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WHAT ABOUT HEART AND MIND IN THE COVID-19 ERA?

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ABSTRACT

From the time of Hippocratic medicine, heart-brain interactions have been recognized and contributed to both mental and physical health. Heart-brain interactions are complex and multifaceted and appear to be bidirectional. Exposure to chronic and daily stressors such as quarantine, or severe psychological trauma like a significant person in danger of life can affect the cardiovascular system and the emotional experience of the individual, leading to an increased risk of developing a cardiovascular disease or mental illness. Subjects with comorbidities between mental disorders and heart diseases are obviously more susceptible to be influenced by emotional burden due to the spread of COVID-19, with emotional responses characterized by fear, panic, anger, frustration. Psychological services and crisis interventions are needed at an early stage to reduce anxiety, depression and post-traumatic stress disorder in such a stressful period, with a special attention to special groups of patients, such as women, children, or the elderly.

Key-words: Heart; Mind; COVID-19; Quarantine; Cardiovascular Disease; Depression; Anxiety.

The “mind-heart-body connection”

It is important to pay great attention to the psychological and physiological milieu in which the heart resides (the so termed “mind-heart-body connection”)¹.

Heart-brain interactions are complex and multifaceted and appear to be bidirectional. Some researchers have hypothesized that stress can play a crucial role in cerebral-cardiac interactions². Exposure to chronic and daily stressors such as quarantine, or severe psychological trauma like a significant person in danger of life can affect the cardiovascular system and the emotional experience of the individual, leading to an increased risk of developing a cardiovascular disease or mental illness. In addition social isolation and loneliness were connected with a 50% increased risk of cardiovascular disease (CVD) events^{3,4}.

Cardiac activity and vascular tone are modulated by the sympathetic and parasympathetic nervous systems, variations to the autonomic nervous system are likewise concerned with the interactions between depressive and anxiety disorders and cardiac consequences⁵. The consequences of heart-brain dysfunction can lead to pathological manifestations involving many organ systems and COVID era may negatively impact on cerebral-cardiac interactions. In this perspective could be useful to actively screen individuals suffering from CVD or mental illness in order to diminish the weight on quality of life and prognosis trying to foster a multidisciplinary collaboration between health professionals.

Cardiovascular disease and emotional burden during quarantine

CVD constitutes a leading worldwide health problem, and the occurrence of depression can worsen cardiovascular morbidity and mortality. It is well known that depressive disorders are more prevalent in women than men (about 20-25% of female population experience depressive symptoms during life), due to the overlap of genetic, hormonal and psychological factors. It is also clear from a huge amount of literature data that women have a doubled incidence of cardiovascular disease related deaths, and there is an increase of angina, heart failure and stroke in females⁶. It has been demonstrated that depression represents an emergent risk factor for cardiovascular disease in women, and underlying mechanism explaining this link include behavioural habits and biological factors, including reduced social support and low self-esteem, emotional attitude in interpersonal relationships, sympathetic nervous system hyperactivity, impairment in hypothalamic-pituitary-adrenal function. It has also been suggested the existence of gender-specific differences in mental activation patterns and biological responses to mental stress^{7,8}. Besides, there is a dramatic increase of coronary heart disease (CHD) in women following menopause, such as a greater prevalence of depressive symptoms in perimenopausal women, probably due to emotional distress related to hormone fluctuation, but also to several psychological implications (stress, body image, sexuality, fertility, aging)⁹.

The outbreak of COVID-19 in China in December 2019 has been identified as a pandemic and a health emergency of global concern. Quarantine is an unpleasant experience for people who experience separation from loved ones, loss of freedom, boredom, uncertainty about disease status and evolution and can create dramatic psychological effects¹⁰. Investigations about prevalence and

predictors of post-traumatic stress symptoms in China hardest-hit areas during COVID-19 outbreak¹¹ have demonstrated that women reported significant higher PTSS in the domains of re-experiencing, negative alterations in cognition or mood, and hyperarousal.

People with heart diseases and mental health disorders in comorbidity result at elevated risk during pandemics and generally more susceptible to infections due to less awareness of risk, cognitive impairment, difficulties in accessing timely health services (also due to discrimination associated with mental disorders in health-care settings), polypharmacotherapies¹². Besides, subjects with comorbidities between mental disorders and heart diseases are obviously more susceptible to be influenced by emotional burden due to the spread of COVID-19, with emotional responses characterized by fear, panic, anger or distress in the short-time, and anxiety and depression as delayed consequences (**Figure 1**).

