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Genetic Predictive Scores in Heart Failure: Possibilities and Expectations

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Abstract

Heart failure (HF) remains a major health problem worldwide. Currently used HF risk prediction scores based on clinical findings, echocardiography features, biomarkers cannot propose an individualized approach to risk stratification, whereas there is variability in predictive value of different scores amongst patients with various HF phenotypes. The editorial commentary is devoted the role of the genetic risk prediction scores in the predisposition of HF development and assay in the HF medical care response. The brand new risk scores reflecting variabilities in genetic and epigenetic features in HF development are discussed also.

Keywords: Heart failure; Phenotypes; Genetics; Epigenetics; Prediction; Scores

Introduction

Heart failure remains a global health and social problem associated with a higher risk of cardiovascular (CV) death and enormous economic burden [1]. Although HF is considered a final pathophysiological stage of any CV disease, the development of several HF phenotypes, i.e., HF with reduced ejection fraction (HFrEF), HF with mid-regional ejection fraction (HFmrEF) and HF with preserved ejection fraction (HFpEF), might be resulted in some distinguishes in etiology, the prevalence of CV risk factors, and co-existing comorbidities, which in particularly impact on nature evolution of the disease [2,3]. Nevertheless, it turns out that prognosis and clinical outcomes of HF phenotypes could be similar and frequently does not closely relate to clinical features, echocardiographic predictors, and biochemical markers' presentation including natriuretic peptides, circulating galectin-3, troponins, and soluble ST2 [4-7]. Moreover, there is large body of evidence regarding that the clinical profile of HF patients who distinguishes 30-day and 1-year mortality and morbidity might bear a strictly similarity and staggering resemblance [8].

The recent clinical studies have shown that inherited forms of cardiomyopathies have a substantial genetic component, which predisposes to the development of several phenotypes of HF [9-11]. By now, genetic testing has incorporated as a part of patient evaluation for suspected inherited cardiomyopathies [10,11]. However, it turns out the epigenetic modifications through DNA methylation, ATP-dependent chromatin remodeling, histone modifications with an involvement of microRNA-related mechanisms might be sufficient pathophysiological factors contributing to adverse cardiac remodeling and altered cardiac function [12]. In this context, the novel risk scores reflecting variabilities in genetic and epigenetic features in HF development appear to be promised [13-15].

Indeed, some early studies have reported interested results with respect to genetic precursors of HFpEF and HFrEF [16-22]. As biomarkers particularly used to scrutiny single nucleotide polymorphisms (SNPs) of genes encoding enzymes related to oxidative stress [16], genotype of guanine nucleotide-binding proteins (G-proteins) β-3 subunit (GNB3) [17], transcription factor Islet-1 gene [18], troponin T [19], CYP2D6 polymorphism [20], cardiac myosin binding protein-C mutations [19], renin-angiotensin-aldosterone system polymorphism [21] etc. Indeed, it is well known that angiotensin-converting enzyme (ACE) I/D gene D allele was associated with higher overall mortality as compared with the I allele in HF patients and that the effect could be modified by ACE inhibitors' given [22]. Additionally, ACE DD and angiotensin-

1-receptor 1166 CC genotypes may synergistically increase the predisposition to HFpEF [23].

Unfortunately, in ARIC (Atherosclerosis Risk in Communities) study was reported that none of the metabolite SNPs including pyroglutamine, dihydroxy docosatrienoic acid were individually associated with incident HF, whereas a genetic risk score created by summing the most sufficient risk alleles from each metabolite determined 11% greater risk of HF per allele [24]. Ganna et al., (2013) [25] have reported that amongst 707 common SNPs associated with 125 diseases including HF it would not be easily obtained explainable results by common genetic variants related to HF development. Consequently, a close gene-gene interaction may determine an individual risk to development of HF through different pathways including epigenetic modifications. All these findings lead to assume that genes score might be a powerful tool for prediction of HF development.

More successful genome-wide linkage studies toward genes-related contribution in HF have been devoted incorporating SNPs of several genes (i.e., the bradykinin type 1 receptor gene, angiotensin-II type I receptor gene, the β1-adrenoceptor gene and CYP2D6 polymorphism) in predictive score to benefit and suffer harm from HF therapy. Although these parmacogenetic studies have focused on promised topics, the obtained results have not been absolutely consistent [26,27]. Nelveg-Kristensen et al, (2015) [27] have found no sufficient association between pharmacogenetic scores and fatal outcomes in HF patients. In contrast, Bondar et al., (2014) [28] have guessed that the gene expression profiling might be useful rather for risk prediction in HF than for choosing HF treatment regime. Thus, the clinical implementation of the HF therapy based on genes scoring remains uncertain and requires more evaluation in the future [29].

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Conclusion

Gene–gene interrelations encompass several mechanisms involved into HF phenotype development. The results of the recent genome-wide linkage studies have improved our understanding of the role of genetics and epigenetics in the HF progression, whereas the predictive value of genes-based scoring remain controversial especially amongst patients who are not referred as inhered cardiomyopathy individuals. However, prospective randomized clinical trials are required to more pretty accurate explain the predictive role of the genetic risk scores in HF development and response of the HF medical care.

Conflict of Interests

No significant financial conflicts of interest relevant to the article topic is declared.

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