Increased serum levels of interleukin-6 and von Willenbrand Factor in early phase of acute coronary syndrome in a young and multiethnic Malaysian population

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ABSTRACT

Objective Interleukin-6 (IL6; proinflammatory marker), von Willebrand Factor (vWF; endothelial dysfunction marker) and P-selectin (platelet activation marker), may play important roles in defining the pathogenesis of vulnerable plaques in acute coronary syndrome (ACS). This study aims to investigate the expression and relationship of these markers in early phases of ACS in a young and multiethnic Malaysian population.

Design Peripheral whole blood mRNA, and serum levels of IL6, vWF and P-selectin were measured in 22 patients with ACS, and in 28 controls with angiographically significant coronary artery disease without previous ACS events. Venous blood from ACS patients was obtained within 1 h of hospital admission.

Results No significant differences of IL6, vWF and P-selectin mRNA levels between ACS and controls were seen. ACS patients had significantly higher serum levels of IL6 and vWF ($p<0.001$), compared with controls. P-selectin correlated with IL6 ($r=0.697$, $p=0.003$) and vWF ($r=0.497$, $p=0.05$) at mRNA levels, indicating a possible association between these three indices of ACS pathogenesis.

Conclusions Increased serum levels of IL6 and vWF suggest that inflammation and endothelial dysfunction may play a prominent role in the pathogenesis of the disease during the early phase of ACS.

INTRODUCTION

Coronary artery disease (CAD), including its manifestation as acute coronary syndrome (ACS) is a well established cause of morbidity and mortality among adults in both developed and developing countries. In recent years, there has been an alarming rise in the incidence of ACS in the Malaysian population, especially in younger age groups.[1] It has been reported that Malaysian ACS patients had a median age of 59 years, which was comparatively younger than the Caucasian population, whose median age was 66 years, as shown by the international multicentre GRACE Registry.[1 2]

Atherosclerosis is the culprit behind the ACS and stable CAD. The pathophysiology of atherosclerosis includes plaque formation and destabilisation ('atherogenesis'), tendency to thrombus formation ('thrombogenesis'), and the loss of endothelial cell integrity ('endothelial dysfunction') within the coronary arteries, as described by Virchow's vascular triad.[3] These processes are intimately linked, and hence, provide a clue of diagnosis of eventual ACS as early as in pathogenesis of disease based on composition and vulnerability of plaque.[4]

Currently available cardiac markers for ACS diagnosis, such as troponin-T and creatine kinase–myocardial band (CK-MB) isoenzyme, only detect consequences of myocardial damage after ACS has occurred, thus the information to identify patients at risk of ACS in early phase is not available.[5] Much interest has focused on identifying upstream markers which can detect an individual at risk of atherosclerotic plaque rupture leading to ACS. These include markers of inflammation, interleukin 6 (IL6); endothelial dysfunction, von Willenbrand Factor (vWF), and platelet activation, P-selectin. Although each of these markers has been shown to predict future cardiovascular events in stable CAD patients, as well as recurrent events and death in patients presenting with ACS,[6–8] their association has yet to be studied in a young, multiethnic group of the Malaysian population.

It now supports the concept that all types of blood constituents appear to play a role in plaque formation,[9] and the peripheral blood gene expression may reflect pathophysiology in the vascular wall or the extent of CAD.[10] With increasing awareness of the practical limitations of collecting primary cardiovascular disease tissue, temporal evaluation of blood RNA profiles that are mechanistically associated with disease processes could provide an additional useful tool for screening for disease in an at-risk population. Moreover, studying both transcriptional and translational profiles of markers could lead us to understand the in vivo molecular pathway of atherogenesis, endothelial dysfunction and platelet activation in patients with ACS.

By specifically choosing different aspects of the pathophysiology of atherosclerotic plaque rupture, the present study sought to investigate whether IL6, vWF and P-selectin can be used as markers to differentiate patients who had developed ACS, compared with patients with stable CAD during an early phase of hospitalisation.

MATERIALS AND METHODS

Study participants

Twenty-two ACS patients, who had transient ST-segment or T-wave changes on a standard 12-lead electrocardiogram, or raised troponin-T levels occurring with their typical symptom onset, were recruited into this study between