Chapter 66

The nurse's role in the care of the cardiotoxicities generated by chemotherapy administration

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ABSTRACT
Cardiac toxicity is severe and an adverse effect of many chemotherapy drugs. The following guiding research question used was: how does the nurse provide health care for prevention and treatment of chemotherapy induced cardiotoxicity? This study is an Integrative Literature Review of which articles were searched in the Scielo, PubMed and BVS databases. The inclusion criteria were complete texts in Portuguese, English, and Spanish, published within a five-year period and indexed with the keywords used. The exclusion criteria were incomplete texts published over five years. The research indicates that there is a need of increasing the literary productions on the theme as well as a need of creating specific tools and guidelines to help nurses and the health care team to coordinate the care of cancer patients with cardiotoxicities generated by chemotherapeutic agents. It was also revealed that the nurse, as the only member of the health team that assists the patient in its entirety and in a holistic manner, has a crucial role in the management of risk factors, being able to act in the detection of the appearance of new signs and symptoms in the patients' routine, as well as guidance to eliminate or minimize their damage.

Keywords: Nurse's Role, Anticarcinogenic Agents, Cardiotoxicity, Antineoplasic Agents, Nursing Care, Teaching.

1 INTRODUCTION

According to a WHO report on cancer (2020), in 2018, 9.6 million people died from this pathology, being the most prevalent lung neoplasm. One in every six global deaths are caused by this disease, and the increase in its incidence can be explained by demographic changes in the population, increased life expectancy, evolution of diagnostic methods, among others. In Brazil, cancer is considered a public health problem and, according to the incidence report issued by INCA (2020), it is estimated that 625,000 new cases will occur annually between 2020 and 2022.

Cancer is the name most commonly used to speak of a malignant neoplasm. Neoplasia is a process of disordered multiplication of abnormal cells that have suffered some alteration in their function due to

Collection of international topics in health science:
The nurse's role in the care of the cardiotoxicities generated by chemotherapy administration

810

hereditary genetic or hormonal factors and/or exposure to biological, physical, chemical or environmental agents with carcinogenic and mutagenic potential. When in its benign form, the cell mass or tumor produced by this uncontrolled growth remains restricted to its place of origin, however, when in the malignant form, it has the ability to migrate to other organs, blood vessels and lymphatic vessels, causing new growth in places far from its origin, which is the process of metastasis (Hoff PMG et al., 2013, p.4-5;10).

Some time ago it was believed that cancer cells had a shorter cell cycle than normal cells and therefore multiplied at a faster rate, however, the hypothesis that there is some failure in the reproduction control mechanism has been studied, and thus they remain in exacerbated proliferation until, due to their large number, there is a lack of nutrients and oxygen, which then decreases their capacity and proliferative rate. Reproducing cells are more sensitive to chemotherapeutic agents and due to this fact, chemotherapy has become one of the main ways to fight cancer (Bonassa & Gato, 2012, pp.2-5). Unlike other treatment modalities such as radiotherapy and surgery, chemotherapy acts systemically, with the potential to act both at the site of the neoplasm, as well as in distant sites, which is necessary due to the migratory characteristic of this disease (Grossman & Porth, 2019, p.190).

The most effective way to plan chemotherapy, in order to reach the largest number of cancerous particles per application, is to combine the agents, since each one has a different mechanism of action in the cell and cell cycle, as well as to associate several treatment approaches. Although there are studies and researches that seek to develop drugs that act only on tumor cells, most chemotherapeutic agents still act in a nonspecific way, also reaching the normal ones (Rodrigues, Martin & Moraes, 2016, pp.187-189) and that is why there are so many adverse effects, among which is the cardiotoxicity that is related to the measurement of the left ventricular ejection fraction (LVEF) (Hoff PMG et al., 2013, p.1130)

Several cardiologic conditions can occur with the use of chemotherapeutic agents, such as metabolic changes, hypertension, acute coronary syndromes, arterial and venous thromboembolism, arrhythmias, and others. There is no consensus on the definition of chemotherapy cardiomyopathy, but according to the European Society of Cardiology (2016), this involvement can be defined as any structural or functional alteration leading to dysfunction of the heart and circulation, whether in the immediate, late or post-traumatic experience of the heart (Melo & Salemi, 2019). Immediate or acute cardiotoxicity manifests itself during treatment and up to 14 days after the end of treatment, and its most common symptoms are electrocardiographic changes, acute coronary syndromes, myocarditis, pericarditis, and acute heart failure. The late or chronic one manifests itself a few months to a year after the end of the chemotherapy infusion, and its main manifestations are systolic or diastolic ventricular dysfunction that can lead to congestive heart failure and even death. The main chemotherapeutic agents that cause cardiac toxicity are antitumor antibiotics, alkylating agents, and antimicrotubule agents, and they can cause reversible or irreversible injury (Bonassa & Gato, 2012, p.350).

Collection of international topics in health science:
The nurse's role in the care of the cardiotoxicities generated by chemotherapy administration

811

Mortality among patients who develop problems due to cardiotoxicity of cancer treatment drugs reaches 60%, so it is extremely important that early detection and active search for manifestations that indicate cardiac involvement is made (Bonassa & Gato, 2012, p.350). It is clear, then, that the nurse's performance is essential in this search, since he is the only professional in the health team that provides care to the patient in its entirety. This professional must monitor patients during treatment (Brunner & Suddarth, 2020, p.334), especially those who have risk factors for the development of cardiotoxic complications, which are patients younger than 2 years of age and older than 70 years of age, previous presence of coronary artery disease, hypertension, diabetes, use in association of chemotherapy drugs with the potential to generate cardiac toxicity, previous or concomitant performance of radiotherapy in the mediastinum, smoking, renal or hepatic dysfunction and genetic predisposition; in addition to being very attentive during nursing consultations to reports and signs of dyspnea, chest pain, fatigue, anorexia, abdominal distension, edema of lower limbs, pulmonary congestion, presence of third heart sound, jugular turgor, ascites, tachycardia, and hepatomegaly, which are signs that may indicate the occurrence of heart involvement (Bonassa & Gato, 2012, p.351-354).

