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Review

Biosensors for cardiac biomarkers detection: A review

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ABSTRACT

The cardiovascular disease (CVD) is considered as a major threat to global health. Therefore, there is a growing demand for a range of portable, rapid and low cost biosensing devices for the detection of CVD. Biosensors can play an important role in the early diagnosis of CVD without having to rely on hospital visits where expensive and time-consuming laboratory tests are recommended. Over the last decade, many biosensors have been developed to detect a wide range of cardiac marker to reduce the costs for healthcare. One of the major challenges is to find a way of predicting the risk that an individual can suffer from CVD. There has been considerable interest in finding diagnostic and prognostic biomarkers that can be detected in blood and predict CVD risk. Of these, C-reactive protein (CRP) is the best known biomarker followed by cardiac troponin I or T (cTnI/T), myoglobin, lipoprotein-associated phospholipase A(2), interlukin-6 (IL-6), interlukin-1 (IL-1), low-density lipoprotein (LDL), myeloperoxidase (MPO) and tumor necrosis factor alpha (TNF-α) has been used to predict cardiovascular events. This review provides an overview of the available biosensor platforms for the detection of various CVD markers and considerations of future prospects for the technology are addressed.

Contents

1. Introduction

Cardiovascular disease (CVD) is a major cause of human death in both developing and developed countries. According to the World

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Health Organization (WHO), an estimated 17.5 million (30%) of all global deaths in 2005 are associated with CVD and it is estimated that by 2015, CVD can be the leading cause of death in the developing countries [1]. Recently, according to the new European cardiovascular disease statistics 2008, a staggering figure of over 4.3 million deaths in Europe alone and 2 million deaths in European Union are caused by CVD, and it is overall estimated to cost the EU economy €192 billion a year [2]. The early and quick diagnosis of cardiovascular disease is extremely important and crucial not for only patient survival but also saving cost and great deal of time in successful prognosis of the diseases. Existing methods of diagnosis for CVD rely heavily on classical methods which are based on tests conducted in central laboratories that may take several hours or even days from when tests are ordered to when results are received [3]. The diagnosis of CVD has been based on the WHO criteria, whereby patients must meet at least two of three conditions: characteristic chest pain, diagnostic electrocardiogram (ECG) changes, and elevation of the biochemical markers in their blood samples [3]. Although, ECG is an important management tool for guiding therapy [4,5], but it is a poor diagnostic test for CVD, because about half of the CVD patients who present to the Emergency Department show normal or no diagnostic electrocardiograms, which makes early diagnosis of CVD more difficult [4–7]. Therefore, measurement of cardiac markers is critical in assisting the diagnosis of CVD. A more sensitive and rapid technology platform is therefore needed to fulfill the rapid diagnosis requirements in CVD detection. The elaboration of biosensors is probably one of the most promising ways to solve some of the problems concerning sensitive, fast and cost effective measurements [8]. Biosensor can help in rapid diagnosis, providing better health care and reducing the waiting time for results dissemination which is highly stressful to the patients. Recently, lab-on-a chip and microfluidics based biosensor technology is reviewed for the detection of cardiac markers [9]. This review provided information on commercially available a few point-of-care immunosensing instruments and chip based technology for the detection of different cardiac biomarkers. In the present paper, we reviewed the developments in application of biosensors over the past 10 years for the detection of cardiovascular risk assessment. This review also summarized the frequently targeted CVD biomarkers in various biosensor platforms and highlighted the major clinically relevant parameters, such as their detection limit/range and designing of bioassay.

2. Cardiac biomarkers

CVD is not a single disease, but it is a group of different disorders that affect heart and blood vessels. CVD includes atherosclerosis condition that develops when a plaque builds up in the walls of the arteries. This plaque narrows the arteries and makes it difficult for blood to flow through and causes a heart attack or stroke. CVD can be caused by a range of factors and disorders that include genetic, gender, age, high blood pressure and cholesterol, diabetes, obesity and overweight, smoking and stress. The causes of CVD are more diverse that clinical testing becomes increasingly complex. There are a number of diseases associated with CVD that affect different parts of the body. Although, great progress has been made in the treatment of this disease, current medical knowledge is unable to effectively predict its risk. With regards to predicting CVD risk, one of the active research areas recently is the use of diagnostic and prognostic biomarkers that can be identified in blood [10]. On the basis of diagnostic and prognostic standpoint, CVD biomarkers can be categorized into pathogenetic and therapeutic types. The diagnostic and prognostic biomarkers also provide therapeutic value in medical applications. The vascular wall releases molecules into the bloodstream that can reflect the pathological processes taking

Fig. 1. Most frequently studied biomarkers in relation to the different mechanism involved in CVD risk [10].

place. In theory, the concentrations of the molecules involved in different pathological processes could be the biomarkers. However, not all of these molecules are suited to this aim but should fulfill certain conditions [10].

There are several important characteristics that an ideal cardiac biomarker should exhibit. These include: (a) high clinical sensitivity and specificity, (b) quick release of biomarker in the blood enabling early diagnosis, (c) capability to remain elevated for longer time in the blood, and (d) ability to be assayed quantitatively [10]. It is difficult to select a specific marker for the diagnosis of CVD. Therefore, a range of biomarkers can potentially be analyzed simultaneously for the accurate disease diagnosis [6,7,10–13]. Anderson et al. reported a set of 177 candidate biomarkers that are potential plasma markers for CVD and stroke [13]. Recently, the most frequently studied biomarkers are summarized in relation to the different mechanisms involved in development and rupture of atherosclerotic plaque, such as endothelial dysfunction, inflammation, oxidative stress, proteolysis, and thrombosis (Fig. 1) [10].

Several other cardiac-specific biomarkers have emerged as strong and reliable risk predictors for coronary heart disease, as listed in Table 1. Of which, CRP has been the most frequently used single biomarker for cardiovascular risk (CVR). The CVR defined by the American Heart Association (AHA) and the Center for Disease Control and Prevention (CDC) is regarded as low risk for a CRP concentration below 1.0 mg L^{-1}, moderate for 1.0–3.0 mg L^{-1}, and high risk for concentrations over 3.0 mg L^{-1} [14]. CRP can rise as high as 1000-fold because of inflammation induced by infection or injury, often leading to CVR [15]. Recent research suggests that patients with elevated basal levels of CRP are at an increased risk of diabetes and hypertension as well as CVD [15].

Myoglobin, although not a very specific marker, but it is the first marker released after the damage occurred to myocardial muscle cells. B-type natriuretic peptide (BNP), cardiac troponin I (cTnI), and CRP are released after myoglobin, but they are specific markers for coronary events. BNP is useful for the emergency diagnosis of heart failure and for the prognosis in patients with acute coronary syndromes (ACS) [16]. CRP is an important prognostic indicator of CVR and ACS. cTnI has become a standard marker for the detection