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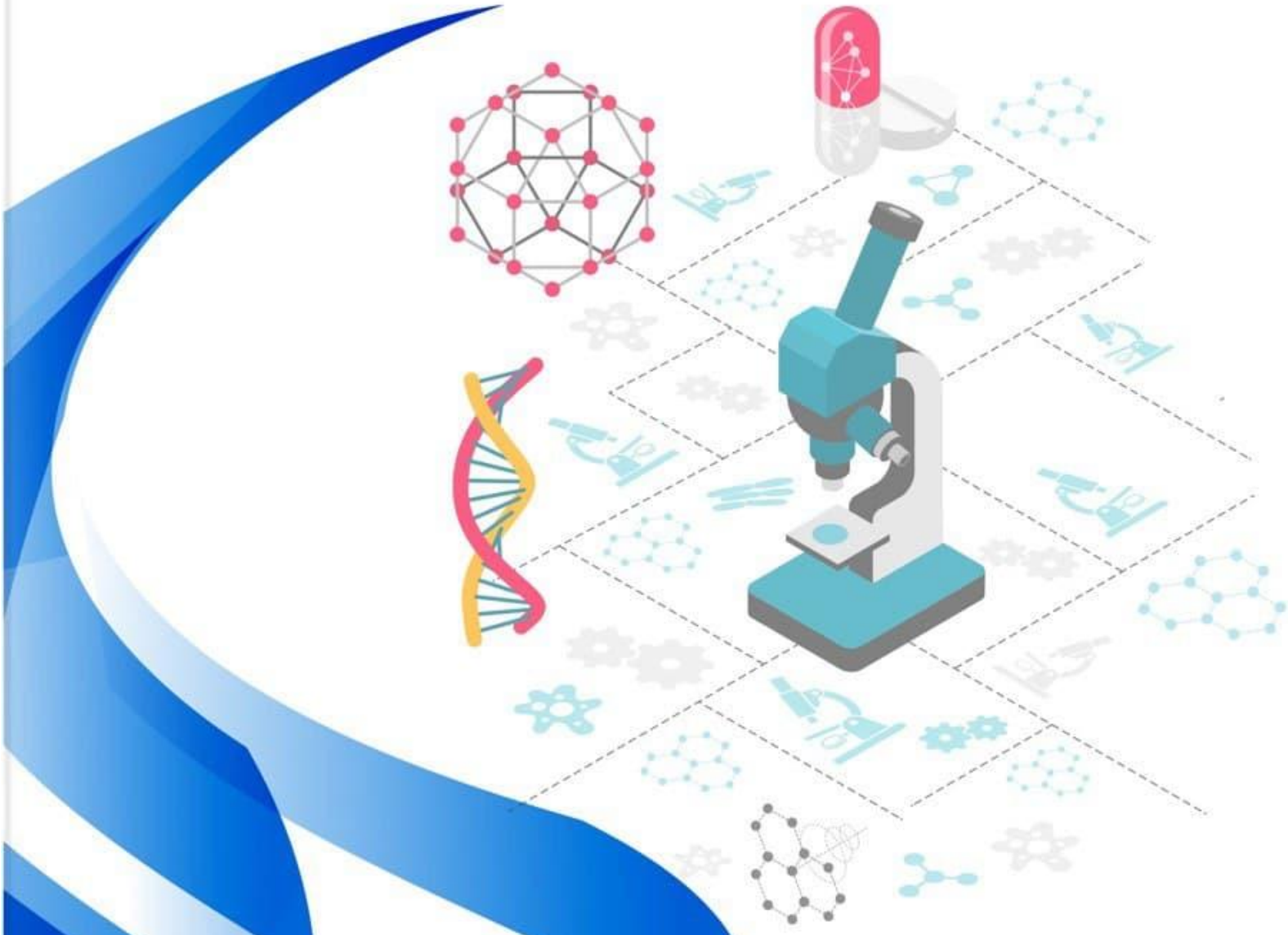

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CANCER PATIENTS COMMONLY EXPERIENCE HEART RHYTHM DISORDERS.

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Abstract. Cardiovascular (CV) disease is increasingly recognized as an important aspect of the clinical spectrum of cancer patients, being the second most common cause of death in this group. Coexisting CV disorders and CV complications of cancer treatments can affect patient outcomes, leading to the emergence of the field of Cardio-Oncology. Among the CV issues in cancer patients, arrhythmias are particularly significant. Patients with cancer may experience a wide range of rhythm disorders, including bradycardia, conduction defects, atrial fibrillation, and ventricular tachycardia.

