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REVIEW ARTICLE

Psychosocial Risk Factors and Ischemic Heart Disease: A New Perspective

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ARTICLE HISTORY

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Abstract: ***Background*:** Cardiovascular disease is the most common cause of morbidity and mortality worldwide, with ischemic heart disease (IHD) accounting for roughly 50% of these events in industrialized nations.

In recent years, the relative importance of IHD in less industrialized countries is also rising at an alarming and steadily-increasing rate.

***Objectives*:** Many experimental, observational and epidemiological studies have demonstrated the importance of psychosocial risk factors in the development and clinical manifestations of IHD. They act both indirectly, associated with an unhealthy lifestyle; and directly, through the activation of inflammatory cascades and the sympathetic nervous system. They also cluster with biological risk factors to increase the incidence and clinical manifestations of IHD. From these assumptions, there emerges the potential that an integrated approach that incorporates psychological therapy in various forms might reduce IHD patients' symptoms and maladaptive behaviors, and thereby enhance their prognosis.

***Methods*:** To date, three psychotherapeutic approaches have been utilized within cardiac psychology practice: (1) cognitive-behavioral psychotherapy; (2) psychodynamic psychotherapy; and (3) ontopsychological psychotherapy. The current article briefly describes these three approaches and how their use might enhance the care of IHD patients.

***Results*:** A range of psychological characteristics influence the development, course and management of cardiac patients' IHD. Among others, these include patients' emotions, attitudes, behaviors, relationships, and stressors. State-of- the-art literature suggests that psychological interventions should be considered in much the same way as medical interventions, in terms of their relevance to both patient management and outcomes.

***Conclusion*:** For this reason, it is essential that professional psychological and psychotherapeutic support be rendered available to cardiology patients, as a means to enhance both the effectiveness and efficiency of care.

Keywords: Cardiac psychology, cognitive-behavioral psychotherapy, ischemic heart disease, ontopsychology, psychodynamic psychotherapy, psychosocial risk factors.

1. INTRODUCTION

Cardiovascular disease (CVD) is the most common source of morbidity and mortality worldwide, with ischemic heart disease (IHD) accounting for roughly 50% of CVD events in industrialized nations.

In recent years, the relative importance of IHD in less-industrialized countries is also rising, and at an alarming and steadily-increasing rate [1, 2]. Indeed, despite advances in its prevention and management [2], IHD still caused 23% of all deaths [3] in Europe in 2015, and resulted in over 165 million disability-adjusted life-years (DALYs) lost in 2012 (accounting for 6% of all disability claims) [4, 5]. Moreover, IHD patients are living longer, given the effectiveness of primary and secondary prevention and management of acute manifestations, meaning that an enlarging cohort of seniors now deals with IHD and its late complications. As such, the independent importance of previously-underestimated factors, like a patient's psycho-social status, is being recognized, particularly given their overlap and interactions with other IHD risk factors, like lifestyle habits, and pathogenic processes, like inflammation; these factors appearing to intertwine in very complex ways [1].

2. PSYCHOSOCIAL RISK FACTORS AND ISCHEMIC HEART DISEASE

Since the mid-20th century, a huge body of scientific research has accumulated evaluating the relationship between

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psychosocial risk factors and IHD. Among these studies, animal experimentation has provided significant insights into the relationship between the heart and brain. Though how generalizable these results of animal experiments are to humans has not yet been documented, they nonetheless offer compelling evidence of an association between psychosocial factors and coronary atherosclerosis [6-9].

Similarly, extensive research has been conducted on humans in laboratories, wherein the physiological responses to mental stress, after a person is exposed to some negative stimulus, have been measured and analyzed. Amongst others, examples of mental stress include individual's being asked to do arithmetic in their head, name colors, make a public speech, and recall an upsetting event [6]. Whilst such stress responses are induced externally (*versus* in a more natural home or work setting), performing such experiments in a laboratory setting is highly advantageous, since it permits the simultaneous measurement of blood biomarkers, heart and brain imaging, vital signs and other measurements of hemodynamics and vascular status, and assessments of heart function, like electro- and echocardiography. An additional advantage is that many potential confounders can be removed since patients typically serve their own control when the physiology of being in a state of stress versus state of rest is compared.