Therefore, the present study aims to highlight the role of nurses in the care of cardiotoxicities generated by the use of chemotherapy drugs.

2 METHODOLOGY

To achieve the proposed objective, an integrative literature review was conducted and four steps were taken to develop this work. The guiding question was formulated, descriptors were defined, data search was performed, and articles were read and discussed. The searches were carried out in the Scielo, BVS and Pubmed databases, with the following descriptors in Portuguese and English: antineoplastic drugs, chemotherapy, cardiotoxicity, nurse's role, nursing care, using the connective 'AND' and 'OR'. The reference of the descriptors used in English was searched in the MeSH Database, which is the English language medical metadata base equivalent to DeCS, which is the database for terms in Portuguese. The equivalent term for chemotherapy drugs in English would be 'drug therapy' which covers not only treatments against cancer, but against any disease, thus, in order to achieve more assertive results, the relative term 'anticarcinogenic drugs' was used instead of this descriptor.

The inclusion criteria were selected texts in Portuguese, English, and Spanish, complete and indexed in the aforementioned descriptors in the period of five years. As exclusion criteria, incomplete texts above the five-year period were not used to compose the database.

Result: The final sample of this review consisted of ten scientific articles selected by the previously established inclusion criteria. Of these, nine articles were found in English, zero articles in Spanish and one article in Portuguese. The ten articles were identified in the Pubmed database, while no articles were found in the VHL and Scielo databases.

Collection of international topics in health science:
The nurse's role in the care of the cardiotoxicities generated by chemotherapy administration

812

The flowchart shows the selection steps of the articles used. Initially, fifty-four articles were found; after reading the abstracts and conclusions, thirty-five remained in the collection. Next, a new concordance check was made between the articles read, thus reducing the sample to twenty-four. After reading the full texts and a new verification, ten articles were selected for the final sample.

Figure 1. Findings in the databases.
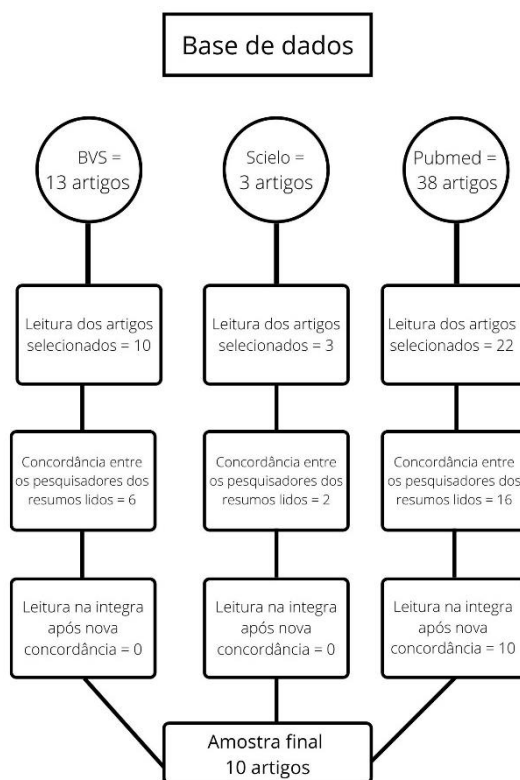
Source: Authors.

3 RESULTS AND DISCUSSION

Chart 1 shows the articles selected by author/year, title and objective of the study, thus facilitating a more detailed view of the material used. The reading of the texts allowed the creation of three thematic categories that will be discussed throughout this study: *1 main diseases caused by chemotherapy drugs: the knowledge that favors the improvement of care; 2 main chemotherapy drugs causing cardiotoxicity: drug identification as a facilitator of complications prevention; 3 the nurse and care with cardiotoxicity: evidence-based knowledge.*

Collection of international topics in health science:
The nurse's role in the care of the cardiotoxicities generated by chemotherapy administration

813

Table 1. Selected articles.

Author / Year	Title	Goal
Clark et al. 2017	Cardiotoxicity and cardiovascular disease risk assessment for patients receiving breast cancer treatment	To identify the patients' previous risk factors for cardiotoxicities, performing early detection by anamnesis through a questionnaire.
Kelly et al. 2017	Symptom practice guide for telephone assessment of patients with cancer treatment-related cardiotoxic dyspnea: Adaptation and evaluation of acceptability	Highlight the lack of tools, knowledge, and clinical practice guidelines available to guide healthcare professionals to assess, screen, and/or provide self-care strategies for patients with dyspnea related to cancer treatment-related cardiotoxicity.
Clark et al. 2019	Cardiotoxicity after cancer treatment: a process map of the patient treatment journey	To describe the journey of patients who developed cardiotoxicity through antitumor treatment, In order to develop and implement evidence-based clinical protocol for management of these patients
Coviello 2018	Cardiovascular and Cancer Risk: The Role of Cardio-oncology	Collaborate in the early identification of risks and development of risks of cardiotoxicities from chemotherapy drugs and improve the quality of life for cancer survivors and decrease mortality.
Austin-Mattison 2018	Joining Forces: Establishing a Cardio-oncology Clinic	To exemplify the importance of creating a clinic with specificity in oncologic cardiology with the objective of prevention and treatment of patients who have developed and may develop cardiotoxicity through anticancer treatment.
Mehta et al. 2018	Cardiovascular Disease and Breast Cancer: Where These Entities Intersect	Provide a comprehensive overview of the prevalence of cardiovascular disease, shared risk factors, and the cardiotoxic effects of anticancer therapy, as well as the prevention and treatment of cardiovascular disease in breast cancer patients.
Gilchrist et al. 2019	Cardio-Oncology Rehabilitation to Manage Cardiovascular Outcomes in Cancer Patients and Survivors	Justify the use of cardiac rehabilitation through structured exercise and provision of ancillary services for cancer patients and survivors and discuss the need for future research to fully implement a multimodal cardiac rehabilitation model.
Higgins et al. 2020	Left ventricular myocardial strain and tissue characterization by cardiac magnetic resonance imaging in immune checkpoint inhibitor associated cardiotoxicity	Evaluate MRI as a screening resource for cardiotoxicities through structural and functional parameters.
Silva et al. 2017	Cardiovascular adverse events associated with oral antineoplastic therapy	To identify in the literature the cardiovascular adverse events resulting from oral antineoplastic therapy.
Fadol 2018	Management of Chemotherapy-Induced Left Ventricular Dysfunction and Heart Failure in Patients With Cancer While Undergoing Cancer Treatment: The MD Anderson Practice	To describe the management of the "Heart Success Program" for chemotherapy-induced cardiomyopathy and heart failure in cancer patients at the MD Anderson Practice.

