

# The association between cardiovascular diseases and depressive symptoms in adults: the classic “chicken or egg” causality dilemma

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by Piwoński et al, see p. 503

For years, the association between depression and cardiovascular diseases (CVDs) in adults has been deemed as the classic “chicken or egg” causality dilemma. In fact, patients with depression often develop CVD, and vice versa. The association between depressive symptoms (DSs) and CVD is of constant great interest for researchers worldwide, but to date, causal mechanisms are not entirely understood. The pathophysiology is likely impacted by a complex interaction of social, emotional, and physiological factors.<sup>1</sup> While biological risk factors, including the sympathetic nervous system hyperactivity and impairment in hypothalamic-pituitary-adrenal function, have also been charged. In addition, some evidence also suggests the existence of gender-specific differences in biological responses to mental stress.<sup>2</sup>

Previous studies identified platelet activation linking DSs, CVD, and thrombotic events.<sup>3,4</sup> Therefore, some authors hypothesized that elevated serotonin levels could be causing platelet activation and coronary vasoconstriction.<sup>3</sup> In fact, Musselman et al<sup>4</sup> showed that levels of platelet factor 4 and other markers of platelet activation were decreased in depressed patients treated with serotonin reuptake inhibitors, suggesting a potential area of study for therapeutic intervention. In contrast, other studies suggest that depressive patients are more likely to experience lethal arrhythmias than nondepressed patients with coronary artery disease (CAD).<sup>5</sup> Anxiety has been associated with diminished heart rate variability, increased QT variability, and baroreflex dysfunction, as well as insulin resistance, hypertension, autonomic nervous system dysfunction, endothelial dysfunction, and inflammation.<sup>6,7</sup>

In line with these evidences, the American Heart Association and the European Society of Cardiology recently adopted and considered depression as a modifiable risk factor in patients

with CAD. However, despite all the efforts to promote and support mental health among patients with CVD, to date, DSs are still under-recognized and under-treated, particularly in women.<sup>8,9</sup>

In this issue, the study by Piwoński et al<sup>10</sup> combined the data set of 3 large cross-sectional studies: WOBASZ, NATPOL 2011, and WOBASZ II, which were designed to examine 3 independent samples from a Polish adult population (more than 20 000), allowing them to get very reliable results. To the best of our knowledge, this is the first analysis of psychosocial risk factors on such a large population in Poland, a population in which DSs were frequently observed. So, the authors here demonstrated an association between CVD and the severity of DSs regardless of age, marital status, education, and concurrent disorders, and therefore confirmed the higher prevalence of DSs in women with CVD: one-third of women as compared with one-fifth of men.

Prevalence of DSs increased with age, was higher in unmarried participants and individuals with a medical history of CVD and decreased with higher education. Individuals with DSs, both men and women, even those with borderline depression, had from 1.5- to more than 2-fold higher risk of either CAD or arrhythmias and from 2- to almost 4-fold higher chance of a previous stroke in their medical history.<sup>10</sup>

Major depression is more common in women than in men in all age groups until late life. Accumulating evidence suggests that depressive symptoms, and possibly clinical depression, increase or escalate during the menopausal transition (perimenopause) compared to premenopause. Emotional distress related to unpredictable hormone fluctuations and stress, body image, sexuality, infertility, and aging may result in mood swings, dysphoria, or depression. Multiple population-based studies reported an increased

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prevalence of DSs and possibly depressive illness in perimenopausal women than in premenopausal women, either with or without a history of depression.<sup>2</sup> Moreover, a potential role for estrogens in modulating the metabolism of antidepressant drugs should be taken into account.<sup>11</sup>

Furthermore, social, emotional, and physiological factors play a key role in this context and can be counteracted by physical exercise, the latter playing an outstanding role both in decreasing mortality associated with DSs and modulating cardiovascular risk factors which are notably increased in patients with DSs.<sup>12</sup>

In this view, the study by Piwoński et al<sup>10</sup> seems to pave the basis to the evidence that probably there is “no egg without a chicken.” In other words, looking at these findings, it seems reasonable to argue that DSs may chronologically precede and promote CVD, while DSs may worsen CVD outcomes. The impact of depression on healthcare is significant, as it acts as one of the primary determinants of quality of life for cardiac patients and it is tightly correlated to disability and work productivity.

In this regard, screening programs and specific tools should be adopted and promoted, even if it remains unknown whether routine screening for psychosocial risk factors contributes to reducing future cardiac events.<sup>13</sup> Multidisciplinary team-based care involving primary care providers, psychiatrists, and cardiologists, may be the key to success in promoting mind and heart wellness in the general population. Focusing on midlife women, especially when they go through the menopausal transition, should be warranted by a cooperation with menopause practitioners and gynecologists promoting lifestyle changes and physical activity.<sup>14</sup>

Further focused clinical trials could probably overcome the current gap in evidence, while additional studies are necessary to characterize the pathophysiological mechanisms, better underlining the link between depression and CVD, as well as gender differences, focusing on metabolism, both in women and men, and its specific interactions with cardiovascular outcomes.<sup>2</sup>

## ARTICLE INFORMATION

**DISCLAIMER** The opinions expressed by the author(s) are not necessarily those of the journal editors, Polish Society of Internal Medicine, or publisher.

**CONFLICT OF INTEREST** None declared.

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