REVIEW ARTICLE

REVISTA ENFERMAGEM ATUAL IN DERME

REPERCUSSIONS OF CHILDHOOD CANCER ON THE CARDIOVASCULAR HEALTH OF SURVIVORS: A REVIEW STUDY

REPERCUSSÕES DO CÂNCER INFANTOJUVENIL NA SAÚDE CARDIOVASCULAR DE SOBREVIVENTES: ESTUDO DE REVISÃO

REPERCUSIONES DEL CÁNCER INFANTIL EN LA SALUD CARDIOVASCULAR DE LOS SUPERVIVIENTES: ESTUDIO DE REVISIÓN

Laura Raquel Soares de Abreu[1]
Samira Silva Santos Soares[2]
Lucas Rodrigo Garcia de Mello[3]
Ana Paula Brito Pinheiro[4]
Eloá Carneiro Carvalho[5]
Karla Biancha Silva de Andrade[6]

[1]Universidade do Estado do Rio de Janeiro, Rio de Janeiro, Brazil. ORCID: https://orcid.org/0000-0003-4331-4483
[2]Universidade Estadual de Santa Cruz, Ilhéus, Brazil. ORCID: https://orcid.org/0000-0001-9133-7044
[3]Universidade do Estado do Rio de Janeiro, Rio de Janeiro, Brazil. ORCID: https://orcid.org/0000-0002-4833-606X
[4]Instituto Nacional de Câncer, Rio de Janeiro, Brazil. ORCID: https://orcid.org/0000-0002-4441-4948
[5]Universidade do Estado do Rio de Janeiro, Rio de Janeiro, Brazil. ORCID: https://orcid.org/0000-0002-1099-370X
[6] Universidade do Estado do Rio de Janeiro, Rio de Janeiro, Brazil. ORCID: https://orcid.org/0000-0002-6216-484X

Corresponding Author
Laura Raquel Soares de Abreu
Rua J, vila 97, casa 7 – Conjunto Habitacional César Maia, Vargem Pequena – Rio de Janeiro, Brazil, CEP 22783111, contact: +55(21) 966261495, E-mail: lauraraquel1421@gmail.com

Submission: 22-04-2024
Approval: 14-05-2025

ABSTRACT
Objective: to analyze scientific production on the repercussions of childhood cancer on the cardiovascular health of survivors. **Method:** integrative review with a qualitative approach. During data collection, a specific instrument was used to search for articles in the MEDLINE/Pubmed, VHL and EMBASE databases, with the following research question: what are the cardiovascular repercussions in survivors of childhood cancer? Articles were included which were freely available in their entirety, in Portuguese, English and Spanish and from the last 10 years (2013-2023). Iramuteq software was used to analyze the data, which was organized using the descending hierarchical classification technique. **Results:** the results showed the extent of the cardiovascular repercussions on the public by presenting the main cardiac events that can occur, including coronary artery disease. The association between chemotherapy, radiotherapy and cardiotoxicity was highlighted, as well as other related risk factors such as dose, bone marrow transplant, gender and family history. **Conclusion:** it can be concluded that the cardiovascular repercussions will accompany this population throughout their lives. In this sense, it is necessary to develop actions that encourage professionals to build awareness and self-care among the survivor population, encouraging them to continue with the monitoring and care plan focused on cardiovascular health.
Keywords: Cancer Survivors; Cardiotoxicity; Patient Care Planning; Oncology Nursing.

RESUMEN
Objetivo: analizar la literatura científica sobre las repercusiones del cáncer infantil en la salud cardiovascular de los supervivientes. **Método:** revisión integradora con enfoque cualitativo. Durante la recogida de datos, se utilizó un instrumento específico para la búsqueda de artículos en las bases de datos MEDLINE/Pubmed, BVS y EMBASE, con la siguiente pregunta de investigación: ¿cuáles son las repercusiones cardiovasculares en los supervivientes de cáncer infantil? Se incluyeron artículos que estuvieran disponibles gratuitamente en su totalidad, en portugués, inglés y español y de los últimos 10 años (2013-2023). Se utilizó el software Iramuteq para el análisis de los datos, que se organizaron mediante la técnica de clasificación jerárquica descendente. **Resultados:** los resultados mostraron la amplitud de las repercusiones cardiovasculares en la población mediante la presentación de los principales eventos cardíacos que pueden producirse, incluida la enfermedad arterial coronaria. Se destacó la asociación entre quimioterapia, radioterapia y cardiotoxicidad, así como otros factores de riesgo relacionados como dosis, trasplante de médula ósea, sexo y antecedentes familiares. **Conclusión:** se puede concluir que las repercusiones cardiovasculares acompañarán a esta población a lo largo de su vida. En este sentido, es necesario desarrollar acciones que favorezcan la construcción de conciencia por parte de los profesionales, el autocuidado de la población sobreviviente, incentivándolos a continuar con el monitoreo y plan de cuidados enfocados en la salud cardiovascular.
Palabras clave: Sobrevivientes de Cáncer; Cardiotoxicidad; Planificación de la atención al paciente; Enfermería Oncológica.

RESUMO
Objetivo: analisar as produções científicas sobre as repercussões do câncer infantojuvenil na saúde cardiovascular de sobreviventes. **Método:** revisão integrativa, com abordagem qualitativa. Durante a coleta de dados, utilizou-se de instrumento próprio para busca de artigos nas bases de dados MEDLINE/Pubmed, BVS e EMBASE, tendo como questão de pesquisa: quais as repercussões cardiovasculares em pessoas sobreviventes de câncer infantojuvenil? Incluíram-se artigos disponíveis na íntegra gratuitamente, nos idiomas português, inglês e espanhol, e recorte temporal dos últimos 10 anos (2013-2023). Adotou-se o software Iramuteq para análise dos dados, sendo organizados a partir da técnica de classificação hierárquica descendente. **Resultados:** os resultados evidenciaram a dimensão das repercussões cardiovasculares no público, a partir da apresentação dos principais eventos cardíacos que podem surgir, dentre eles, a doença arterial coronariana. Destaca-se a associação entre quimioterapia, radioterapia e cardiotoxicidade, bem como outros fatores de risco relacionados, como dose, transplante de medula, sexo e histórico familiar. **Conclusão:** as repercussões cardiovasculares irão acompanhar essa população durante toda vida, neste sentido, urge elaborar ações que favoreçam a construção de conscientização por parte dos profissionais, o autocuidado da população sobrevivente, incentivando-os a prosseguir o acompanhamento e o plano de cuidados focados na saúde cardiovascular.
Palavras-chave: Sobreviventes de Câncer; Cardiotoxicidade; Planejamento de Assistência ao Paciente; Enfermagem Oncológica.

REVISTA ENFERMAGEM ATUAL IN DERME

INTRODUCTION

Cancer is defined as uncontrolled cell growth characterized by affecting different tissues and organs, and in the context of childhood cancer, this involvement occurs mainly in the blood and supporting systems[1]. Furthermore, according to the National Cancer Institute, cancer is currently the leading cause of death in the population between the ages of one and 19, with embryonic mutations being the main agents that lead to the onset of the development of the disease in this population.

For the three-year period 2023-2025, 7,930 new cases are expected for each year of the three-year period, 4,230 for males and 3,700 for females[2]. Currently, the South Region has the highest number of cases, both in the male population, approximately 153.29/million, and in the female population, approximately 151.19/million[2]. That said, among the different types of cancer, leukemia, central nervous system cancers and lymphomas are, respectively, the malignant neoplasms that most affect this population[2].

Regarding the death rate in Brazil due to childhood cancer, in 2017, approximately 1,467 deaths were recorded among males and 1,086 deaths among females. Regarding survival in Brazil, the Ministry of Health[3] estimated that the survival rate of pediatric cancer patients reached 64% in 2016. For the three-year period 2023-2025, it is estimated that 80% of children and adolescents with cancer, if diagnosed and treated early, tend to be cured[2]. However, due to the correlation between survival and cure and survival, discussions are needed about the quality of this survival rate and the possible repercussions that may impact this period[4].

