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Editorial

Anxiety weights down the heart – New evidence for a toxic cardiovascular risk factor

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"*…. As early as 1806 Napoleon's physician, Corvisart, described the main features of cardiac psychosis: depression, restlessness and irritability, rising in some cases to excitement with confusion, and continuous anxiety*."

[*Joseph Wortis* [1]]

Global point prevalence of any anxiety disorder is estimated at approximately 7% and mounts to a prevalence of approximately 16% in cardiovascular disease (CVD) populations [2]. Several meta-analyses revealed an increased moderate risk associated with anxiety in CVD, often attenuated by depression. A recent meta-analysis with more than thirty thousand CVD patients [3] revealed that the increased risk was restricted to anxiety in stable CVD but not in the post-acute acute coronary syndrome (ACS) phase. Robust evidence compiled in a meta-analysis of studies with more than one million included participants and more than 58,000 cardiac events indicates that among anxiety disorder subtypes, panic disorder is associated with an increased relative risk of 47% for incident coronary heart disease (CHD), a major contributor to CVD [4].

Yet, compared to depression, anxiety continues to be waved aside. Depression is widely acknowledged as an etiological risk factor with a solid standing among the classical somatic risk factors [5]. As prognostic risk factor, it has received recognition in a scientific statement by the American Heart Association. The most extended randomized controlled trials in psychotherapy targeting depression have been performed with many thousands of CVD patients while there remains a paucity of treatment studies focusing on anxiety making systematic reviews a challenge.

The Janus face of anxiety itself may account for this depreciation. Opposing an overhasty interpretation of anxiety as an adverse mental state, perceiving anxiety, even when sustained, may be a completely natural reaction. Surviving a life threatening event which comes mostly unprepared, forcing the victim from 1 min to the next to give up many aspects of his/hers former biography; being entrapped in an emerging chronic disease condition where he/she lacks control over the progression of the disease and perceives the inability to escape the situation – all this may cause sustained feelings of anxiety which may make it difficult to judge these feelings as out of proportion. Furthermore - comparable to the pain system - feelings of fear and anxiety may serve as a psycho-biological survivor tool for mankind. It may prevent people from engaging in destructive and self-damaging behavior. Anxiety has been found to be a 'driver' for individuals to address their health needs more regularly. A systemic review including 15 studies evidenced that being 'anxious' has a significant positive effect on decision making in help seeking behavior at the early signs of the disease [6]. Parker et al. [7] found that patients with Generalized Anxiety Disorder (GAD) received more medical tests and were more engaged in post-AMI rehabilitation programs. Fang et al. [8] showed that anxiety was associated with a favorable reduced delay time of patients to reach emergency facilities when facing an AMI.

The prospective multicenter study of Hoang Tran et al. [9] adds new important insights to this puzzle and helps to clarify conflicting evidence. In a large study sample of 1909 ACS patients, the investigators assessed anxiety by the well-established Generalized Anxiety Disorder (GAD-7) questionnaire while patients were hospitalized for their index ACS. However, they also determined by review of each patient's medical history records – and this makes their study unique - whether the patients had been suffering from any anxiety disorder in the past. At baseline, almost 19% of patients qualified for clinical relevant anxiety symptoms and 10.4% of patients had an established diagnosis of an anxiety disorder. The anxiety symptom burden was neither associated with unscheduled 30 days hospital readmission rates nor was it associated with 2-years mortality. A confirmed diagnosis of any anxiety disorder, however, was a strong predictor for 2-years mortality – most notably

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after adjustment for somatic severity indexes and even for depression! Thus, these findings support the assumption that the experience of anxiety in the face of an ACS is a non-pathological adjustment condition on a life threating condition and may act as a grief reaction supporting the patient to regain a future perspective. An established anxiety disorder, however, unfolds fatal effects on the ACS.

As often, excellent research findings open new and burning questions. In this case, the researchers found that the toxic effect of an anxiety disorder was independent from its symptom burden and was even apparent in patients under successful psychopharmacological treatment. How then should we treat our cardiac patients with comorbid anxiety? How could we explain this finding which is likely to be counterintuitive? It is not unlikely that we will have to look into the molecular underpinning and into the changes in the architecture of DNA provoked by anxiety to answer this question [10]. It is of note that the investigators, in modeling the adjustment strategy for their 2-years follow up investigation, focused on an extended disease severity score involving age, heart rate, systolic blood pressure, creatinine, ST-deviations, cardiac enzymes and comorbid disease conditions. But they were less rigorous with adjusting for potential life style factors – thus, leaving room for clarifying the role of lifestyle factors associated with the diagnosis of anxiety in the future.

Conflict of interest

The author reports no relationships that could be construed as a conflict of interest.

References

[1] J. Wortis, Cardiac psychosis and the symptom of anxiety, Am. Heart J. 13 (4) (1937) 394–412.
[2] P.J. Tully, S.M. Cosh, H. Baumeister, The anxious heart in whose mind? A systematic review and meta-regression of factors associated with anxiety disorder diagnosis, treatment and morbidity risk in coronary heart disease, J. Psychosom. Res. 77 (6) (2014) 439–448.
[3] C.M. Celano, R.A. Millstein, C.A. Bedoya, B.C. Healy, A.M. Roest, J.C. Huffman, Association between anxiety and mortality in patients with coronary artery disease: a meta-analysis, Am. Heart J. 170 (6) (2015) 1105–1115.
[4] P.J. Tully, D.A. Turnbull, J. Beltrame, J. Horowitz, S. Cosh, H. Baumeister, et al., Panic disorder and incident coronary heart disease: a systematic review and meta-regression in 1131612 persons and 58111 cardiac events, Psychol. Med. 45 (14) (2015) 2909–2920.
[5] K.H. Ladwig, J. Baumert, B. Marten-Mittag, K. Lukaschek, H. Johar, X.Y. Fang, et al., Room for depressed and exhausted mood as a risk predictor for all-cause and cardiovascular mortality beyond the contribution of the classical somatic risk factors in men, Atherosclerosis 257 (2017) 224–231.
[6] T. Dubayova, J.P. van Dijk, I. Nagyova, J. Rosenberger, E. Havlikova, Z. Gdovinova, et al., The impact of the intensity of fear on patient's delay regarding health care seeking behavior: a systematic review, Int. J. Public Health 55 (5) (2010) 459–468.
[7] G. Parker, M. Hyett, D. Hadzi-Pavlovic, H. Brotchie, W. Walsh, GAD is good? Generalized anxiety disorder predicts a superior five-year outcome following an acute coronary syndrome, Psychiatry Res. 188 (3) (2011) 383–389.
[8] X.Y. Fang, D. Spieler, L. Albarqouni, J. Ronel, K.H. Ladwig, Impact of generalized anxiety disorder (GAD) on prehospital delay of acute myocardial infarction patients. Findings from the multicenter MEDEA study, Clin. Res. Cardiol. 107 (6) (2018) 471–478.
[9] H. Tran, N. Byatt, N. Erskine, D. Lessard, R.S. Devereaux, J. Saczynski, et al., Impact of anxiety on the post-discharge outcomes of patients discharged from the hospital after an acute coronary syndrome, Int. J. Cardiol. 278 (2019) 28–33.
[10] R.T. Emeny, J. Baumert, A.S. Zannas, S. Kunze, S. Wahl, S. Iurato, et al., Anxiety associated increased CpG methylation in the promoter of Asb1: a translational approach evidenced by epidemiological and clinical studies and a murine model, Neuropsychopharmacology 43 (2) (2018) 342–353.