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REVIEW

Cardio-oncology for the general physician: 'old' and 'new' cardiovascular toxicities and how to manage them

Michael Mallouppas[1,2]

J Malcolm Walker[1,2]

Avirup Guha[3]

Rebecca Dobson[4]

Arjun K Ghosh[1,2,5]

Author details can be found at the end of this article

Correspondence to:
Arjun K Ghosh;
arjun.ghosh@nhs.net

Abstract

Cardio-oncology is the care of cancer patients with cardiovascular disease. The need for a dedicated subspecialty emerged to address heart failure caused by drugs such as anthracyclines and anti-human epidermal growth factor receptor 2 (HER2) therapies, but over time has expanded into an exciting subspecialty with widening horizons. While still dealing with a lot of commonly recognised toxicities, such as heart failure, hypertension and coronary disease, new and revolutionary cancer therapies have been associated with challenging cardiovascular complications, requiring specialist input to manage effectively. Echocardiography is a key investigation, with advanced techniques such as three-dimensional and strain assessment allowing more accurate diagnosis and earlier detection of subtle changes. Cardiac magnetic resonance and biomarkers are useful adjuncts to aid diagnosis and management. With increasing cancer incidence and improved cancer survival rates, it is important that general cardiologists and physicians are aware of cardiac complications associated with cancer and how to manage them.

Key words: Cancer; Cardio-oncology; Cardiotoxicity; Heart failure; Myocarditis; Toxicity

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What is cardio-oncology?

Cardio-oncology is the care of cancer patients with cardiovascular disease (Ghosh and Walker, 2017). Although often thought to be a new subspecialty, cardio-oncology has a considerable history. Anthracyclines were discovered in the 1960s and were soon found to have significant anti-tumour properties, but this came with a considerable cardiotoxic profile (Von Hoff et al, 1977). The anti-human-epidermal growth factor receptor 2 (anti-HER2) therapies revolutionised survival for some patients with breast cancer, but were soon noted to be associated with deleterious effects on cardiac function (Slamon et al, 2001). It was recognised that with these cancer successes came an unmet need for oncologists and cardiologists to collaborate and develop appropriate strategies to manage these two important cohorts of cancer patients.

The introduction of new cancer therapies has led to a variety of cardiovascular complications encountered by clinicians and potentially impacting on the outcome for cancer patients. Cardiotoxicity is commonly used as an umbrella term to refer to these complications without a precise definition. Confusingly, the term is often used interchangeably with chemotherapy-related cardiac dysfunction; while detection and treatment of heart failure plays a major part, cardio-oncology is not only about heart failure (Chung et al, 2018). Therefore, even though 'cardiotoxicity' is a useful generic term, the specific cardiovascular complications of each therapy need to be detailed in patient records. Despite the implications for cancer care when they occur, there is an opportunity to learn from these toxicities. Cancer therapies are being developed with precise cellular and molecular targets and when these impact on cardiovascular function, insight can be gained into the mechanisms underlying certain aspects of cardiovascular disease (Manouchehri et al, 2020). Table 1 details the cardiovascular complications of the cardio-oncology patient.

Given the increasing number of patients being diagnosed with and also surviving cancer, having an understanding of common cardiac complications of cancer treatment is useful for general physicians. This review provides an outline of these complications, covering diagnosis and management with a focus on newer toxicities.

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Table 1. Cardiovascular complications of the cardio-oncology patient
Perimyocardial disease
Pulmonary hypertension
Thromboembolic disease
Systemic hypertension
Arrhythmic disease
Valvular heart disease
Coronary artery disease
Heart failure and myocardial dysfunction

Table 2. Mechanisms of action of common chemotherapeutic agents

Type of agent	Examples	Mechanism of action
Cytotoxic agents	Anthracyclines – doxorubicin, daunorubicin, epirubicin	DNA intercalation, topoisomerase II inhibition, disruption of cell transcription and division, free radical generation
	Taxanes – docetaxel, paclitaxel	Disruption of cell division
Molecular targeted therapy	Human epidermal growth factor 2 receptor (HER2) antibody – trastuzumab, pertuzumab	Monoclonal antibody against the HER2 protein
	Tyrosine kinase inhibitors of vascular endothelial growth factor – lapatinib, sunitinib, imatinib	Blocking signal transduction cascades
	Vascular endothelial growth factor inhibitors – bevacizumab	Inhibit angiogenesis
	Immune checkpoint inhibitors – ipilumab, nivolumab, pembrolizumab	Monoclonal antibody against immune checkpoint receptors and their ligands

