Psychosocial perspectives in cardiovascular disease

Pedersen, Susanne S.; von Känel, Roland; Tully, Phillip J; Denollet, Johan

Published in:
European Journal of Preventive Cardiology

DOI:
10.1177/2047487317703827

Publication date:
2017

Document version
Peer reviewed version

Citation for published version (APA):
Psychosocial perspectives in cardiovascular disease

Susanne S Pedersen (PhD)\textsuperscript{a,b}, Roland von Känel (MD)\textsuperscript{c,d,e,}, Phillip J. Tully (PhD)\textsuperscript{g,h}, Johan Denollet (PhD)\textsuperscript{i,j}

\textsuperscript{a}Department of Psychology, University of Southern Denmark, Odense, Denmark
\textsuperscript{b}Department of Cardiology, Odense University Hospital, Odense, Denmark
\textsuperscript{c}Department of Neurology, Inselspital, Bern University Hospital and University of Bern, Switzerland
\textsuperscript{d}Neuropsychosomatic and Stress Biology Group, Department of Clinical Research, University of Bern, Switzerland
\textsuperscript{e}Department of Psychosomatic Medicine, Clinic Barmelweid, Barmelweid, Switzerland
\textsuperscript{f}Hypertension in Africa Research Team, Faculty of Health Sciences, North-West University, Potchefstroom Campus, South Africa
\textsuperscript{g}Bordeaux Population Health, U1219, University of Bordeaux, France
\textsuperscript{h}Freemasons Foundation Centre for Men's Health, Discipline of Medicine, School of Medicine, The University of Adelaide, Australia
\textsuperscript{i}CoRPS – Department of Medical and Clinical Psychology, Tilburg University, the Netherlands
\textsuperscript{j}Department of Cardiology, Antwerp University Hospital, Antwerp, Belgium

Word count (text and references only): 3322
Total number of tables and figures: 5

\textbf*{Corresponding author:} Susanne S Pedersen (PhD), Department of Psychology, University of Southern Denmark, Campusvej 55, DK-5230 Odense M, Denmark. \textit{Phone:} +45 65 50 79 92; \textit{Fax (none); E-mail:} sspedersen@health.sdu.dk
Abstract

Adaptation to living with cardiovascular disease (CVD) may differ from patient to patient and is influenced not only by disease severity and limitations incurred by the disease but also socio-economic factors (e.g. health literacy), the patients’ psychological make-up, and susceptibility to distress. Co-morbid depression and/or anxiety is prevalent in 20% of patients with CVD, which may be either transient or chronic. Distress, such as depression, reduces adherence, serves as a barrier to behaviour change and the adoption of a healthy lifestyle, and increases the risk that patients drop out of cardiac rehabilitation, impacting on patients’ quality of life, risk of hospitalisation and mortality. Hence, it is paramount to identify this subset of high-risk patients in clinical practice. This review provides a general overview of the prevalence of selected psychosocial risk factors, their impact on patient-reported and clinical outcomes, and biological and behavioural mechanisms that may explain the association between psychosocial factors and health outcomes. The review also provides recommendations on which self-report screening measures to use to identify patients at high risk due to their psychosocial profile and the effectiveness of available trials that target these risk factors. Despite challenges and barriers associated with screening of patients combined with appropriate treatment, it is paramount that we treat not only the heart but also the mind in order to improve the quality of care and patient and clinical outcomes.

Keywords: Mechanisms; interventions; psychosocial factors; patient-reported outcomes; prognosis; screening

Word count (abstract): 229
Considerable knowledge on the role of psychosocial risk factors in cardiovascular disease (CVD) has been accumulated during the last 30 years. The aim of this state-of-the-art review is to provide an overview of the main psychosocial risk factors, their prevalence and association with patient- and clinical outcomes, mechanisms that may explain these associations, and how to target these factors in clinical practice.