Cancer is a complex and multifactorial disease. Therefore, even if the person is cured, depending on the development of the disease and the treatment implemented, the consequences may be experienced for a long time or even forever. Among these consequences, cardiovascular repercussions stand out. The literature shows that, due to the widespread use of doxorubicin, a chemotherapy drug from the anthracycline class, widely used in the treatment of childhood and adolescent cancers, the risks of cardiovascular complications in the survival of these individuals are greater[5].

One in eight patients undergoing treatment with anthracyclines or chest radiotherapy will experience some life-threatening cardiovascular problem 30 years after treatment for childhood and adolescent cancer[6]. Furthermore, if the patient already has an uncontrolled disease that compromises cardiovascular health, such as Systemic Arterial Hypertension (SAH), according to the Ministry of Health[7], the cardiovascular risks will be greater[8].

Thus, this study aimed to analyze scientific productions about the repercussions of childhood cancer on the cardiovascular health of survivors.

METHODS

This is an integrative review with a qualitative approach. For this study, the research

REVISTA ENFERMAGEM ATUAL IN DERME

was conducted via the National Library of Medicine (MEDLINE/PubMed), Excerpta Medica database (EMBASE) and the Virtual Health Library (BVS), based on the implementation of controlled descriptors related to each database.

For the search in MEDLINE/PubMed, the Medical Subject Headings (MeSH) were used for descriptors in English. For the search in EMBASE, the Embase thesaurus (EMTREE). For the descriptors in Portuguese, used in the BVS, the Health Science Descriptors (DeCS) were applied. At the time of the search, the descriptors were arranged with the Boolean operators OR and AND, "OR" between synonymous terms and "AND" between distinct descriptors. For the MEDLINE/Pubmed database, the following MeSH descriptors were used: "child", "adolescent", "cancer survivors", "neoplasms", "antineoplastic protocols", "drug therapy", "antineoplastic agents", "radiotherapy", "cardiotoxicity", "heart injuries", "heart diseases".

For EMBASE, the following descriptors were used: "childhood cancer survivor", "neoplasm", "drug therapy", "chemotherapy", "radiotherapy", "cardiotoxicity", "heart injury". For BVS, the following DeCS descriptors were used: "child", "adolescent", "cancer survivors", "neoplasms", "antineoplastic agents", "radiotherapy", "heart", "cardiotoxicity". The research question was based on the anagram PICo – population, intervention (or phenomenon of interest) and context, in which the population was made up of survivors of childhood cancer, the intervention was related to exposure to treatment and its respective cardiovascular repercussions, and the context did not apply to this research. Thus, the research question of this study was: what are the cardiovascular repercussions in survivors of childhood cancer?

To construct this work, articles available in full for free, in Portuguese, English and Spanish, were included, following a time frame of the last 10 years (2013-2023), considering that, in the last decade, there has been an evolution in oncological treatments and progress in the view of survival in this population, starting with the publication of the First Brazilian Guideline for Cardio-oncology of 2011[9], which directs actions for safe cardiovascular care; and studies carried out in humans that addressed the cardiovascular repercussions in survivors of childhood cancer. Articles whose title or abstract did not correspond to the object, the study question and the research objectives were excluded; review articles, letters, guidelines, theses, dissertations or books.

The selection followed the three stages of the flowchart of the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) 2020 recommendations. For data collection, a specific instrument was adopted, consisting of database, year of publication, article title, authors, objectives, type of study, summary of findings, conclusion and level of evidence. The data collection period was between March and April 2023. To certify the level of evidence of each article, the Joanna Briggs Institute[10] was used as a reference.

REVISTA ENFERMAGEM ATUAL IN DERME

Subsequently, from the collection of articles, the data were processed using the software Interface de R pour les Analyses Multidimensionneles de Textes et de Questionnaires (Iramuteq) for further analysis. This is software that quantifies the frequency of words in a text, after organizing it into "text segments", thus automatically creating an organization of vocabularies that can be easily assessed visually[11], thus allowing subsequent exploration, correlation and analysis of the most frequent terms with what the literature describes. The use of this tool ensures precision, agility and less interference from subjectivity during data analysis[11].

To this end, the findings (results) found in each article were summarized and organized according to the Iramuteq manual standards in a single text, the "textual corpus" [12]. The textual corpus was made up of command lines that identify and differentiate each article included in the research. In addition, synonymous words were standardized to avoid duplication, such as the words pediatric cancer and childhood cancer, which were standardized to "childhood and youth cancer," and the words cardiac and similar were standardized to "cardiovascular." In addition, a table was created with the variables and codes of each of these articles for later identification.

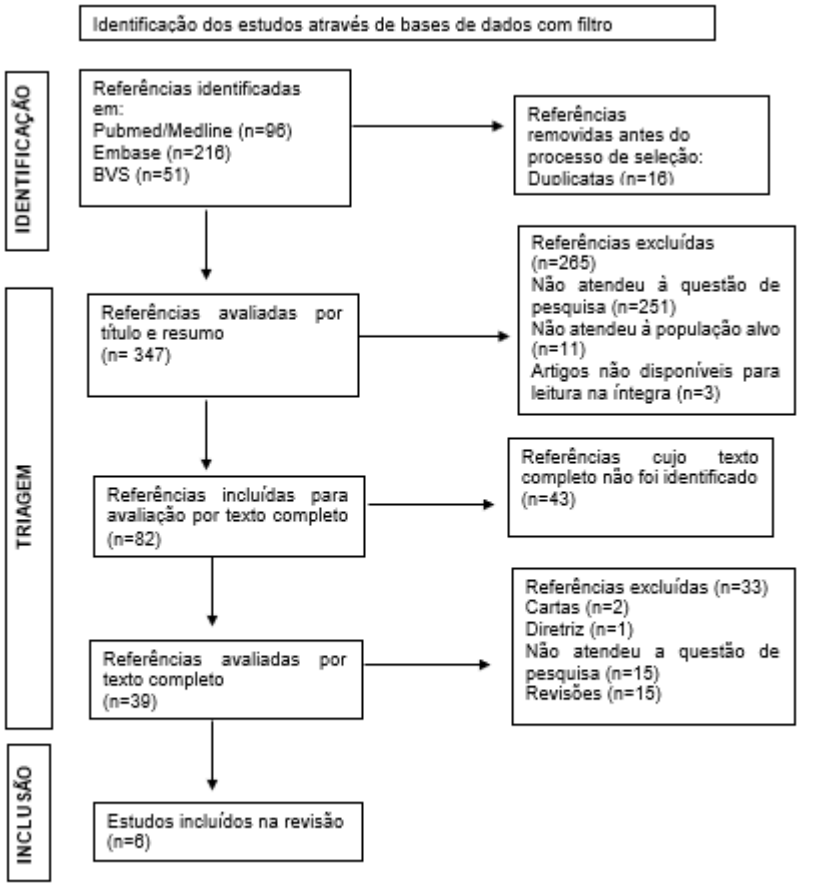
The finished textual corpus was processed by Iramuteq and organized according to a Descending Hierarchical Classification (DHC) that performed lexical analysis of the corpus. From this, Iramuteq generated a visual instrument for discussing the findings, known as a dendrogram, which presents the classes and lexicons (words) that represent the context to be discussed. Finally, the lexicons found in the contexts were explored and the text segments interpreted, based on the conceptual theoretical framework[13].

It is emphasized that the classes generated came from the articles analyzed, and may be correlating text segments from several articles or just one; this variation occurred according to the specificity of the texts. Some themes that differentiate and were not discussed by other authors, that is, classes could be generated from a single article, due to their singularity.