Source: Authors.

Collection of international topics in health science:
The nurse's role in the care of the cardiotoxicities generated by chemotherapy administration

814

Category 1 - Main health problems caused by chemotherapy: the knowledge that favors the improvement of care

Cardiovascular disease is a concurrent cause of death in early-stage cancer patients (Gilchrist et al., 2019). The use of antineoplastic drugs bring changes in muscle electrophysiology and damage to the muscles of the heart, making it weaker in its ejection function (Ministry of Health, 2020). Cancer treatment can result in early or late cardiotoxicity, which can range from impaired left ventricular ejection fraction, cardiomyopathies, hypertension, arrhythmias, myocardial ischemia, valvular disease, thromboembolic disease, myocarditis, and pericarditis (Mehta et al., 2018).

Hypertension is one of the most common cardiovascular diseases seen in the adult population. High blood pressure causes the heart to exert a greater effort than normal to ensure that the blood is properly distributed in the body and is one of the main risk factors for the occurrence of stroke, myocardial infarction, arterial and cardiac aneurysm (Ministério da Saúde, 2020). It presents a risk factor associated with left ventricular dysfunction in both anthracycline and trastuzumab use and is also associated with the onset of renal cancer (Coviello, 2018). Values greater than 90 mmHg diastolic and 140 mmHg systolic are used as references for diagnosing hypertension, and increasing these diastolic and systolic levels cause an increased risk of atherosclerosis (Robbins, 2013, p.332).

Furthermore, hypertension is a precursor to heart failure, which is characterized by a condition in which the heart cannot pump enough blood to meet the body's needs, and may affect predominantly the left or right side of the heart. The morphological and clinical effects of heart failure come from decreased systemic perfusion and elevated return pressures within the pulmonary circulation. The manifestation of left ventricular failure includes an enlarged heart size (cardiomegaly), tachycardia, presence of a third heart sound, and thin rales at the base of the lungs caused by the opening of edematous pulmonary alveoli. Dilatation of the left atrium can cause atrial fibrillation, which presents as an irregular heartbeat (Robbins 2013, p.367). Some authors point out that the main symptoms found were fatigue and dyspnea (Silva et al., 2017). Right heart failure is usually the consequence of left heart failure and its main morphological and clinical effects are given by engorgement of the venous system that causes the increase in size of the liver and spleen, peripheral edema, pleural effusion and ascites (Robbins, 2013, p.368).

When talking about cardiac hemostasis, we know that the heart is defined as a contractile machine with a sophisticated conduction system influenced by neural stimuli. The stimulus reaches the atrial sinus node that propagates to the whole heart, dictating the rhythm of its beating. The alteration of this homeostasis leads to a condition called arrhythmia. By definition cardiac arrhythmia is characterized by a lack of rhythm in the heart's beats (Robbins, 2013, p.385). The most frequent chemotherapy-generated arrhythmias reported by authors are atrial fibrillation, ventricular tachyarrhythmias, atrial fibrillation, ventricular tachycardia, and ventricular fibrillation (Mehta et al., 2018). Patients may be unaware of the

Collection of international topics in health science:
The nurse's role in the care of the cardiotoxicities generated by chemotherapy administration

815

rhythmic disturbance or feel their heart racing, i.e., have palpitations; the loss of adequate cardiac output that results from a prolonged arrhythmia can produce dizziness, syncope, or sudden death.

Ischemic injury is the most common cause of rhythm disturbances (Robbins, 2013, p.386). Myocardial ischemia or angina occurs when the blood flow to the heart through the coronary arteries is interrupted, generating a low oxygen delivery or hypoxemia to the heart muscle that needs it for its contractility. Factors that alter oxygen demand and supply, therefore, are responsible for the evolution of the patient to syndromes such as angina, coronary artery disease (atherosclerosis), coronary artery spasm and blood clot (Robbins, 2013 pp.401-402).

The blood clot, also known as thrombus, is characterized by the formation of blood clots inside the veins, partially or completely blocking the passage of blood. The clot is formed when there is some imbalance in the coagulation mechanism, because patients with neoplasms have increased circulating levels of tissue factor, present in the subendothelium, platelets, and leukocytes. Tissue factor is an essential physiological component in the initiation of the coagulation cascade and plays an important role in the pathophysiology of thromboembolism associated with neoplasms (Albuquerque, Serrano Júnior, Mady, Ramires, Hajjar, Kalil Filho, 2014, p.66). During treatment with chemotherapy drugs, the incidence of thromboembolism is 20% in the absence of prophylactic anticoagulants, which makes it necessary to adopt this medication to prevent thrombotic events (Silva et al., 2017).

As for the pericardial tissue, which is a layer of **fibrous connective tissue** that surrounds the entire heart, the authors surveyed reported many problems with pericarditis (**Frank H. Netter, MD, 2018, pp.111-114)** which is the inflammation or infection of the serous layer of the heart. The heart is lined by a triple membranous layer called the fibrous pericardium (outer layer of connective tissue) and serous pericardium (layer that lines the inner surface of the fibrous pericardium) which is meant to protect and anchor the heart. Infection can lead to thickening of the serous lining and has the consequence of heartbeats that produce a grinding sound called pericardial friction. The most serious consequence results in the heart adhering to the outer wall of the pericardium or thickening to the point where there is inhibition of heart movements. The most common symptom of acute pericarditis is an intense chest pain that usually worsens during deep inspiration (Guyton & Hall, 2017, p.103). During antitumor radiation therapy treatment there are improved techniques that limit radiation to the cardiac field reducing the incidence of pericarditis, although it remains a potential side effect, particularly when radiation is combined with certain chemotherapies (Coviello, 2018).

