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Management Of Cardiac Disease In Cancer Patients Throughout Oncological Treatment

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Abstract

Cancer and cardiovascular (CV) disease are the most prevalent diseases in the developed world. Evidence increasingly shows that these conditions are interlinked through common risk factors, coincident in an ageing population, and are connected biologically through some deleterious effects of anticancer treatment on CV health. Anticancer therapies can cause a wide spectrum of short- and long-term cardiotoxic effects. An explosion of novel cancer therapies has revolutionised this field and dramatically altered cancer prognosis. Nevertheless, these new therapies have introduced unexpected CV complications beyond heart failure. Common CV toxicities related to cancer therapy are defined, along with suggested strategies for prevention, detection and treatment. This ESMO consensus article proposes to define CV toxicities related to cancer or its therapies and provide guidance regarding prevention, screening, monitoring and treatment of CV toxicity. The majority of anticancer therapies are associated with some CV toxicity, ranging from asymptomatic and transient to more clinically significant and long-lasting cardiac events. It is critical however, that concerns about potential CV damage resulting from anticancer therapies should be weighed against the potential benefits of cancer therapy, including benefits in overall survival. CV disease in patients with cancer is complex and treatment needs to be individualised. The scope of cardio-oncology is wide and includes prevention, detection, monitoring and treatment of CV toxicity related to cancer therapy, and also ensuring the safe development of future novel cancer treatments that minimise the impact on CV health. It is anticipated that the management strategies discussed herein will be suitable for the majority of patients. Nonetheless, the clinical judgment of physicians remains extremely important; hence, when using these best clinical practices to inform treatment options and decisions, practitioners should also consider the individual circumstances of their patients on a case-by-case basis.

Keywords: cardiac disease, cardiovascular toxicity, Clinical Practice Guidelines, diagnosis, recommendations

Introduction

Heart disease and cancer are the two major causes of morbidity and mortality worldwide, accounting for at least 70% of the medical reasons for mortality across the globe.[1] Cancer patients often have multiple comorbidities [e.g. diabetes, hypertension (HTN)] that can profoundly influence their cancer care and clinical outcomes.[2] Additionally, the concern for survivorship care is particularly relevant, given that, for many forms of cancer, the 5-year survival rate has dramatically risen over the past 30 years.[3]

Many anticancer therapies are known to have deleterious effects on the cardiovascular (CV) system.[4,5]

Although many health care providers are aware of the potential short-term cardiotoxicities associated with anticancer therapies, there is frequently less appreciation for the long-term consequences of such treatments on cardiac health.
The majority of clinical trials of anticancer therapeutics associated with CV toxicity are lacking in the ascertainment of relevant cardiac outcomes.[6]
A fundamental aspect of caring for a patient undergoing potentially cardiotoxic anticancer therapy is interdisciplinary communication, especially between cardiology, oncology and haematology departments and, ultimately, primary care providers. In particular, the cardiologist should have a thorough understanding of the prognosis, intended treatment plan, estimated benefit of the proposed treatment, cardiac and relevant non-cardiac toxicities and alternative treatment options. Conversely, oncologists and haematologists should be informed of the patient's CV risk factors and the status of pre-existing CV disease (CVD) along with their prognosis.
These ESMO consensus recommendations attempt to summarise best practices for the care of cancer patients exposed to potential cardiotoxic therapy, including chemotherapeutic agents, targeted therapies and radiotherapy (RT).

Materials and Methods

The recommendations that are detailed represent a unanimous agreement among the writing group. The literature review was done at the onset of deliberations, ongoing through the collaborative discussions, and then was finalised in June 2011. A complete literature search was done through PubMed index and included adult studies published from 1975 to the present. The author search incorporated the text words and Medical Subject Headings (MeSH) for chemotherapy (ChT), targeted therapy, RT, immunotherapy, individual drug names, adverse events, cardiac events, cardiotoxicity, cardio-oncology and vascular toxicity. References of reviewed articles were also searched for relevant titles. Priority was given first to evidence from randomised, controlled trials (RCTs) or meta-analysis (levels I and II), then to evidence from cohort and case control studies (level III), and finally to expert opinion based on the synthesis of retrospective or observational studies and clinical practice (levels IV and V). The authors also searched clinicaltrials.gov for any ongoing appropriate clinical trials.

Result

Anticancer therapy, including RT and some ChT drugs/targeted agents, can substantially affect the heart and vascular system. Any anticancer therapy that impacts cardiac safety requires monitoring.

Screening.

Cancer patients with pre-existing CVD or CV risk factors are at a greater risk of cardiac complications from anticancer therapies. The treatment of CV risk factors in any patient is important and the significance of this principle is equally valid in a patient population that has cancer.[8–10] In many contexts of anticancer therapy, there is ample information to validate the recommendation to treat CV risk factors effectively.[11–17]

Anticancer therapy risk factors for CV toxicities.

Many large-scale randomised prospective clinical trials and follow-on studies have indicated certain ChT and/or targeted therapies are associated with CV toxicities (supplementary Table S1, available at *Annals of Oncology* online).[18–23] It is also widely recognised that radiation to CV structures has an important impact on CV health,[5,24–26] with radiation exposure potentially having a profound impact on the vascular structures, valves, pericardium/myocardium and conduction system, as well as the autonomic system.[5,27–32] When planning anticancer therapy, the potential adverse CV effects of anticancer therapy should be balanced against the expected benefits.

Collaborative approach.

There is a high level of evidence that cardiac monitoring in certain anticancer settings helps limit the cardiac impact of a patient's cancer therapy.[18–21] The cardiology consultation can be associated with improved cardioprotection, therapy adherence and survival in patients receiving anthracyclines.[33] The multidisciplinary team's goal should be a balanced approach to minimising CV toxicity while also limiting reduction or discontinuation of anticancer therapy. Intensive, multidisciplinary team intervention, compared with usual care to prevent cardiotoxicity, is currently being tested in an RCT (TITAN, NCT01621659), with results expected soon.[34]

Recommendation 1.1.

Screening for known CV risk factors in patients with cancer is recommended; treatment of identified CV risk factors according to current guidelines is recommended [I, A].

Recommendation 1.2.

Many types of cancer therapy, especially mediastinal and left-sided chest radiation and certain ChT and targeted agents, can substantially affect the heart and vascular system and it is recommended that CV safety be monitored [I, A].

Recommendation 1.3.

Close and early collaboration between cardiologists, oncologists, haematologists and radiation oncologists is recommended to ensure lifelong CV health and to avoid unnecessary discontinuation of cancer therapy [III, A].

Conclusion

CVD in patients with cancer is complex, and it is paramount that individual patient management and treatment is personalised. Although cancer treatment-related cardiotoxicity was initially observed as early as the 1970s, the current landscape has changed dramatically with the introduction of novel targeted therapies. The scope of cardio-oncology is wide and includes not just prevention, detection, monitoring and treatment of CV toxicity related to anticancer therapy, but also the development of future novel anticancer treatments that have minimal impact on CV health.

Close collaboration between oncologists, cardiologists and allied health care professionals will ensure delivery of optimal care for cancer patients, based on current best clinical practices, without compromising CV health. Research will help define best strategies for prevention, early detection and management of CV complications related to anticancer therapy. The incorporation of surveillance strategies in cancer survivors will help prevent the potential long-term CV morbidity and mortality associated with oncological treatments. Education of health care providers, particularly the next generation of cardiologists and haemato-oncologists, along with patients, on the importance of CV health and anticancer treatment should translate into better cancer and CV clinical outcomes.

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