REVISTA ENFERMAGEM ATUAL IN DERME

RESULTS

Figure 1 – Preferred Reporting Items for Systematic Reviews and Metaanalysis flow diagram of studies identified and selected for inclusion in the integrative review. Rio de Janeiro, 2023.



Fonte: O autor. 2023.

Table 1 – Summary of articles included in the review. Rio de Janeiro, 2023.

DATABASE	Year	Code/Authors/Titles	Summary of findings	Objectives	Type of study	Conclusion	Level of evidence
Embase	2022	Art. 1 Nathan et al.[14] Incidence and risk factors of anthracycline-induced cardiotoxicity in long-term survivors of pediatric cancer: A population based cohort study	Anthracycline therapy has also been associated with congestive heart failure, arrhythmias, pericardial and valvular disease, myocardial infarction, and hypertension. There is evidence of late deterioration and death >10 years after anthracycline therapy due to replacement of degenerated cardiomyocytes by fibrosis. Risk factors for early and late anthracycline-induced	To report the incidence and risk factors for Anthracycline-Induced Cardiotoxicity (AIC) in long-term pediatric cancer survivors.	Cohort type observational	The incidence of cardiotoxicity was 5.98%, while the incidence of symptomatic cardiotoxicity requiring interventions due to anthracyclines was low (2.17%). Only a cumulative dose of 300 mg/m2 of anthracycline was significantly associated with symptomatic anthracycline-induced	III

REVISTA ENFERMAGEM ATUAL IN DERME

			cardiotoxicity (AIC) have been studied and include a higher cumulative anthracycline dose, female sex, younger age at treatment, radiation to the chest, hematopoietic stem cell transplantation, and longer follow-up.			cardiotoxicity.	
Embase	2019	Art. 2 Abdelhameid et al.[15] Long term effects of therapy among childhood cancer survivors treated in the last two decades	Six participants had an abnormal echocardiogram, showing decreased Ejection Fraction (EF) and/or Shortening Fraction (SF). Fifteen (12%) reported having a chronic cardiovascular comorbidity on the questionnaire, including diabetes, hypertension, high cholesterol, and heart disease.	To assess the burden of significant long-term complications related to cancer therapy in survivors of childhood cancer diagnosed and treated after 1990.	Cohort type observational	There are several limitations to this study. This is not a longitudinal study and there is likely to be underreporting of late effects as the prevalence increases over time. The sample size was small and may not accurately reflect the prevalence of these outcomes in the general population of childhood cancer survivors. Data were predominantly obtained from questionnaires and medical records. No objective neurocognitive testing was performed to assess neurocognitive outcomes in this cohort. Although data were collected prospectively, there was no control group in the study. Despite these limitations, this study was representative of the burden of long-term complications among childhood cancer survivors treated with newer treatment regimens..	III
Embase	2022	Art. 3 Lipshultz et al.[16] Cardiometabol	30.5% of survivors were at moderate risk of ischemic heart disease	To assess the burden of traditional, potentially	Clinical trial	Childhood cancer survivors exhibit similar or better cardiometabolic and	I

REVISTA ENFERMAGEM ATUAL IN DERME

		ic risk in childhood cancer survivors: a report from the Children's Oncology Group	and >95% at moderate/high risk of heart failure, with an expected incidence of 9% to 12% of these conditions by age 50 years.	modifiable cardiometabolic risk factors (CRF) among young adult survivors previously treated in clinical trials investigating the use of dexrazoxane in anthracycline-based regimens; and to compare these results with population-matched controls.		lifestyle profiles compared with the general population without cancer, but are still at risk for future clinically significant cardiovascular disease.	
BVS	2020	Art. 4 Mulrooney et al.[17] Major cardiac events for adult survivors of childhood cancer diagnosed between 1970 and 1999: report from the Childhood Cancer Survivor Study cohort	Hazard ratios for heart failure and coronary artery disease suggested a decline across treatment eras, but were attenuated by the addition of treatment variables (mean cardiac and anthracycline doses) and cardiovascular risk factors. Risk factors associated with heart failure included female sex (1.51 (1.10–2.06)), higher cardiac radiation exposure and anthracycline dose, and reported diagnosis of diabetes, dyslipidemia, or hypertension. For coronary artery disease, a dose–response was evident, with increasing mean cardiac radiation exposure (2.26 (1.32–3.84) for 15–35 Gy and 5.86 (3.69–9.28) for ≥35 Gy)..	To investigate the impact of modifications to contemporary cancer protocols, designed to minimize cardiotoxic exposures and preserve long-term health, on serious cardiac outcomes among adult survivors of childhood cancer.	Observational type Retrospective cohort	Among adult survivors of childhood cancer, the risk of coronary artery disease has decreased significantly. This decrease may be associated with historical reductions in cardiac radiation exposure, particularly among survivors of Hodgkin lymphoma. This is important because childhood cancer survival rates are increasing and these young adults acquire cardiovascular disease prematurely.	III
BVS	2021	Art. 5 Goldberg et al.[18] Cardiovascular Family	Among survivors exposed to chest-directed radiation and/or anthracycline chemotherapy (n=824),	To examine the contribution of family history of cardiovascular disease and	Cohort type observational	Family history of cardiovascular disease and cardiovascular risk factors independently	III

		History Increases Risk for Late-Onset Adverse Cardiovascular Outcomes in Childhood Cancer Survivors: A St. Jude Lifetime Cohort Report.	7% reported a first-degree family history of heart failure; 19%, myocardial infarction; 11%, stroke; 26%, atherosclerotic disease (myocardial infarction and/or stroke); 62%, hypertension; and 31%, diabetes mellitus. Eighteen percent of exposed survivors developed heart failure; 9%, myocardial infarction; 3%, stroke; 11%, atherosclerotic disease; 30%, hypertension; and 9%, diabetes mellitus. Having a first-degree family history of atherosclerotic disease was independently associated with the development of treatment-related heart failure among exposed survivors. The risk of hypertension was increased among exposed survivors with a first-degree family history of hypertension or any cardiovascular disease [myocardial infarction,stroke, or heart failure].	cardiovascular risk factors to the development of these conditions among childhood cancer survivors exposed and unexposed to cardiotoxic therapies.		increased the risk of heart failure and hypertension among childhood cancer survivors exposed to cardiotoxic therapies.	
BVS	2016	Art. 6 Mulrooney et al. [19] Cardiac Outcomes in Adult Survivors of Childhood Cancer Exposed to Cardiotoxic Therapy: A Cross-Sectional Study from the St. Jude Lifetime Cohort.	Cardiomyopathy was present in 7.4% (newly identified at evaluation in 4.7%), coronary artery disease (CAD) in 3.8% (newly identified in 2.2%), valvular regurgitation/stenosis in 28.0% (newly identified in 24.8%), and conduction/rhythm abnormalities in 4.6% (newly identified in 1.4%). Almost all (99.7%) were asymptomatic. The prevalence of cardiac disease increased with age at evaluation, ranging from 3-24% in	Systematically evaluate cardiac outcomes among childhood cancer survivors	Cohort type observational	Cardiovascular screening has identified considerable subclinical disease among adult survivors of childhood cancer.	IV

