



LETTER TO THE EDITOR

Cardio-oncology guidelines, structural heart disease and Kounis syndrome in the upcoming guidelines



Recomendações de cardio-oncologia, doença cardíaca estrutural e síndrome de Kounis nas próximas recomendações

The Cardio-Oncology Study Group of the Portuguese Society of Cardiology and the Portuguese Association of Cardiovascular Intervention have collaborated to produce a position paper that addresses the topic of cardiac intervention in cancer patients, with an emphasis on percutaneous techniques.¹ The authors of this outstanding work underlined the scarcity of currently available evidence or recommendations for treating structural or coronary heart disease. Another important point to remember is that, possibly more so than in the general population, the manifestations of coronary artery disease in cancer patients are frequently caused by microvascular disease, classical atherosclerotic disease, vasospasm and hypersensitivity to cancer drugs leading to hypersensitivity-associated acute coronary syndrome, so-called Kounis syndrome (KS).² Furthermore, this subject is only touched upon in passing in the most recent (2022) European Society of Cardiology (ESC) guidelines on cardio-oncology,³ for which the ESC collaborated with the European Hematology Association, the European Society for Therapeutic Radiology and Oncology, and the International Cardio-Oncology Society. However, a noteworthy omission from the ESC guidelines is hypersensitivity reactions and the Kounis hypersensitivity-associated coronary syndrome, despite the fact that these conditions have been identified as serious side effects of cancer therapy in many reports in the medical literature.

KS is an acute coronary syndrome that results from hypersensitivity or anaphylactic reactions. It can manifest as vasospastic angina (type 1), myocardial infarction (type 2), stent thrombosis with an occluding thrombus (type 3A), or stent restenosis (type 3B). Mast cells, which are best known for inducing hypersensitivity, are found in cardiac tissue and especially in the vulnerable shoulder region of atheroma of coronary arteries.⁴

During the hypersensitivity reaction, inflammatory mediators are released, with effects including vasoconstriction and coronary artery spasm facilitated by histamine, platelet-activating factor, and eicosanoids. In the US

National Inpatient Sample, KS was associated with an in-hospital mortality of 7.0% as opposed to 0.4% in the anaphylaxis non-KS group.⁵ Three entities resembling KS may involve the mesenteric, cerebral and peripheral arteries. One of the main differential diagnoses to take into account in KS is stress-induced cardiomyopathy, or Takotsubo syndrome, in patients taking anti-cancer therapy.⁶ Additionally, patients can have both of those entities present at the same time during the ATAK complex (adrenaline, Takotsubo, anaphylaxis, and Kounis syndrome).⁶

In order to reduce morbidity and mortality in KS, prompt intervention is essential. The guidelines on acute coronary syndromes (ACS) should be followed when treating patients with ACS. Sadly, there are no precise instructions on how to handle ACS due to KS in these guidelines. Clinical challenges arise in the management of KS because certain medications used to treat the cardiac clinical picture can also worsen allergic signs and symptoms. Guidelines on hypersensitivity reactions to cancer chemotherapy have been released by the Spanish Multidisciplinary Research Network for Allergy Diseases, but they do not mention cardiotoxicity.⁷ Instead, they emphasize the importance of diagnosis, management, and desensitization procedures. Similarly, a task force has been established by the European Network on Drug Allergy and the Drug Allergy Interest Group of the European Academy of Allergy and Clinical Immunology to furnish information and suggestions concerning allergological research in the area of hypersensitivity reactions to chemotherapy, without making reference to cardiotoxicity.⁸

For the benefit of both researchers and practicing physicians, there needs to be close coordination and understanding among all these great organizations. Looking ahead, the ESC cardio-oncology guidelines, which are set to be released shortly, ought to take structural heart disease and KS into account.

Conflicts of interest

The authors have no conflicts of interest to declare.

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Nicholas G. Kounis

Department of Cardiology, University of Patras Medical School, Patras, Greece

E-mail address: ngkounis@otenet.gr