Although there is an increasing amount of papers in these weeks focusing on the impact of depressive and anxious symptoms in frontline health care workers facing the coronavirus disease 2019 (COVID-19) in China and in other countries, they lack in data regarding pre-existing rates of psychopathology in this cohort (health workers act daily in stressful settings) and necessarily lack of adequate follow-ups¹³. Even prior to this pandemic the high prevalence of burnout, the complex causes and critical consequences have been reported among medical staff. Lai et al.¹⁴ have found that frontline workers treating patients with COVID-19 in multiple regions of China reported more severe symptoms (depression, anxiety, distress), with especially women nurses in Wuhan experiencing severe psychological burden. Noteworthy, most health professionals working in isolation units and hospital do not receive any training for providing mental health care¹⁵.

It has been suggested that intimate partner violence might increase the risk of cardiovascular disease in women¹⁶. In quarantine due to COVID-19 home risks to become a very dangerous place for victims of domestic violence, because they are required to stay the whole day with partners and away from people who can validate their experiences and give help.

Psychological services and crisis interventions are needed at an early stage to reduce anxiety, depression and post-traumatic stress disorder in such a stressful period, with a special attention to special groups of patients, such as women, children, or the elderly. Psychiatrists and counselors are suggested to work over phone or internet and there is an increased need of psychological hotlines for the support of public mental health in order to exert protective effects of stress reduction and increase perception of social support. At the same time is extremely important to identify high-risk individuals to avoid the occurrence of extreme events such as suicide or impulsive behaviour. During the COVID-19 outbreak in China mental health professionals and health authorities have provided several mental health services: online mental health surveys, online mental health education with communication programmes (WeChat, Weibo, TikTok), online psychological counseling services, online psychological self-help intervention systems, artificial intelligence programmes as interventions for psychological crises (for example recognition of individuals at risk for suicide)¹⁷. It has been demonstrated that survivors of life-threatening infectious diseases like SARS and quarantine can be affected by considerable psychological distress and develop post-traumatic stress disorder and depressive symptoms^{18,19}, so it is mandatory to prevent possible psychological sequelae of isolation (**Figure 2**).

Large prospective epidemiologic studies and meta-analysis have firmly established a connection between anxiety and a higher risk of coronary disease, myocardial infarction and cardiovascular death^{20,21}. In a critical review and meta-analysis²² it has been reported that anxiety was linked to a 52% increased prevalence of CVD. Anxiety is a predictor of death in middle-aged women^{23,24} and Janszky et al.²⁰ found that patients suffering from anxiety disorders doubled the risk of developing CHD. There also is evidence that phobic anxiety may increase risk of mortality in CHD^{25,26}. A

prospective study²⁷ confirmed a strong relationship between phobic anxiety and the risk of sudden cardiac death and fatal myocardial infarction (MI). The overall literature supports that the coexistence of anxiety and depressive disorders may confer a higher risk of cardiovascular disease^{24,28}.

It has been reported a cardiac involvement may happen with COVID-19 (Inciardi, 2019), among the victims of COVID-19 arterial hypertension and cardiovascular disease represented two of the most common comorbidities²⁹. Inciardi et al.³⁰ suggested that the pathogenesis of heart involvement linked to SARS-CoV-2 may reproduce a process of replication and dissemination of the virus through the blood or the lymphatic system from the respiratory tract.

From the time of Hippocratic medicine, heart-brain interactions have been recognized and contributed to both mental and physical health. Researchers have investigated potential behavioural and biological mechanisms⁴ as pathways connecting depressive and anxiety disorders with CVD. By focusing on behavioural aspects, mood disorders may greatly worsen the course and prognosis of CVD by decreasing healthy lifestyle habits such as physical activity level, smoking, body weight, alcohol intake and also with a poor adherence to cardiovascular medications. The biological mechanisms linking depression with CVD may be related to inflammatory processes, autonomic nervous system dysfunction, with increased risk of myocardial ischemia and impaired coronary flow reserve⁴.