Increased reactivity has been linked to negative cardiac outcomes. On the other hand, blunted reactivity also appears to portend negative cardiac events [10]. In addition, poor recovery from stress (defined as sustained cardiovascular activation above baseline levels during a post-task period) is predictive of negative cardiovascular outcomes, including elevated blood pressure and an increased rate of negative cardiovascular events [10].

Though most published data on psychological risk factors and heart disease in humans have been collected in observational studies (ecological, cross-sectional, or longitudinal) - and therefore, cannot prove causality and are subject to confounding - they generally are translatable to humans in real-life circumstances [6]. Globally, these studies provide evidence that acute stress [11-13], chronic stress, post-traumatic stress disorder [14], work-related stress [15, 16], marital stress [17, 18], low socioeconomic status [19], mood disorders including especially depression [20-25], and anxiety [26], are strongly associated with the development of ischemic heart disease in general, and of atherosclerosis in particular. More controversial is the role of personality traits, particularly anger and hostility, in the development of IHD [27].

One of the most influential and sizable studies to evaluate the relationship between combined stress factors and coronary artery disease (CAD) has been the INTERHEART study [28]. In this international case-control study, data were collected in 52 countries around the world. Amongst the subjects were 11,119 patients with at least one prior myocardial infarction (MI) and 13,648 controls. Per protocol, subjects were briefly assessed for depression, locus of control, perceived stress at home and/or work, financial stress, and negative life events, with general stress defined as the summation of stress at home and work. The investigators found that permanent general stress was statistically linked to a two-fold increase in the odds of MI, when adjusted for subjects' geographic region, age, gender, and smoking history. This two-fold increase also was consistent across regions, ethnic groups and the two genders. In addition, each individual stress factor was significantly associated with an increased risk of myocardial infarction (MI). Assuming a reversible, cause-and-effect relationship, the authors predicted that eliminating such sources of stress would reduce the incidence of MI by approximately a third.

All psychosocial risk factors act both indirectly, and directly. They act indirectly through an individual's behaviors: for example, how sedentary they are; how much sleep they get; how healthy or unhealthy their diet is; whether they smoke; and how adherent versus non-adherent they are with their medications and other therapy. They act directly by activating inflammatory cascades and the sympathetic nervous system.

Beyond depression's effect on lifestyle, numerous biologically-feasible explanations exist to justify this increased risk of IHD in those who are depressed. Depression has been linked to both the hypothalamic-pituitary-adrenal axis and sympathoadrenal dysfunction. These, in turn, might be secondary to the persistent negative thinking that characterizes depression, or to whatever adverse life events have triggered or contributed to the person's depression. These abnormalities may further lead to circadian rhythm disruption, which may elevate patients' blood pressure, heart rate, blood sugar and serum lipid levels [29]. Autonomic dysregulation, reflected by reduced 24-hour heart rate variability, also may occur [30]. Depressed patients also may have hypercoagulable blood, associated with hyperactive platelets; endothelial dysfunction, exhibited as the impaired ability to vasodilate under certain conditions [31]; and increased inflammation, indicated by increases in various inflammatory markers [32, 33].

Combined with this is that such exposures to stress often are interconnected; for example, in addition to financial stress, individuals from low socioeconomic backgrounds are more likely to experience repeated exposure to trauma and family instability. In addition, psychosocial risk factors may cluster with biological risk factors, greatly increasing IHD risk, as they can reciprocally strengthen themselves.