Cardiovascular complications of cancer therapy

To appreciate the cardiovascular complications of cancer therapies, a basic understanding of how these agents work is needed. Chemotherapeutic agents can be broadly divided into two categories: cytotoxic agents (eg anthracyclines) or molecular-targeted therapy agents (eg trastuzumab). The mechanism of action of some common chemotherapeutic agents is shown in Table 2.

Heart failure

Heart failure is one of the most common and most serious complications of cancer therapy. Survivors of paediatric cancer have a 15-fold increase in the risk of congestive heart failure compared to healthy siblings (Oeffinger et al, 2006). Adults treated for aggressive non-Hodgkin's lymphoma have a 17% incidence of clinical heart failure at 5 years (Limat et al, 2014). Agents that commonly cause heart failure are listed in Table 3.

Previously, cancer therapy-related cardiac dysfunction was divided into type 1 and type 2 (Ewer and Lippman, 2005). Type 1, typically caused by anthracyclines, was felt to be dose related, irreversible and characterised by vacuolar swelling, myofibrillar disarray and ultimately myocyte death (Plana et al, 2014). Type 2, typically caused by trastuzumab, was described as not dose related, reversible and without any apparent ultrastructural abnormalities on electron microscopy (Ewer and Lippman, 2005). However, this distinction is too simplistic, as it does not take into account the synergistic effect of combination chemotherapies. Additionally, anthracycline-induced cardiac injury is

Table 3. Common and new cardiovascular complications of chemotherapeutic agents

Complication	Causative agent	Comments
Heart failure	Anthracyclines	Multifactorial – free radical generation most likely (Gewirtz, 1999)
	Alkylating agents (cyclophosphamide, ifosfamide)	Toxic endothelial damage with subsequent cardiomyocyte death (Allegra et al, 2010)
	Anti-human epidermal growth factor 2 receptor (HER2) therapies	HER2 protein blockage blocking Erb2 signalling and impairing cardiac contractility and structure (Ewer and Lippman, 2005)
	Tyrosine kinase inhibitors of vascular endothelial growth factor (VEGF) receptors (e.g. imatinib, dasatinib)	'Off target' effects affecting a variety of intracellular signalling pathways in cardiomyocytes (Force et al, 2007)
Coronary ischaemia	Fluoropyrimidines (fluorouracil, capecitabine)	Multifactorial. Coronary spasm one commonly quoted mechanism (Polk et al, 2014)
	Platinum agents (cisplatin)	Arterial thrombosis as a result of the procoagulant state (Zamorano et al, 2016)
Hypertension	Vascular endothelial growth factor inhibitors	Increase in systemic vascular resistance (Izzedine et al, 2009)
Myocarditis	Immune checkpoint inhibitors	Possible molecular mimicry (Palaskas et al, 2020)
Hypotension and shock	Chimeric antigen receptor (CAR)-T cell therapy	Unclear. Likely part of generalised cytokine release syndrome (Ghosh et al, 2020)

reversible if treated early (Cardinale et al, 2015) and trastuzumab-induced injury does not always reverse (Cardinale and Sandri, 2010).

Treatment of chemotherapy-induced heart failure does not differ from other types of heart failure and should follow published guidelines. A cut-off of a change in left ventricular ejection fraction of ≥10% from baseline to a level below the lower limit of normal, or with symptoms, often prompts initiation of treatment.

Attempts to identify potential agents for use in primary prevention of cardiac dysfunction, particularly from anthracyclines, have generated mixed results. There is limited evidence that enalapril prevents reductions in left ventricular ejection fraction compared to placebo in high-risk patients (Cardinale and Sandri, 2010), whereas there is no such evidence for carvedilol in the same patient cohort (Avila et al, 2018). Combined therapy with carvedilol and enalapril prevents small reductions in left ventricular ejection fraction (Bosch et al, 2013). In breast cancer patients treated with anthracyclines and/or trastuzumab, candesartan prevents a small but significant reduction in left ventricular ejection fraction compared to placebo (Gulati et al, 2016).

