European Heart Journal Supplements (2019) **21** (Supplement B), B1–B2
The Heart of the Matter
doi:10.1093/eurheartj/suz025

ESC
European Society
of Cardiology

Introductory editorial

Francesco Prati, Eloisa Arbustini, and Mario Albertucci

Is personalized medicine entering clinical practice?

This issue of EHJs collects the contributions presented at the 35th Conoscere e Curare il Cuore (CCC) 2018 Congress. The meeting has provided the national cardiology community with a *participated state of the art* on the latest translational scientific advances in the setting of heart failure (acute and chronic, past and new medications, resynchronization, up to percutaneous treatment of tricuspid valve in refractory right heart failure); ischaemic heart disease (from risk factors prevention and new medications to the problem of the residual angina in incomplete revascularization, up to the innovative absorbable stents and the imaging-based characterization and scoring system of the vulnerable plaques); aortic stenosis as potentially preventable disease, and its management in old frail patients, including those with heart failure); myocarditis (biopsy and imaging diagnosis and treatment up to the management of post-myocarditis dilated cardiomyopathy). Of common interest and shared to all the topics were the big data (as they are already today an instrument of epidemiological and scientific knowledge in medicine, but as in fact we still do not have an impact in clinical practice) and genetics of cardiovascular diseases (cardiomyopathies, aneurysmal aortopathies, arrhythmogenic atrial diseases, pulmonary hypertension, and cardio-oncology). The discussion of each topic invariably brought out the slow but now necessary entering of personalized and precision cardiology in the clinical practice. The growing knowledge of the pathophysiological mechanisms and the specific causes of the different phenotypic manifestations of cardiovascular diseases are slowly changing the clinical vision. Today the power of our magnifying glasses increases: imaging, genetics, and biomarkers lead from symptoms and phenotypes to molecules and pathogenic pathways that are potential targets for new therapeutic developments. Despite the future lies in the roots of knowledge, these new knowledge and tools bring out differences, even within the same groups of diseases. Moving from the robust tradition of evidence-based medicine to the innovative vision of personalized precision cardiology requires a critical cultural and professional revolution. The new personalized precision medicine does not deny the past evidence-based medicine but represents its natural evolution. The on-going effort is to distinguish patients and their diseases rather than grouping them, even forcibly, under the same umbrella. Similarity is not sameness. In front of today's patient, we look for diagnostic, classificatory, and therapeutic certainties but we also face the challenges of uncertainty. Uncertainty deserves research and today more than ever, research is the most robust and solid tool to face this cultural revolution and to govern technological development that also risks conditioning clinical paths and therapeutic choices.

The example of coronary artery disease

Some medical specialties, particularly oncology, are currently applying the rules of precision medicine; patients are being treated with the goal of targeting the disease cause or, alternatively, specific phenotype. Such approach is emerging with prudence and carefulness in cardiology. Still, the most of therapeutic solutions for ischaemic heart disease are applied indiscriminately to all patients either in primary or secondary prevention. The identification and quantitative assessment of the individual burden of atherosclerosis are key in a programme of primary prevention of cardiovascular diseases. A recent study that addressed the prevalence of coronary artery disease (CAD) in the Tsimane Aborigines of Amazon rainforest, who conduct a subsistence lifestyle, demonstrated the lowest global prevalence of CAD. Yet the risk of developing coronary artery disease was not completely turned down, despite a healthy lifestyle. The development of atherosclerosis is therefore compatible with low LDL values, especially in aged individuals. The study did not clarify the role of inflammation for promoting atherosclerosis. In fact in the indigenous populations an elevated inflammatory burden of inflammation due to infections and environmental exposure was found.

The role of systemic inflammation is certainly into the spotlight since the CANTOS showed that Canakinumab, a drug able to reduce inflammation without affecting the LDL levels, improves clinical outcome. This finding, along with the launch of PCSK9 inhibitors that reduce LDL cholesterols to unprecedented levels, open new perspectives as for the first time separates the inflammatory component from the cholesterol levels. Unfortunately, the systemic marker of inflammation (C-reactive protein/hsPCR)

Published on behalf of the European Society of Cardiology. © The Author(s) 2019.
This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (http://creativecommons.org/licenses/by-nc/4.0/), which permits non-commercial re-use, distribution, and reproduction in any medium, provided the original work is properly cited. For commercial re-use, please contact journals.permissions@oup.com

does not provide a direct assessment of coronary artery disease. Local assessment of inflammations with imaging modalities may become a major player in the next future, with macrophage detection at optical coherence tomography, being so far the most valid approach.

The characterization of atherosclerotic plaques is another valuable aspect in the search for a personalized treatment approach, complementary to blood markers characterization. The CLIMA study showed for the first time, in a secondary prevention study, that the application of four metrics of vulnerability in the same coronary lesions, obtained with optical coherence tomography, a high intracoronary imaging modality, can identify patients at risk of hard events. Clinical applications of these concepts are not immediate; in fact it is still unclear how to treat patients with vulnerable plaques. However, the study reinforces the concept of selectively identifying different manifestations of CAD, searching for individual specific phenotypes and personalized treatments. Envisioning future scenarios, it is reasonable to foresee a therapeutic strategy that takes into account a clinical stratification (risk factors) with blood markers and characterization of atherosclerosis by imaging technique.

Technology innovation and big data

Medicine has always followed the technological innovations, albeit at its own pace. The availability of digital personal devices, along with the information and opportunities they provide, is presenting the occasion to collect unprecedented numbers of data, in a manner not previously available. The most significant change in clinical research is the ever more frequent acceptance of observational data, both through the use of registry of rare or common conditions and the implementation of capillary networks recording the daily clinical practice. Once all the glitches will be corrected, *precision medicine*, that is assigning specific treatment to individual patients, will be possible.

To make this lofty goal possible a keen understanding of pathophysiology will be paramount. As for the dispensation of diuretic treatment in patients with heart failure a familiarity with renal physiology is instrumental in achieving the desired result in the specific patient. We now have (with more coming in the future) different compounds to obtain similar effects, and deciding will require extensive knowledge of the pathophysiology in general, and of the patient in particular. One fits all approach is not enough anymore. Multiple data on patient's genetics, specific conditions, medical history, habits, attitudes, pharmacogenomics, nutrition, and *microbioma* will enter the medical decision making process, which will select *just* the individual patient.

Is Steve Jobs somehow responsible for this new era in medicine? . . . Quite possibly!