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Review

Preoperative cardiac evaluation and anesthetic considerations for cancer patients who underwent chemotherapy

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ABSTRACT

Cardiotoxicity is a serious side effect of some common cancer treatments. Although the cardiotoxic potential of anthracycline and trastuzumab is well known, many other chemotherapeutic agents can produce clinical and subclinical heart injury in the course of chemotherapy or after days, weeks or years after completion of chemotherapy. Consequently, patients with confirmed cardiotoxicity attributable to chemotherapy should be treated as high risk for potential cardiac events during anaesthesia. Because cancer patients and survivors cancer patients may be subjected to anesthesia for elective or emergency surgery, a careful cardiac assessment is mandatory especially for detecting patients with subclinical heart failure. While heart failure and left ventricular dysfunction are the main findings of chemotherapy-related cardiotoxicity, QT prolongation, arrhythmias, myocardial ischemia, pericarditis and/or myocarditis-like syndromes, and changes in blood pressure are other significant side effects. These overt or sub-clinical changes require a careful pre-, intra- and post-operative anesthetic management in patients who underwent anticancer therapy. This review discusses the features of chemotherapy-related cardiotoxicity, the role of the preoperative cardiac evaluation and the anesthetic considerations for patients with a previous history of chemotherapy, with the purpose of providing some practical suggestions for the clinical decision-making process.

Contents

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1. Introduction

The perioperative management of patients receiving chemotherapy for cancer diseases is often an underappreciated topic by clinicians, as chemotherapy-induced organ injury has been widely documented for the majority of drugs commonly used by oncologists. Chemotherapy can causes acute [1] or irreversible chronic bone marrow injury [2], cognitive impairment (chemo-brain) [3], peripheral neurotoxicity [4], pulmonary toxicity [5], and hepatotoxicity [6]. Additionally, almost 25% of patients receiving cisplatin experience acute kidney injury and must discontinue therapy [7]. Moreover, a serious side effect of some common cancer treatments is cardiotoxicity. The cardiotoxic potential of anthracyclines [8] and trastuzumab is well known [9], but many other chemotherapeutic agents can produce clinical and subclinical heart injury. Some of these side-effects induce reversible dysfunction with no long-term cardiac damage to the patient (Type II cardiotoxicity, e.g due to trastuzumab, imatinib, sunitinib, and bevacizumab), while others are irreversible, leading to progressive heart failure (HF) (Type I cardiotoxicity, e.g., due to anthracyclines) [10]. (See Table 1 for more details about the cardiotoxicity of chemotherapeutic agents).

This review discusses the features of chemotherapy-induced cardiotoxicity, the role of the preoperative cardiac evaluation and the anesthetic considerations for patients who underwent chemotherapy, with the purpose of providing some practical suggestions for the clinical decision-making process. Thrombotic and vascular side effects, such as pulmonary embolism, deep vein thrombosis, and stroke, are not addressed in this review, as these complications require a more detailed discussion on the relationship between cancer, anticancer therapies and thrombosis, which is not the aim of this work.

2. Cardiac effects of anticancer therapy

Cardiotoxicity due to cancer drugs is the presence of heart injury in the course of chemotherapy or after days/weeks (acute and subacute cardiotoxicity), or many years after the end of the cancer therapy (chronic cardiotoxicity) [11]. The acute effects might manifest especially as arrhythmias, myocardial ischemia, pericarditis and/or myocarditis-like syndromes, HF or systolic dysfunction. Overt or sub-clinical ventricular dysfunction is the main finding of chronic cardiotoxicity. Moreover, drug-induced long QT syndrome (LQTS) is the most common cause of acquired LQTS [12], and this severe side effect has been described for many chemotherapies [12]. In QT prolongation, this abnormal ventricular repolarization, when amplified by sympathetic activity, can lead to the formation of reentry circuits and may present with syncope, seizures, or torsades de pointes (TdP), ventricular fibrillation and, therefore

Table 1
Cardiotoxicity of anticancer drugs.

