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A SURVEY ON RISK PREDICTION OF CARDIOVASCULAR DISEASE USING GENETIC INFORMATION

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ABSTRACT- Cardiovascular disease (CVD) has become the world's number one cause of morbidity and mortality. It leads to millions of deaths every year which are supposed to occur decades later. Around two-thirds of these deaths are due to acute events, which frequently occur suddenly and are often fatal before medical care can be given. Unexpected acute events are resulting in affliction and high treatment costs. Hence CVD becoming huge burdens even for developed countries. So, early prediction and intervention would be a huge benefit to society. Many groups have developed prediction models for CVD by classifying its risk based on risk factors such as age, sex, etc. Recent studies have uncovered that many genetic variants are associated with CVD outcomes. However, the potential clinical utility of genetic information has been uncovered initially and is expected for further development.

Keywords: Cardiovascular disease (CVD), genetic variants.

1 Introduction

Cardiovascular disease such as heart attack, stroke, and hypertension is caused by disorders of the heart and blood vessels and by far continues to be the leading cause of death in the world for both developed and developing countries. Vulnerable plaque easily ruptures in blood vessels, thereby including the occurrence of a stroke, heart attack, etc. The deaths related to CVD are mainly due to acute events, which frequently occur suddenly. According to health informatics, which has been listed by the U.S. National Academy of Engineering as one of the 14 grand engineering challenges of the 21st century, deals with the acquisition, transmission, processing, storage and retrieval of health information for early detection, early diagnosis and early treatment of diseases.

Therefore risk prediction is of utmost importance to allow early intervention and treatment of complex CVD to prevent the occurrence of acute events and decrease costs. It is for this reason that

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risk prediction has become an important field to study. It is therefore, in addition to traditional approaches, new strategies for screening and early intervening CVD are demanded. The art of electro-cardiograph (ECG) interpretation is basically one of the pattern recognition. To date, in addition to this traditional ECG approach and demographic information some risk prediction models have been built such as Framingham, ATP-III, SCORE, PROCAM, QRISK and MUCA. These current risk prediction models have had some initial success in CVD prediction. However, they did not have good performance in predicting the end point of individuals who were assessed to have an intermediate risk of developing CVD.

The traditional risk factors or biomarkers for predicting CVD outcomes include age, sex, systolic blood pressure, smoking habits, diabetes, total cholesterol, high-density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) cholesterol, diabetes mellitus, family history, etc. While traditional risk factors can explains only half of the incidence of CVD. Therefore further efforts are needed to improve the performance of risk prediction models. For further efforts, Genome-Wide Association Studies (GWAS) for CVD outcomes/traits can be overviewed. Genomics summarized recent studies on genetic variants that are associated with CVD outcomes/traits and perspective of using genetic information for developing a personalized risk prediction model for CVD. The genetic variants associated with CVD outcomes and other complex disease can also be searched in web of science and PubMed.

The genetic markers reviewed were those associated with CVD outcomes (coronary heart disease, stroke, heart failure, etc) established traditional factors (systolic blood pressure, total cholesterol, HDL cholesterol, LDL cholesterol, body mass index, hypertension, etc) and biomarker. It is now becoming apparent that new and personalized biomarkers are needed in order to predict acute CVD outcomes more accurately. Recent studies have been focusing on looking for new genetic, molecular, imaging or physiological biomarkers with better clinical prediction outcomes and for this advancements in different computing and information technologies are needed.

The common CVD outcomes/traits are Myocardial Infarction (MI), stroke, Heart Failure (HF). Myocardial infarction (MI) is the diseased state of the heart that leads to the damage in the depolarizing myocardium (heart muscle), resulting in heart attack. Stroke is a kind of severe disease which has been one of the most frequent diseases that can cause sudden deaths. Even if the unattended patients attacked stroke and survived, a great or small part of the heart will still be always affected, and work of heart involvement and the possibility of chronic HF will be produced. Moreover, arrhythmias will be caused. There are other severe cardiovascular outcomes, such as HF,

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a kind of common disease, which can cause leg swelling, shortness of breath, and the other severe symptoms. HF can be led by other diseases, such as rheumatic heart disease, anemic heart disease and toxic heart disease.