Besides this, depression is also a major contributor to medication non-adherence [34]. From these assumptions, there emerges the possibility that an integrated approach that incorporates psychological therapy, in various forms, might reduce symptoms and maladaptive behaviors, and thereby enhance IHD patients' prognosis. As such, the multimodal integration of cardiologists and psychologists in IHD diagnosis and treatment has become a new frontier for cardiac patient management [35].

3. PSYCHOTHERAPY IN PATIENTS WITH ISCHEMIC HEART DISEASE

Psychotherapy, combined with ancillary psychological interventions, has the potential to augment the outlook and

outcomes of IHD patients, providing benefits which integrate and complement those provided by more mundane interventions - like pills, surgery, devices, and stem cells. Biondi Zoccai *et al*. recently conducted an updated review of the literature on this topic [36], synthesizing four systematic reviews and 24 randomized trials. Their synthesis suggests that, in the current era of modern multi-faceted cardiovascular care, psychotherapy and ancillary psychological interventions may indeed improve the prognosis of IHD patients, particularly if several unsettled issues remain [36].

Currently, three psychotherapeutic approaches are being utilized in the field of Cardiac Psychology:

(1) Cognitive-behavioral psychotherapy; (2) psychodynamic psychotherapy; and (3) ontopsychological psychotherapy. The most widely adopted of these, worldwide, is the first.

Cognitive behavioral psychotherapy (CBT) encompasses a range of therapies, with the patient working collaboratively with a therapist using a shared formulation to achieve specific treatment goals. Such goals might include recognizing the impact of behavioral and/or thinking patterns on feeling states and encouraging alternative cognitive and/or behavioral coping skills to reduce the severity of target symptoms and issues [37]. This treatment approach, pioneered by Beck [38] and Ellis [39], has, as its core premise, the belief that maladaptive thinking feeds emotional distress and behavioral problems. Synthetically, the main methodological approaches used in CBT are:

1) Cognitive restructuring, which entails identifying certain schemas and automatic thoughts and restructuring them to be more realistic and adaptive [40];
2) Behavioral activation, which entails assigning and scheduling weekly activities, so patients resume discontinued activities and engage in new ones;
3) Problem-solving techniques, which increase patients' ability to make choices, when they must face difficult situations or make everyday decisions that have become overwhelming;
4) Positive self-statements, which serve to boost patient's sense of self-esteem;
5) Distraction and refocusing, which patients are taught to employ when they have difficulty concentrating or are overwhelmed with emotion;
6) Relaxation therapy [41], which is a well-established component of psychological therapy, utilized to help alleviate patients' psychological distress, including patients dealing with chronic illness.

Among the various relaxation techniques available are procedures standardized and validated by Bernstein and Borkovic for progressive muscle relaxation (PMR), based upon a classic muscle relaxation program developed by Jacobson. Other basic relaxation strategies include imagery exercises [37].

Other more complex approaches developed from the original CBT are: mindfulness-based cognitive therapy [MBCT], metacognitive therapy (MCT), and acceptance and commitment therapy [ACT].

Mindfulness-based cognitive therapy [MBCT] integrates aspects of CBT for depression into the mindfulness-based stress reduction (MBSR) program initially developed and described by Kabat-Zinn [42]. MBCT includes such strategies as slow, simple breathing, meditation, and yoga to help individuals become more in touch with moment-to-moment changes that are occurring in their mind and body. In this way, MBCT helps individuals to develop the ability to permit distressing moods, thoughts and sensations to come and go, without having to battle against them. It also helps them to stay in touch with their present moment [37].

