

EDITORIAL COMMENT

Cardiometabolic Diseases and Depression



Which Came First, the Chicken or the Egg?

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Cardiovascular disease (CVD) and depression are leading causes of disability worldwide and a major component of health care expenditures due to the increased use of health care services.¹ In particular, CardioMetabolic Syndrome (C-MetS) is rapidly increasing and a major cause for CVD. In accordance with the harmonizing worldwide consensus criteria of metabolic syndrome issued by International Diabetes Federation, American Heart Association, and modified National Cholesterol Education Program Adult Treatment Panel III criteria,² metabolic syndrome was defined as the presence of 3 or more of the following components: 1) abdominal obesity, defined as a waist circumference of ≥ 90 cm for males or ≥ 85 cm for females (following Korean specific cut-offs for abdominal obesity defined by the Korean Society of Obesity)³; 2) hypertriglyceridemia, defined as a serum triglyceride concentration of ≥ 150 mg/dL, or specific treatment for this lipid abnormality; 3) low high-density lipoprotein cholesterol level, defined as a serum high-density lipoprotein cholesterol concentration of < 40 mg/dL for males or < 50 mg/dL for females, or specific treatment for this lipid abnormality; 4) high blood pressure, defined as a systolic blood pressure of ≥ 130 mmHg and a diastolic blood pressure of ≥ 85 mmHg, or treatment with antihypertensive agents; and 5) high fasting glucose level, defined as a fasting serum glucose level

of ≥ 100 mg/dL or current use of antidiabetic medication. The Korean Society of CardioMetabolic Syndrome releases a Fact Sheet presenting the current prevalence of C-MetS every 3 years. The C-MetS Fact Sheet 2021 reported that current prevalence in adults aged older than 19 years was 23%, and socioeconomic factors are closely related to prevalence of C-MetS and lower socioeconomic status and poor lifestyle habits were associated with higher prevalence of C-MetS.⁴

More than half a century ago, Wynn⁵ found that the prevalence of unrecognized depression in male patients with ischemic heart disease was high, up to 40%, which had not been previously reported. Since then, accumulating evidence has shown that the presence of various types of CVD increases the development of depression ranging from mild forms of depression to major depression. Similarly, the contribution of individual depressive symptoms to the incident CVD has recently been studied worldwide.^{6,7} In 2005, a remarkable report demonstrating the phenomenon of “stress-induced” cardiomyopathy highlighted the importance of the mind-heart connection.⁸ We have also demonstrated the possible role of depression in the development of subclinical left ventricular dysfunction as one of the plausible mechanisms for CVD events.⁹

In this issue of *JACC: Asia*, Zhou et al¹⁰ performed several analyses based on data from 5 aging cohorts from 19 countries in Asia, North America, and Europe to investigate a bidirectional association between CVD and depression. In addition, the authors focused on whether certain specific lifestyle factors would mediate a reciprocal relationship in middle-aged and elderly populations. Although there were unavoidable limitations due to study heterogeneity, including the observational study design, short-term follow-up, use of different depressive symptom questionnaires, and so on, the current study raises important

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implications for clinical practice and public health policy regarding the bidirectional associations between depression and CVD. First, the reciprocal effect of these conditions, whereby the onset of either one significantly increases the risk of developing the other, was analyzed simultaneously with the same data. Second, to overcome the limitation of the generalizability due to ethnic or racial differences, the authors collected the data using a broader range of nationally representative samples from 19 countries, thereby reinforcing the reliability of the previous studies that examined the association between depression and incident CVD in a single ethnic group.^{6,7} Third, although there were no clear explanations such as social and cultural differences or genetic variation, the bidirectional associations between depression and CVD were more pronounced in Western countries than in Asian countries. As noted by Zhou et al,¹⁰ further research with a large sample population from different cultural backgrounds is needed to elucidate potential mechanisms for this issue. Fourth, according to a recent study, which has been published in *JACC: Asia*, a significant association between depression and subsequent CVD events was more pronounced in women than in men in Japan.⁶ However, in this study, which included Asians and Westerners, the gender did not modify the bidirectional associations between depression and CVD in subgroup analyses. Although being “female” may be a significant contributor to the association between depression and CVD events, it remains unclear whether the associations are stronger in women than in men. Finally, among various lifestyle factors,

the authors found that both alcohol consumption and physical activity significantly mediated a bidirectional association between depression and CVD. In particular, because these modifiable lifestyle factors were significantly involved in the association between depression and incident CVD, routine systematic screening protocol is needed for early identification of CVD events in patients with depression.

In conclusion, because it does not matter which one comes first, there is a need to develop targeted prevention and management strategies to mitigate the observed bidirectional associations between depression and CVD, regardless of gender and ethnicity. The earlier the depression is detected, the greater the impact on the prevention of incident CVD will be and vice versa. Overall, further collaborative work between cardiologists and psychiatrists would be a key solution to improve mental health and CVD outcomes.

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