In the complexity of the current moment, the pandemic can take very intense effects on the individual and social bond, passing through the anguish of an anticipatory mourning in which the environment and the affectively invested objects can be experienced in an atmosphere of incipient loss and impending fear of the end. This can determine the risk of the withdrawal of the affected from the objects perceived as damaged or damageable, that is the psychic condition that can expressively show itself as apathy.

The comparison and dialogue between different knowledge, experiences and sciences can lay the foundations for an ethics of collaboration and solidarity, trying to help individuals to accept the uncertainty of the vicissitudes of existence, avoiding the uneconomic illusion of thinking of to be able to govern what is not completely governable. At a time when fear for the destiny of the individual predominates, mental health professionals can help people to react to the feelings of catastrophe, drawing on the work of symbolization and helping to revive the ability to think and dream of a better future, allow individuals to discover unknown energies, to be used for oneself and made available to others.

REFERENCES

1. Levine GN. The Mind-Heart-Body Connection. *Circulation*. 2019;140(17):1363-1365.
2. Layon J, Gabrielli A, William A. *Textbook of Neurointensive Care*. Springer, New York, 2013, p. 256.

3. Steptoe A, Kivimäki M. Stress and cardiovascular disease: an update on current knowledge. *Annu Rev Public Health*. 2013;34:337-54.
4. Cohen BE, Edmondson D, Kronish IM. State of the Art Review: Depression, Stress, Anxiety, and Cardiovascular Disease. *Am J Hypertens*. 2015 Nov;28(11):1295-302.
5. Celano CM¹, Villegas AC, Albanese AM, Gaggin HK, Huffman JC. Depression and Anxiety in Heart Failure: A Review. *Harv Rev Psychiatry*. 2018;26(4):175-184.
6. Bucciarelli V, Caterino AL, Bianco F, Caputi CG, Salerno S, Sciomer S, Maffei S, Gallina S. Depression and cardiovascular disease: The deep blue sea of women's heart. *Trends Cardiovasc Med*. 2020;30(3):170-176.
7. Kasher N, Wittbrodt MT, Alam ZS, Lima BB, Nye JA, Campanella C, Ladd S, Hammadah M, Shah AJ, Raggi P, Quyyumi AA, Vaccarino V, Bremner JD. Sex differences in brain activation patterns with mental stress in patients with coronary artery disease. *Biol Sex Differ*. 2019 ;10(1):35.
8. Samad Z, Boyle S, Ersboll M, Vora AN, Zhang Y, Becker RC, Williams R, Kuhn C, Ortel TL, Rogers JG, O'Connor CM, Velazquez EJ, Jiang W; REMIT Investigators. Sex differences in platelet reactivity and cardiovascular and psychological response to mental stress in patients with stable ischemic heart disease: insights from the REMIT study. *J Am Coll Cardiol*. 2014;64(16):1669-78.
9. Jiang XD. Editorial commentary: The menopausal transition: A critical time for promoting midlife women's mind and heart wellness. *Trends Cardiovasc Med*. 2020;30(3):177-178.
10. Brooks SK, Webster RK, Smith LE, Woodland L, Wessely S, Greenberg N, Rubin GJ. The psychological impact of quarantine and how to reduce it: rapid review of the evidence. *Lancet*. 2020;395(10227):912-920.
11. Liu S, Yang L, Zhang C, Xiang YT, Liu Z, Hu S, Zhang B. Online mental health services in China during the COVID-19 outbreak. *Lancet Psychiatry*. 2020;7(4):e17-e18.
12. Yao H, Chen JH, Xu YF. Patients with mental health disorders in the COVID-19 epidemic. *Lancet Psychiatry*. 2020;7(4):e21.
13. Perlis RH. Exercising Heart and Head in Managing Coronavirus Disease 2019 in Wuhan. *JAMA Netw Open*. 2020;3(3):e204006.
14. Lai J, Ma S, Wang Y, Cai Z, Hu J, Wei N, Wu J, Du H, Chen T, Li R, Tan H, Kang L, Yao L, Huang M, Wang H, Wang G, Liu Z, Hu S. Factors Associated With Mental Health Outcomes Among Health Care Workers Exposed to Coronavirus Disease 2019. *JAMA Netw Open*. 2020;3(3):e203976.