To date, no medications have been routinely used for the primary prevention of anthracycline-induced cardiomyopathy. Dexrazoxane is an iron chelator which prevents free radical generation, thus interfering with one of the prevailing hypothesised mechanisms of anthracycline-induced cardiotoxicity. It has been shown to prevent development of left ventricular dysfunction in phase III trials of patients with advanced breast cancer (Swain et al, 1997). Owing to initial concerns of an increased risk of infection, myelosuppression, second primary malignancies and reduction of anthracycline efficacy in adults and particularly children there was a general reluctance to use it and it was initially restricted for certain indications. Since then, systematic reviews of its use have shown an overall net benefit (van Dalen et al, 2011) and some of the restrictions have been lifted (European Medicines Agency, 2017). It is currently the only agent that is approved for the primary prevention of anthracycline-induced cardiomyopathy in patients with advanced breast cancer, who are to receive high-dose anthracyclines.

In cases of cardiac dysfunction resulting from anti-HER2 therapy, it is not uncommon to adopt a start/stop approach to allow left ventricular function to recover, even in asymptomatic patients. However, there are concerns that this approach may affect oncological outcomes. Emerging data suggest that in asymptomatic patients who have

a mild reduction of left ventricular ejection fraction (as low as 40%), who are treated appropriately (usually with beta blockers and angiotensin-converting enzyme inhibitors), may be able to continue anti-HER2 therapy without interruptions with close monitoring (Lynce et al, 2019; Curigliano et al, 2020). Therefore, surveillance for cardiotoxicity is crucial in the management of these patients. In the latest European Society of Medical Oncology (ESMO) consensus recommendations, asymptomatic patients on adjuvant trastuzumab therapy in the non-metastatic setting should be considered for routine surveillance with cardiac imaging every 3 months during therapy to detect early onset cardiotoxicity, although this may need to be even more frequent in high-risk patients (Curigliano et al, 2020). Cardiac biomarkers, in particular troponin and N-terminal pro-brain natriuretic peptide (NT-proBNP), may also be an additional valuable tool, as an abnormal elevation predicts a higher risk of developing heart failure. However, the exact timing of when to measure biomarkers and the level of elevation is deemed abnormal is yet to be determined. In patients with metastatic disease, general cardiac surveillance with clinical, imaging and biomarker assessment is recommended, although the exact frequency is not specified (Curigliano et al, 2020).

Ischaemia

Coronary disease and ischaemia can be caused by a variety of different agents (Table 3). While most of these accelerate atherosclerosis, there are other proposed mechanisms (Das et al, 2019). Fluoropyrimidines, commonly used in the treatment of bowel cancer, are thought to cause endothelial injury and coronary vasoconstriction that can lead to ischaemia (Chong and Ghosh, 2019). Patients will commonly present with angina, either during therapy or a few days after, sometimes associated with electrocardiogram changes and less commonly with an acute coronary syndrome, presenting with elevations in cardiac enzymes and/or wall motion abnormalities on echocardiography (Chong and Ghosh, 2019). Depending on the clinical presentation and each individual patient, investigations are performed to rule out significant coronary disease.

In the acute setting of electrocardiogram changes with cardiac biomarker elevation and/or echocardiographic changes, an urgent inpatient coronary angiogram is often performed. In the non-acute setting, if other patient factors like thrombocytopenia are present, non-invasive investigations with either computed tomography coronary angiography or functional testing (stress echocardiography, cardiac magnetic resonance or stress perfusion nuclear imaging) are often performed (Das et al, 2019). In the absence of significant coronary disease, patients are often treated for presumed vasospasm with calcium-channel blockers with varying success.

The mode of administration may have a role to play, as retrospective analyses of patients on different fluoropyrimidine regimens suggest an increased risk of cardiac events (with angina being the most common) with continuous (72%) vs bolus (23%), or intermediate (3%) infusions or oral preparations (2%) (Saif et al, 2009). In true coronary ischaemia, fluoropyrimidine therapy may need to be interrupted, or avoided completely, leading to complex issues regarding cancer chemotherapy regimens and needing close cooperation between specialties to quantify risks and achieve the best outcomes for individual patients.

