REVIEW

Cardio-Psychiatric Intersections: Updated Perspectives

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Abstract: The bidirectional relationship between mental health disorders and cardiovascular disease (CVD) represents a major clinical challenge with significant impact on morbidity and mortality. Patients with coexisting psychiatric and cardiovascular conditions experience a mutually reinforcing deterioration, driven by complex neuroendocrine, autonomic, inflammatory, and metabolic mechanisms. Dysregulation of the hypothalamic–pituitary–adrenal axis promotes water and sodium retention and increases circulating free fatty acids, thereby worsening heart failure. Sympathetic overactivity, elevated catecholamines, and reduced heart rate variability contribute to arrhythmogenesis and myocardial dysfunction. This interplay creates a vicious cycle in which depression and anxiety amplify cardiovascular vulnerability, and cardiovascular disease exacerbates psychiatric symptoms. Integrating mental health evaluation into cardiovascular care is essential for optimizing outcomes, improving treatment adherence, and reducing long-term risk. Comprehensive management includes lifestyle interventions, behavioural support, metabolic monitoring, and psychotropic regimens tailored to the cardiovascular profile. Recognition of the intricate links between psychiatric and cardiovascular pathology underscores the central role of psychocardiology in modern preventive and therapeutic strategies.

Keywords*: cardiovascular disease, depression, anxiety, psychiatric drugs, drug interactions.*

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INTRODUCTION

Mental and cardiovascular health influence each other, interacting in a complex and multidirectional manner. The coexistence of cardiovascular disease and mental health disorders generates a negative bidirectional interaction that contributes to the worsening of both conditions and is associated with an unfavourable clinical prognosis. In current cardiovascular clinical practice, there is insufficient integration and a lack of a systematic framework for the screening, evaluation, communication, and appropriate management of mental health problems.

PATHOPHYSIOLOGY

At the core of the relationship between mental and cardiovascular health lies the interaction among heart failure, depression, and anxiety, which influence each other through multiple pathophysiological pathways. Activation of the hypothalamic–pituitary–adrenal

(HPA) axis leads to elevated levels of free fatty acids and increased water and sodium retention, contributing to the worsening of heart failure symptoms [1,2]. Dysregulation of the autonomic nervous system manifests as heightened catecholamine levels and reduced heart rate variability, thereby promoting arrhythmogenesis and myocardial dysfunction. In parallel, activation of the cytokine cascade induces immunosuppression, inflammation, and myocardial remodelling—processes that accelerate the decline in cardiac function [3]. Platelet activation further increases thrombotic risk, creating an additional burden for patients with atherosclerotic disease. Through the combined effects of these mechanisms—HPA activation, autonomic imbalance, inflammation, and platelet activation—a vicious cycle develops between depression and heart failure, with each condition exacerbating the severity of the other. Therefore, mental health has significant influence on cardiovascular risk [4]. Positive psychological indicators, such as optimism, life satisfaction, and emotional well-being, are associated with reduced cardiovascular risk, while adverse psychosocial factors—including social isolation, occupational stress, and financial strain—contribute to an increased risk of cardiovascular disease [5]. Psychiatric disorders such as depression, anxiety, and post-traumatic stress disorder (PTSD) are also strongly linked to higher cardiovascular morbidity. Healthcare professionals play a crucial role in recognizing these associations by identifying psychosocial and psychiatric risk factors during clinical assessment, providing education and counselling, referring vulnerable patients when needed, and supporting system-level interventions that promote mental health. In this context, psychosocial stress management and mental health promotion are essential components of integrated cardiovascular prevention, and routine screening for depression, anxiety, and PTSD should be incorporated into standard cardiovascular risk evaluation [6].

EPIDEMIOLOGY OF CARDIO-PSYCHIATRIC OVERLAP

The prevalence of depression and anxiety is significantly higher among patients with cardiovascular disease compared with the general population, in which depression occurs in approximately 15% of individuals and anxiety in 4% [7]. The highest rates are observed in patients with chronic heart failure, where depression is present in 72% of cases and anxiety in 21.5% [7]. Elevated rates are also reported in acute coronary syndrome or post–myocardial infarction, in pulmonary hypertension, in patients with implantable cardioverter–defibrillators, and in those with atrial fibrillation [7]. Depression represents an independent risk factor for mortality in patients with heart failure, irrespective of NYHA functional class, and individuals with psychiatric disorders exhibit substantially higher rates of cardiovascular morbidity and mortality compared with the general population. These findings underscore the importance of systematic mental health evaluation and management in the care of cardiac patients, with the aim of reducing risk and improving overall prognosis [8].

