Eur J Vasc Endovasc Surg (2019) 57, 329–330

EDITORIAL

Metabolomics as an Innovative Tool for a Personalised Approach to Vascular Disease

During the past decade, patient care and treatments have continuously evolved to a more personalised approach, centring the medical care on the patient, which probably represents the most promising paradigm change in modern medicine. As reported by the Food and Drug Administration (FDA), personalised/precision medicine is to become a key issue for the present and probably a key determinant factor for the future of treatment and drug development.[1] About 30% of the new drug FDA approval last year was for personalised medicines.[2] This approach, defined as the study of the most appropriate and tailored way to treat patients affected by a disease, is expected to significantly improve the quality of life of the patient and to reduce the healthcare cost and the duration of hospital stay.[3] For this purpose, personalised medicine will attempt to identify the drugs and therapies that ensure optimal patient care and follow up. Indeed, depending on the pathology, current pharmaceutical treatments appear to be poorly effective and/or toxic for 30–60% of patients.[4] This should be correlated with the notion that the effects and progression of diseases are not homogeneous but highly dependent on different and complex parameters such as the patient's genotype but also phenotype, lifestyle, environment, etc. It is obvious that, in the near future, patients will not be compared with a vast control population but will become their own control. Such an approach requires (a) to stratify or classify patients into groups, (b) to select and/or adapt treatment according to the group characteristics, and (c) to follow the patient's evolution. An improved knowledge of patients (genotype, phenotype, lifestyle), pathology status (grade, evolution), and treatment (dose, timing, repetition) is then mandatory. Personalised medicine must combine modern and innovative tools to measure, integrate, and model informative data that could help clinicians choose the best option for the care of the individual patient.

In the search for new methodologies and tools applicable to personalised medicine and vascular diseases, "omics" sciences and their holistic point of view are of great interest.[5] Indeed, cells, organs, and organisms are composed of several interconnected classes of building block molecules (DNA, RNA, proteins, and metabolites) that jointly contribute to the functioning of a very complex network. Digging deeper into this network by a better exploration of the relationships between all the constituent molecules is mandatory to understand how physiological but also pathological processes occur. Evidently, the study of the genome, the transcriptome, and the proteome by genomics, transcriptomics, and proteomics approaches is important but not sufficient for this comprehension. Indeed, all these "omics" lack an essential part of the complexity of the organisms, which is the interaction with the environment (i.e. nutrition, microbiome, lifestyle, pathogens, etc.). In other words, to describe how a living system is evolving or will evolve, one needs to assess phenotype more than genotype and to obtain information about functionalities and not only about capabilities. Metabolomics, described as the qualitative but also the quantitative measurement of low molecular weight biomolecules (metabolites) is a powerful and essential tool to assess the phenotype and to correlate it with genes, lifestyle, environment, and physiology or pathology.[6,7] The term "metabolites" is used for various and diverse endogenous and exogenous compounds of different biochemical classes (e.g., amino acids, sugars, fatty acids, lipids, nucleotides, drugs, and drug metabolites) coming from food, microbiota, biochemical pathways, treatments, etc. This innovative approach is used in diverse and various applications such as quality control (food, plants, drugs, etc.), taxonomy (plants and animals), biology and biochemistry (functional genomics, biological systems, biochemical pathways, etc.), and obviously medicine (diagnostics, toxicology, drug discovery, and epidemiology).[8–11] Because it provides a unique insight into the relationships between physiological status, lifestyle, pathologies, and patients, and because it correlates with a patient's disease phenotype, metabolomics is particularly adapted to obtain relevant and helpful information for a personalised approach to treatment. Genomics or genetics study focuses on the identification of a predisposition for a disease and/or a pathology subtype while metabolomics approaches the characterisation of the disease at a certain time point and helps follow its evolution and its response to drugs or treatment. Moreover, metabolomics is also particularly adapted to study the impact of exposome on the population, which can lead to essential information about pathology development (i.e. cancer).

While the development of metabolomics is relatively recent, this emerging technology has already proved its high efficacy in many clinical areas such as in the assessment and personalisation of pharmacotherapy (pharmacometabolomics),[12] in the development of new diagnostic tools (more than 300 approved by the FDA), in discovery of biomarkers, and in understanding the aetiology of some pathologies.

Linked to a high prevalence and mortality, vascular diseases are clearly within the scope of this personalised approach. Indeed, vascular care has evolved enormously in the past two decades, with the development of endovascular techniques and the optimisation of medical treatment. Still, some barriers

https://doi.org/10.1016/j.ejvs.2019.01.003

remain challenging. In spite of unquestionable progress in the unravelling of plaque physiopathology, much remains obscure about how and why plaque complication is triggered. The same can be said about abdominal aortic aneurysm growth dynamics and ultimate rupture. Another important area of research is the behaviour of plaque and vessel wall after endoluminal angioplasty, leading to either successful and lasting results or early restenosis and failure. Similarly, restenosis in anastomotic sites can jeopardise effective open revascularisation and often requires re-intervention.

The number of studies involving "omics" sciences and metabolomics in the context of precision/personalised medicine in vascular diseases remains limited, but recent publications on cardiac hypertrophy, heart failure, or myocardial infarction clearly indicate that such tools will be helpful to assess some of the critical challenges, such as the identification of risk factors, the prevention of cardiovascular events, and the improvement of overall cardiovascular health.[13–18] This is not surprising if we take into account the important effect of exposome on the pathogenesis of these pathologies and the evidence that systemic and local metabolism modifications could negatively influence cardiovascular outcome. As metabolomics could also be applied in pre-clinical models, it could be helpful to validate research hypotheses or to accelerate transitional verification.

In this issue of the Journal, Zhou et al.[19] report the results of a study assessing serum metabolomics markers in 35 patients with type A or type B acute aortic dissection (AAD). They found that lysophosphatidylcholines and sphingolipids are altered in patients with AAD, and that several sphingolipids (sphinganine, phytosphingosine, and ceramide) are significantly decreased in patients with Stanford type A AAD. These findings raise the possibility that a combination of these two families of metabolites could serve as a biomarker for the diagnosis of AAD and contribute to distinguishing between Stanford type A and type B AAD.[19]

In conclusion, combining metabolomics with other omics approaches (named panomics) together with the study of microbiome and with classical clinical and/or lifestyle data will certainly result in relevant improvement in the understanding of cardiovascular disease occurrence, evolution, and patients' response to treatment and lead to more precise therapies. The editors of the EJVES are looking forward to receiving high quality manuscripts in this exciting field of omics, with the overall aim of advancing our knowledge and improving the (personalised) care that we provide to our patients suffering from vascular diseases.[20]

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