Prevalence of psychosocial risk factors and association with cardiovascular events

Negative emotions
Among those with known CVD, depression and anxiety are linked to major adverse cardiac events (MACE), rehospitalisation, and death, independent of traditional risk factors. Depression disorder prevalence is between 15% and 20% in CVDs and clinically relevant depressive symptom estimates are much higher. Depression is especially deleterious to cardiovascular prognosis post-myocardial infarction (MI). There does not appear to be a meaningful difference in prognosis for persons with pre-existing depression or those developing depression post-MI, suggesting both subtypes are equally important. Anxiety is investigated to a lesser extent than depression in CVD populations, but a recent meta-analysis indicated a 16% prevalence rate of anxiety disorders, although individual disorder prevalence varies markedly (Table 1). Among the anxiety disorders, evidence implicates generalised anxiety disorder (GAD) with poorer CVD prognosis in a recent meta-analysis.

Positive emotions
Positive emotions appear to benefit cardiovascular prognosis. An exploratory meta-analysis on positive emotions (e.g. positive affect, optimism) indicated a reduced rate of rehospitalisation or mortality in adjusted analyses (odds ratio [OR] = .88; 95% confidence interval [CI] .84 to .91; p < .001).
Stress

In the broadest sense, stress encompasses mental and environmental stress, posttraumatic stress, and low perceived social support. Empirical work on stress in CVD reveals associations with adverse CVD prognosis, regardless of the definition of stress studied. A wealth of literature supports that low social support portends MACE risk. Findings for posttraumatic stress and ACS prognosis have emerged more recently, but appear to signify higher mortality and MACE risk.

Personality

A longstanding body of work has investigated personality traits in CVDs. Recent studies with contemporary conceptualizations of personality traits implicate hostility and anger with adverse CVD prognosis. Another conceptualization of personality traits known as Type D personality is defined as the co-occurrence of negative affect and social inhibition. A recent review of 12 studies corroborated an association between Type D personality with hard endpoints such as MACE and death (adjusted hazard ratio (HR) of 2.24 (95% CI [1.37-3.66]).

In summary, collective findings demonstrate that depression, other negative emotions, stress and personality factors are associated with MACE risk, whereas positive emotions appear to be associated with better CVD prognosis.

Biological and behavioural pathways linking psychosocial risk factors to cardiovascular disease

Risk for incident cardiovascular disease

Meta-analysis of large-scale population-based studies of apparently healthy individuals show that psychosocial factors, such as depression, anxiety, anger/hostility, social isolation/low social support, chronic stress, and PTSD are associated with an approximate 1.5-fold excess risk of incident cardiovascular events, including acute coronary syndromes (ACS) and death. The direction of this relationship rules out reverse causality, supporting the status of psychosocial factors as causal risk factors for CVD. A long-term follow-up study in 1,107,524
young Swedish men supports this notion. In spite of abundant statistical adjustments for various socio-demographic and CVD risk factors, residual confounding by unmeasured common causes remains a possible explanation in these prospective observational studies. As an example, epigenetic programming of a hyperactive stress response system in utero in offspring of stressed mothers may carry over to adulthood. As a consequence of such biographical/epigenetic and environmental antecedents, autonomic, neuroendocrine and immune system dysfunction facilitate both atherosclerosis progression and, as part of the sickness response, signalling of negative affect and social withdrawal to the brain through an interoceptive route many years before CVD events do occur. Moreover, congruent with the concept of allostasis, sustained adaptive changes in the cardiovascular system to taxing environmental ("stressful") situations lead to allostatic load and overload in the form of cardiometabolic and structural arterial changes; the resulting endothelial dysfunction, subclinical atherosclerosis, overt CVD and poor prognosis reflect the long-term cardiovascular costs of adaptation to stress. To sum up the above reasoning, it is likely that some individuals experience low psychological well being and feelings of distress many years before the clinical manifestation of CVD. In turn, cardiac events may provoke profound psychological and acute phase reactions, from which incident psychosocial risk factors may arise, like depression, anxiety and PTSD.