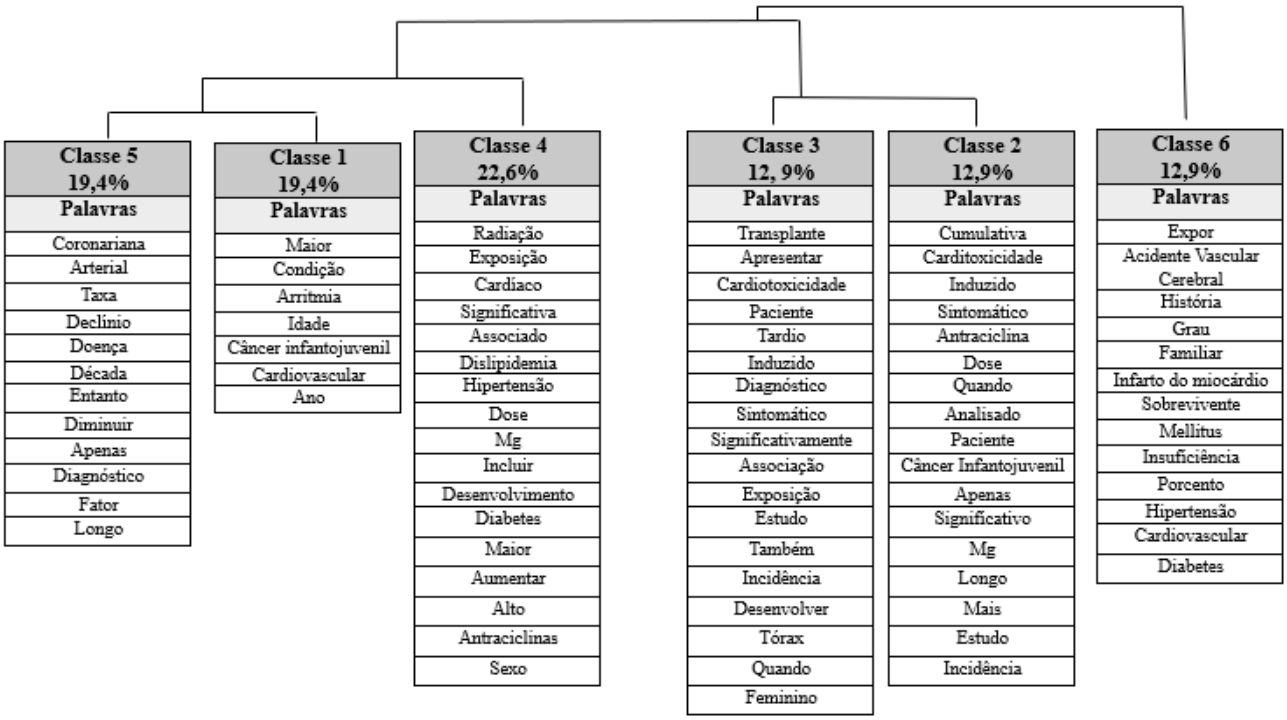
REVISTA ENFERMAGEM ATUAL IN DERME

			those 30-39 years to 10-37% in those ≥40 years. In multivariate analysis, anthracycline exposure ≥250 mg/m2 increased the odds of cardiomyopathy (odds ratio [OR] 2.7, 95% CI 1.1-6.9) compared with survivors not exposed to anthracycline. Radiation to the heart increased the odds of cardiomyopathy (OR 1.9, 95% CI 1.1-3.7) compared with survivors not exposed to radiation.				

Fonte: O autor, 2023

The six articles constituted the textual corpus for processing via Iramuteq. When performing the Descending Hierarchical Classification (CHD), a utilization rate of 77.50% was achieved and 31 Text Segments (TS) were distributed into six classes, with the separation into three thematic blocks being observed, as evidenced by the following dendrogram.

Figure 2 – Dendrogram of the classes established by the software Interface de Rpour lesAnalyses Multidimensionnelles de Textes et de Questionnaires (Iramuteq), through the Descending Hierarchical Classification. Rio de Janeiro, 2023.



Source: Authors, 2023.

REVISTA ENFERMAGEM ATUAL IN DERME

By analyzing the lexicons that composed the classes presented and exploring the text segments in which they appeared, it was possible to name the classes formed.

The first thematic block was composed of classes 5, 1, 4. Class 1 (19.4%) represents "cardiovascular impairment in survivors of childhood cancer", class 5 (19.4%) points to the "risk of coronary artery disease in survivors of childhood cancer". In class 4 (22.6%), "cardiac damage related to exposure to radiation" stands out.

The second thematic block highlighted "anthracycline-induced cardiotoxicity and possible repercussions" (class 2 – 12.9%) and "risk factors for anthracycline-induced cardiotoxicity" (class 3 – 12.9%). Finally, in the third thematic block, "family history as a factor related to the greater risk of cardiovascular repercussions in survivors of childhood cancer" (class 6 – 12.9%) stood out, a difference that can be observed in the dendrogram, when verifying the separation of the other groups.

The dendrogram is a tool that highlights a set of words, separated by classes. In each class, the word can have a strength, expressed by frequency or by the chi-square value. And, the evident words in each class are the most representative of a text segment. The term "hypertension", for example, appeared in classes 4 and 6. In class 4, its frequency was 50%, while in class 6, it was 30%. Furthermore, the same word can have different meanings. This was the case with the word "hypertension", which, in class 4, was discussed as a risk factor for increased cardiovascular impairment.

And, in class 6, hypertension emerged as a consequence after cardiac damage due to cardiotoxic therapies linked to family history. Thus, Descending Hierarchical Classification (DHC) is a method that aims to identify not only classes with different text segments, but also with similar vocabularies[12].

Class 5: Risk of coronary artery disease in childhood cancer survivors

In this class, the most frequent words were "coronary", "arterial" and "rate". This is because coronary artery disease is one of the cardiovascular diseases that can also affect survivors of childhood cancer. As shown in the ST below, which shows the rate of Coronary Artery Disease (CAD) in 1,853 survivors of childhood cancer who were previously exposed to cardiotoxic therapies, such as chemotherapy and radiotherapy.

> "Cardiomyopathy was present in 7.4%; Coronary Artery Disease (CAD), in 3.8% [...]". (Art. 6)

Class 1: Cardiovascular impairment in childhood cancer survivors

In class 1, the words "major", "condition", "arrhythmia" were the most mentioned in the scope of the literature analyzed, as well as the words "cardiovascular" and "childhood cancer". This occurred because the therapeutic approach implemented in childhood cancers is associated with damage to cardiac

REVISTA ENFERMAGEM ATUAL IN DERME

health, conferring a greater risk of cardiovascular diseases, even after a longer period of time after therapy. As stated by the ST:

> "Treatment with anthracyclines has also been associated with congestive cardiovascular failure, arrhythmias, pericardial and valvular disease, myocardial infarction and hypertension. There is evidence of late deterioration and death greater than 10 years after anthracycline therapy [...]". (Art. 1)

Furthermore, from this, survivors of childhood cancer constitute a public with greater vulnerability to the development of cardiovascular conditions, when compared to an individual without cancer. As stated in the text segments.

> "Childhood cancer survivors have a higher risk of developing cardiovascular disease." (Art. 2)

> "[...] 30.5% of survivors had a moderate risk of developing ischemic cardiovascular disease and >95% had a moderate or high risk of developing cardiovascular failure [...]." (Art. 3)

Class 4: Heart damage related to radiation exposure

Radiation is one of the treatment modalities implemented in childhood and adolescent cancers and also poses a risk of cardiac damage. In this study, the class stood out as the most recurrent (22.6%), with the words "radiation", "exposure", and "cardiac" being the most cited. In this sense, survivors previously exposed to radiation have a greater chance of developing heart disease, as stated in the text segments below.

