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Research Article

Therapeutic Approach to Depression and Cardiovascular Diseases in a Hospital Setting at the Mustapha University Hospital Center of Algiers in Algeria

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Abstract

Introduction: Ischemic heart disease and depression are inseparable conditions, with increasing incidence and prevalence with the aging of the population. When combined, they reduce quality of life, and require long-term care and exorbitant cost for care.

Activation of stress pathways has often been indexed as a neurochemical mechanism that links depression and ischemic heart disease. Anxiety resulting from cardiac involvement, the complexity of treatment and repeated hospitalizations facilitate the onset of depressive syndrome. Untreated depression can be a risk factor for heart disease over time.

Early detection and treatment of depression is recommended in patients with ischemic heart disease.

Methods: We conducted a case study reported in a cardiology department of the University Hospital of Algiers, as part of the consultations of the liaison psychiatry. We included patients regardless of age, sex, origin, hospitalized for cardiovascular pathologies. The parameters studied were sociodemographic data: age, sex, marital status, cardiovascular risk factors as well as clinical signs, diagnosis of hospitalization and the existence of anxiety and/or depression. Our comprehensive psychiatric assessments with psychiatric history, mental examination with structured interviews according to DSM-5 and also the passing of questionnaires: Beck Depression Inventory-(IDB-13) «PHQ-9: Patient Heath Questionnaire» to inpatients in the cardiology department as mentioned above.

Results: Of the two selected cases followed for cardiovascular pathologies mainly coronary syndrome on the one hand and myocardial infarction on the other hand in the cardiology department of the University Hospital of Algiers. We have seen that depression would explain this cardiovascular event although this subject, young woman of 25 years mentioned in case N ° 1 and without cardiovascular risk factors identified on the one hand and on the other hand with all the cardiovascular risks of making a myocardial infarction despite effective revascularization. For the 2nd case of this 42-year-old man, the management was longer and complicated by a recurrent, resistant major depression. Treatment of comorbidity has made it possible to eliminate the risk of mortality through the intervention of psychiatry in conjunction with the appropriate treatment of this depression.

Conclusion: At the end of this study we can conclude that depression and cardiovascular disease are inseparable and linked to each other. The follow-up must be multidisciplinary, early detection of depression using scales such as the PHQ-9 in cardiac patients could reduce the risk of occurrence of depression but also its complications, reduce the cost and duration of hospitalization this promoting the survival and well-being of our patients. SSRIs and particularly Sertraline, Citalopram and Escitalopram are the recommended first-line pharmacological treatment for the management of depression in coronary patients. Non-pharmacological treatment involves cognitive-behavioral psychotherapy and cardiovascular rehabilitation or even repetitive transcranial magnetic stimulation (rTMS) in some severe or resistant depressions.

Keywords: Ischemic Heart Disease; Depression; Cardiovascular Diseases

General Introduction

Ischemic heart disease and depression are conditions with increasing incidence and prevalence with the aging of the population [1]. These pathological disorders impair and reduce quality of life, increase morbidity and mortality, and justify long-term, expensive care. They represent a heavy financial burden for society [2].

Cardiovascular diseases as a whole and depressive syndromes appear to be intimately linked [3]. A patient's awareness of the severity of cardiac involvement and the feeling of imminent death have an impact on their mood and emotional state [4]. Thus, the anxiety generated by cardiac involvement, the difficulties and complexity of treatment, and repeated hospitalizations facilitate the onset of depressive syndrome [5].

Depressive symptomatology (psychomotor slowdown, asthenia, indifference) has repercussions on the lifestyle of patients, in particular the anarchic intake of cardiac drugs including cholesterol drugs, the follow-up of a low-fat diet, the practice of physical exercise and the reduction of tobacco**.**

Depression is one of the important risk factors for cardiovascular disease independently of commonly known risk factors such as high blood pressure, diabetes, smoking etc. with a relative risk of 1.64 of developing coronary artery disease in a patient with major depressive disorder [6].