**Biological and behavioural pathways**

*Figure 1* illustrates that psychosocial factors impact on cardiovascular health by different pathways and mechanisms, many of which are linked with each other. Newly emerging, but also pre-existent psychosocial factors that persist in the wake of a cardiac event, like personality characteristics or job stress, affect atherosclerosis development and progression through behavioural and biological pathways.
Psychosocial factors are associated with altered hypothalamic pituitary adrenal axis function, increased output of the sympathetic nervous system, and parasympathetic/vagal withdrawal. Against a background of endothelial dysfunction, chronic alterations in these central outputs induce distinct pathophysiologic responses, summarized in Table 2\textsuperscript{17}. Low-grade inflammation and coagulation activation play particularly important roles, as they facilitate growth, vulnerability, and hemodynamically-induced erosion/rupture of an atherosclerotic plaque with thrombotic coronary occlusion\textsuperscript{18}. As shown in Figure 2, the latter is a key mechanism in the biology of emotionally triggered ACS, such as with outbursts of anger\textsuperscript{19}.

Psychosocial factors and stress are associated with more adverse lifestyle behaviours related to smoking, physical activity, diet, alcohol consumption, and sleep health\textsuperscript{16}. Further consequences of psychosocial factors are non-adherence with medication, poor consultation behaviour, and low attendance in cardiac rehabilitation\textsuperscript{16}. Stress-related health behaviours and biological mechanisms additionally contribute to the development of modifiable traditional cardiometabolic risk factors, including high blood pressure and hypertension, dyslipidaemia and high cholesterol, insulin sensitivity and type 2 diabetes, as well as weight gain and increased body mass index\textsuperscript{12}. In a vicious cycle, traditional cardiovascular risk factors (e.g., obesity and diabetes) and secondary complications (e.g., physical immobility and peripheral arterial disease) act in concert with psychosocial factors as profound barriers to lifestyle change (e.g. starting a regular exercise program)\textsuperscript{16}.

**Implications for clinical research and practice**

*The patient perspective*

Patient-reported outcomes, such as symptoms, perceived health status, and quality of life, represent powerful measures to inform clinicians, patients, and professional societies\textsuperscript{20}, and may influence the uptake of these outcomes in clinical research and practice\textsuperscript{21}.
Importantly, psychosocial risk factors such as depression, anxiety, Type D personality, and perceived social isolation may significantly contribute to poorer perceived health status, quality of life and other important patient-reported outcomes. For example, a meta-analysis of prospective studies in various cardiovascular patient groups showed that Type D personality was associated with a more than 2-fold increased odds for impaired physical and mental health status. Cardiologists and other health professionals should be aware of these substantial individual differences in patient-reported outcomes in order to identify high-risk patients and improve their perceived health status.

Effects of interventions targeting psychosocial risk factors

Psychotropic medication, cognitive-behavioural therapy and psychotherapy all address psychosocial risk factors but evidence for a beneficial effect on cardiac prognosis is inconclusive. A number of clinical trials have examined the effect of treating depression in patients with CVD. Overall, these trials only showed reductions in depressive symptoms that are not clinically significant, and could not show that depression treatment decreased the risk of (recurrent) cardiac events or improved health status in cardiac patients. However, these studies yielded a number of important insights that may enhance the effectiveness of future interventions.

First, secondary analyses of these depression trials suggest that cardiac prognosis seems to improve when the intervention is effective in improving depression. Second, evidence suggests that cardiac rehabilitation should also integrate counselling for psychosocial risk factors, as the combination of cardiac rehabilitation and stress management training seems to produce greater reductions in anxiety, distress and stress levels than cardiac rehabilitation alone. Third, intervention trials need to take into account the moderating effects of sample and patient characteristics and should also be targeted to the individual patient’s needs and preferences. A meta-analysis suggests that depression treatment may be more useful in coronary artery bypass graft patients, while anxiety treatment may be
particularly useful in patients with an implantable cardioverter defibrillator \(^{26}\). A recent trial in depressed patients with CVD found a significant treatment-by-Type D interaction on change in depression, suggesting that psychotherapy might be beneficial for depressed patients with Type D personality but not for non-Type D patients \(^{27}\).