> "Exposure to anthracyclines and thoracic radiation are the most important risk factors for the development of cardiovascular disease". (Art. 2)

> "Radiation greater than 1500cgy with any exposure to anthracycline conferred the greatest chances of valvular findings. The chances of cardiomyopathy were significantly associated with male gender, anthracycline doses greater than or equal to 250 mg, exposure to cardiac radiation greater than 1500cgy, and hypertension". (Art. 6)

In addition, if the patient has comorbidities, the chances of cardiovascular diseases will be greater. As a result, it was possible to observe the high frequency of the words "diabetes", "dyslipidemia" and "hypertension", as highlighted by the ST:

> "Risk factors associated with cardiovascular failure included female gender, greater exposure to cardiovascular radiation and anthracycline dose and report of diagnosis of diabetes, dyslipidemia or hypertension". (Art. 4)

Class 3: Risk factors for anthracycline-induced cardiotoxicity

For the development of cardiotoxicity and, consequently, heart disease, there are factors that, when associated, can contribute to a greater chance of this cardiovascular condition occurring. In addition to a high cumulative dose, class 3 addressed other risk factors that can also contribute to heart disease, which explains the multiple citations of the words "transplant", "present", "cardiotoxicity", "patient", "late", "diagnosis", as highlighted in the text segments:

> "When analyzed, all patients who presented anthracycline-induced

REVISTA ENFERMAGEM ATUAL IN DERME

> cardiotoxicity, bone marrow transplantation and the diagnosis of acute myeloid leukemia and sarcoma were significantly associated with anthracycline-induced cardiotoxicity". (Art. 1)

> "Our study found that hematopoietic stem cell transplantation and the diagnosis of acute myeloid leukemia and sarcoma are significantly associated with anthracycline-induced cardiotoxicity". (Art. 1)

Furthermore, cardiotoxicity can be defined according to the period in which it appears. Thus, late cardiotoxicity is one of the possible definitions of this damage – which can be associated with patients diagnosed and subjected to the events previously mentioned, as mentioned by the ST:

> "Among the four patients who presented symptomatic cardiotoxicity, two patients presented late-onset cardiotoxicity. Late onset is defined as occurring more than one year after the end of exposure to anthracycline". (Art. 1)

The mention of the words "female" and "thorax" is emphasized, as both constitute the set of risk factors for anthracycline-induced cardiotoxicity, indicating that the female sex and radiation exposure in the chest region have a greater risk of cardiac damage, as ratified by the following ST:

> "Of the four patients who presented cardiotoxicity, 75% were female, 25% had radiation exposure in the chest [...]". (Art. 1)

It is worth noting that article 1 was the only one among the other articles that addressed the risk factors related to anthracycline-induced cardiotoxicity, which is why it supports class 3.

Class 2: Anthracycline-induced cardiotoxicity and possible repercussions

In this class, the words "cumulative", "cardiotoxicity", "induced", "symptomatic" and "anthracycline" stood out. As mentioned, oncological treatment confers a greater cardiovascular risk to previously exposed survivors. Thus, in the oncological scenario, anthracyclines have gained notoriety, as they are frequent drugs in treatment protocols for children and adolescents and induce cardiotoxicity to the heart, especially if the cumulative dose is high and exposure occurs at a young age, which characterizes it as a risk factor for this population, as highlighted by the following ST:

> "However, when only symptomatic patients are analyzed, only a cumulative anthracycline dose of 300 mg/m² has a significant relationship with anthracycline-induced cardiotoxicity. Although a cumulative anthracycline dose of 300 mg/m² poses a significant risk of cardiotoxicity, doses below this level have been shown to cause cardiovascular changes." (Art. 1)

> "Risk factors for early and late anthracycline-induced cardiotoxicity have been studied and include a higher cumulative anthracycline dose, female gender, and young age at treatment [...]." (Art. 1)

Furthermore, regarding the repercussions on cardiovascular health, childhood cancer survivors can be divided into asymptomatic

REVISTA ENFERMAGEM ATUAL IN DERME

patients, i.e., those who do not present symptoms characteristic of cardiotoxicity; and symptomatic patients, those who have symptoms of cardiotoxicity in the period after treatment. For this reason, the term "symptomatic" appeared in the group of most frequent words, symptoms associated with the cumulative dose of anthracycline, according to the ST below.

> "When analyzing only symptomatic patients, the only significant outcome associated with cardiovascular events was a cumulative anthracycline dose of 300 mg/m²." (Art. 1)

Class 6: Family history as a factor related to the increased risk of cardiovascular repercussions in survivors of childhood cancer

In addition to the risk factors for the repercussions on the cardiovascular health of childhood cancer survivors, as mentioned, family history appears in this class as a new factor. Article 5 stood out among the others, as it discussed the relevance of this family history for the increased risk of adverse cardiovascular events, which gave rise to class 6. In this class, the most mentioned terms were "expose", "vascular", "cerebral", "accident", "history", "degree", "familial" and others associated with the theme, according to the following ST.

> "The risk of hypertension increased among exposed survivors with a first-degree family history of hypertension or any cardiovascular disease, myocardial infarction, stroke, or cardiovascular failure." (Art. 5)

Therefore, if the survivor, previously exposed to cardiotoxic therapies, has a family history of some cardiovascular disease, the risk of developing heart disease will be greater, also highlighted in the ST:

> "Having a first-degree family history of atherosclerotic disease was independently associated with the development of treatment-related cardiovascular failure among exposed survivors." (Art. 5)

In view of these findings, three themes were developed: **Compromise of cardiovascular health in survivors of childhood cancer; Radiotherapy as a risk factor for cardiovascular impairment; and Risk factors associated with cardiovascular events in survivors of childhood cancer.**

DISCUSSION

Cardiovascular health impact of childhood cancer survivors

As found in the results of this research, the repercussions on the cardiovascular health of childhood cancer survivors are diverse, among which the risk of Coronary Artery Disease (CAD) addressed in class 5[17] stands out. CAD is a heart disease characterized by endothelial damage that culminates in a continuous inflammatory response in the vessel, which progresses to endothelial dysfunction. In this scenario, childhood cancer survivors are included. According to the results presented, approximately 3.8% of childhood cancer survivors presented CAD[19]. This association indicates that chemotherapy treatment and

REVISTA ENFERMAGEM ATUAL IN DERME

cardiac radiation are additional risk factors for coronary artery disease, given that they induce the formation of Reactive Oxygen Species (ROS) that damage myocardial tissue[20].

The incidence of coronary artery disease increases in survivors previously exposed to cardiac irradiation[21]. Radiation causes damage to endothelial cells, activation of growth factors and consequent inflammatory response, generating recruitment of cytokines, such as tumor necrosis factor and interleukins (IL), and fibroblasts. As a result, there is progressive fibrosis of cardiac tissue and subsequent myocardial dysfunction[20].

CAD is one of the most common late cardiovascular diseases resulting from radiotherapy, even 10 to 15 years after treatment[22]. Furthermore, the incidence of CAD in survivors of Hodgkin lymphoma exposed to radiotherapy is 20%, even 40 years after therapeutic intervention[23].

In addition to CAD, according to the results, other cardiovascular diseases can affect survivors of childhood cancer, as there is an association between cancer treatment and arrhythmias, pericardial and valvular disease, acute myocardial infarction and congestive heart failure, in which one of the mechanisms is the replacement of degenerated cardiomyocytes by fibrosis, which can lead to late deterioration, even after a period of more than 10 years[14].

Similarly, survivors of childhood cancer have a 5-15 times greater risk of Congestive Heart Failure (CHF), compared to the general population[24]. If the diagnosis is confirmed, the chance of survival in five years is less than 50%. In addition, another cause associated with heart failure is the irreversible loss of cardiomyocytes induced by anthracyclines[4]. It should also be added that treatment with anthracyclines confers a 15-fold greater risk of chronic heart failure for survivors[25].

As found in the results of this research, the repercussions on the cardiovascular health of childhood cancer survivors are diverse, among which the risk of Coronary Artery Disease (CAD) addressed in class 5[17] stands out. CAD is a heart disease characterized by endothelial damage that culminates in a continuous inflammatory response in the vessel, which progresses to endothelial dysfunction. In this scenario, childhood cancer survivors are included. According to the results presented, approximately 3.8% of childhood cancer survivors presented CAD(19). This association indicates that chemotherapy treatment and cardiac radiation are additional risk factors for coronary artery disease, given that they induce the formation of Reactive Oxygen Species (ROS) that damage myocardial tissue[20].