Radiotherapy, particularly to the chest, significantly increases the risk of premature coronary artery disease through accelerating atherosclerosis (Zamorano et al, 2016). Critical proximal lesions are more common and depend on the radiation field. For instance, left anterior descending lesions are more common in patients who received left-sided radiation for breast cancer (Nilsson et al, 2012), whereas patients who previously received mantle radiotherapy for Hodgkin's lymphoma may develop a variety of coronary and non-coronary complications. Therefore, aggressive control of cardiovascular risk factors (possibly at a younger age than usual) as well as a low threshold for investigating symptoms is paramount, particularly because of the latent period of presentation (which can be more than 10 years after treatment; Handa et al, 1999). This is important, as ongoing screening of these patients should occur on a long-term basis, preferably in a 'late-effects clinic' setting. Furthermore, radiotherapy is a well-recognised cause of premature valvular disease, with an even more latent period compared to coronary disease (Hull et al, 2003), as well as pericardial disease (Ghosh et al, 2018).

Hypertension

Hypertension is common in cancer patients, found in 38% of hospital-based cancer registry data. It is the most common comorbidity (Piccirillo et al, 2004), but can also be induced by cancer treatment. This is particularly true for vascular endothelial growth factor (VEGF) inhibitors (eg bevacizumab, sorafenib, sunitinib) with an incidence of all grades of hypertension between 15 and 44% (Zamorano et al, 2016). Diagnosis and treatment should follow international guidelines with treatment initiated if blood pressure is ≥140/90 mmHg or if there is ≥20 mmHg increase in diastolic blood pressure from baseline (Maitland et al, 2010). Renin–aldosterone system blockers or dihydropiridine calcium-channel blockers are usually first-line therapies, with beta blockers and thiazide diuretics as alternative options, although ultimately each treatment needs to be individualised, taking into account cancer therapy interactions (Maitland et al, 2010). Sometimes, the VEGF inhibitor may need to be adjusted or completely stopped if blood pressure remains high despite treatment, in cases of symptomatic severe hypertension (malignant hypertension) or if cardiovascular complications occur, necessitating urgent blood pressure control. A useful approach when monitoring blood pressure during treatment includes an initial assessment of risk (including clinical history and examination, assessment of risk factors and blood pressure measurement on two occasions, 3 minutes apart, ideally on two separate visits). This should be followed by weekly monitoring of blood pressure during the first cycle of therapy and, if stable, every 2–3 weeks thereafter for the duration of therapy (Maitland et al, 2010).

‘Newer’ toxicities

Cardiac arrhythmias

Cardiac arrhythmias are common (and not new) in cancer patients. They are either present at baseline or occur as a consequence of cancer and its treatment. QT prolongation is a commonly quoted and feared complication, as it can lead to life-threatening torsades de pointes polymorphic ventricular tachycardia. Arsenic (a treatment for a variety of haematological malignancies) significantly increases the risk of QT prolongation (Zamorano et al, 2016).

Atrial arrhythmias, in particular atrial fibrillation, are increasingly recognised as a problem in cancer, especially as these can lead to complex and difficult decisions with regard to anticoagulation (Ganatra et al, 2018). Several of the offending chemotherapeutic drugs have been described as triggers (Zamorano et al, 2016). The tyrosine kinase inhibitors, in particular ibrutinib (a novel tyrosine kinase inhibitor approved in 2015 for a variety of haematological malignancies), have been identified as increasing the risk of atrial fibrillation over and above that of the general population, with rates of 5.8 per 100 person-years (adjusted incidence 8%) in systematic reviews (Ganatra et al, 2018). Management of atrial fibrillation in patients with ibrutinib who are haemodynamically stable is often based on a rate control strategy, because of the high risk of recurrence. It is preferably treated with a beta blocker as calcium-channel blockers and digoxin both interact with ibrutinib (Ganatra et al, 2018). Anticoagulation can be challenging, as ibrutinib increases the risk of bleeding and seems to interact with both classes of the newer oral anticoagulants. However, anticoagulation should be offered to those with high thromboembolic risk and low baseline bleeding risk regardless (Ganatra et al, 2018).