Myocarditis is defined as inflammation of the heart tissue (Robbins, 2013, p.396). The **myocardium** is the middle **muscle layer of the** heart wall, its structural function is to support the heart chambers and its functional function is to aid in the contraction and relaxation of the heart walls so that blood can pass between the chambers, as well as conducting electrostimulation, through its own tissues and the epicardium **(Frank H. Netter, MD, 2018, pp.111-114).** Myocarditis is the most frequently reported

Collection of international topics in health science:
The nurse's role in the care of the cardiotoxicities generated by chemotherapy administration

816

cardiotoxicity during treatment with immune checkpoint inhibitors (Higgins et al., 2020). Symptoms can vary and may include fatigue, shortness of breath, edema, palpitations, and sudden death. Diagnosis is based on electrocardiogram, cardiac biomarker measurements, imaging tests of the heart, and biopsy of the heart muscle (Albuquerque et al, 2014, p.85).

Category 2. Major chemotherapeutic agents causing cardiotoxicity: drug identification as a facilitator for the prevention of complications

As the survival rate in cancer patients increases, the cardiotoxicities caused by chemotherapeutic drugs become more evident and worrisome, since cardiomyopathies have a higher mortality rate worldwide than cancers (WHO, 2020).

The chemotherapeutic agents most commonly associated with the occurrence of cardiotoxicity are anthracyclines (1 to 26%), high-dose cyclophosphamide (7 to 28%), trastuzamab (2 to 28%), and tyrosine kinase enzyme inhibitors (0.05 to 11%). Concomitant use of chest radiotherapy (used in breast, lung, and blood cancer cases) increases the potential for inducing cardiotoxicity (Clark et al., 2019). Nevertheless, most of the articles reviewed mentioned only anthracyclines, especially doxorubicin, as the main drugs causing cardiac damage.

Patients with risk factors for developing cardiovascular disease such as smoking, diabetes mellitus, hypertension, obesity, dyslipidemia, with a history of heart disease prior to cancer treatment (Fadol, 2018), older than 65 years or younger than 5 years, female, with a nutrient-poor diet, sedentary, genetically prone, and on concomitant radiotherapy treatment are more vulnerable to cardiovascular injuries caused by the toxicity of antineoplastic agents (Coviello, 2018).

Although there are several cardiac side effects that can be considered as cytotoxicities caused by chemotherapy drugs, asymptomatic decrease in left ventricular ejection fraction (LVEF) should be the major concern for the healthcare team, since it happens in up to 20% of patients undergoing antineoplastic therapy, particularly with anthracyclines and/or radiation in the mediastinum (Coviello, 2018).

The main antitumor agents, also called anthracyclines, are doxorubicin, epirubicin, and idarubicin, the latter being of oral use and less cardiotoxic than intravenous ones (Silva et al., 2018).

With its cardiovascular events being able to present up to 20 years after the end of treatment (Austin-Mattison, 2018), anthracycline cardiotoxicity is dose-cumulative and can develop in up to 48% of patients receiving the highest dose of 700mg/m², with the risk of presentation being lower in patients receiving lower cumulative doses (Mehta et al., 2018). The immediate or acute manifestations of these antitumor antibiotics (from infusion to one week after) may be related to inflammation and edema resulting in pericarditis and myocarditis, manifesting mainly in changes in the electrocardiogram and arrhythmias, which may be reversible with suspension of drug administration. Late manifestations are more common

Collection of international topics in health science:
The nurse's role in the care of the cardiotoxicities generated by chemotherapy administration

817

and present in a chronic form, they result from damage to myocytes that generate cardiac dysfunction and can lead to congestive heart failure (Coviello, 2018).

The main alkylating agents are cyclophosphamide, ifosphamide and cisplatin. Their main cytotoxic effects occur in the gastrointestinal, reproductive and hematopoietic systems (Bonassa & Gato, 2012, p.18). Its cardiotoxic effects are rare and are apparently correlated to high doses, when associated with the use of anthracyclines and/or radiotherapy in the mediastinum, to ventricular dysfunction prior to treatment or to risk factors for cardiomyopathies. Its presentation may present asymptomatic changes in electrocardiogram, and may reach myocarditis associated with necrosis (Hoff PMG et al., 2013, p.715).

Studies have reported rare cardiac involvement such as myocarditis, pericarditis, bradycardia, and atrial fibrillation (Mehta et al., 2018).

After the antitumor antibiotics, the antimetabolite agents are the most associated with cardiotoxicity, especially fluoruracil, occurring in approximately 8% of patients, with manifestations such as chest pain, electrocardiogram alterations, or myocardial infarction. In most cases the cardiotoxic effects are reversed after termination of therapy or with the use of calcium channel blockers and nitrate. The use of concomitant cisplatin or anthracycline and previous cardiomyopathies are factors that increase the risk of cardiac toxicity (Hoff PMG et al., 2013, p.737).

The most commonly reported adverse effect is angina, usually attributed to vasospasm caused by the medication, although there are also rare reports of acute myocardial infarction, heart failure, and arrhythmias. Fluoruracil cardiotoxicity can be acute (during intravenous infusion) or delayed (2 to 5 days after infusion); later cardiologic effects are uncommon. Arrhythmias caused by fluoruracil and capecitabine, including ventricular fibrillation and ventricular tachycardia, are mostly ischemic in origin and usually occur due to arterial vasospasm, however, atrial fibrillation and QT segment prolongations are also reported (Mehta et al., 2018).

Regarding antimicrotubule agents, the most common are vincristine (vinca alkaloid), paclitaxel and docetaxel (both taxanes). Docetaxel is dose-cumulative and can cause severe hypotension in 3% of cases, rare heart failure, atrial flutter, sinus tachycardia, arrhythmias, angina, and hypertension. Paclitaxel can cause asymptomatic and transient bradycardia, chest pain, ventricular tachycardia, hypotension, and acute myocardial infarction. Vincristine, in turn, can present ischemic cardiotoxicity, hypotension, and hypertension (Bonassa & Gato, 2012, p.126-136).

It is still uncertain whether the rhythm changes observed with paclitaxel administration are caused by the agent itself, the polyoxyethylated castor oil present in the formulation, or the H1 and H2 receptor antagonists administered prior to this medication to prevent hypersensitivity reactions (Mehta et al., 2018).

