Towards personalized prevention in special patient populations

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Personalized medicine is a vision of the future in many disciplines, including cardiology.1,2 Although genetics have had an enormous impact on science,3,4 their clinical value in cardiovascular medicine has been disappointing so far. With the exception of rare monogenic diseases,5,6 some of which are discussed in this issue,7 genetic information only marginally improves risk stratification in patients with atherosclerotic vascular disease8 or heart failure.9 Nevertheless, while waiting for progress and a better understanding of products of non-coding DNA10,11 and post-transcriptional modification of proteins,12,13 we should not forget that personalized medicine is already here today.

Beyond the known classical risk factors such as high blood pressure, LDL-cholesterol, smoking, and diabetes, many special features of individual patients may be relevant to the prevention of future events. Patients with congenital heart disease of any kind need personalized attention when they reach reproductive age, and this applies in particular to women who might become pregnant.14,15 As outlined in a Clinical Review entitled ‘Contraception and cardiovascular disease’ by Jolien W. Roos-Hesselink from Erasmus MC, Rotterdam in The Netherlands,16 contraceptive counselling should begin early in females with heart disease, preferably directly after the start of menstruation. In coming to a decision about the method of contraception, the following issues should be considered: (i) the risk of pregnancy for the mother and the consequences of an unplanned pregnancy; (ii) the risks of the contraceptive method; (iii) failure rates; (iv) the non-contraceptive benefits; (v) the availability; (vi) the individual’s preferences; (vii) protection against infection; and (viii) costs. In some women with heart disease, the issues may be complex and require the input of both a cardiologist and an obstetrician (or other foeto-maternal expert) to identify the optimal approach. No studies have been performed in women with heart disease to investigate the relative risks and benefits of different contraceptive methods.

Another special patient group requiring personalized attention are diabetics. Not only are they at increased risk of coronary artery disease and stroke,17 but they may also develop diabetic cardiomyopathy, as discussed in the Clinical Review article ‘Clinical diabetic cardiomyopathy: a two-faced disease with restrictive and dilated phenotypes’ by Walter J. Paulus from the Free University Medical Center (VUMC) in Amsterdam, The Netherlands.18 Originally described as dilated cardiomyopathy with systolic dysfunction, this currently presents mainly with a restrictive pattern and diastolic dysfunction. This review is the first to approach clinical diabetic cardiomyopathy as two distinct phenotypes with specific pathophysiological mechanisms, diagnostic algorithms, and treatment strategies.

Arrhythmogenic right ventricular cardiomyopathy (ARVC) is a rare disease which characteristic features,19,20 which also deserves a personalized approach, particularly related to lifestyle recommendations. It has been proposed that competitive sport increases the risk of ventricular tachyarrhythmias and death in such patients, although it is unknown whether this applies exclusively to competitive sport or also to recreational sporting activities. To address this, Anne-Christine Ruwald from the University of Rochester Medical Center in the USA investigated 108 individuals with ARVC. In the paper entitled ‘Association of competitive and recreational sport participation with cardiac events in patients with arrhythmogenic right ventricular cardiomyopathy: results from the North American multidisciplinary study of arrhythmogenic right ventricular cardiomyopathy’,21 study participants were questioned at the time of enrolment about their exercise habits prior to and after ARVC diagnosis, within three categories of sports participation, i.e. competitive, recreational, and inactive. Competitive sport was associated with a two-fold increased risk of ventricular tachyarrhythmia or death compared with both recreational sport and inactive patients. Interestingly, no increased risk of ventricular tachyarrhythmia or death was noted with recreational sport when compared with inactive patients. Furthermore, symptoms developed at ~30 years of age in patients who participated in competitive sport and 8 to 11 years later in patients who participated in recreational sport or were inactive, respectively.

