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Silent Casualties of War: Stress-Driven Cardiotoxicity in Patients with Cancer Receiving Chemotherapy

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The interaction among war-related psychological stress, limited access to health care, and chemotherapy-induced cardiotoxicity in patients with cancer remains critically underexplored. Patients living in conflict zones not only experience substantial psychological stress but also face significant barriers to timely medical care, which may increase the risk of cancer therapy-related cardiac dysfunction. The combined effects of psychological stress and limited access to health care remain insufficiently studied.

Patients receiving chemotherapy are inherently at increased risk of cardiotoxicity. Recent advances in anticancer therapy have substantially improved patient prognosis. Some patients achieve durable complete responses, whereas many others experience prolonged remission, effectively transforming certain malignancies into chronic diseases. However, these therapeutic gains are accompanied by notable cardiovascular adverse effects (1). Fluoropyrimidines, such as 5-fluorouracil, and alkylating agents, such as cyclophosphamide, can cause epicardial coronary artery spasm (2). Targeted anticancer agents, including human epidermal growth factor receptor 2 (HER2) inhibitors and tyrosine kinase inhibitors, can increase the risk of cardiotoxicity. Chimeric antigen receptor T-cell therapy is associated with left ventricular dysfunction, heart failure, and arrhythmias, usually mediated by cytokine release syndrome. Anthracyclines directly impair cardiomyocytes by inducing oxidative stress, DNA injury, and mitochondrial damage; they also affect endothelial cells and fibroblasts by inducing reactive oxygen species. Immune checkpoint inhibitors can cause myocarditis and dilated cardiomyopathy through immune dysregulation (1, 3, 4).

Acute stress exerts its effects through the release of epinephrine, norepinephrine, cortisol, and free fatty acids, as well as activation of the renin-angiotensin-aldosterone system. The hypothalamic-pituitary-adrenal axis is a key neuroendocrine regulator that coordinates adaptation to acute stressors and maintains homeostasis. In contrast, chronic stress is associated with suppression of both cellular and humoral immunity. Chronic stress also creates a proinflammatory microenvironment by promoting activation of signal transducer and activator of transcription 3 and nuclear factor kappa-light-chain-enhancer of activated B cells in immune cells. Prolonged activation sustains the production of proinflammatory mediators, such as interleukin 6 and tumor necrosis factor α, decreases the effectiveness of cancer therapies, and increases cardiovascular complications (5, 6).

At our center, we observed a substantial increase in acute cardiac events among patients receiving chemotherapy during and after regional conflict compared with the preconflict period. Patients reported new-onset palpitations, arrhythmias, and chest pain despite having no previous history of cardiovascular disease. Pulmonary edema was also observed in patients with preexisting heart failure who had no previous history of pulmonary edema. Clinical observations from war-affected regions suggest that stressors such as displacement, widespread fear, and compromised access to health facilities may increase susceptibility to chemotherapy-related cardiotoxicity. Increased levels of stress hormones, including cortisol and catecholamines, which are commonly observed after trauma exposure, may also adversely affect the myocardium.

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Although potential confounding factors can be controlled to some extent, the temporal relationship between war-related stress and symptom development supports the need for careful, systematic clinical evaluation. Effective care in conflict zones requires stress screening and close collaboration among oncologists, psycho-oncologists, and cardio-oncologists. Patients in these settings experience psychological stress and limited access to medical care, both of which may increase the risk of chemotherapy-related cardiotoxicity. Prospective studies are needed to examine the relationships among psychological stress, restricted access to health care, and treatment-related cardiac complications. Incorporating psychosocial support, lifestyle interventions, and enhanced cardiac monitoring into oncology protocols through multidisciplinary collaboration may reduce preventable morbidity, optimize oncologic efficacy, improve cardiovascular safety, and enhance outcomes in this vulnerable population.

Footnotes

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