In hormone therapy, tamoxifen is the most commonly used antiestrogen, especially in breast cancer. It binds to the cancer cell, preventing its estrogen stimulation. It is usually well tolerated, but can cause menopause-like symptoms (Bonassa & Gato, 2012, p.26).

Collection of international topics in health science:
The nurse's role in the care of the cardiotoxicities generated by chemotherapy administration

818

In most organs, such as the uterus, bones, and organs of the cardiovascular system, tamoxifen acts as an estrogen agonist, which will cause beneficial or harmful effects depending on the affected tissue. At the expense of its protective action on lipid metabolism, its action as an estrogen agonist generates increased thrombogenicity, which can cause deep vein thrombosis and thromboembolism (Mehta et al., 2018).

Angina, ischemia, and acute myocardial infarction have also been reported in treatment with tamoxifen and anastrozole (the latter being an Aromatase Inhibitor) (Silva et al., 2018).

Aromatase inhibitors are also used in hormone therapy and their main agents are anastrozole and letrozole; because they cause a reduction in estrogen levels, they are widely indicated for breast cancer treatment (Bonassa & Gato, 2012, p.26).

Because aromatase inhibitors reduce endogenous estrogen production, it is hypothesized that patients using these medications are at an increased risk of developing cardiovascular diseases such as dysrhythmia, valve dysfunction, pericarditis, heart failure, or cardiomyopathies, however, further investigations should be done to confirm or not confirm this hypothesis (Mehta et al., 2018).

The anti-androgens, on the other hand, bind to the androgen receptors of the cancer cells, preventing their growth by stimulating mainly testosterone. They are indicated for the treatment of prostate cancer and their main drugs are bicalutamide and flutamide. The recorded cardiovascular adverse effects of bicalutamide and flutamide are hypertension, angina, and congestive heart failure (Bonassa & Gato, 2012, p.156).

Antibodies are proteins of the immune system that recognize antigens, specific targets of foreign cells in the body. Since cancer cells express a large number of antigens, they become attractive to monoclonal antibodies, which are an antineoplastic target therapy. Some of them specifically inhibit HER2 (human epithelial growth factor receptor-2) signaling, which plays an important role in breast cancer growth. The main monoclonal antibodies currently are rituximab, alentuzumab, and trastuzumab (HER-2). They can be used alone or in combination with other cytotoxic agents (Bonassa & Gato, 2012, pp.40-41).

Target therapy-associated left ventricular dysfunction has been studied more extensively in a breast cancer population treated with trastuzumab. Compared to anthracycline-induced cardiotoxicity, left ventricular dysfunction and heart failure caused by trastuzumab are generally reversible. People at greatest risk of cardiotoxicity from exposure to this drug are those older than 50 years, those with hypertension, those with an LVEF below 55%, and those who have already used antitumor antibiotics. Studies have pointed to the occurrence of heart failure and severe cardiac events in therapies using trastuzumab (Mehta et al., 2018).

Hypertension is one of the most common cardiovascular risk factors among the adult population and, when associated with trastuzumab use, increases the likelihood of developing left ventricular dysfunction (Coviello, 2018).

Collection of international topics in health science:
The nurse's role in the care of the cardiotoxicities generated by chemotherapy administration

819

Tyrosine kinase inhibitors (TKIs) are an alternative for inhibiting HER2 signaling. Lapatinib is often given in combination with capecitabine or hormone therapy and is approved for the treatment of women with HER2-positive metastatic breast cancer. A study comparing the use of lapatinib alone and its use in combination with trastuzumab reported a higher incidence of severe cardiac events of systolic dysfunction when on combination therapy (Mehta et al., 2018).

Hypertension is a common adverse effect of tyrosine kinase inhibitors (11%-45%). It is common for these drugs to destabilize cases of previously controlled systemic hypertension, accounting for 2%-20% of severe cases. Lapatinib and other ITQ's can cause QT segment prolongation, while between 16% and 36% of patients who need to undergo antineoplastic treatment already have arrhythmias before the start of treatment. Thus, it is critical that healthcare professionals anticipate this increase in arrhythmias in the cancer population through regular assessments with electrocardiograms (Coviello, 2018).

A literature review study demonstrated that among the oral chemotherapeutics, tyrosine kinase inhibitors such as sunitinib, sorafenib, pazopanib, nilotinib, imatinib, and lapatinib caused the most cardiac adverse events, including: decreased left ventricular ejection fraction, angina, acute myocardial infarction, congestive heart failure, and electrocardiogram changes (conduction disturbances, T-wave change, ST depression and elevation, change in QT interval, change in QRS amplitude, premature atrial beats, decreased heart rate, atrial fibrillation). In treatment with sunitinib, pericardial effusion and changes in cardiac enzymes were also reported. These drugs were also the most associated with changes in blood pressure, which highlighted the great need for medical monitoring during the use of these drugs (Silva et al., 2018).

As part of immunotherapy, interferons are glycoproteins produced by immune system cells that inhibit viral replication. Alpha interferons are the only ones approved for use in anti-cancer treatment. Studies prove that they improve the way the body fights cancer cells (Bonassa & Gato, 2012, p.31).

The risk of cardiac toxicity from interferon alpha is higher in older patients and those with previous heart disease. Reversible cardiomyopathies after treatment, supraventricular arrhythmias and acute myocardial infarction may occur in rare cases (Hoff PMG et al., 2013, p.796).

Interleukin-2 is a cytokine produced by lymphocytes that are responsible for controlling the body's immune response. It has antitumor capabilities when used alone or in combination with other cytotoxic agents. Its main cardiac cytotoxic effects are decreased cardiac ejection fraction and increased heart rate (Bonassa & Gato, 2012, p.30)

There are other chemotherapy drugs that have cardiotoxic potential; in this study, the main ones mentioned in the analyzed articles and supporting literature were listed (Table 2).

Collection of international topics in health science:
The nurse's role in the care of the cardiotoxicities generated by chemotherapy administration

820

Table 2. Major antineoplastic drugs and possible cardiovascular effects.

