaker. The population comprised 253 patients with on average four syncopes, mostly without or with short prodromal symptoms. Of these patients, 47% received a pacemaker and 42% were followed for about a year. Syncope recurred in total in 9% and 15% at 2 years. The recurrence rate was similar in patients that were carotid sinus massage positive or tilt table test positive and was significantly lower than that observed in those with non-diagnostic tests. The authors conclude that about half of older patients with severe recurrent syncopes without prodromal symptoms have an asymptotic reflex for which cardiac pacing goes along with a low recurrence rate. Although randomized controlled trials would be mandatory in the future, this study is hypothesis generating and suggests that their algorithm for the selection of candidates for cardiac pacing in everyday clinical practice might be useful to reduce recurrence of syncopes in this population. The editors hope that the readers will find this issue of the \textit{European Heart Journal} of interest.

**References**