2 Reviews

A. GWAS

GWAS are developed to identifying inherited genetic variants that are associated with complex disease. This identification enables a clarification of the disease mechanisms and improves the efficacy of disease diagnostics and therapeutics. Currently, the procedures involved in introducing the genetic information into the developed risk prediction models are: (1) Identifying the genes that will be used in the prediction by studying the disease mechanism. (2) Identifying the association between the genes and the risk of disease using GWAS. (3) Developing clinical trials to make sure that the genes can predict the risk of the disease. (4) Using the outcomes of gene detection, predict whether the sample suffer from the diseases. (5) If the detected gene is found in the human blood, the person will suffer from the disease. Therefore the person should take appropriate therapy to prevent the disease earlier.

In the case of complex diseases, associated genetic variants will refer to hundreds or thousands of Single-Nucleotide Polymorphisms (SNPs), which are distributed in large regions with a particular locus on different chromosomes. Traditional methods (fragment length polymorphism, single-strand conformation polymorphism) are hard to apply on a large-scale population and multiple SNPs. The method for SNP genotyping should be high-throughput, low-cost, robust, automated, easily developed, accurate analysis of high volume data, simple operation and so on. It is difficult to combine all of these attributes into a single technology.

B. Personalized Risk Prediction Models

Personalized risk prediction modeling, in addition to the traditional population-based modeling is an emerging field of studies in health informatics. To assist the development in this area, the National Public University Center in Uruguay with the aim of developing and applying strategies to improve cardiovascular risk stratification and sub clinical vascular disease detection. The data can be valuable for the development of patient-specific evaluation metrics for CVD outcomes.

At present, combination of imaging biomarkers of atherosclerotic plaques with clinical features for better prediction of stroke on over 1000 patients. These models present interesting ideas on combing images with physiological or clinical information for CV risk prediction.

C. Critical Analysis

By combining or mining both GWAS and National Public University center we can gain large amount

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of sufficient information about gene variants which are associated with several diseases including CVD. Further this information can also be used for disease detection of individuals. Further new CVD outcomes can also be identified using different kind of genes.

3 Challenges of Genetic Association into CVD

Several studies have the potential of adding genetic variants into CVD risk prediction which can improve the performance of the risk prediction model and clinical utility. Even though there is a need of better performance on developing individual CVD risk prediction. It is still hard to carry out because it needs abundant studies with clinical trials. There are many challenges that are existed in large-size samples in the clinical trials.

Firstly, there are a large number of genes that have or will be discovered to associate with complex disease. The established risk factors have been explained half of the CVD risk. Secondly, different races, lifestyles, and living environments could induce these genetic variants to be differently explained. Many genes were detected in the subject's body, but they did not explain the disease because of the special life styles and the living environments. Thirdly, it takes too much time to genotype SNP and collects useful information for evaluating the merits of genetic CVD risk prediction for clinical use.

Lifestyle changes have been found to be an effective approach to prevent CVD. Few objective and quantifiable indices are currently available in clinical practice to assist the assessment of lifestyle changes, for example, via exercise.

4 Conclusion

CVD is one of the most common causes of death worldwide and represents a major financial burden for national economies. The epidemic of CVD has caused huge losses and caught the attention of society. Effective prediction and prevention of CV disease, particularly which resulted from high-risk asymptomatic atherosclerosis, has now become a top priority. With the advancement of technologies, screening and improved selection of individuals for more effective prevention is now possible through (1) Preclinical atherosclerotic plaques develop slowly over several decades before they rupture or obstruct an artery becoming clinically manifest. (2) Screening methods are now available for detecting the presence and severity of such plaques. (3) Current prophylaxis with aggressive risk factor modification can largely reduce morbidity and mortality from heart attacks and strokes by 50%.

Genes will be generally stable in human body for a long time after birth, so gene detection will play an important role in predicting and preventing all kinds of diseases (including CVD),

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and also extends and improves human life. However, more efforts should still be made before integrating genetic information into CVD risk prediction model clinically, because the genes that can fully explain complex CVD have not yet been identified.

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