Classe		Antineoplásico	Tratamento	Possíveis Efeitos Cardiovasculares
QUIMIOTERÁPICOS CLÁSSICOS	ANTRACICLINA	Doxorrubicina / Epirrubicina / Idarrubicina	mama, pulmão, bexiga, tireoide, estômago, pâncreas, ovário, sarcomas ósseos e nos tecidos moles, linfoma de Hodgkin, leucemias, mieloma múltiplo, outros	alterações no ECG (inversão ou achatamento da onda T, depressão de segmento ST), arritmias, disfunção ventricular esquerda, ICC
	AGENTES ALQUILANTES	Ciclofosfamida / Ifosfamida / Cisplatina	mama, pulmão, testículo, estômago, ginecológicos, sarcomas, bexiga, mieloma, leucemias, linfomas, neuroblastoma, outros	hipertensão arterial, alterações no ECG, arritmias, miocardite, pericardite, isquemia, disfunção ventricular esquerda, ICC
	ANTIMETABÓLITOS	Fluoruracil / Capecitabine	colorretal, mama, pâncreas, ovário, útero, em cabeça e pescoço, estômago, pele, canal anal, próstata	isquemia, angina, alterações no ECG, vasoespasmo coronariano, arritmias, disfunção ventricular esquerda, ICC, IAM
	AGENTES ANTIMICROTÚBULOS	Vincristina / Paclitaxel / Docetaxel	mama, pulmão, próstata, ovário, em cabeça e pescoço, pâncreas, sarcomas em tecidos moles, melanoma, leucemias, linfomas, outros	isquemia, bradicardia, síncope, arritmias, angina, IAM
TERAPIA HORMONAL	ANTIESTROGÊNIOS	Tamoxifeno	mama, melanoma, pâncreas, endométrio, fígado, próstata	angina, isquemia, IAM, desordem arterial coronariana, hipertensão arterial, eventos tromboembólicos
	INIBIDORES DE AROMATASE	Anastrozole / Letrozole	mama	angina, hipertensão, tromboflebite, isquemia, IAM
	ANTIANDROGÊNIOS	Bicalutamida / Flutamida	próstata	hipertensão, angina, ICC
TERAPIA-ALVO MOLECULAR	ANTICORPOS MONOCLONAIS	Trastuzumabe / Alentuzumabe / Rituximabe / Bevacizumabe	mama, pulmão, colorretal, renal, leucemias, mieloma múltiplo, linfoma não Hodgkin, outros	arritmia/hiper ou hipotensão durante infusão, angina, redução na FEVE, disfunção ventricular esquerda, ICC, hipertensão arterial, tromboembolia, síncope, trombose venosa profunda, trombose arterial
	INIBIDORES DA TIROSINA QUINASE	Imatinibe / Lapatinibe / Sunitinibe / Sorafenibe	leucemia, tumor estromal, mama, renal, fígado	ICC, taquicardia, palpitação, hiper ou hipotensão arterial, redução da FEVE, isquemia, IAM, alterações no ECG
TERAPIA BIOLÓGICA	IMUNOTERAPIA	Interferon alfa	tricoleucemia, melanoma, leucemias, linfoma, sarcoma de Kaposi, mieloma múltiplo, outros	arritmias, taquicardia, dor torácica, IAM, fibrilação atrial, hipotensão após administração ou crônica, hipertensão
		Interleucina-2	renal, melanoma	aumento da frequência cardíaca, diminuição da FEVE, taquicardia, bradicardia, arritmias, isquemia, IAM
OUTROS		Talidomida	mieloma múltiplo	batimento cardíaco irregular, hiper ou hipotensão, angina, ICC, bradicardia, taquicardia, fibrilação atrial, pericardite, IAM, trombose
		Azacitidina	leucemia mielomonocítica crônica e mielocítica aguda	hipotensão arterial, dor torácica, taquicardia, sopro cardíaco, síncope

Source: Authors.

Category 3. The nurse and cardiotoxicity care: evidence-based knowledge

The advances made concerning the ways of early detection, screening, and treatment of cancer have increased the survival rate among patients with this disease, while also increasing the incidence of morbidity and mortality caused by adverse effects of the treatment of neoplasms. Cardiotoxicity is one of the most common effects caused by cancer treatments and can lead to the accelerated development of heart disease, especially when in the presence of traditional cardiovascular risk factors (Clark et al., 2017). Patients with risk factors such as diabetes mellitus, dyslipidemia, hypertension, smoking, obesity, sedentary lifestyle, or who already have a history of heart disease are more vulnerable to the development of chemotherapeutic agent-related cardiac toxicity and have their risk of premature death from cardiovascular causes increased

Collection of international topics in health science:
The nurse's role in the care of the cardiotoxicities generated by chemotherapy administration

821

(Fadol, 2018). The elevated risk of developing cardiomyopathies in cancer survivors is a likely result of pathologies typically related to aging in conjunction with the direct (e.g., cardiotoxicity) and indirect (e.g., weight gain, physical deconditioning) effects of antineoplastic therapies (Gilchrist et al., 2019).

The prevalence of cardiovascular disease related to chemotherapy treatment is increasing and its control requires a multidisciplinary approach from the entire healthcare team (Fadol, 2018). The risk of developing and/or existence of risk factors should be checked before, during and after chemotherapy and the choice of treatment should be made on risk-benefit, with an emphasis on improving prognosis and quality of life and not just eradicating the cancer (Austin-Mattison, 2018). It is no longer enough to focus only on cancer diagnosis and its treatment, healthcare professionals must expand their focus to include pre-existing chronic diseases as well as diseases and disabilities caused by treatment (Fadol, 2018).

Cancer survival impacts not only the health of the patient and his/her family, but also socioeconomic, cultural, and psychological aspects (Potter & Perry, 2013, pp.94-95). As one of the functions of nurses is to assist patients and their families in an integral manner, aiming at increasing the quality of life of clients (COFEN, 1998), it is necessary for them to have knowledge about the effects of cancer and its treatment, how it affects the quality of life, as well as the meaning of health for the patient, so that it is possible to guarantee health care to a cancer survivor in its entirety (Potter & Perry, 2013, pp.94-95).