THERAPY CONSIDERATIONS

Identification, prevention, and management of mental health problems in patients with cardiovascular disease require the involvement of specialized psycho-cardiology teams capable of developing structured protocols for assessment and intervention. This process consists of three essential steps: screening, specialist referral, and treatment. During the screening stage, validated instruments such as PHQ-2 (Patient Health Questionnaire-2) and PHQ-9 (Patient Health Questionnaire-9) questionnaires are used to detect depressive symptoms, while GAD-2 (Generalized Anxiety Disorder-2) and GAD-7 (Generalized Anxiety Disorder-7)

assess anxiety [9]. Based on the screening results, patients requiring further evaluation are referred to psychiatric care facilities, where a comprehensive diagnosis and an optimal therapeutic plan can be established. Treatment involves individualized pharmacological and non-pharmacological options tailored to the patient's needs, ensuring an integrated and effective approach to mental health within the context of cardiovascular disease. Benzodiazepines are not recommended as first-line therapy for anxiety or depression, and their use—as well as the use of other anxiolytics, sedatives, and hypnotics—must be approached with caution, particularly in older adults and individuals with mental health disorders [10]. By contrast, antidepressants are indicated for moderate to severe anxiety and depression, but their administration requires psychiatric supervision. In patients with ventricular arrhythmias, antidepressants that prolong the QTc interval—such as tricyclics or high-dose citalopram/escitalopram—should be replaced with safer alternatives. Careful monitoring of pharmacotherapy is essential to optimize efficacy, ensure safety, and prevent clinically relevant drug interactions [11]. The clinical process begins with symptom screening. Patients with mild symptoms or those in remission may receive psychological support, whereas individuals with moderate or severe symptoms should undergo psychiatric evaluation. Decisions to continue or modify psychotropic therapy depend on factors such as weight gain, diabetes, QTc prolongation, or dyslipidemia [12]. Initiation of a new antidepressant requires consideration of symptom severity, cardiovascular comorbidities, medication-related risks, and patient preferences. In all cases, cardiovascular risk factor assessment and management, along with behavioural interventions that promote a healthy lifestyle, are recommended. Psychotropic-induced weight gain results from complex mechanisms involving interactions with multiple receptors involved in appetite regulation and metabolism. Many of these medications act as antagonists of H1 histamine receptors, serotonergic receptors (5-HT2A and 5-HT2C), and α1-adrenergic receptors. All of them increase central appetite drive, leading to increased caloric intake, while H1-receptor blockade specifically enhances carbohydrate craving. Beyond central receptor actions, psychotropic drugs may interfere with leptin- and adiponectin-regulated signalling pathways, two key hormones involved in satiety and energy metabolism. When leptin's capacity to reduce appetite is inhibited, caloric intake rises and progressive weight gain ensues [13]. Depending on their receptor affinity profiles, different medications exert distinct effects on body weight: fluoxetine is often associated with weight loss, whereas amitriptyline and mirtazapine are well known to promote weight gain. Conversely, bupropion tends to facilitate weight reduction due to its dopaminergic activity. The mechanisms underlying psychotropic-associated dyslipidemia include several complex metabolic alterations. One of the most common contributors is weight gain, particularly with second-generation antipsychotics such as clozapine and olanzapine, which carry the highest risk of inducing significant weight increase. Triglyceride and cholesterol levels may rise early in treatment—sometimes even before weight gain becomes evident—indicating the presence of direct molecular mechanisms independent of adiposity. These mechanisms include increased lipid biosynthesis driven by the overexpression of genes encoding enzymes involved in lipogenesis, as well as alterations in hepatic and peripheral lipid metabolism. In patients with schizophrenia, statin therapy reduces LDL-cholesterol, total cholesterol, and triglycerides, without affecting HDL-cholesterol levels, representing a useful strategy for managing medication-induced dyslipidemia. These mechanisms highlight the importance of informed psychotropic

selection, with careful consideration of the potential for weight gain and its broader implications for the patient's overall health.