The incidence of coronary artery disease increases in survivors previously exposed to cardiac irradiation[21]. Radiation causes damage to endothelial cells, activation of growth factors and consequent inflammatory response, generating recruitment of cytokines, such as tumor necrosis factor and interleukins (IL), and fibroblasts. As a result, there is progressive fibrosis of cardiac tissue and subsequent myocardial dysfunction[20].

REVISTA ENFERMAGEM ATUAL IN DERME

CAD is one of the most common late cardiovascular diseases resulting from radiotherapy, even 10 to 15 years after treatment[22]. Furthermore, the incidence of CAD in survivors of Hodgkin lymphoma exposed to radiotherapy is 20%, even 40 years after therapeutic intervention[23].

In addition to CAD, according to the results, other cardiovascular diseases can affect survivors of childhood cancer, as there is an association between cancer treatment and arrhythmias, pericardial and valvular disease, acute myocardial infarction and congestive heart failure, in which one of the mechanisms is the replacement of degenerated cardiomyocytes by fibrosis, which can lead to late deterioration, even after a period of more than 10 years[14].

Similarly, survivors of childhood cancer have a 5-15 times greater risk of Congestive Heart Failure (CHF), compared to the general population[24]. If the diagnosis is confirmed, the chance of survival in five years is less than 50%. In addition, another cause associated with heart failure is the irreversible loss of cardiomyocytes induced by anthracyclines[4]. It should also be added that treatment with anthracyclines confers a 15-fold greater risk of chronic heart failure for survivors[25].

Radiotherapy as a risk factor for cardiovascular impairment

Radiotherapy is an important therapeutic modality for the treatment of malignancies and is characterized by the release of ionizing radiation to destroy cancer cells, as well as to stop their multiplication[27]. As evidenced in the results of this research, radiotherapy is an important risk factor for the development of cardiovascular diseases[15]. Ionizing radiation causes endothelial damage, and as a result, the cells release molecules and growth factors that induce an acute inflammatory response. Subsequently, this response will cause progressive fibrosis of the cardiac tissue, leading to pericardial, myocardial and valvular dysfunctions[20].

In this sense, radiotherapy is one of the factors associated with damage to cardiac valves, pericarditis and heart failure[26,28]. Therefore, survivors of childhood cancer exposed to radiotherapy are susceptible to cardiomyopathy, pericardial disease, atherosclerosis, valvular disease and other cardiovascular events[29]. Thus, exposure to radiotherapy in the mediastinal region, combined with chemotherapy, increases the chances of cardiovascular events, possibly due to the anatomical location of the heart and increased cardiotoxic effects[22].

In the same sense, if there is a diagnosis of comorbidities, such as diabetes, hypertension, dyslipidemia and others, the chances of heart disease are greater, given that these are widely known cardiovascular risk factors and that their association has already been confirmed[17,21,23].

Risk factors associated with cardiovascular events in childhood cancer survivors

In addition to the aforementioned risk factors, different literature describes other factors associated with the risk of cardiovascular disease, such as bone marrow transplantation,

REVISTA ENFERMAGEM ATUAL IN DERME

diagnosis of Acute Myeloid Leukemia (AML), gender, exposure to anthracyclines and family history, evidenced in classes 3, 2 and 6, respectively. Acute myeloid leukemia is characterized by being a malignancy that results in the replacement of normal blood cells by abnormal and immature cells in the bone marrow, which leads to the emergence of signs and symptoms characteristic of the disease and the need for specific treatments[30].

Patients previously diagnosed with AML are susceptible to a higher risk of anthracycline-induced cardiotoxicity (topic to be discussed later)[14], possibly because this class of chemotherapy is widely used in leukemia treatment protocols, which includes acute myeloid leukemia(24). Furthermore, some studies state that children diagnosed with leukemia presented considerable values of troponin T and NTproBNP, biomarkers that demonstrate cardiac damage, after treatment with anthracyclines[25,31], which explains the link between the diagnosis of leukemia and anthracycline-induced cardiotoxicity and the resulting damage.

Furthermore, one of the treatments used, including in the treatment of leukemia, is bone marrow transplantation, also known as Hematopoietic Stem Cell Transplantation (HSCT). This procedure is a risk factor for the development of cardiac repercussions, being associated with anthracycline-induced cardiotoxicity[14]. Furthermore, the National Cancer Institute[32] also states that HSCT confers a higher risk of metabolic syndrome, which is associated with a greater chance of early onset of cardiovascular diseases in young people undergoing this therapy in childhood.

Another important factor of discussion is gender, with females being at greater risk for the development of cardiotoxicity associated with anthracyclines[14,21,22]. This finding still presents gaps regarding the reason for it, however, some studies report that one of the possible reasons is the difference that females present compared to males, regarding the pharmacokinetics and pharmacodynamics of antineoplastics[22]. One of these associations is body composition, which can influence the toxicity of the antineoplastic; however, more studies are still needed to corroborate this statement[33].

Regarding anthracyclines, there is extensive mention in the literature of a strong association with cardiac repercussions[15,20,24]. Especially in childhood cancer, the cardiotoxicity associated with anthracyclines is widely discussed, considering that these are drugs frequently used in chemotherapy protocols for the treatment of the main hematologic and solid cancers that affect this population, among them, leukemias[4,25].

Anthracyclines are a class of chemotherapy drugs used to treat different types of cancer, whose mechanism of action involves the impairment of DNA and RNA synthesis, as well as the production of Reactive Oxygen Species (ROS) that damage the cell membrane, which prevents tumor growth[34]. Among the antineoplastics that represent this class, we can mention doxorubicin, daunorubicin, epirubicin

REVISTA ENFERMAGEM ATUAL IN DERME

and idarubicin[24]. However, despite the positive influence on the establishment of healing, considerable losses are associated with this mechanism.

The production of ROS causes considerable oxidative damage, which induces lipid peroxidation, mitochondrial dysfunction and, subsequently, activation of the apoptosis pathway[25]. Because cardiomyocytes do not have a considerable amount of ROS scavengers, they become more susceptible to this damage, which leads to subsequent loss of these cells[22]. In addition, due to the low regenerative capacity, damage to cardiac tissue tends to be irreversible[4].

These lesions to cardiac tissue vary according to the cumulative dose of anthracycline to be administered, with doses greater than 250 mg/m2 being those that confer the greatest chance of cardiotoxicity, leading some studies to state that there is no safe dose[14,21]. Thus, the possible cardiovascular events associated with this therapy are conduction disorders, damage to the microvasculature, heart failure, myocarditis, pericarditis and coronary syndromes[4,22,26]. Furthermore, according to the I Brazilian Guideline for Cardio-oncology of the Brazilian Society of Cardiology[9], exposure to anthracyclines at a young age is one of the risk factors for cardiotoxicity, which increases the chances of childhood cancer survivors developing a cardiovascular event.

Another important factor for the emergence of repercussions for the cardiac health of childhood cancer survivors is family history, in which, if the survivor has a first-degree relative diagnosed with hypertension or cerebrovascular diseases, such as stroke, the risks for developing hypertension or heart failure will be greater[18].

A study reiterates that genetic/familial predisposition to dilated cardiomyopathy may be a possible risk factor for anthracycline-associated cardiomyopathy[35]. This is due to the fact that in a previous study[36], two patients who underwent cancer treatment in childhood presented cardiac alterations, as well as family members who also presented alterations. However, the studies highlighted the need for further research in the area to fully elucidate this.

Therefore, another field of research and investment has emerged, of extreme importance to health professionals, especially nurses, with possible tools for this investigation being family cardiovascular screening, before and after the diagnosis of cancer in childhood. In this way, the possibility of early and assertive intervention is increased. In addition, the chances of ensuring survival with a lower rate of morbidity and mortality associated with cardiac repercussions will be greater[18].

