Co-morbidities

The Future Role of Cardio-oncologists

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Abstract
Cardiovascular (CV) disease and cancer remain the two most common causes of mortality in developed countries; however, progress in the treatment of malignant diseases significantly improved survival of oncological patients. Similarly, there is an increased number of the patients with malignancy who have a history of CV disease or an increased CV risk. Rates of CV problems from cancer-related therapeutics are high, and cardiotoxicity is the second most common cause of morbidity and mortality in cancer survivors. Therefore, there is a need for the development of an efficient programme to manage the problem of cardiotoxicity with the aim to decrease morbidity and mortality in patients and to improve their quality of life. For this purpose, cardio-oncological clinics should be an essential part of the strategy.

Keywords
Cardiotoxicity, cardio-oncology clinic, detection, management, risk factors

Cardiovascular (CV) disease and cancer remain the two most common causes of mortality in developed countries. According to recent data from the American Cancer Society, the lifetime probability of being diagnosed with an invasive cancer is higher for men (43 %) than for women (38 %).\(^1\) Within the last few decades the progress in the treatment of malignant diseases significantly improved survival of oncological patients. The decreased mortality is driven by both improved diagnostic and therapeutic modalities; however, the improved survival of oncological patients can be limited by adverse effects associated with intensive antitumorous treatment. In particular, cardiotoxicity may compromise the effectiveness of the anticancer therapy, independently of the oncological prognosis, and can negatively affect survival and quality of life of oncological patients. This includes the development of newly diagnosed CV problems, or the exacerbation of previously identified CV disease. Rates of CV problems from cancer-related therapeutics have been reported to be in excess of 30 %, and cardiotoxicity is the second most common cause of morbidity and mortality in cancer survivors.\(^2,3\) The number of patients at risk of problems is high. According to the latest data, on 1 January 2016 more than 15.5 million Americans with a history of cancer were alive, and this number is projected to reach more than 20 million by 1 January 2026. Furthermore, 56 % of survivors were diagnosed within the past 10 years, and almost half (47 %) were aged 70 years or older.\(^4\) Similarly, there is an increasing number of patients with malignancy who have a history of CV disease or an increased CV risk. Therefore, the CV problems in oncological patients are not only medical but also social and economic problems, and new strategies to solve this topic are needed.\(^5\) This brief review focuses on some issues that need to be addressed in the near future.

Wide Spectrum of Cardiovascular Complications of Cancer Treatment

The first clinical manifestation of adverse effects from anticancer drugs on the CV system was depression of the left ventricle function leading to heart failure in patients treated with anthracyclines. Therefore, the term cardiotoxicity of cancer therapy was established for the development of heart failure as a result of anticancer treatment. Until now, myocardial dysfunction and heart failure are the most concerning CV complications of cancer therapy due to their role in an increase in morbidity and mortality in cancer patients. Myocardial dysfunction is associated with a broad spectrum of anticancer treatment (anthracyclines, alkylating agents, tyrosine kinase inhibitors, antimetabolites, etc.) with the incidence ranging from 2–40 %.\(^6\) Diagnosis of myocardial dysfunction was based on a decrease of left ventricular ejection fraction (LVEF) of at least 10 % to a level below normal from methods such as 2D and 3D echocardiography, cardiac MRI and multigated radionuclide angiography.\(^7,8\) Some studies revealed a potential beneficial role of cardiomarkers (troponins and natriuretic peptides) in the detection of early manifestation of cardiotoxicity.\(^9\) Serial evaluation of symptoms, ECG and echocardiography focused on left ventricle function were seen to be sufficient to cover all cardiotoxicity problems; however, further observations revealed a much wider spectrum of CV complications of cancer therapy.\(^10\) They are divided into nine categories according to their pathophysiology and clinical manifestation: myocardial dysfunction and heart failure; coronary artery disease; valvular disease; arrhythmias, especially those induced by QT-prolonging drugs; arterial hypertension; thromboembolic disease; peripheral vascular disease and stroke; pulmonary hypertension; and pericardial complications.\(^11\) Detection of CV complications from the cancer treatment requires the use of a broad spectrum of diagnostic techniques, such as ECG, blood pressure monitoring, CV imaging methods, biomarker testing, coronary arteriography, cardiac catheterization, etc. Therefore, there is a need for collaboration from a broad spectrum of specialists covering not only oncology, but all fields of cardiology.

