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ORIGINAL ARTICLE

Osteometabolic changes in patients under antineoplastic treatment: scoping review

Alterações osteometabólicas em pacientes em tratamento antineoplásico: revisão de escopo

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KEYWORDS

Antineoplastics
Bones
Chemotherapy
Metabolic bone diseases
Oncology

ABSTRACT

Objective: To summarize the main evidence regarding osteometabolic changes in patients undergoing antineoplastic treatment.
Methods: This is a scoping review, following the methodology of the Joanna Briggs Institute, using PubMed/MedLine, Cochrane Library, LILACS, The British Library, and Google Scholar. This review is registered in the Open Science Framework.
Results: Many antineoplastics affect bone architecture by reducing its density, such as selective estrogen receptor modulators, aromatase inhibitors, androgen deprivation therapy, and glucocorticoids. To avoid such outcomes, treatment and prevention can be achieved by calcium and vitamin D supplementation, physical exercise, use of bisphosphonates, denosumab, and selective estrogen receptor modulators.
Conclusion: people at a higher risk of developing cancer also have a higher risk of osteopenia and osteoporosis when the process is already established and undergoing antineoplastic treatment because of the grouping of risk factors. The need for bone densitometry in patients undergoing cancer treatment to prevent and promote bone health in these patients is evident, in addition to more research with a high level of evidence to support such use.

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PALAVRAS-CHAVE

Antineoplásicos
Doenças ósseas metabólicas
Oncologia
Ossos
Quimioterapia

RESUMO

Objetivo: sintetizar as principais evidências acerca das alterações osteometabólicas presentes nos pacientes em tratamento antineoplásico.
Métodos: trata-se de uma revisão de escopo, seguindo a metodologia do Instituto Joanna Briggs, nas bases de dados PubMed/MedLine, Cochrane Library, LILACS, The British Library e Google Scholar. A revisão está protocolada no Open Science Framework.
Resultados: muitos antineoplásicos possuem efeito na arquitetura óssea, reduzindo sua densidade, tais como moduladores seletivos de receptores de estrogênio, inibidores da aromatase, terapia de privação androgênica, e glicocorticoides. Para evitar tais desfechos, o tratamento e prevenção podem ser realizados pela suplementação de cálcio e vitamina D, exercícios físicos, uso de bifosfonatos, denosumab, e moduladores seletivos do receptor de estrogênio.
Conclusão: pessoas com maior risco de desenvolver câncer também possuem maior risco de osteopenia e osteoporose, quando processo já estabelecido e em tratamento antineoplásico, devido ao compartilhamento de fatores de risco. Torna-se evidente a necessidade da densitometria óssea nos pacientes em tratamento contra o câncer para de prevenção e promoção de saúde óssea nesses pacientes, além de mais pesquisas com alto nivel de evidência para subsidiar tal uso.

INTRODUCTION

Cancer is among the leading causes of death in approximately 112 countries, reflecting the decline in mortality rates from stroke and cardiovascular disease. The International Agency for Research on Cancer (IARC) published estimates of approximately 19.3 million cases and 10 million deaths caused by cancer in 2020, revealing a true public health crisis with an urgent demand for new efficient therapies that reduce mortality[1].

Skeletal changes in cancer patients are already known even before the introduction of antineoplastic therapies because of the direct effect of the underlying neoplasia[3]. However, the current therapies used have a synergistic effect in reducing bone mineral matrix (BMM). Furthermore, the bone is a frequent site of metastases, occasionally leading to fractures and chronic pain[2]. Regardless of the type of malignancy presented, the reduction in BMM may evolve into changes in the mineralization pattern; however, the literature does not indicate specific screening programs for this disorder[3].

Thus, the loss of bone mineralization in cancer patients reflects both the effects of carcinogenesis and responses to therapies used for cancer treatment, such as glucocorticoids, aromatase inhibitors, and androgen deprivation therapy. Antineoplastic agents are associated with various adverse musculoskeletal effects, including arthralgias, peripheral neuropathies, joint stiffness, myositis, osteopenia, and fragility fractures[4]. When seen from the point of view of increased survival, efforts to minimize bone loss can significantly improve the patient's quality of life to maximize their treatment and prevent complications[2,3,5,6].

Based on the increasing incidence of cancer diagnoses and the scarce evidence regarding the musculoskeletal consequences of the therapy used, this study aims to synthesize the primary evidence on the osteometabolic changes present in patients undergoing antineoplastic treatment to facilitate and better understand their possible complications and *clusters* of oncological symptoms.

METHODS

This scoping review had the research protocol registered in the *Open Science Framework* (DOI: 10.17605/OSF.IO/HVWBY).

The search strategy was conducted in November 2022 in four electronic databases: Medical Literature Analysis and Retrieval System Online – MEDLINE/PubMed, Cochrane Library, Latin American and Caribbean Literature in Health Sciences (Lilacs), The British Library, and Google Scholar. The acronym PECO (population, exposure, comparison and outcomes) was used to develop the research'sguiding question, considering P = (People undergoing antineoplastic treatment), E = (Symptoms and osteometabolic changes resulting from antineoplastic therapy), C = (Patients cancer patients without the use of osteotoxic medication), and O = (Patient prognosis and knowledge of the main changes)[7-9]. Thus, the research question was: *"What scientific evidence is available on the impact of the use of antineoplastics on the signs and symptoms of the* osteometabolic system?".