Depression would promote the onset of coronary heart disease and increase cardiac mortality. According to the study by Empana., *et al.* [7]: «depression appears to be a risk factor for cardiovascular disease through decreased heart rate variability, endothelial dysfunction and increased platelet aggregation». The severity of depression is proportional to the risk of developing coronary artery disease [8].

Several studies have shown a higher frequency of major depressive illness in patients who have suffered a major cardiac event such as myocardial infarction with prevalence's varying between 35 and 74% depending on the studies [9-16].

A better understanding of common etiological pathways would be useful for appropriate management of depression during ischemic heart disease.

The occurrence of depression during heart disease is always a factor of poor prognosis, promoting poor adherence to treatment, accelerating the progression of heart disease, facilitating complications, and causing excess mortality regardless of the severity of coronary artery disease [17].

Depression too often goes unnoticed, because significant anxiety, reactive sadness, after an illness as serious as acute coronary syndrome, are too often considered understandable, justified reactions after a painful and distressing event [18]. The most common clinical aspects are represented by minor forms of depression without obvious sadness often masked by somatic symptoms: irritability, asthenia (increasing fatigability), atypical precordialgia, palpitation discomfort etc. Sometimes, there appears an indifference to cardiac symptoms or, on the contrary, a real psychological suffering towards the slightest manifestations of the underlying cardiac pathology and its treatment with difficulties in compliance with treatment [19]. These signs should suggest the presence of depression and look for other symptoms, such as a loss of vital momentum, anhedonia (loss of the ability to experience pleasure), or a loss of hope regarding the evolution of cardiovascular status, or suicidal ideation to accelerate the process to shorten their suffering. Early detection is important for early management.

Possible mechanisms by which depression can lead to cardiac events*

Many lifestyle behavioral factors have long been known to play a role in increasing the risk of coronary heart disease in depressed patients. The psychological stress experienced by people with Major Depressive Disorder (MDD) can also cause dysregulation of the sympathetic nervous system and the hypothalamic-pituitary-adrenal axis (HHS) [20,21]. This has many deleterious effects, including the development of hypertension, left ventricular hypertrophy [22], coronary vasoconstriction, endothelial dysfunction [23-25], platelet activation, and production of pro-inflammatory cytokines [26,27]. A possible consequence of this is an increased risk of ventricular arrhythmias [28] and myocardial infarction [29].

Mechanisms by which depression can lead to increased heart risk. This is multifactorial, including sympathetic activation, hypothalamic-pituitary activation, endothelial dysfunction, activation of platelet aggregation, pro-inflammatory cytokines, development of atherosclerosis, and vascular and cardiac arrhythmias.

Behavioural factors and lifestyle

It is well known that patients with MDD have many lifestyle-related behavioral factors that can increase their risk of developing coronary artery disease [30]. These include increased smoking, alcohol consumption, physical inactivity associated with lack of physical activity and obesity [31]. As expected for other disorders, major depression predicts poor adherence to medication [32], lifestyle [33-35] and rehabilitation programs [36] in coronary heart patients. In fact, cardiovascular rehabilitation failure rates have been shown to be approximately 44% vs. 29% in the non-depressed group [37]. Therefore, depressed coronary patients may be demotivated and adhere to cardiovascular rehabilitation programs. MDD also makes lifestyle changes less likely after a major cardiac event to reduce classic risk factors for coronary heart disease. This is seen in association with smoking less frequently and more strongly in people with MDD [38].

Disruption of the autonomic nervous system

It has long been known that «stress» is associated with heart disease [39,40]. Stressful events such as terrorist attacks [41], natural disasters [42] and even high-stakes knockout football matches are positively associated with an increase in acute cardiovascular events [43]. Psychological stress is one of many cognitive symptoms experienced by people with MDD. Laboratory psychological stress tests have been shown to activate sympathetic production in non-cardiac patients [44]. The sympathetic nervous system is preferentially activated by such psychological stress [45]. Animal models and clinical settings [28,46] have demonstrated the importance of cardiac sympathetic nerve fiber activation to disrupt heart rhythm, resulting in ventricular arrhythmias, decreased perfusion [47] and left ventricular hypertrophy [22,47]. increases the risk of myocardial infarction (MI) and sudden death [25]. Depressed patients with coronary artery disease have been shown to have elevated resting heart rates, which may also be due to sympathetic hyperactivity in these patients [48].

