

Article

# Association of Stress, Mental Health, and *VEGFR-2* Gene Polymorphisms with Cardiometabolic Risk in Chinese Malaysian Adults

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**Abstract:** Gene-environment ( $G \times E$ ) interactions involving job stress and mental health on risk factors of cardiovascular disease (CVD) are minimally explored. This study examined the association and  $G \times E$  interaction effects of vascular endothelial growth factor receptor-2 (*VEGFR-2*) gene polymorphisms (rs1870377, rs2071559) on cardiometabolic risk in Chinese Malaysian adults. Questionnaires: Job Stress Scale (JSS); Depression, Anxiety, and Stress Scale (DASS-21); and Rhode Island Stress and Coping Inventory (RISCI) were used to measure job stress, mental health, and coping with perceived stress. Cardiometabolic risk parameters were evaluated in plasma and genotyping analysis was performed by real-time polymerase chain reaction. The subjects were 127 Chinese Malaysian adults. The allele frequencies for rs1870377 (A allele and T allele) and rs2071557 (A allele and T allele) polymorphisms were 0.48 and 0.52, and 0.37 and 0.63, respectively. Significant correlations include scores from JSS dimensions with blood glucose (BG) ( $p = 0.025\text{--}0.045$ ), DASS-21 dimensions with blood pressure, BMI, and uric acid ( $p = 0.029\text{--}0.047$ ), and RISCI with blood pressure and BG ( $p = 0.016\text{--}0.049$ ). Significant  $G \times E$  interactions were obtained for: rs1870377 with stress on total cholesterol ( $p = 0.035$ ), low density lipoprotein cholesterol ( $p = 0.019$ ), and apolipoprotein B100 ( $p = 0.004$ ); and rs2071559 with anxiety on blood pressure ( $p = 0.006\text{--}0.045$ ). The significant  $G \times E$  interactions prompt actions for managing stress and anxiety for the prevention of CVD.

**Keywords:** gene-environment interaction; *VEGFR-2* gene; rs1870377; rs2071559; job stress; mental health; cardiometabolic risk; Chinese Malaysian adults

## 1. Introduction

Cardiovascular diseases (CVDs), especially heart attack and stroke, are still the number one killer above any other cause, which affect several countries globally [1]. Similarly, in Malaysia, CVDs contribute to the main cause of death, with a combined total of 20.1% in 2016 from coronary heart disease (CHD) and cerebrovascular disease [2]. In addition, the prevalence of metabolic risk factors of CVD, namely hypertension, diabetes mellitus, hypercholesterolemia, and overweight or obesity, is high among Malaysian adults, with a total of 30.3%, 17.5%, 47.7%, and 47.7%, respectively, in 2015 [3].

The known etiology of CVD includes non-modifiable risk factors (age, sex, family history, and genes) and modifiable, behavioral, and environmental risk factors (unhealthy diet, physical inactivity, tobacco use, and harmful use of alcohol). However, there are two interrelated environmental risk