CONCLUSION

Based on the results obtained, it was possible to understand the wide range of heart diseases that survivors of childhood cancer are susceptible to, such as CAD, arrhythmias and heart failure. Therefore, based on the correlation of treatments used for childhood cancer with a

REVISTA ENFERMAGEM ATUAL IN DERME

higher risk of heart disease, it is understood that the cure is effective at the expense of heart health.

Because this is a recent subject with a restricted target population, this study was limited by the minimum number of field research and correlated studies. In this sense, further investigations and publications on the subject are also suggested, especially to increase the actions of nurses within the scope of the nursing process.

In addition, it is necessary for the oncology scientific community to reevaluate therapeutic protocols, as well as improve discussions and studies on the doses used in chemotherapy protocols, especially with regard to anthracyclines and radiotherapy, in order to balance therapeutic action and toxicity.

Finally, it is understood that the survival process is not restricted to the act of continuing to live; a cure does not guarantee full safety and quality of life. Cardiovascular repercussions will accompany this population throughout their lives; ensuring the aforementioned actions favors the construction of awareness by professionals and self-care by the surviving population, encouraging them to continue with the monitoring and the established care plan.

REFERENCES

1. Instituto Nacional de Câncer (BR). Câncer infantojuvenil [Internet]. Rio de Janeiro: INCA; c2022- [citado 2022 Set 14]. Disponível em: https://www.gov.br/inca/pt-br/assuntos/cancer/tipos/infantojuvenil

2. Instituto Nacional de Câncer (BR). Estimativa 2023: Incidência de câncer no Brasil [Internet]. Rio de Janeiro: INCA; 2022 [citado 2023 Maio 22]. Disponível em: https://www.inca.gov.br/sites/ufu.sti.inca.local/files/media/document/estimativa-2023.pdf

3. Instituto Nacional de Câncer (BR). Incidência, mortalidade e morbidade hospitalar por câncer em crianças, adolescentes e adultos jovens no Brasil: informações dos registros de câncer e do sistema de mortalidade [Internet]. Rio de Janeiro: INCA; 2016 [citado 2022 Set 14]. Disponível em: https://www.inca.gov.br/sites/ufu.sti.inca.local/files//media/document//incidencia-mortalidade-morbidade-hospitalar-por-cancer.pdf

4. Lazăr DR, Farcaş AD, Blag C, Neaga A, Zdrenghea MT, Căinap C, et al. Cardiotoxicity: A Major Setback in Childhood Leukemia Treatment. Dis Markers [Internet]. 2021 [citado 2022 Set 14];2021:8828410. Disponível em: https://www.hindawi.com/journals/dm/2021/8828410/

5. Mancilla TR, Iskra B, Aune GJ. Doxorubicin-Induced Cardiomyopathy in Children. Compr Physiol [Internet]. 2020 [citado 2022 Set 14];9(3):905-31. Disponível em: 10.1002/cphy.c180017. Acesso em: 14 set. 2022.

6. Pal HJVD, et al. High Risk of Symptomatic Cardiac Events in Childhood Cancer Survivors. J Clin Oncol [Internet]. 2012 [citado 2022 Set 14];30(13):1429-37. Disponível em: https://onlinelibrary.wiley.com/doi/10.1002/cphy.c180017

7. Ministério da Saúde (BR). Plano de ações estratégicas para enfrentamento das doenças crônicas não transmissíveis (DCNT) no Brasil 2011-2022 [Internet]. Brasília-DF: Ministério da Saúde; 2011 [citado 2022 Set 14]. 160 p. Disponível em: https://bvsms.saude.gov.br/bvs/publicacoes/plano_acoes_enfrent_dcnt_2011.pdf

8. Baker KS, Syrjala KL. Long-term complications in adolescent and young adult leukemia survivors. Am Soc Hematol [Internet]. 2018 [citado 2022 Set 14];1:146-53. Disponível em: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6245964/#:~:text=Long%2Dterm%20toxicities%20of%20AML,%2C%20venous%20thrombosis%2C%20and%20ON.&text=Both%20AML%20and%20ALL%20survivors,for%20cardiomyopathy%20and%20cardiometabolic%20abnormalities.

9. Karil Filho R, Hajjar LA, Bacal F, Hoff PMG, Diz MDS, Galas FRBG, et al. I Diretriz Brasileira de Cardio-Oncologia da Sociedade Brasileira de Cardiologia. Arq Bras Cardiol [Internet]. 2011 [citado 2023 Jun 07];96(2):1-52. Disponível em: https://www.scielo.br/j/abc/a/KkGBNtQtyfF9yLy5jn3KXsL/?format=pdf&lang=pt

10. Joanna Briggs Institute. JBI Levels of Evidence [Internet]. Adelaide: JBI; 2013 [citado 2022 Nov 20]. Disponível em: https://jbi.global/sites/default/files/2019-05/JBI-Levels-of-evidence_2014_0.pdf

11. Andrade JV, Moura D, Cristina J, Polati AM. Uso de software para análise de dados em pesquisas qualitativas: abordagem das ferramentas NVivo, MAXQDA e IRAMUTEQ. Revista Enfermagem Atual In Derme [Internet]. 2024 [citado 2025 Mar 24]; 98(4):e024410-0. Disponível em: https://revistaenfermagematual.com.br/index.php/revista/article/view/2415

12. Camargo BV, Justo AM. Tutorial para uso do software de análise textual IRAMUTEQ [Internet]. Florianópolis: Universidade Federal de Santa Catarina; 2021 [citado 2022 Nov 20]. Disponível em: http://www.iramuteq.org/documentation/fichiers/Tutorial%20IRaMuTeQ%20em%20portugues_22.11.2021.pdf

13. Sousa YSO. O uso do software Iramuteq: Fundamentos de Lexicometria para Pesquisas Qualitativas. Estud Pesqui Psicol [Internet]. 2021 [citado 2023 Jan 09];21(4):1542-60. Disponível em: https://www.e-publicacoes.uerj.br/index.php/revispsi/article/view/64034/40133

14. Nathan P, Kulkarni K, MacDonald T. Incidence and risk factors of anthracycline-induced cardiotoxicity in long-term survivors of pediatric cancer: A population based cohort study. Pediatr Hematol Oncol J [Internet]. 2022 [citado 2023 Jun 07];7:136-41. Disponível em: https://www.sciencedirect.com/science/article/pii/S2468124522002431

15. Abdelhameid D, Mills A, Dean J, Piguet N, Shankar S. Long term effects of therapy among childhood cancer survivors treated in the last two decades. Pediatr Hematol Oncol J [Internet]. 2019 [citado 2023 Jun 07];4(1):12-6. Disponível em: https://www.sciencedirect.com/science/article/pii/S2468124518300676

16. Lipshultz ER, Chow EJ, Doody DR, Armenian SH, Asselin BL, Baker KS, et al. Cardiometabolic risk in childhood cancer survivors: a report from the Children's Oncology Group. Cancer Epidemiol Biomarkers Prev [Internet]. 2022 [citado 2022 Set 14];31(3):536-42. Disponível em: https://aacrjournals.org/cebp/article/31/3/536/681946/Cardiometabolic-Risk-in-Childhood-Cancer-Survivors

17. Mulrooney DA, Hyun G, Ness KK, Ehrhardt MJ, Yasui Y, Duprez D, et al. Major cardiac events for adult survivors of childhood cancer diagnosed between 1970 and 1999: report from the Childhood Cancer Survivor Study cohort. BMJ [Internet]. 2020 [citado 2023 Jun 07];368:l6794. Disponível em: https://www.bmj.com/content/368/bmj.l6794

