PERSONALIZED MEDICINE IN CARDIOLOGY

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Background

Personalized medicine implies a tailored approach to patients that offers more effective therapy for each individual, reduces risks and avoids unnecessary treatments or diagnostic interventions. Treatment of patients with cardiovascular diseases (CVDs) has markedly improved through the evaluation of new therapy concepts in large, controlled trials that provide evidence-based guidance. Conditions such as atrial fibrillation, acute heart failure, or sudden cardiac death still cause unacceptable morbidity and mortality in the population. Furthermore, patients who survive acute cardiac events often require long-term treatment for chronic conditions. The development and implementation of a more personalized management offer potential to significantly improve outcome.

State of Art in Cardiovascular Medicine

Large randomized clinical trials (RCTs) and population studies have identified the benefit of novel therapies such as β-blockers, ACE-inhibitors, anticoagulants, PCI and stents,1-3 defibrillators, and pacemakers.4 The evidence-based approach has led to major reductions in mortality in acute coronary syndromes and stroke5-6 in a time when progress in other areas has been much slower.6 Recently, however, some limitations to the evidence-based medicine have emerged. For example, it has been recognized that this approach is driven by the enrolment criteria of the trials and may not provide results that are applicable to other subgroups of patients such as those excluded by the trial.

Existing and Emerging Approaches: Genomics in CVD

The genomic gold rush of the past decades has brought major insights in the spectrum of the genetic contribution to CVD. 'Classical' genetic techniques and functional assessment of the gene defect have identified arrhythmia mechanisms in the long QT syndrome and other inherited arrhythmic diseases.7,8 These insights are now shaping "genotype-specific therapy " providing a role model for the future use of novel, genomic information in CVD management. Large-scale GWAS studies have identified a number of relevant alleles in common chronic diseases such as coronary artery disease or atrial fibrillation. The potential to identify new disease mechanisms and approaches for individualized therapy based on genotype has yet to be harvested. PCSK9 and PITX2 provide first examples for the potential of 'polygenic' genetic predispositions in common CVDs. In contrast,personalized medicine is a novel medical model with all decisions and practices being tailored to individual patients in whatever ways possible. Personalized medicine may allow the physician to provide a better therapy for patients in terms of efficiency, safety and treatment length to reduce the associated costs. We review the concepts, strengths, limitations and challenges of personalized medicine with a particular focus on cardiovascular diseases (CVDs). Individualized medicine serves a pivotal role in the evolution of national and global healthcare reform, especially, in the CVDs fields. Interestingly, if drugs are not accounted for inter-individual differences, they are either 'ineffective' or 'not completely effective' in 30-60% of patients.9-10 One tends to scotomize that on average, a drug on the market works for only 50 percent of the people who take it.11 The use of personalized medicine may allow the physician to provide a better therapy for patients in terms of efficiency, safety and treatment length, as well as to reduce the associated costs for the community. In this respect, it worth mentioning that adverse drug reactions represent the fourth leading cause of hospitalization in the US, accounting for 100000 deaths

per year and $150 billion in US healthcare costs annually,7,9 about 5.3 percent of hospital admissions are associated with adverse drug reactions (ADRs),10 many of them potentially preventable by an individualized approach in therapy. In the era of genomic, personalized medicine through the combination of genetic information with other biomarkers may add additional benefits for preventive and therapeutic strategies in individuals.12 As a result, due to such advances, personalized medicine has become increasingly important in cardiology. However, only very few cardiologists in the world are incorporating personalized medicine into clinical treatment (7%) thus far. A majority of doctors believe that personalized medicine will have a positive impact on their practice; however, only 51% think that there is sufficient evidence to order personalized genetic tests at present. However, before adapting personalized medicine for everyone and every day in clinical practice, we should be aware of the strengths, limitations and challenges of personalized medicine.

Summary and Definition of Personalized Medicine

Thus, human genome information now allows providers to create optimized care plans at every stage of the disease, shifting the focus from reactive to preventive health care.7 We often use expressions, such as personalized medicine, individualized medicine, tailored medicine, or stratified medicine, which could give the impression of a total individualized pharmacotherapy (i.e., targeting drugs for each unique genetic profile). Further, we use the expression such as predictive medicine, preventive medicine, protective medicine related with personalized medicine. Personalized medicine needs a multidisciplinary team approach, with different disciplines that must work together (Fig.1). It is an approach that may help to solve medical challenges faced in the 21th century. For example, current healthcare model is expensive, reactive, inefficient, and focuses largely on «one-size-fits-all» treatments for events of late stage diseases. With personalized, individualized, tailored, predictive, preventive, and participatory medicine and etc.