Concerted efforts are needed to develop more effective psychosocial interventions, based on better insights into biobehavioural mechanisms of stress-related disease and the identification of high-risk subgroups \(^{23}\). Until such interventions are available, at the individual patient level, it is important to continue to refer patients with clinically significant levels of distress for specialised psychopharmacological or psychological treatment, due to the impact of distress on adherence, participation in cardiac rehabilitation, lifestyle changes, and patient-reported and clinical outcomes \(^{16, 28, 29}\).

*Recognition of psychosocial risk factors in clinical practice*

In order to identify patients at high-risk due to their psychosocial profile, it is paramount that we are able to identify this subset. Although the evidence for screening protocols making a difference to patient outcomes is scare and barriers for implementation plentiful, the alternative of doing nothing with the knowledge that depression is a treatable condition seems unacceptable \(^{30}\). A selection of psychosocial measures used to screen and identify at risk patients in a cardiac setting is presented in Table 4. These include the Patient Health Questionnaire (PHQ) 2 and 9 that have been recommended by the American Heart Association \(^{31}\). All measures are generic and available in several languages. Although disease-specific measures are available for specific subsets of patients [e.g. the ICD Patients concern questionnaire (ICDC)\(^{32}\) and the Cardiac Anxiety Questionnaire (CAQ)\(^{33}\), etc.], it is beyond the scope of this paper to provide an exhaustive list.
**Recommendations and future perspectives**

Focus on psychosocial factors in the ESC Textbook of Cardiovascular Medicine in 2009 and the European Guidelines on CVD prevention in clinical practice in 2012 have paved the way for more research in the field of cardiac psychology/behavioural cardiology and a greater understanding of the role of psychosocial factors in cardiovascular health. However, we are still far from treating the body and mind together. In order to advance the field and enhance the quality of care for patients with CVD we need to:

- Implement screening of patients in clinical practice in order to identify the subset of patients at risk. We have core questions available for the physicians to include in their interview and full, standardized and validated questionnaires to make a more extended assessment that have been shown to predict patient and clinical outcomes.

- Start incorporating psychosocial factors into CVD risk prediction models at an equal level to standards risk factors, such as age and smoking, as psychosocial factors are not only risk modifiers but also independent risk factors for poor patient and clinical outcomes.

- Design effective interventions that target psychosocial risk factors and that use a more precision medicine rather than a 'one-size-fits-all' approach. This warrants that we gain a better understanding of individual patients’ needs and preferences but also knowledge about barriers and facilitators of their implementation in clinical practice.

- Start treating body and mind together, as successful risk factor management at the patient level has a large behavioural component. Hence, we need to strive for more integrated care in general but also in the cardiac rehabilitation setting. In cardiac rehabilitation, physical training, setting goals for risk factor management, psycho-education, and psychosocial intervention should be integrated, while also taking into account the patient’s context (e.g family, health literacy, and other vulnerability factors). This requires that we work together in an integrated fashion across disciplines placing the patient center-stage.
Contributions of authors

All authors (SSP, RvK, PJT, JD) contributed to the conception of the manuscript, acquisition and interpretation of data (literature), drafting of the manuscript, and critical revision of the manuscript. All gave final approval and agree to be accountable for all aspects of work ensuring integrity and accuracy.

Declaration of conflicting interests

The authors have no conflicts of interest to declare.
References


41. Pedersen SS, Mathiasen K, Christensen KB and Makransky G. Psychometric analysis of the Patient Health Questionnaire in Danish patients with an implantable cardioverter defibrillator (The DEFIB-WOMEN study). *J Psychosom Res.* 2016; 90: 105-12.