Disorders of the hypothalamic-pituitary-adrenal axis

Major depression is associated with stress-induced activation of the HPA axis [49]. High levels of cortisol have been repeatedly found in patients with MDD [50]. This hypercortisolism leads to an increased risk of diseases such as metabolic syndrome, including impaired glucose tolerance, hyperlipidemia, and increased visceral fat mass. This metabolic syndrome has been shown to increase not only the risk of cardiovascular disease and diabetes, but also sympathetic activation. Platelets, inflammation, and autoimmune mechanisms.

Stress and anxiety, two common symptoms of major depression, can contribute to atherosclerosis. Increased platelet activation and endothelial dysfunction have been implicated as potential pathophysiological pathways linking MDD and CHD. Prolonged psychological stress, common in people with MDD, has been shown to lead to long-term endothelial dysfunction [24,25]. This endothelial dysfunction has been shown to be one of the first signs of future cardiovascular deterioration. In fact, oxidative stress itself has been reported in many psychiatric disorders. Inflammatory pathways have been proposed as one of the etiological pathways responsible for MDD, increasing the risk of coronary heart disease via atherosclerosis. Patients with depression have elevated levels of inflammatory markers such as C-reactive protein (CRP) and pro-inflammatory cytokines such as interleukins 1, 2, 6 and tumor necrosis factor. Many of these inflammatory markers are consistently associated with poor cardiovascular outcomes, and CRP can predict MI.

Potential biological mechanisms

- Alterations of the autonomic nervous system, reduction of vagal tone;
- Hyperactivity of the sympathetic system and hypothalamic-pituitary-adrenal axis;

- Activation, platelet hyper-aggregability, thrombogenic tendency;
- Increased levels of catecholamines and serotonin;
- Chronic inflammation, dysimmunity;
- Ischemia induced by mental stresses;
- Reduction of membrane contents of polyunsaturated fatty acids;
- Cardiotoxic effects of tricyclic antidepressants.

Behavioural mechanisms

- Absence of exercise;
- Food gaps;
- Medication non-adherence;
- Social isolation and sedentary lifestyle;
- Smoking, alcoholism, various addictions.

It should be noted that the appearance of depressive symptoms is not correlated with the «objective» severity of cardiovascular disease. Rather, depression appears to depend on the person's degree of vulnerability and the quality of support and empathy they find around them, including caregivers and family.

The occurrence of depression after myocardial infarction is an event fraught with consequences, which should not be neglected. Anxiolytics of the benzodiazepine family can reduce anxiety disorders, but they are insufficient to treat even minor depressive syndrome, hence the interest of an antidepressant that requires the intervention of a psychiatric specialist, because some may be contraindicated or even dangerous.

Diagram illustrating the Behavioural Mechanisms (Diagram-1).

Diagram 1

Associations between adverse psychological factors, such as depression, and cardiovascular disease (CVD) are well established. However, a growing body of evidence suggests that positive psychological well-being (hereinafter, psychological well-being) – which includes positive thoughts and feelings such as purpose in life, optimism and happiness – has its own independent associations with a lower risk of CVD and may promote cardiovascular health (CVH).

Diagram illustrating the Synergy between Biological Mechanisms and Behavioral Mechanisms.

Diagram 2

Psychosocial factors can affect all biological steps leading to atherothrombosis, as shown by the measurement of circulating biomarkers of endothelial dysfunction in patients with DD. Endothelial dysfunction plays a primary role in the pathophysiology of coronary artery disease. In fact, acute non-obstructive coronary events such as MI with non-obstructive coronary arteries (MINOCA) and Takotsubo cardiomyopathy are more common in women than men, highlighting the importance of these processes. In addition, the immune and hemostatic systems could be negative. Affected by chronic stress-related adaptations in the activity of the hypothalamic-pituitary-adrenal axis and autonomic nervous system, leading to increased platelet inflammation, coagulation, and activation.