Basic Concept for the Management of Patients Treated with Potentially Cardiotoxic Drugs

It has been shown that early detection and adequate treatment of CV complications can improve survival and the quality of life of oncological
patients. The main part of the general strategy to minimise the CV risks of anticancer treatment is baseline risk assessment with the aim to identify patients who are at higher risk of CV complications. There are four factors for CV risk: current myocardial disease (heart failure including asymptomatic left ventricular dysfunction; evidence of coronary artery disease; moderate or severe valvular heart disease; arterial hypertension with impaired LVEF; hypertrophic, dilated or restrictive cardiomyopathy; cardiac sarcoidosis; and arrhythmias [AF and ventricular arrhythmias]); previous cardiotoxic cancer treatment (prior anthracycline medication, and chest and mediastinal irradiation); demographic risk factors (age, family history of premature CV disease, arterial hypertension, diabetes mellitus and hypercholesterolemia); and lifestyle risk factors (high alcohol intake, obesity, sedentary lifestyle and smoking). In patients treated with potentially cardiotoxic therapy, baseline risk assessment and LVEF should be determined before and periodically during the treatment using the same method. The regimen of the diagnostic tools for the detection of cardiotoxicity consists of ECG (resting tachycardia, ST-T changes, conduction disturbances and QT interval prolongation); echocardiography (2D or 3D LVEF assessment, global longitudinal strain, pericardial effusion, etc.); nuclear cardiac imaging (LVEF assessment using multigated radionuclide angiography); cardiac MRI (LVEF and structural changes of the myocardium); and biomarker assessment (challenging data were published on troponins and natriuretic peptides, which seems to be helpful to identify the patients at higher risk or those with early manifestation of cardiotoxicity). According to the current recommendations, precise timing and frequency of imaging and/or biomarkers sampling depends on the specific cancer treatment, total cumulative dose, delivery protocol and the patient’s baseline CV risk profile. In asymptomatic patients with significantly decreased ejection fraction, the treatment with angiotensin-converting enzyme inhibitors in combination with beta-blockers should be considered as a prevention of further decrease of LVEF. These drugs are indicated for those with symptomatic left ventricular dysfunction; thus, the timing of the cardiotoxicity surveillance should be personalised to the patient with the aim to avoid cardiotoxicity, to detect early phases of the cardiotoxicity and to start appropriate measures (type and schedule of anticancer regimen, and treatment of heart failure).

The optimal surveillance strategy to minimise the risk of cardiotoxicity has gaps in evidence and this strategy is frequently based on expert opinion; therefore, further studies are needed.

Cardio-oncology Team and Cardio-oncology Subspecialty

Historically, oncologists were the first medical professionals to observe CV complications from cancer treatment. These patients were referred to cardiologist for further examination and CV treatment. This approach was shown to be ineffective in appropriate treatment of the cardiac problems in cancer patients, but mainly it was impossible to detect early phases of cardiotoxicity and avoid complications. Nowadays, the complexity of the cancer treatment requires tight co-operation between oncologist and cardiologist in the identification of at-risk patients, planning of treatment, and patient surveillance with the aim to prevent cardiotoxicity, detect early signs of cardiotoxicity and to take appropriate measures to solve complications. This new situation has led to the development of the new cardiology subspecialty in cardio-oncology, which is a multidisciplinary field with the aim to prevent and treat CV complications from cancer therapy. The cardio-oncology clinic must be able to cover all needs required to fulfil its aims, that is, they must be able to provide all examinations of the CV system (ECG, echocardiography and biomarkers), and have access to patients or provide other examinations (nuclear cardiology examinations, cardiac magnetic resonance, cardiac catheterization, etc.).

Cardio-oncology Clinic

Cardio-oncology clinics are currently expanding in both academic centres and community practices. Some key components for the effective work of the cardio-oncology centre are:

- High level of programme leadership (collaborative work of cardiologist and oncologist on all aspects of programme development).
- Appropriate location (within cancer centre, in close proximity to those specialities that refer large numbers of patients, and adequate space to allow for future expansion and growth).
- Experienced staff (patient evaluation must be provided by individuals who understand the complexities of cancer patients).
- CV testing (onsite echocardiography with access to advanced echo technologies, and access to additional imaging modalities including cardiac MRI and coronary arteriography).

The cardio-oncology nurse coordinator can be a useful member of the cardio-oncology team. The aim of the co-ordinator should be patient care co-ordination, triaging urgent CV issues and patient education. Education and research are also important functions of the successful centre. Education should be focused on staff education (oncology meetings, tumour boards, etc.), trainee education (conferences and workshops for residents and fellows) and community education (to increase public awareness about cardio-oncology problems), and research should be one of the essential functions of the academic centre.

Conclusion

Effective cardiotoxicity management needs to be comprehensive. It requires not only the building of a network of cardio-oncology clinics near oncology centres but also a tight co-operation with other primary healthcare clinics and providers who care for patients after the completion of oncology treatment. This requires close co-operation between medical professionals (oncologists and cardiologists) and education not only within the medical community but also for the general public. This must all be supported by adequate financial resources. Therefore, it is necessary to create standards for the effective functioning of such a system, aiming not only at minimising the mortality and mobility of this group of patients, but primarily for improving the quality of life, including the return-to-work process.

In summary, these are the processes that must be led by medical societies in a discussion with other partners involved in the treatment of oncological patients: healthcare providers, the healthcare industry, health insurers, institutions involved in healthcare and the general public.
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