Key words: cancer, arrhythmias, cancer therapy, anticancer therapy, cardiotoxicity

Arrhythmias in cancer can result from the interaction of three main factors: patient characteristics, cancer, and anticancer therapy [1]. Patient-related factors that may predispose to arrhythmias include: (i) coexisting cardiovascular disease, (ii) aging, which is associated with rhythm disorders such as atrial fibrillation or sick sinus syndrome, (iii) comorbid conditions such as diabetes mellitus or chronic kidney disease, and (iv) genetic predisposition [2]. On the other hand, cancer may induce arrhythmias by direct invasion of the heart from a primary cardiac neoplasm, or more commonly, a metastatic tumor, and by causing systemic abnormalities such as autonomic nervous system derangement and inflammation [3]. Finally, cancer therapy may induce or contribute to rhythm disorders, including systemic anticancer therapies (e.g. chemotherapy, targeted therapies, immunotherapies), radiotherapy with chest irradiation involving cardiac tissue, and supportive medications such as antiemetics [4]. Certain anticancer agents have been associated with pro-arrhythmic properties, with QT prolongation being the most typical. Anticancer drugs may also predispose to arrhythmias by causing other forms of cardiovascular disease such as ventricular dysfunction and heart failure or myocardial ischemia as part of their cardiotoxicity profile, or by inducing electrolyte and metabolic disorders due to gastrointestinal and other toxicities [5].

The role of a Cardio-Oncology specialist in preventing and managing arrhythmias in cancer patients is multifaceted. It involves conducting a baseline assessment when the cancer is diagnosed, monitoring and managing during active

cancer treatment, and providing long-term surveillance for cancer survivors [4,5]. The baseline assessment aims to stratify the risk of patients, identifying those who need close monitoring during and after cancer therapy, and optimizing cardiovascular therapies. In this context, identifying patients with pre-existing rhythm disorders such as atrial fibrillation or risk factors for arrhythmias, such as QT prolongation, can help in taking special precautions during cancer therapy or making proper adaptations to anticancer therapies, in collaboration with the attending oncologist or hematologist.

During cancer treatment, it's important to monitor high-risk patients to promptly diagnose and manage arrhythmias and other potential cardiovascular complications. Although arrhythmias can often be treated in an emergency setting, it's essential to take precautions when managing rhythm disorders in cancer patients. This includes carefully assessing potential drug interactions between antiarrhythmics or anticoagulants (for atrial fibrillation) and anticancer medications. When making decisions about interventions like device implantation, it's important to consider the patient's prognosis and life expectancy. Managing anticoagulation for atrial fibrillation in patients with active cancer can be challenging due to higher thromboembolic and bleeding risks. Additionally, adjusting ongoing cancer therapies may be necessary after the development of an arrhythmia [3].

It is important to consider long-term monitoring for cancer survivors with coexisting cardiovascular disease or those who have undergone treatments with significant cardiotoxic effects. This is because arrhythmias may develop as part of late cardiotoxicity. For instance, chest irradiation can lead to degeneration and fibrosis of the conduction system, which may result in atrioventricular block several years after radiotherapy [7].

In the latest release of the Journal, Anker and colleagues present the results of a case-control study comparing ventricular arrhythmias in patients with advanced cancer and healthy age- and sex-matched controls. The study found that patients with cancer had a higher incidence of non-sustained ventricular tachycardia (NSVT) during ambulatory electrocardiographic monitoring. The authors propose a new perspective on the relationship between cancer and arrhythmias, beyond the prevention and management of rhythm disorders during or after cancer therapy.The study indicates that ventricular arrhythmias may have prognostic significance in patients with advanced malignancies as the burden of either NSVT or premature ventricular contractions independently predicted all-cause mortality. Similarly, previous studies have shown that atrial fibrillation, even if related to transient stressors such as surgery, is an independent predictor of worse outcomes in patients with malignancies.In addition to the prognostic impact of ventricular arrhythmias,

Anker and colleagues suggest that rhythm disorders may represent a therapeutic target in cancer and that cardioactive medications may impact mortality by mitigating ventricular arrhythmias [6,8].

This concept is a hypothesis that needs to be investigated through proper clinical studies and should consider the type and stage of cancer. It highlights the importance of addressing cardiovascular disease in cancer patients. Previous research has shown that conducting a thorough initial cardiovascular assessment, risk stratification, and monitoring and management of cancer patients makes the majority of them suitable to receive the best available cancer therapy without interruptions. This, in turn, increases the likelihood of a positive outcome. Additionally, timely detection and management of cardiovascular issues during cancer treatment also improves patient survival. Further progress is expected as ongoing research provides solid evidence for the primary prevention of cardiotoxicity and when long-term cardiovascular surveillance of cancer survivors is well established. All of these efforts form the basis of a comprehensive Cardio-Oncology service.

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