Metacognitive therapy (MCT) is a recently-constructed strategy designed to facilitate some understanding of whatever has caused a patient's mental health problems, and using this knowledge to then treat them [43]. Metacognition, itself, is that component of awareness that controls mental processes and thinking. Most people have some direct conscious awareness of metacognition. Meta-cognitive therapy helps patients to develop new ways of controlling this, when negative thoughts and beliefs arise and modifying metacognitive beliefs that give rise to unhelpful thinking patterns [37]. The results of the main trial conducted with CBT have been introduced in the guidelines on psychological activities in cardiac rehabilitation, elaborated by the GICR-IACPR (Gruppo Italiano di Cardiologia Riabilitativa e Preventiva - Italian Association for Cardiovascular Prevention, Rehabilitation and Epidemiology) [44]. The GICR-IACPR board promotes excellence in research, education and the organization of preventative and rehabilitative cardiovascular programs in Italian Cardiological activities.

Psychodynamic psychotherapy is another methodology used by therapists working in cardiac psychology. It is an empirical, speculative discipline that incorporates a broad range of theoretical mind and psychopathology models, in addition to a wide range of psychotherapeutic techniques. Since its initial creation, based upon Freud's psychoanalytic theory, it has been received contributions from various other theoretical approaches, like ethology, and both the cognitive and neuro sciences [45]. The two pillars of therapy are: 1) the patient's free associations; and 2) the analyst's free-floating attention. The main rule behind free association is that patients are invited to say whatever comes into their mind without censorship or judgment, and thereby experience their most authentic and open self-expression [46]. Over time, most patients start to gain confidence in this approach and the relationship they have developed with their therapist. They also begin to learn how to best reflect on their emotions and affective reactions to guide their own behaviors and the content of their free-association 'stories'. Too, they gain the ability to "associate" - that is, to connect their emotions and memories, their suffering and thoughts, and their relationship experiences in a meaningful way, both with their therapist and others. This activation affords them the capacity to create a "new self-experience"; or what Jung called an "individuation process" and Winnicott "development of the true-Self"[47].

Despite these important premises and the long-standing tradition of psychoanalytic psychotherapy, the literature on psychodynamics in cardiology has numerous short-comings, as noted in a 2007 systematic review paper published by Jordan and Barde [48]. In their article, the two authors listed several methodological limits of prior studies, like small subject samples and high drop-out rates. Furthermore, the studies that the authors reviewed focused not on treatment, but on the personality characteristics of cardiovascular disease patients.

A ten-year longitudinal study, published by Lantz and Gregoire in 2003 [49], evaluated the impact of a couple psychotherapy. In this study, in which 24 post-MI patients and their partners were treated, there was a significant improvement in patients' ability to elaborate on their feelings about their heart attack, their awareness of defense strategies adopted, and disease management. The partner's role in this study pertained to the patient's need to elaborate regarding the defense mechanisms that the couple or family used to cope with the trauma caused by the heart attack. Sometimes, such trauma circumvents a couple's or family's capacity to "transform" it into healthy manifestations of existence.

The third psychotherapeutic methodology more recently used in the field of Cardiac Psychology is the Ontopsychological approach [50]. Ontopsychological psychotherapy [50] is a complex and pioneering approach largely drawing from psychoanalysis [51], analytic psychology [52] and humanistic-existential psychotherapy, as hypothesized by Maslow [53]. It was used for the first time in Cardiac Psychology in a randomized controlled trial called step-in-AMI, into which 101 patients with an acute MI, treated with urgent percutaneous coronary angioplasty (PTCA), were recruited and randomized to two groups: one group treated with rehabilitative and medical therapy; the second group receiving the same treatment plus short-term psychotherapy [54, 55]. The study's main objectives were: 1) to evaluate the role of the psychological dimension in AMI and the potential of short-term psychotherapy to modify and improve psychological symptoms; and 2) to assess the effects of such therapy on cardiac and medical outcomes in this age of more advanced pharmaceutical and interventional therapies. The combined treatment group received, for the first time, a novel humanistic-existential form of short-term psychotherapy, extracted from the Ontopsychological method and adapted for acute cardiac care patients. At one-year follow-up, the patient group that had received short-term psychotherapy, in addition to standard cardiac care, exhibited significant improvements in cardiac symptoms, quality of life, and both psychological and medical outcomes, as well as a lower rate of re-hospitalization [54-56].