15. Lima CKT, Carvalho PMM, Lima IAAS, Nunes JVAO, Saraiva JS, de Souza RI, da Silva CGL, Neto MLR. The emotional impact of Coronavirus 2019-nCoV (new Coronavirus disease). *Psychiatry Res.* 2020;287:112915.
16. El-Serag R, Thurston RC. Matters of the Heart and Mind: Interpersonal Violence and Cardiovascular Disease in Women. *J Am Heart Assoc.* 2020;9(4): e015479.
17. Liu N, Zhang F, Wei C, Jia Y, Shang Z, Sun L, Wu L, Sun Z, Zhou Y, Wang Y, Liu W. Prevalence and predictors of PTSS during COVID-19 outbreak in China hardest-hit areas: Gender differences matter. *Psychiatry Res.* 2020;287:112921.
18. Hawryluck L, Gold WL, Robinson S, Pogorski S, Galea S, Styra R. SARS control and psychological effects of quarantine, Toronto, Canada. *Emerg Infect Dis.* 2004;10(7):1206-12.
19. Wu KK, Chan SK, Ma TM. Posttraumatic stress after SARS. *Emerg Infect Dis.* 2005;11(8):1297-300.
20. Janszky I, Ahnve S, Lundberg I, Hemmingsson T. Early-onset depression, anxiety, and risk of subsequent coronary heart disease: 37-year follow-up of 49,321 young Swedish men. *J Am Coll Cardiol.* 2010;56(1):31-7.
21. Roest AM, Martens EJ, Denollet J, de Jonge P. Prognostic association of anxiety post myocardial infarction with mortality and new cardiac events: a meta-analysis. *Psychosom Med.* 2010;72(6):563-9.
22. Batelaan NM, Seldenrijk A, Bot M, van Balkom AJ, Penninx BW. Anxiety and new onset of cardiovascular disease: critical review and meta-analysis. *Br J Psychiatry.* 2016;208(3):223-31.
23. Denollet J, Maas K, Knottnerus A, Keyzer JJ, Pop VJ. Anxiety predicted premature all-cause and cardiovascular death in a 10-year follow-up of middle-aged women. *J Clin Epidemiol.* 2009;62(4):452-6.
24. Angermann CE, Ertl G. Depression, Anxiety, and Cognitive Impairment : Comorbid Mental Health Disorders in Heart Failure. *Curr Heart Fail Rep.* 2018;15(6):398-410.
25. Watkins LL, Blumenthal JA, Babyak MA, Davidson JR, McCants CB Jr, O'Connor C, Sketch MH Jr. Phobic anxiety and increased risk of mortality in coronary heart disease. *Psychosom Med.* 2010;72(7):664-71.
26. Smith PJ, Blumenthal JA. Psychiatric and behavioral aspects of cardiovascular disease: epidemiology, mechanisms, and treatment. *Rev Esp Cardiol.* 2011;64(10):924-33.

27. Albert CM, Chae CU, Rexrode KM, Manson JE, Kawachi I. Phobic anxiety and risk of coronary heart disease and sudden cardiac death among women. *Circulation* 2000;111(4):480-7.
28. Marano G, Harnic D, Lotrionte M, Biondi-Zoccai G, Abbate A, Romagnoli E, Mazza M. Depression and the cardiovascular system: increasing evidence of a link and therapeutic implications. *Expert Rev Cardiovasc Ther.* 2009;7(9):1123-47.
29. Inciardi RM, Lupi L, Zaccone G, Italia L, Raffo M, Tomasoni D, Cani DS, Cerini M, Farina D, Gavazzi E, Maroldi R, Adamo M, Ammirati E, Sinagra G, Lombardi CM, Metra M. Cardiac Involvement in a Patient With Coronavirus Disease 2019 (COVID-19). *JAMA Cardiol.* 2020 Mar 27. doi: 10.1001/jamacardio.2020.1096. [Epub ahead of print]
30. Strabelli TMV, Uip DE. COVID-19 and the Heart. *Arq Bras Cardiol.* 2020 Mar 30. [Epub ahead of print]

Figure legends

Figure 1. Impact of quarantine on physical and mental well-being: short and long-term consequences.

Figure 2. Possible interventions during COVID-19 lock-down.