Myocarditis

Myocarditis is an increasingly recognised complication of immune checkpoint inhibitors (Curigliano et al, 2020). Immune checkpoint inhibitors are monoclonal antibodies that target immune checkpoint receptors on the surface of cytotoxic T-cells, preventing their ligands from binding together; an interaction which in some cancer cell lines protects them from T-cell-mediated death (Brahmer et al, 2018). There are currently seven immune checkpoint inhibitors (ipilimumab, nivolumab, pembrolizumab, cemipilimab, avelumab, atezolizumab, durvalumab), with indications including melanoma, renal cell carcinoma, lung cancer, lymphoma and colorectal cancer, among others (Palaskas et al, 2020).

Despite having very specific molecular targets, immune checkpoint inhibitors can lead to a variety of immune-related adverse events that can affect any part of the body (Brahmer et al, 2018). Myocarditis is rare, with a prevalence of 1.14% in one series (Palaskas et al, 2020) but, when encountered, it carries a significant mortality rate of up to 50% (Wang et al, 2018).

Patients can present in a variety of ways, ranging from asymptomatic elevation of cardiac enzymes to full blown cardiogenic shock with ventricular arrhythmias, requiring cardiac support. Myocarditis can be associated with myositis and myasthenia gravis (Wang et al, 2018). Useful investigations include cardiac biomarkers, cardiac magnetic resonance, electrocardiogram and echocardiography, with myocardial biopsy needed only if the diagnosis remains unclear. Re-challenging with the same immune checkpoint inhibitor leads to a recurrence rate of the same immune-related adverse event of 29% and a different immune-related adverse event of 4%, suggesting it may be possible to restart therapy in selected cases with close monitoring (Dolladille et al, 2020).

First-line therapy is the discontinuation of the immune checkpoint inhibitor and intravenous or oral steroids. Clinical, biochemical (troponin) and electrocardiogram monitoring is advocated to assess response and, if inadequate, secondary immunomodulatory agents may be considered such as intravenous immunoglobulin, mycophenolate mofetil, and others (Palaskas et al, 2020).

Chimeric antigen receptor T-cell therapy and cardiotoxicity

Chimeric antigen receptor (CAR) T-cell therapy is a revolutionary new treatment for refractory haematological malignancies in adults and children, often given as a last resort if conventional therapy has failed. The therapy is based upon genetically modifying the patient's own T cells ex vivo, altering them to recognise tumour-associated antigens (Ghosh et al, 2020). This very promising approach to managing refractory cancers has unfortunately been associated with various systemic toxicities, principally cytokine release syndrome and neurotoxicity. However, there is increasing recognition of cardiovascular involvement (Ghosh et al, 2020). Commonly associated with severe cytokine release syndrome (grade 3 or 4), patients may progress to left ventricular dysfunction, arrhythmia and cardiogenic shock, in association with grossly elevated levels of cardiac biomarkers. It is possible that the cardiovascular complications are merely secondary to the cytokine release syndrome, but the underlying pathophysiological mechanisms affecting the heart are not entirely understood and may represent a specific off-target entity (Ganatra et al, 2019).

Presentation

Owing to the varied nature of cardiovascular complications of cancer therapy, unsurprisingly, patients can present with any cardiovascular symptoms and signs. Furthermore, they can present at any stage of the cancer treatment pathway, either during treatment, or at a much later date. In addition, they can present acutely through the emergency department, or sub-acutely in the outpatient or community setting. Therefore, a high index of suspicion is needed and any cardiovascular symptoms should prompt further investigation.

In view of the multidisciplinary nature of cancer care, patients with cardiovascular complications can present to any number of different healthcare professionals before they come to the attention of cardiologists. Therefore, it is vital that the whole multidisciplinary team is educated about the cardiovascular complications of cancer therapy. A careful and detailed history of each patient's symptoms and oncological history, including therapies received, is needed to guide further cardiac investigations.

Investigations

Cardiac investigations will depend upon the suspected cardiotoxicity and the questions asked by the oncology team. Cardiac imaging, in particular echocardiography, is a crucial part of any cardio-oncology service.

Echocardiography

Echocardiography is widely available, does not involve any radiation and can give detailed information on cardiac structure and function, as well as assessing for pericardial effusions and valve disease. It has traditionally been the investigation of choice for monitoring

cardiac function during and post-chemotherapy, particularly with anthracycline and anti-HER2 therapies.