There is a strong association between the use of psychotropic medications and the development of insulin resistance, the worsening of pre-existing insulin resistance, or the onset of diabetes mellitus (DM). Patients treated with antipsychotics or valproate derivatives have a 2.5-fold higher prevalence of DM compared with the general population. The potential mechanisms involved in antipsychotic-induced diabetes are complex and may act simultaneously through multiple pathways. A primary mechanism is insulin resistance secondary to weight gain and obesity, which are frequently associated with certain antipsychotics. In addition to this indirect effect, some antipsychotics can induce insulin resistance through direct mechanisms, independent of body weight, by interfering with intracellular insulin-signalling pathways. Moreover, antipsychotics may directly impair pancreatic β-cell function, potentially causing dysfunction or even apoptosis, thereby reducing insulin secretion and contributing to diabetes onset. In animal studies, olanzapine administration has been associated with dose-dependent increases in blood glucose, as well as alterations in fatty-acid profiles, characterized by elevated plasma saturated fatty acids and reduced monounsaturated fatty acids. Olanzapine activates hypothalamic AMPK, stimulating hepatic gluconeogenesis via sympathetic nervous system pathways. Psychotropic medications may also promote insulin resistance through epigenetic mechanisms, particularly by reducing global DNA methylation. The use of these medications is further associated with dose-dependent increases in blood pressure, mediated by direct effects on neurotransmitter systems. When using norepinephrine reuptake inhibitors, hypertension may occur from selective blockade of the norepinephrine transporter in peripheral sympathetic neurons. First-generation antipsychotics, such as chlorpromazine and haloperidol, may contribute to elevated blood pressure through anticholinergic effects.

RELEVANT DRUG INTERACTIONS

The concomitant use of fluoxetine and warfarin increases anticoagulant activity—and therefore bleeding risk—through inhibition of warfarin metabolism via CYP2C9, making close monitoring for signs and symptoms of bleeding essential. Co-administration of SSRIs or SNRIs with antiplatelet agents or anticoagulants also increases hemorrhagic risk by inhibiting serotonin reuptake in platelets, requiring similar clinical vigilance. Combining an SSRI with a beta-blocker may increase beta-blocker plasma concentrations through CYP2D6 inhibition; therefore, monitoring of heart rate and dose adjustment when needed is recommended. The combination of SSRIs, TCAs, or trazodone with amiodarone or class IA antiarrhythmics can increase the risk of cardiotoxicity through additive QT-interval prolongation. For antipsychotics with QT-prolonging potential, the lowest effective dose should be used, concomitant medications with similar risks must be reviewed; drug–drug interactions should be evaluated, careful monitoring performed when initiating any new therapy, electrolyte disturbances corrected and updated resources such as crediblemeds.org consulted. Reversible factors that may prolong the QT interval include bradycardia, hypothyroidism, starvation or eating disorders, alcohol or substance misuse, and myocardial ischemia. Irreversible factors include heart failure, ventricular hypertrophy, recently converted atrial fibrillation, hepatic or renal impairment, female sex, and age over 65 years. If the QTc interval exceeds 470 ms, treatment initiation is not recommended without strict risk–benefit assessment conducted by a multidisciplinary Psychiatry–Cardiology team. Most patients remain asymptomatic, but symptoms suggestive of torsades de pointes include palpitations, dizziness, and syncopal

episodes, which may progress to cardiopulmonary arrest. Electrocardiographic monitoring with a 12-lead ECG is mandatory at baseline and at 1 week, 6 weeks, and 12 weeks after treatment initiation, with additional assessments if QT prolongation occurs. Biochemical evaluation should include serum potassium, calcium, and magnesium levels, given their role in myocardial electrical stability. Overall, most antipsychotics carry a relatively low risk of clinically significant QT prolongation; however, identification and management of predisposing factors remain essential for minimizing risk in the context of psychotropic therapy [14].

CONCLUSIONS

Depression, anxiety, and other psychiatric disorders significantly increase cardiovascular morbidity and mortality, while cardiovascular disease itself heightens the risk of mental health deterioration through neurohormonal, inflammatory, and autonomic mechanisms. Despite this well-established bidirectional relationship, mental health remains under-recognized and under-managed in routine cardiovascular practice. Early identification through systematic screening, timely referral, and integrated treatment delivered by coordinated psycho-cardiology teams are essential to improving outcomes. Psychotropic therapies—while often necessary—require careful selection and vigilant monitoring due to their metabolic effects, potential to exacerbate cardiovascular risk factors, and clinically relevant drug interactions, including QT prolongation, dyslipidemia, weight gain, insulin resistance, and increased bleeding risk. Optimizing care for these patients requires a multidisciplinary approach that addresses both psychiatric and cardiovascular needs, corrects modifiable risk factors, and ensures the safe use of psychotropic medications. Integrating mental health evaluation into standard cardiovascular care pathways is therefore critical to improving prognosis and enhancing overall quality of life for this vulnerable population.

Author Contributions

M.M.P. conceived the original draft preparation. M.M.P., L.G.G., and C.C.D. were responsible for conception and design of the review. M.M.P., L.G.G., and C.C.D. were responsible for the data acquisition, collection and assembly of the articles/published data, and their inclusion and interpretation in this review. All authors contributed to the critical revision of the manuscript for valuable intellectual content. All authors have read and agreed with the final version of the manuscript.

Conflict of interest

The authors declare no conflict of interest regarding this article.

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