18. Goldberg JF, Ness KK, Chi X, Santucci AK, Plana JC, Joshi VM, et al. Cardiovascular Family History Increases Risk for Late-Onset Adverse Cardiovascular Outcomes in Childhood Cancer Survivors: A St. Jude Lifetime Cohort Report. Cancer Epidemiol Biomarkers Prev [Internet]. 2021 [citado 2023 Jun 07];30(1):123-32. Disponível em:

https://aacrjournals.org/cebp/article/30/1/123/72510/Cardiovascular-Family-History-Increases-Risk-for

19. Mulrooney DA, Armstrong GT, Huang S, Ness KK, Ehrhardt MJ, Joshi VM, et al. Cardiac Outcomes in Adult Survivors of Childhood Cancer Exposed to Cardiotoxic Therapy: A Cross-Sectional Study from the St. Jude Lifetime Cohort. Ann Intern Med [Internet]. 2016 [citado 2023 Jun 07];164(2):93-101. Disponível em: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4809016/

20. Bansal N, Blanco JG, Sharma U, Pokharel S, Shisler S, Lipshultz SE. Cardiovascular Diseases in Survivors of Childhood Cancer. Cancer Metastasis Rev [Internet]. 2020 [citado 2023 Jun 07];39(1):55-68. Disponível em: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7123498/#:~:text=Survivors%20of%20cancer%20are%20significantly,or%20valvar%20abnormalities%20%5B5%5D

21. Chow EJ, Leger KJ, Bhatt NS, Mulrooney DA, Ross CJ, Aggarwal S, et al. Paediatric cardio-oncology: epidemiology, screening, prevention, and treatment. Cardiovasc Res [Internet]. 2019 [citado 2023 Jun 07];115(5):922-34. Disponível em: https://academic.oup.com/cardiovascres/article/115/5/922/5320534?login=false

22. Sadurska E. Current Views on Anthracycline Cardiotoxicity in Childhood Cancer Survivors. Pediatr Cardiol [Internet]. 2015 [citado 2023 Jun 07];36:1112-9. Disponível em: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4495714/

23. Petropoulos AC, Moschovi M. Cardiotoxicity among adult survivors suffered from childhood malignancies. Hell J Nucl Med [Internet]. 2019 [citado 2023 Jun 07];2:34-40. Disponível em: https://www.nuclmed.gr/wp/wp-content/uploads/2019/12/SUPPLEMENT-5th-OLYMPIAD.pdf

24. Armenian S, Bhatia S. Predicting and Preventing Anthracycline-Related Cardiotoxicity. Am Soc Clin Oncol Educ Book [Internet]. 2018 [citado 2023 Jun 07];23(38):3-12. Disponível em: https://ascopubs.org/doi/10.1200/EDBK_100015

25. Bennati E, Girolami F, Spaziani G, Calabri GB, Favre C, Parrini I, et al. Cardio-Oncology in Childhood: State of the Art. Curr Oncol Rep [Internet]. 2022 [citado 2023 Jun 07];24:1765-77. Disponível em: https://link.springer.com/article/10.1007/s11912-022-01329-6

26. Lipshultz SE, Karnik R, Sambatakos P, Franco VI, Ross SW, Miller TL. Anthracycline-related cardiotoxicity in childhood cancer survivors. Curr Opin Cardiol [Internet]. 2014 [citado 2023 Jun 07];29(1):103-12. Disponível em: https://journals.lww.com/co-cardiology/abstract/2014/01000/anthracycline_related_cardiotoxicity_in_childhood.15.aspx

27. Instituto Nacional de Câncer (BR). Radioterapia [Internet]. Rio de Janeiro: INCA; c2023- [citado 2023 Jun 07]. Disponível em: https://www.gov.br/inca/pt-br/assuntos/cancer/tratamento/radioterapia#:~:text=O%20que%20%C3%A9%20radioterapia%3F,sente%20nada%20durante%20a%20aplica%C3%A7%C3%A3o

28. Benetou DR, Stergianos E, Geropeppa M, Ntinopoulou E, Tzanni M, Pourtsidis A, et al. Late-onset cardiomyopathy among survivors of childhood lymphoma treated with anthracyclines: a systematic review. Hell J Cardiol [Internet]. 2019 [citado 2022 Set 14];60(3):152-64. Disponível em: https://www.sciencedirect.com/science/article/pii/S1109966618302999

29. Lipshultz EE, Franco VI, Miller TL, Colan SD, Sallan SE. Cardiovascular Disease in Adult Survivors of Childhood Cancer. Annu Rev Med [Internet]. 2015 [citado 2023 Jun 07];66:161-76. Disponível em: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5057395/#:~:text=The%20leading%20noncancer

%2Drelated%20cause,%2Drelated%20disease%20(9).

30. Instituto Nacional de Câncer (BR) [Internet]. Rio de Janeiro: INCA; c2022- [citado 2023 Jun 07]. Leucemia. Disponível em: https://www.gov.br/inca/pt-br/assuntos/cancer/tipos/leucemia

31. Rato J, Rebelo M, Borges A. Uso pediátrico de antraciclinas e cardiotoxicidade: Revisão de novos métodos de rastreio e terapêutica a propósito de um caso clínico. Rev Port Oncol [Internet]. 2019 [citado 2023 Jun 07];3(1). Disponível em: https://rponcologia.com/index.php/rpo/article/view/8

32. Instituto Nacional de Câncer (BR). Tópicos em Transplante de Células-Tronco Hematopoéticas [Internet]. Rio de Janeiro: INCA; 2012 [citado 2023 Jun 07]. Disponível em: https://www.inca.gov.br/sites/ufu.sti.inca.local/files//media/document//topicos-transplantes-medula.pdf

33. Lipshultz EE, Lipsitz SR, Mone SM, Goorin AM, Sallan SE, Sanders SP, et al. Female sex and higher drug dose as risk factors for late cardiotoxic effects of doxorubicin therapy for childhood cancer. N Engl J Med [Internet]. 1995 [citado 2023 Jun 07];332(26):1738-43. Disponível em: https://www.nejm.org/doi/full/10.1056/NEJM199506293322602

34. Gatto M, Mota GAF. Influência do Tratamento com Doxorrubicina no Metabolismo da Heme em Cardiomioblastos: Estudo In Vitro. Arq Bras Cardiol [Internet]. 2021 [citado 2023 Jun 07];116(2):323-4. Disponível em: https://abccardiol.org/short-editorial/influencia-do-tratamento-com-doxorrubicina-no-metabolismo-da-heme-em-cardiomioblastos-estudo-in-vitro/

35. Wasielewski M, van Spaendonck-Zwarts KY, Westerink NDL, Jongbloed JDH, Postma A, Gietema JA, et al. Potential genetic predisposition for anthracycline-associated cardiomyopathy in families with dilated cardiomyopathy. Open Heart [Internet]. 2014 [citado 2023 Jun 07];1(1):1-9. Disponível em: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4195921/

36. van den Berg MP, van Spaendonck-Zwarts KY, van Veldhuisen DJ, Gietema JA, Postma A, van Tintelen JP. Familial dilated cardiomyopathy: another risk factor for anthracycline-induced cardiotoxicity? Eur J Heart Fail [Internet]. 2010 [citado 2023 Jun 07];12:1297-9. Disponível em: https://onlinelibrary.wiley.com/doi/10.1093/eurjhf/hfq175

Declaration of conflict of interests
Nothing to declare.

Funding and Acknowledgements:
The research did not receive funding.

Authorship criteria (authors' contributions)

Laura Raquel Soares de Abreu and Karla Biancha Silva de Andrade contributed substantially to the conception, planning, data collection and analysis, writing, critical review and final approval of the study.

Samira Silva Santos Soares, Lucas Rodrigo Garcia Mello, Ana Paula Brito Pinheiro, Eloá Carneiro Carvalho contributed substantially to the critical review and final approval of the study.

Scientific Editor: Ítalo Arão Pereira Ribeiro. Orcid: https://orcid.org/0000-0003-0778-1447