Historically, left ventricular ejection fraction has been used as marker of cardiac function during and post-anthracycline therapy. Over the years, a variety of methods has been developed to calculate left ventricular ejection fraction, all with their limitations. Two-dimensional echocardiography methods are commonly used, with the modified biplane Simpson's method being the most popular. In cancer patients undergoing chemotherapy requiring serial echocardiograms, two-dimensional left ventricular ejection fraction and volume calculations have a temporal and observer variability of about 10% (Thavendiranathan et al, 2013). This is also the cut-off of a change in left ventricular ejection fraction that would prompt discontinuation of chemotherapy (Curigliano et al, 2020). Clearly there is a problem when the coefficient of variation of the test approximates the threshold for cancer therapy discontinuation. Three-dimensional, volumetric assessments reduce this variability to around 6% (Thavendiranathan et al, 2013). If endocardial definition allows, three-dimensional is the preferred method to calculate left ventricular ejection fraction in cancer patients undergoing monitoring (Plana et al, 2014; Zamorano et al, 2016; Curigliano et al, 2020).

Nonetheless, changes in left ventricular ejection fraction may be a late feature of cardiotoxicity. Ejection fraction is a composite measure of longitudinal, radial and circumferential contractility and if one of these deteriorates, the other types may overcompensate to keep ejection fraction unchanged (Ghosh and Walker, 2017). Thus, other measures are becoming more relevant. Myocardial deformation indices, in particular global longitudinal strain, have been found to be an early predictor of subclinical cardiac dysfunction, which predicts subsequent deterioration in left ventricular ejection fraction (Negishi et al, 2013), with a change in global longitudinal strain of more than 15% from baseline indicative of toxicity (Plana et al, 2014; Zamorano et al, 2016). The usefulness of early predictors of dysfunction, such as global longitudinal strain, becomes evident in patients treated with anti-HER2 therapies. As a general rule, in patients with symptoms and signs of heart failure or with an asymptomatic deterioration of left ventricular ejection fraction ≤ 40%, anti-HER2 therapy needs to be withheld and heart failure treatment started (Curigliano et al, 2020). However, discontinuing anti-HER2 therapy can have a significant impact on cancer outcomes, particularly in the metastatic setting, where it can significantly reduce the risk of death compared to no anti-HER2 therapy (Slamon et al, 2001). Therefore, early identification of left ventricular dysfunction, before left ventricular ejection fraction reduction, may allow the initiation of cardioprotective medication and continuation of cancer therapy. It has been shown that in these patients, deterioration in global longitudinal strain not only pre-dates reductions in left ventricular ejection fraction, but also early treatment with carvedilol prevents deterioration in left ventricular ejection fraction, thus providing a possible window of opportunity to prevent discontinuation of cancer therapy, although this requires further research (Curigliano et al, 2020).

Cardiac magnetic resonance

This is increasingly recognised as a very useful adjunctive investigation to assess left ventricular volumes and function, as well to detect ischaemia. It is often indicated when echocardiography is non-diagnostic, which may be in up to 25% of cases (Menacho et al, 2019). Uniquely, cardiac magnetic resonance can provide 'tissue characterisation', which can be used to determine causality of left ventricular dysfunction and diagnose cardiac infiltration, while providing anatomical details to characterise cardiac tumours.

Biomarkers

Cardiac biomarkers are increasingly being used in the assessment and monitoring of patients undergoing chemotherapy, although it is not clear how exactly to interpret them. In the context of anthracyclines, elevations in troponin levels that persist after chemotherapy predict the development of cardiac dysfunction (Cardinale and Sandri, 2010). The role of N-terminal pro-hormone brain natriuretic peptide (NT-pro-BNP) is even less clear (Cardinale and Sandri, 2010).