Ontopsychology borrows some techniques from psychoanalysis and analytic psychology, like dreams analysis. This being said, ontopsychology has several highly-unique characteristics that differentiate it from other psychodynamic and humanistic-existential approaches. In particular is the epistemological criterion represented by the concept of In Self (more appropriately labelled, the ontic In Self) [45, 56]. With this approach, each person's emotional structure is sustained by a positive core, which has been termed the 'ontic In Self' ('In Sé ontico'). The ontic In Self can be considered a person's first reality, the positive core of their unconscious, which coincides with the projection of each person's intrinsic nature. In this way, just like one's DNA contains all the drives responsible for a body's growth and functional development, the project of nature referred to as the In Self contains all the psychological drives responsible for an individual's life-long development and self-realization.

Other fundamental, distinct Ontopsychological concepts include a different and more complex characterization of the SuperEgo than in psychoanalysis; and the tremendous importance afforded, particularly, non-verbal communication. Based upon its peculiar topographic and dynamic conception of unconsciousness, the meaning of symbolic dream images has also been in largely re-codified, as per the theory of interpretation [50]. During the very initial phase of psychotherapy, the therapist focusses entirely on listening to patients' personal history, including their feelings, emotions, discomfort, suffering, and uneasiness. Subsequently, the therapist gradually transitions the analysis towards the two main expressions of unconscious drive: dreams and body language [56].

After thoroughly analyzing each patient's situation, a gifted therapist might be able to determine the root of the suffering the patient has described, then help them identify some initial solution to address that core issue. The psychotherapist largely focusses on the patient's deeper reality, represented by the ontic In Self. In this second phase of the therapeutic process, dialogue is used by the psychotherapist for the sole purpose of accessing the patient's most real and most profound ego, one that is inaccessible to the patient's consciousness. In this way, the therapist acts as a 'mirror', reflecting an image that is closer to the patient's true identity; and language is an irreplaceable instrument to restore authenticity to the objects present in the Ego's consciousness [45].

Above all, the entire psychotherapeutic process might be considered an instrument to help patients to regain full contact with their true identity, which fundamentally coincides with the intentionality of nature expressed by their ontic In Self. In this way, a psychotherapist is a tool guiding patients through the process of self-awareness. This being said, the 'true' therapist and enactor of any change is, in all actuality, the In Self. The psychotherapist merely helps the patient to read and de-codify messages expressed by the In Self, and then to translate them into messages that the patient might understand at a conscious and rational level. Upon re-contacting their own true identity, each patient becomes the solely responsible subject, the one to decide if and how to change their personal life, life-style, relationships, job, financial choices, *etc*.

At San Filippo Neri Hospital in Rome, based upon the promising one -year follow-up results observed in the STEP-IN-AMI trial, as well as the frequent, spontaneous requests of many patients admitted to the Department of Cardiovascular Medicine, an outpatient cardiac psychology clinic has been created within the Interventional Cardiology Unit. In

actuality, this service is dedicated both to clinical psychotherapy and research on the role of psychosocial risk factors in cardiac disease. Psychotherapy must be provided as an adjunct to optimal medical and interventional therapy, and can be applied only after appropriate and comprehensive secondary preventative measures have been undertaken, including lifestyle changes and the reduction or elimination of modifiable biomedical risk factors [57].

CONCLUSION

The genesis of heart disease, its course, and how effectively it can be treated, all are dependent on a patient's psyche, behaviors, attitudes and relationships, as well as the many stresses that life and the illness itself brings. For this reason, it is increasingly being recognized that professional psychological and psychotherapeutic support is essential to cardiology care, impacting both the effectiveness and efficiency of treatment. In fact, their role is also being recognized as being as essential as medical interventions, in terms of influencing patient outcomes [35]. The care that psychologists deliver must balance the essentials of standard medical practice and the individual needs of patients.

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