Drug Class	Drug	Features of Cardiotoxicity
Anthracycline	Epirubicin, Doxorubicin, Daunorubicin	Acute and dose related cardiotoxicity occurs in <1% of patients immediately after infusion and manifests as an acute, transient and reversible decline in myocardial contractility. Early-onset chronic progressive form in 1.6%–2.1% of patients (during therapy or within the first year after treatment). Lateonset chronic progressive anthracycline-induced cardiotoxicity occurs at least 1 year after completion of therapy (1.6%–5% patients), but may not become clinically evident until 10–30 years after treatment. Early- and late-onset chronic progressive cardiotoxicity typically present as dilated cardiomyopathy.[8]
Monoclonal antibodies	Trastuzamab	1% of patients develop HF (while 5% develop systolic dysfunction and 1% symptomatic cardiomyopathy).[9] Not-cumulative dose related and predominantly reversible.[10]
	Bevacizumab	Cardiatoxicity mostly in anthracycline-pretreated population. Increased risk of cardiac ischemic events[38] and high-grade hypertension.[39]
[a]Small molecule tyrosine kinase inhibitors	Imatinib, Sunitinib, Sorafenib, Dasatinib, Nilotinib, Lapatinib	10% incidence of asymptomatic drop in LVEF to >10% with full recovery when treatment was completed.[16] QT prolongation (Nilotinib).[82]
Alkylating agents	Cyclophosphamide, Ifosfamide, Cisplatin, Carboplatin	Cyclophosphamide and Ifosfamide can lead to LVD, pericardial effusions and myopericarditis in acute, and QT prolongation.[27] HF up to 28% for high-dose cyclophosphamides.[43] Subclinical myocardial toxicity in the short term in older patients who have been exposed to anthracyclines (platinum compounds).[20]
Inhibitors of microtubule polymerization (taxanes)	Paclitaxel, Docetaxel Cabazitaxel	Low incidence of HF, conduction abnormalities (sinus bradycardia) and ischemic heart diseases in patients who have been exposed to anthracyclines.[32]
Tyrosine kinase inhibitors and other targeted agents	Lapatinib	Symptomatic cardiac failure (1.4%) in a population with prior exposure to anthracycline and trastuzumab.[24] QT prolongation.[27]
Vinca alkaloids	Vinblastine, Vincristine, Vinorelbine	Cardiac events (mostly acute coronary syndrome) in about 1% of patients.[35]
Anti metabolites	Fluorouracil, Capecitabine, Gemcitabine	Angina-like chest pain, cardiac arrhythmias or myocardial infarction (1.2–18% of patients) especially after continuous infusion.[34] Acute coronary syndrome in patients without underlying cardiovascular disease has been reported with capecitabine.[36] Cardiac arrhythmias (0.7–1.4%), significant reduction in LVEF (0.2%) and the development of exudative pericarditis in 0.2% of the patients treated with gemcitabine.[31]
LHRH analogs (also called GnRH agonists)	Leuprolide, Triptorelin, Goserelin, Histrelin	Some research has suggested the risk of arrhythmia (supraventricular tachycardia) or coronary heart disease.[41]
LHRH antagonists	Histrelin, Degarelix	Increased cardiovascular morbidity. Among men with preexisting cardiovascular disease, the risk of cardiac events is lower in those treated with a GnRH antagonist compared with GnRH agonists.[42]
Antiandrogens	Cyproterone acetate, Flutamide, Nilutamide, Bicalutamide, Enzalutamide	Increase cardiovascular disease risk by increasing body weight, reducing insulin sensitivity, and/or resulting in dyslipidemia.[40]
Selective estrogen-receptor modulator	Tamoxifen	QT prolongation.[82]

HF: Heart Failure; LVEF: Left ventricular ejection fraction; LVD: Left Ventricular Dysfunction; LHRH: Luteinizing hormone-releasing hormone.
[a] Gefitinib and erlotinib have not been related to toxic effect on the heart.

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