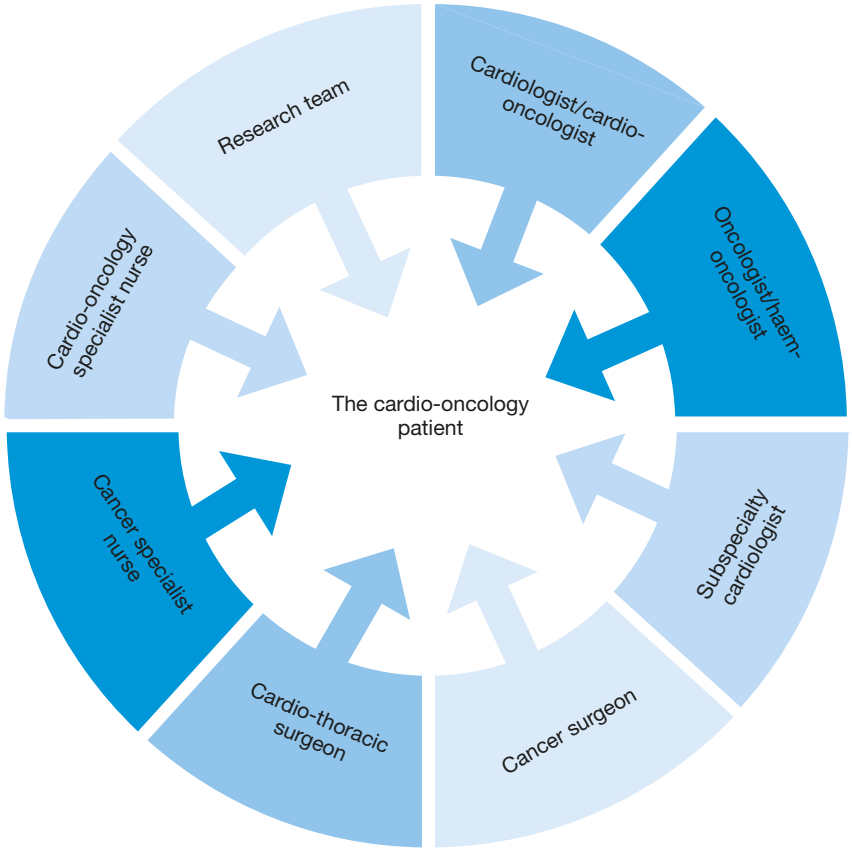

Figure 1. The members of the cardio-oncology multidisciplinary team.

Cardio-oncology service set up

Cardio-oncology services are increasingly being set up across the UK and elsewhere. The European Society of Cardiology Cardio-Oncology council has published guidance on service set up (Lancellotti et al, 2019). This should be organised according to the size of the hospital and the number of patients seen. District general hospitals with small numbers of cancer patients will have a basic cardio-oncology team or a dedicated cardiologist with a specialist interest and basic cardiac investigations, namely echocardiography and increasingly cardiac magnetic resonance. Bigger tertiary centres require dedicated cardio-oncology teams with access to all cardiac investigations, catheter laboratories and cardiac surgeons. An integral part of any service is the multidisciplinary team, where cardiology and oncology teams come together to discuss difficult cases and make decisions on the best management (**Figure 1**).

Conclusions

Cardio-oncology is an exciting and growing sub-specialty within cardiovascular medicine, with an ever-increasing relevance to the acute and general physician because of the varied nature of presentation of the cardio-oncology patient. With multiple new cancer therapies being developed, 'new' cardiovascular toxicities are emerging and therefore continual education is important.

Author details

[1]Cardio-Oncology Service, University College London Hospital NHS Foundation Trust, London, UK

[2]Hatter Cardiovascular Institute, University College London, London, UK

[3]Harrington Heart and Vascular Institute, Case Western Reserve University School of Medicine, Cleveland, OH, USA

[4]Liverpool Heart and Chest Hospital, Liverpool, UK

[5]Cardio-Oncology Service, Bart's Heart Centre, St Bartholomew's Hospital, London, UK

Key points

- Cardio-oncology is the care of cancer patients with cardiovascular disease, involving the detection, prevention and timely treatment of heart disease.
- Common cardiovascular complications include heart failure, coronary ischaemia, hypertension and arrhythmias, but any part of the cardiovascular system can be affected.
- Immune checkpoint inhibitor myocarditis is an increasingly recognised complication which can be fatal if not treated adequately.
- Newer echocardiographic techniques, like three-dimensional assessment of cardiac function and global longitudinal strain, are better at detecting subtle cardiac changes and are increasingly encouraged to be used.
- The use of inhibitors of the angiotensin system and beta-blockers for the primary prevention of cardiac dysfunction has shown mixed results in the latest studies.
- Cardio-oncology services require input from various specialists, with the multidisciplinary team approach at its core.

Conflicts of interest
The authors declare no conflicts of interest.

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