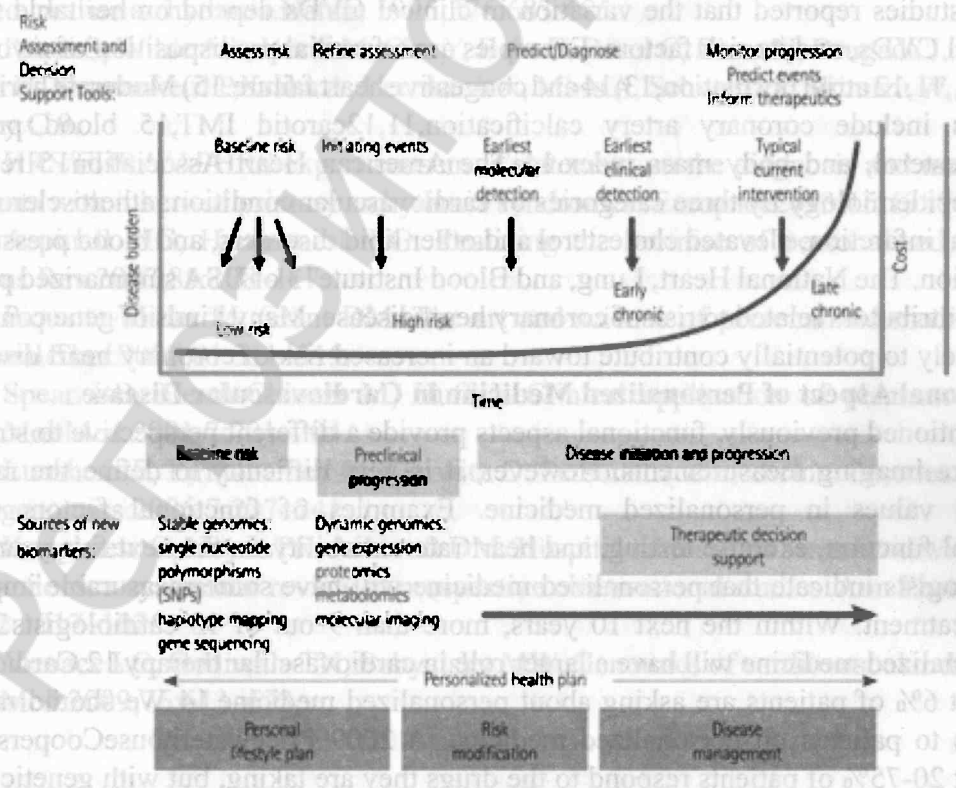

Fig.1 – The role of genomic-based information across the continuum of health to disease

The role of genome-based information across the continuum of health to disease. Currently, in the time course of a chronic disease (line), treatment usually occurs at the point in the disease process indicated by «typical current intervention»-a point . There may be many benefits of personalized medicine; making better medication choices (100000 Americans die from adverse reactions to medications); select optimal therapy (on average, only 50% of people respond, 30% in hypertension8; safer dosing options (one size does not fix all); improvements in drug development (focused drug testing); decrease health care costs; decrease ADRs (Avoiding ADRs the fourth leading of cause of death according to FDA); potential to improve patient safety; reduce inappropriate testing and procedures; increased patient empowerment and awareness. Cardiovascular diseases is the most common cause of death worldwide. Today CVDs accounts for 30% of deaths worldwide, including nearly 40% in high-income countries and about 28% in low- and middle-income countries.9 CVDs increases the global health burden and total cost of medical care. Such situation of health care demands the evidence, optimum quality and cost. Moreover, research funding challenge will grow also. After the Human Genome Project, many technologies aiming to use genome-wide predisposition markers, pharmacogenetics, and genomic signatures in complex CVDs have been developed. Monogenic cardiac diseases have provided insight into pathophysiological mechanisms and the genetic underpinnings of a growing number of complex cardiovascular disorders that are caused by interactions between multiple genes and environmental factors.6 Examples of monogenic CVDs are the long QT syndrome (LQTS), hypertrophic cardiomyopathy, factor V Leiden, and familial dyslipidemias.10 In understanding the CVDs continuum, we can identify the unmet medical needs of personalized medicine along this continuum (patient engagement for disease risk and lifestyle change, tailoring prevention, improved diagnostic decisions, tailored therapy).

Genetic Contributors in Cardiovascular Diseases

Many studies reported that the variation in clinical CVDs depend on heritable factors, subclinical CVDs, and its risk factors. Examples are a familial predisposition of myocardial infarction,,11,12 atrial fibrillation,13,14 and congestive heart failure.15) Moderate heritability conditions include coronary artery calcification,11,12carotid IMT,15 blood pressure, total cholesterol, and body mass index.14 The American Heart Association15 reviewed genomic epidemiology by three categories of cardiovascular condition: atherosclerosis and myocardial infarction, elevated cholesterol and other lipid disorders, and blood pressure and hypertension. The National Heart, Lung, and Blood Institute13 of USA summarized possible genetic contributors related to risk of coronary heart disease. Many kinds of gene considered mostly likely to potentially contribute toward an increased risk of coronary heart disease.

Functional Aspect of Personalized Medicine in Cardiovascular Disease

As mentioned previously, functional aspects provide a different perspective to structural aspect, like imaging measurements. However, it is very difficulty to define the range of functional values in personalized medicine. Examples of functional factors include endothelial function, exercise testing, and heart rate variability. In the next five years, 73% of cardiologists indicate that personalized medicine will have some measurable impact on patient treatment. Within the next 10 years, more than 9 out of 10 cardiologists believe that personalized medicine will have a larger role in cardiovascular therapy.12 Cardiologists report that 6% of patients are asking about personalized medicine.14 We should raise the awareness to patients on personalized medicine. A 2009 PricewaterhouseCoopers report found that 20-75% of patients respond to the drugs they are taking, but with genetic testing that response rate could improve «dramatically»

Conclusion

Individualized medicine contributes to the evolution of health management practice, especially in CVDs fields. Ultimately, it will affect the entire landscape of healthcare system. The overall outcome is the well-being of each individual through the continuum of life, transforming the future of personalized health care.

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