Scheme-1 (+) Scheme-2 (+) Scheme-3

However, hormonal status alone is not sufficient to explain the different prevalence of DD between women and men. The higher frequency among families highlights the potential role, and interaction, between genetic predisposition and psychological adjustment, particularly in daily activities, where women are more vulnerable to depression.

Diagram 3

Clinical cases

Clinical case N°1

Miss F aged 25 admitted to the intensive care unit of cardiology for acute coronary syndrome with ST segment shifts successfully treated by the care team after percutaneous revascularization by angioplasty?

The patient always presents with persistent asthenia with somatic complaints such as: rebellious headaches, atypical precordialgia, cervical and/or thoracic constrictions, hypertensive or hypotensive flare-ups, malaise, dizziness, and tinnitus. During hospitalization, there is prostration, invincible sadness. The patient isolates herself, remains indifferent to the encouragement, support of doctors and her family. She is convinced of the uselessness of any treatment, expresses the desire to end it and wishes for his imminent death. Miss F, dejected, no longer communicates with the staff, wanting the care stopped, and remains in her bed. The patient refuses to see her family and especially her fiancé and expresses no desire to heal or leave the hospital. Mademoiselle F ruminates on dark ideas, incurability, damnation, and blocked future.

The somatic state deteriorates due to food refusal and clinophilia with the appearance of dehydration and ionic disorders as well as functional renal failure. The patient is mute, opponent with therapeutic refusal contrasting with a good cardiac condition which finally motivated the care team to seek psychiatric advice urgently.

The psychiatrist traces the history of the depressive illness and finds that the onset of the disorders goes back well before the acute coronary syndrome that only aggravated the depression, which was due to conflicts with her fiancé. According to the patient, he wanted to break up with her to get together with his younger sister. These conflicts were accentuated when her sister and parents did not support her, approving the proposal to marry her sister, and that in turn she had to accept their feelings, and put an end to her own feelings. This situation caused great emotional distress followed by his heart attack.

Hospitalization has curbed the vital emergency allowing to put the finger on this depression remained in the background for a long time. The psychiatrist prescribed a benzodiazepine Lorazepam®, an antidepressant Sertraline® and supportive psychotherapy, with no apparent benefit for several weeks. It was only after hospitalization in a psychiatric setting with prolonged cognitive-behavioral psychotherapy that his psychological state improved.

Clinical case N°2

Mr. D., 42 years old, is hospitalized in the intensive care unit of cardiology for an intense chest pain syndrome with several risk factors including heavy smoking (more than a pack of cigarettes a day since age 20), dyslipidemia with LDL-C at 2.40 g/L and neglected moderate hypertension. Upon entry to the coronary intensive care unit, sinus tachycardia at 110 b/min, BP at 100/70 mm Hg was observed. The electrical plot shows a major elevation of ST/T and small Q waves from V2 to V6. In the territory of the anterior interventricular artery (VIA). Mr. D. is treated properly but remains anxious, refuses any effort, thinking that a recurrence is inevitable. This patient, single, with a poor family environment, and professional worries.

Gradually, he expresses his desire to no longer fight, expressing his anxieties, his desire to disappear. The cardiology condition is excellent, but day by day, despite the injunctions of the care team, an indifference to the treatment that he follows only partially, is taking hold. He no longer sleeps, has no appetite, and only talks about his imminent end. The patient expresses disgust with existence and suicidal tendency. He demands an end to medical care, remains prostrate in his room, refuses any contact with members of his family or entourage.

Mr. D. is entrusted to a psychiatrist who prescribes treatment with the benzodiazepines Prazepam®, an antidepressant Fluoxetine®, and undertakes cognitive-behavioral psychotherapy. The convalescence of this myocardial infarction, after effective revascularization was very prolonged, the evolution being

complicated by this depressive syndrome. The patient remains very anxious and his condition requires very regular and prolonged medical, cardiology and psychiatric supervision.