Recognizing the short- and long-term effects of cancer and chemotherapy allows for the early diagnosis of conditions, which might develop for other reasons, but have their manifestation caused or exacerbated by chemotherapeutic agents (Potter & Perry, 2013, pp.95-96). According to Robyn (Clark et al., 2017), nurses providing care to patients with symptoms of cardiotoxicity require additional evidence-based cardiologic knowledge to guide their patients in managing their symptoms.

Nurses are in a position to act as leaders in combating the long-term consequences of cancer by being part of the development of the survivors' health plan. In the nursing consultation, it is possible to collect very important data about the patient's current and past health status, family history, social, psychological, spiritual needs, and available resources; these data will allow for the best guidance on symptom management, self-care, and lifestyle changes (Potter & Perry, 2013, p.99). Screening for cardiovascular risk is a comprehensive assessment that includes, in addition to laboratory and imaging tests, a collection of medical and family history, blood pressure measurement, weight, abdominal circumference, and physical examination (Coviello, 2018). Thus, the importance of the nursing consultation in the detection and management of these risks is evident.

A study that verified the feasibility of implementing a "practical symptom guide" to be used by nurses in the evaluation, triage, and management of patients with dyspnea caused by cardiotoxicity related to chemotherapy showed that nurses have difficulty in identifying the cause of dyspnea to make an assertive triage. Even though nurses are responsible for assessing and triaging patients with dyspnea and can propose

Collection of international topics in health science:
The nurse's role in the care of the cardiotoxicities generated by chemotherapy administration

822

strategies to relieve this symptom, there are no tools available that can assist them in the specific management of these patients (Kelly et al., 2017).

A cardio-oncology project carried out with breast cancer patients with chemotherapy prescription observed that the follow-up nursing consultations, in stable patients, with risk assessment for developing cardiomyopathies and control of cardiovascular risk factors such as hyperlipidemia, hypertension and diabetes mellitus, before and during treatment, proved to be the key element for the success of the project that succeeded in preventing the onset of chemotherapy-induced cardiotoxicity, as well as preventing patients at high risk of developing cardiac conditions from receiving more cardiotoxic drugs (Austin-Mattison, 2018).

The interdisciplinary, patient-centered program that was designed at MD Anderson Cancer Center in Texas was successful in decreasing the readmission rate after 30 days of discharge and also focused on identifying decompensated cardiovascular risk factors and symptoms of cardiomyopathies through regular nursing consultations, so that the nurse could keep the healthcare team informed. In addition, this program highlighted the importance of the nurse's role as a health educator by guiding patients and their families about the disease, its treatment, adverse effects, acute signs and symptoms of heart failure, when to seek medical assistance, how to continue their treatment at home, and emphasizing points about medications, activities, constant weight monitoring, and hyposodium diet, with the goal of making patients co-responsible for their health (Fadol, 2018). Patient empowerment requires improving their understanding of the disease process and ways to manage their symptoms in order to prevent unplanned hospital admissions/attendances (Fadol, 2018).

Since nurses have the responsibility of educating cancer survivors and their families about the effects of the disease and its treatment, providing strategies for self-management of care, helping them gain self-efficacy, and giving them confidence to cope (POTTER; PERRY, 2013, p.100), the importance of this professional as a health educator and counselor in providing patients, their families, and caregivers with the necessary tools to take control of their health maintenance process and well-being is evident.

In the research conducted by Robin (Clark et al., 2019), the biggest concern of patients was the lack of communication from the healthcare team regarding the cardiotoxic potential of antitumor treatments prior to their initiation, as well as the lack of other treatment strategies. They had insufficient knowledge about risk factors for heart failure and prevention measures and would have liked to have been warned about the possibility, even if minimal, of developing heart failure prior to treatment. None of the participants could clearly articulate about their heart care needs, and more than half adopted healthy eating habits after their cancer diagnosis, but seemed to have no clear understanding of what a balanced diet is for heart health. This makes it clear that in many cases nurses are not exercising their role as health educators, which can directly affect patients' quality of life.

Collection of international topics in health science:
The nurse's role in the care of the cardiotoxicities generated by chemotherapy administration

823

4 CONCLUSION

The fact that nurses do not act as health educators prevents patients from having full knowledge of their condition, reducing their autonomy and making it difficult for them to act as co-responsible caregivers, which has a negative impact on their quality of life.

The purpose of this study was to contribute to the increase of knowledge regarding the role of nurses with cardiotoxicities generated by the administration of chemotherapeutic drugs, enabling further research on the subject, thus demonstrating that the role of this professional is extremely important and makes a difference in the care of patients undergoing chemotherapy.

Although most articles did not specify the importance of nurses in the process of identification, prevention, and treatment of cardiotoxicities caused by chemotherapy, all of them mentioned the cardiovascular risk factors associated as potentiators of these events, as well as the management of these risks being an essential action for increasing survival after treatment and, especially, for increasing the quality of life of patients. The prompt detection and treatment of this side effect of antitumor drugs is also mentioned as fundamental for reversing or minimizing cardiac problems. In addition, the articles brought light to the primordiality of care to be centered on the patient and not on the disease and the need for multidisciplinary work for the care of patients with cancer.

Thus, nurses, as the only member of the health team who assists patients in their entirety and holistically, play a crucial role in the management of these risk factors, and can act to detect the emergence of new factors in the routine of patients, as well as to guide them to eliminate or minimize their damage. Thus, it is necessary to create specific care protocols for patients with chemotherapy-induced cardiotoxicity that establish a relevant periodicity of follow-up and guide the nurse's actions so that their evaluation, screening, and guidance are more assertive and individualized to the needs of each patient.

Collection of international topics in health science:
The nurse's role in the care of the cardiotoxicities generated by chemotherapy administration

824

REFERENCES

Austin-Mattison C. (2018). Joining Forces: Establishing a Cardio-oncology Clinic. *Journal of the advanced practitioner in oncology*, *9*(2), 222–229.

Bonassa, Edva Moreno Aguilar; Gato, Maria Inês Rodrigues. (2012). *Terapêutica oncológica para enfermeiros e farmacêuticos*. Atheneu.