In patients who have undergone percutaneous coronary interventions (PCIs) with stenting, the prevention of stent thrombosis is the greatest concern, particularly in certain patients, depending on the intervention and the stent type.23 Stent thrombosis is a potentially lethal complication. Platelet reactivity during treatment with P2Y12 inhibitors is known to be associated with stent thrombosis, but also with bleeding, another important prognostic factor in this patient population.24 In the second clinical research paper, ‘Bleeding and stent thrombosis on P2Y12 inhibitors: collaborative analysis...’ by Domenico Corrado from the University of Padua in Italy,22...
on the role of platelet reactivity for risk stratification after percutaneous coronary intervention. 25 Dániel Aradi and colleagues from the Heart Center in Balatonfured, Hungary sought to determine the prognostic value of low, optimal, or high platelet reactivity by applying uniform cut-off values for standardized devices that are currently available. To that end, authors of studies published before January 2015, reporting associations between platelet reactivity, stent thrombosis, and major bleeding, were contacted for a collaborative analysis using consensus-defined, uniform cut-offs for standardized platelet function assays. Seventeen studies including 20 839 patients treated mainly with clopidogrel were used for the analysis; patients with high platelet reactivity had a 2.7-fold higher risk for stent thrombosis, yet a slight (15%) reduction in bleeding compared with those with optimal platelet reactivity. In contrast, patients with low platelet reactivity had an almost 2-fold higher risk for bleeding, without any further benefit as regards stent thrombosis. As expected, mortality was significantly higher in patients with high platelet reactivity compared with other groups. The authors conclude that the assessment of platelet reactivity in patients on thienopyridine-type P2Y12 inhibitors identifies PCI-treated patients at higher risk for mortality and stent thrombosis and at elevated risk for bleeding. The paper is accompanied by a critical Editorial by Robert Storey from the University of Sheffield in the UK. 26

The fifth patient group under consideration in this issue is those with chronic obstructive pulmonary disease (COPD). COPD is associated with chronic inflammation and hypoxia, mechanisms that are involved in both myocardial infarction and sudden cardiac death. In the third manuscript, Chronic obstructive pulmonary disease and sudden cardiac death: the Rotterdam Study. Maartje Nieske Niemeijer and colleagues from the University Medical Center Rotterdam, The Netherlands investigated whether there is an association between COPD and sudden cardiac death in the general population. 27 The Rotterdam Study is a population-based cohort study that enrolled 14 926 subjects aged 45 years and older with up to 24 years of follow-up. Of the 13 471 persons included in this analysis, 1615 had a diagnosis of COPD in which the risk of sudden cardiac death overall was increased 1.34-fold, but increased up to 2-fold 5 years after the diagnosis of COPD and increased further to a >3-fold higher risk in those with frequent COPD exacerbations during follow-up. The authors conclude that COPD is associated with an increased risk for sudden cardiac death, especially in persons with frequent exacerbations of the disease process. This risk indicator might therefore provide new targets for the prevention of sudden cardiac death.

Finally, in patients with ischaemic heart failure, most currently approved treatment options may fail. Thus, regenerative treatment with peripheral blood or mesenchymal cells has been considered, but this novel approach needs confirmation in larger randomized trials. 28 In the fourth clinical research paper Bone marrow-derived mesenchymal stromal cell treatment in patients with severe ischaemic heart failure: a randomized placebo-controlled trial (MSC-HF trial), Anders Bruun Mathiasen and colleagues from the Copenhagen University Hospital in Denmark studied the effects of intramyocardial autologous bone marrow-derived mesenchymal stromal cell (MSC) treatment in patients with severe ischaemic heart failure. 29 The MSC-HF trial was a double-blind, placebo-controlled trial randomizing patients 2:1 to intramyocardial injections of MSCs or placebo, respectively. The primary endpoint was change in left ventricular end-systolic volume (LVESV), measured by magnetic resonance imaging or computed tomography at 6 months. Sixty patients aged 30–80 years with severe ischaemic heart failure, New York Heart Association (NYHA) class II–III, left ventricular ejection fraction (LVEF) <45%, and no further treatment options were randomized and 55 completed the 6-month follow-up. At 6 months, LVESV was significantly reduced in the MSC group by ~8 mL, while it had increased in the placebo group by 5.4 mL. Compared with placebo, LVEF also improved by 6.2% in the MSC group, as did stroke volume by 18.4 mL and myocardial mass by 5.7 g. No differences were found in NYHA class, 6-min walking test, and Kansas City Cardiomyopathy Questionnaire, and no side effects were identified. The authors therefore conclude that intramyocardial injections of an autologous culture of expanded MSCs are safe and improve myocardial function in patients with severe ischaemic heart failure. The paper is discussed in a comprehensive Editorial by James T. Willerson from the University of Texas Health Science Center in Houston, USA. 30

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

References