Discussion

In the 1st case, we saw how depression would have led to a cardiovascular accident, despite the young age of the patient and the absence of cardiovascular risk factors. In the 2nd case, we saw the patient who had all the risks of doing a MI and that despite effective revascularization, his management was longer and complicated by depression, which increased comorbidity and mortality.

In summary, various case-control studies suggest, without proving it, that depression increases cardiovascular risk and that coronary events can have a significant psychological impact and facilitate the onset of a depressive syndrome which in turn will increase the morbidity and mortality of coronary artery patients.

The fact to emphasize is therefore the difficulty of treating depressive syndromes in cardiac and coronary patients in particular. Treatment should be conducted by well-experienced psychiatrists collaborating with cardiologists or internists, to initiate treatment that will have better tolerance on cardiac activity.

The major elements of management are the conventional treatment of secondary prevention of infarction, which should not be modified or interrupted, with antidepressants. Note that tricyclic antidepressants are very active, but they have cardiovascular toxicity due to their side effects, while these are low with selective serotonin reuptake inhibitors (SSRIs) such as: Citalopram, Escitalopram, Fluoxetine, Paroxetine, Sertraline, Fluvoxamine. SSRIs even have cardioprotective effects because of their positive actions on vagal tone and baroreflex, and as antiplatelet agents, thus they restore sinus rhythm variability.

The contribution of cognitive-behavioral psychotherapy, as well as regular follow-up of these patients with exercise rehabilitation in specialized settings such as in the Cardiovascular Rehabilitation Centres (CRCV), Psychosomatic and Musculoskeletal Rehabilitation Centres (PMS) or the offer of certain short-stay and even outpatient inpatient cardiovascular rehabilitation programs (PRCCs) remain essential for the gradual recovery of these patients in some countries in Europe. and North America. These types of PRCC programs, whether inpatient or outpatient, require an adapted technical table with above all a transdisciplinary team where patients meet different interlocutors for an optimal treatment plan during their stay, these are professionals such as:

- An internist and a cardiologist
- A psychiatrist, psychotherapist, and psychopharmacology specialist
- A doctor specialized in clinical pharmacology
- Nurses and orderlies in the unit
- Specialized physiotherapists
- A dietician or nutritionist
- An occupational therapist
- Clinical nurse specialists in various fields (e.g. Tobacco, diabetes, etc.)
- A psychologist specializing in cognitive behavioural therapy (cbt)
- A hypnotherapist
- A reflexologist-masseur
- An art therapist
- A recreation therapist
- Etc.

Recommendations

Screening for depressive symptoms in patients with coronary artery disease should be systematic for early and appropriate management.

The HQP is a depression screening instrument that is easy for most unassisted patients to complete in less than 5 minutes. It provides two questions (PHQ-2) that are recommended for identifying depressed patients. If the answer is «yes» to either or both questions, it is recommended to ask all 9 HQP items (HQP-9). It gives both a provisional diagnosis of depression and a severity score that can be used for treatment selection and monitoring. PHQ-9 has been shown to have reasonable sensitivity and specificity for patients with coronary artery disease. For patients with mild symptoms, follow-up at a subsequent visit is advised. In patients with high depression scores, a physician or nurse should review the responses with the patient. Other assessment tools and their use for research purposes have been discussed elsewhere. Any of these tools can provide a useful initial assessment, but it must be recognized that depressive symptoms may present in the context of a complex medical condition. This current scientific opinion builds on the approach developed by the MacArthur Initiative on Depression and Primary Care, which provides empirical tools and procedures for the recognition and treatment of depression in primary care settings for depression screening and care guidelines

for cardiologists. However, patients whose screening scores indicate a high probability of depression (PHQ-9 score of 10 or higher) should be referred for a more complete clinical evaluation by a qualified professional to assess and determine an appropriate individualized treatment plan. Patients who meet the threshold for a more complete clinical evaluation should be evaluated for the presence of other mental disorders (e.g., anxiety) that have also been associated with adverse outcomes in cardiac patients.

We recommend for the biopsychosocial management of patients with depression with Coronary Syndrome: antidepressant treatment from the family of Selective Serotonin Reuptake Inhibitors (SSRIs), cognitive behavioral therapy and adapted physical activity and exercise and cardiovascular rehabilitation.