Brunner & Suddarth. Tratado de Enfermagem Médico-cirúrgica. Janice L. Hinkle, Kerry H. Cheever. 14. ed. – Rio de Janeiro, Guanabara Koogan, 2020.

COFEN (1998) Resolução 210. http://www.cofen.gov.br/resoluo-cofen-2101998_4257.html

Correction to: Cardiovascular Disease and Breast Cancer: Where These Entities Intersect: A Scientific Statement From the American Heart Association. (2019). *Circulation*, *140*(9), e543. https://doi.org/10.1161/CIR.0000000000000728

Coviello JS (2018). Cardiovascular and Cancer Risk: The Role of Cardio-oncology. *Journal of the advanced* prater *in oncology*, *9* (2), 160-176.

Curigliano et al. Cardiovascular toxicity induced by chemotherapy, targeted agents and radiotherapy: ESMO Clinical Practice Guidelines†, Annals of Oncology,Volume 23, Supplement 7, 2012,Pages vii155-vii166, ISSN 0923-7534, https://doi.org/10.1093/annonc/mds293

Curigliano, G., Fradley, M., Ganatra, S., Barac, A., Blaes. A., Herrmann, J., ... Jordan, K., on behalf of the ESMO Guidelines Committee. (2020). Management of cardiac disease in cancer patients throughout oncological treatment: ESMO consensus recommendations. Annals of Oncology,Volume 31, Issue 2, P171-190 https://doi.org/10.1016/j.annonc.2019.10.023

Clark, RA, Marin, TS, Berry, NM *et al.* Avaliação de cardiotoxicidade e risco de doença cardiovascular em pacientes recebendo tratamento para câncer de mama. *Cardio-Oncology* **3,** 6 (2017). https://doi.org/10.1186/s40959-017-0025-7

Clark, RA, Marin, TS, McCarthy, AL *et al.* Cardiotoxicidade após o tratamento do câncer: um mapa do processo da jornada de tratamento do paciente. *Cardio-Oncology* 5**,** 14 (2019). https://doi.org/10.1186/s40959-019-0046-5

Fadol A. P. (2018). Management of Chemotherapy-Induced Left Ventricular Dysfunction and Heart Failure in Patients With Cancer While Undergoing Cancer Treatment: The MD Anderson Practice. *Frontiers in cardiovascular medicine*, *5*, 24. https://doi.org/10.3389/fcvm.2018.00024

Susan C. Gilchrist et al. (2019) Cardio-oncology rehabilitation to manage cardiovascular outcomes in cancer patients and survivors: a scientific statement from the American heart association. Circulation. 2019;139:e997–e1012. https://doi.org/10.1161/CIR.0000000000000679

Grossman, Sheila C.; Porth, Carol Mattson. (2019). *Fisiopatologia*. Guanabara Koogan.

Guyton, A.C. e Hall J.E. (2017). Tratado de Fisiologia Médica. Elsevier. 13ª ed.

Hajjar et al., (2020). Diretriz Brasileira de Cardio-oncologia – 2020. *Arquivos Brasileiros de Cardiologia*, *115*(5), 1006-1043. Epub December. https://doi.org/10.36660/abc.20201006

Higgins, A. Y et al., (2021). Left ventricular myocardial strain and tissue characterization by cardiac magnetic resonance imaging in immune checkpoint inhibitor associated cardiotoxicity. *PloS one*, *16*(2), e0246764. https://doi.org/10.1371/journal.pone.0246764

Hoff PMG et al. (2013). *Tratado de Oncologia*. Atheneu.

Kelly, F., Carroll, S. L., Carley, M., Dent, S., Shorr, R., Hu, J., Morash, R., & Stacey, D. (2017). Symptom practice guide for telephone assessment of patients with cancer treatment-related cardiotoxic

Collection of international topics in health science:
The nurse's role in the care of the cardiotoxicities generated by chemotherapy administration

825

dyspnea: Adaptation and evaluation of acceptability. *Cardio-oncology (London, England)*, *3*, 7. https://doi.org/10.1186/s40959-017-0026-6

Kumar, V.; Abbas, A.K.; Aster. (2013). J.C. Patologia Básica. 9. ed. Rio de Janeiro: Elsevier.

Melo, Marcelo Dantas Tavares de, & Salemi, Vera Maria Cury. (2019). Utilidade dos Índices de Deformação Miocárdica na Prevenção da Cardiotoxicidade em Pacientes com Câncer de Mama. *Arquivos Brasileiros de Cardiologia*, *112*(1), 57-58. https://doi.org/10.5935/abc.20190009

Ministério da Saúde. INCA. (2019). *Estimativa 2020: incidência de câncer no Brasil.* https://www.inca.gov.br/sites/ufu.sti.inca.local/files//media/document//estimativa-2020-incidencia-de-cancer-no-brasil.pdf

Netter, Frank H. (2018). **Atlas de Anatomia Humana.** 7ed. Porto Alegre: Artmed.

Potter, Patricia A.; Perry, Anne G. (2013). Fundamentos de Enfermagem. Elsevier.

Rodrigues, Andrea Bezerra; Martin, Leila Gonçalves Rocha; Moraes, Márcia Wanderley de. (2016). *Oncologia multiprofissional: bases para assistência.* Série manuais de especialização Einstein. Manole.

Silva, Jacqueline Mota da, Lima, Beatriz da Silva, Araújo, Thelma Leite de, Lima, Francisca Elisângela Teixeira, & Cunha, Gilmara Holanda da. (2018). Cardiovascular adverse events associated with oral antineoplastic therapy. *Revista Brasileira de Enfermagem*, *71*(5), 2561-2569. https://dx.doi.org/10.1590/0034-7167-2017-0450

OMS. (2020). *WHO report on cancer: setting priorities, investing wisely and providing care for all.* https://www.who.int/publications/i/item/who-report-on-cancer-setting-priorities-investing-wisely-and-providing-care-for-all

OMS. (2020). The top 10 causes of death. https://www.who.int/news-room/fact-sheets/detail/the-top-10-causes-of-death

Collection of international topics in health science:
The nurse's role in the care of the cardiotoxicities generated by chemotherapy administration

826