Selective serotonin reuptake inhibitor antidepressants (SSRIs) are safe for patients with coronary artery disease and effective for severe or recurrent depression. Sertraline and citalopram are the first-line antidepressants for patients with coronary artery disease. They have cardiovascular safety in depressed patients with angina pectoris or recent myocardial infarction, they reduce the risk of cardiac events and improve both survival and mood. Patients treated with an SSRI have a 42% reduction in recurrent deaths or MIs compared to depressed patients not receiving an antidepressant. Antidepressant treatment improves mood and quality of life, but also improves treatment adherence in patients after AMI. Tricyclic antidepressants and monoamine oxidase inhibitors are, however, contraindicated for many patients with heart disease because of their cardiotoxic side effects. After introduction of antidepressant therapy, monitoring of adverse treatment effects, suicidal risk, adherence to treatment should be monitored and potential drug interactions should be monitored.

Cognitive behavioral therapy may be beneficial for depression in heart patients. This may be an alternative for heart patients who do not tolerate antidepressants or who may prefer a non-pharmacological or counseling approach to treatment. In addition, many patients with moderate to severe depression may respond better to the combination of an antidepressant and psychotherapy than to either treatment alone. Referral to a qualified psychotherapist is necessary. At least 12 to 16 sessions of cognitive behavioural therapy over 12 weeks have been recommended for remission of moderate to severe depression.

Aerobic exercise and cardiovascular rehabilitation can reduce depressive symptoms in addition to improving cardiovascular fitness. While depression can be a barrier to participation in cardiac rehabilitation and exercise programs, cardiologists can help depressed patients overcome this barrier by offering encouragement and follow-up contacts. They should also seek the help of the patient's entourage to improve adherence. Exercise prescription should be evaluated individually based on the individual's heart condition and exercise capacity. Adapted and assisted exercise in a cardiovascular rehabilitation unit can be considered the first-line treatment plan for depression in patients with acute coronary syndrome.

The rTMS used in addition to drug therapy can also be used in resistant depression associated with coronary heart disease. The antidepressant efficacy of rTMS was evaluated at follow-up in patients with unipolar depression, less severe MDD episodes, treatment-resistant depression, non-psychotic depression, and those treated with concomitant antidepressants with rTMS.

The multidisciplinary and biopsychosocial approach should be considered for the best management of depression in patients with cardiovascular disease. This approach involves the cardiologist, psychotherapist, liaison psychiatrist, and other specialists in physical medicine and cardiovascular rehabilitation.

Implications for treatment

If major depression develops in a patient who has had a major cardiac event, depressive symptoms are expected to persist 4 months after discharge. Although it is important to recognize depression in coronary heart disease, most cases go undiagnosed and untreated.

Conclusion

Depression is often unknown by doctors and the family circle of patients suffering from coronary heart disease. It is too often considered normal or even banal, that a subject, whose life is threatened by a serious heart disease, sinks into discouragement accompanied by invincible sadness. In fact, a depressive tendency should not be considered a normal reaction to an acute coronary event and should be treated seriously as much as coronary artery disease.

Screening for depression in patients with coronary artery disease should be systematic for optimal management. The HQP scale is an excellent quick, convenient, and easy-to-use tool for early detection for referral to a psychiatrist for early management. Antidepressants from the SSRI family including

sertraline, citalopram and escitalopram are the first-line treatment for coronary patients. This pharmacological management can be supplemented by CBT-type psychotherapy and cardiovascular rehabilitation.

Treatment of depression in a patient with coronary syndrome seems to improve cardiovascular prognosis, because recovery from depression in these patients leads to the disappearance of psychomotor slowdown, increases motivation and adherence to treatment with good complacency to the cardiovascular rehabilitation program and CBT [.....].

Improving the quality of life and prognosis of depressed coronary patients likely combines biopsychosocial treatment combining cognitive-behavioural and drug treatment, and cardiovascular rehabilitation after infarction.

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