Mendeley Reference Management Software® was used to organize and manage the studies found in the databases. The selection of studies was performed by three researchers independently and double-blindly using Rayyan® software. The Boolean operators "AND" and "OR" were used to obtain restrictive and additive combinations and to combine the Medical Subjects Headings (MeSH) "Antineoplastics", "Chemotherapy", "Oncology", "Metabolic bone diseases" and "Bones", and translated into Portuguese and Spanish.

Eligibility Criteria

All observational, experimental, and qualitative study designs and literature reviews published until the beginning of November 2022and studies covering the use of antineoplastics in cancer patients and their bone changes were included. Productions in the following languages were selected: English, Portuguese, Spanish, and French.

Case reports, articles that addressed menopausal women (as they may already have some bone changes), and pediatric oncology cases were excluded from the review. For the temporal criterion, a 5-year cutoff was set for the search in electronic databases. Because of the innovativeness of the topic concerning osteometabolic changes, we decided to limit the number of most recent articles in the literature and conduct a review with the most recent evidence for clinical practice.

Study selection

All files examined from the four electronic databases were initially imported into Mendeley; thus, duplicate studies were removed. Three independent researchers searched and filtered the records by abstract and title using the Rayyan® application. After the first screening, the full texts of the retrieved studies were evaluated for inclusion or exclusion using the same application. A fourth author was consulted to decide in case of disagreement between the authors. The Preferred Statement Reporting Items for Systematic Review and Meta-Analyses extension for Scoping Reviews (PRISMA- ScR) was used to summarize the study selection process and its stages[10].

Data extraction and synthesis

The extracted data included: 1) type of methodological study; 2) population, if applicable; 3) recruitment method; 4) measurement/monitoring time; 5) main findings; 6) relevance for clinical practice[9,11,12].

Assessment of the included studies

The level of evidence (LE) was identified according to the evidence hierarchy, a strategy chosen because it is widely used and effective for classifying evidence for literature reviews. This system is divided into seven hierarchical levels, as shown in Table 1. This review considers levels I to III as strong, IV to VI as moderate, and VII as weak.

For data synthesis, the characteristics of the studies are summarized and shown in tables, and the results are presented according to the study design. Tables that present the results contain the citation, country of origin, objective, main results, LE, and clinical applicability. The discussion was subdivided into topics related to the main findings of this review for better clinical debate.

Furthermore, the quantitative tool by Law et al. (1998)[13] was used, which includes 12 criteria for evaluating the methodological quality of the studies selected for the review. A score of 1 or 0 was established for each criterion assessed by the tool and converted into a percentage for interpretation. Therefore, a study with a score of 100% is considered to be a good methodological study. The scores for each study were independently and blindly evaluated using two nurses experienced in the field of reviews and oncology.

Table 1 — Hierarchical level and study design.

Level of evidence	Study design
I	Systematic reviews or meta-analyses of randomized clinical trials
II	Well-designed randomized controlled trial
III	Well-designed controlled clinical trial without randomization
IV	Well-designed cohort, case-control, cross-sectional study
V	Systematic review of qualitative studies and descriptive studies
SAW	Single descriptive or qualitative study
VII	Authoritative opinion and/or expert report

RESULTS

In the search stage, 58 productions were identified in the six selected databases. Of these, we found 2 duplicates, which were excluded using Mendeley. The selection phase continued with 56 articles, among which 38 productions were excluded according to the title, with 18 being analyzed by summary and full reading. After reading, 6 articles were excluded because they did not address the guiding question, totaling 12 articles for review. Figure 1 demonstrates the steps for selecting articles for this scoping review.

Five productions (41.66%) were literature reviews without meta-analysis of the results, which only discussed the findings superficially, without analyzing the quality or LE of the productions. Three cohort studies (25%) were obtained: 1 (33.3%) prospective and 2 (66.66%) retrospective studies. Four productions were characterized as clinical trials (33.33%); of these, only one was a nonrandomized clinical trial, and the other three were randomized and double-blind (Table 2).

When analyzing the study population, 1 (8.33%) patient addressed pediatric cancer, correlating kidney and metabolic bone changes after cancer treatment. The majority (n = 11; 91.67%) had cancer in adulthood, including breast, prostate cancer and lymphoma. Regarding the country of origin, most studies were conducted in Europe (n = 11; 91.67%) and only one in the USA (8.33%). Regarding the LE of the selected articles, 5 (41.66%) were classified as LE V, 3 (25%) as LE IV, 3 (25%) as LE II, and only 1 (8.33%) as LE III (Table 3). Regarding the methodological quality of the 12 studies, based on the generic quantitative assessment tool, we obtained 8 productions of good quality and 4 of moderate quality (Table 4).

DISCUSSION

Osteoporosis is a bone disease characterized by compromised bone strength and microarchitecture deterioration. Bone mineral density (BMD) can be assessed using dual-energy X-ray absorptiometry, known as bone densitometry (DXA). The diagnostic result is

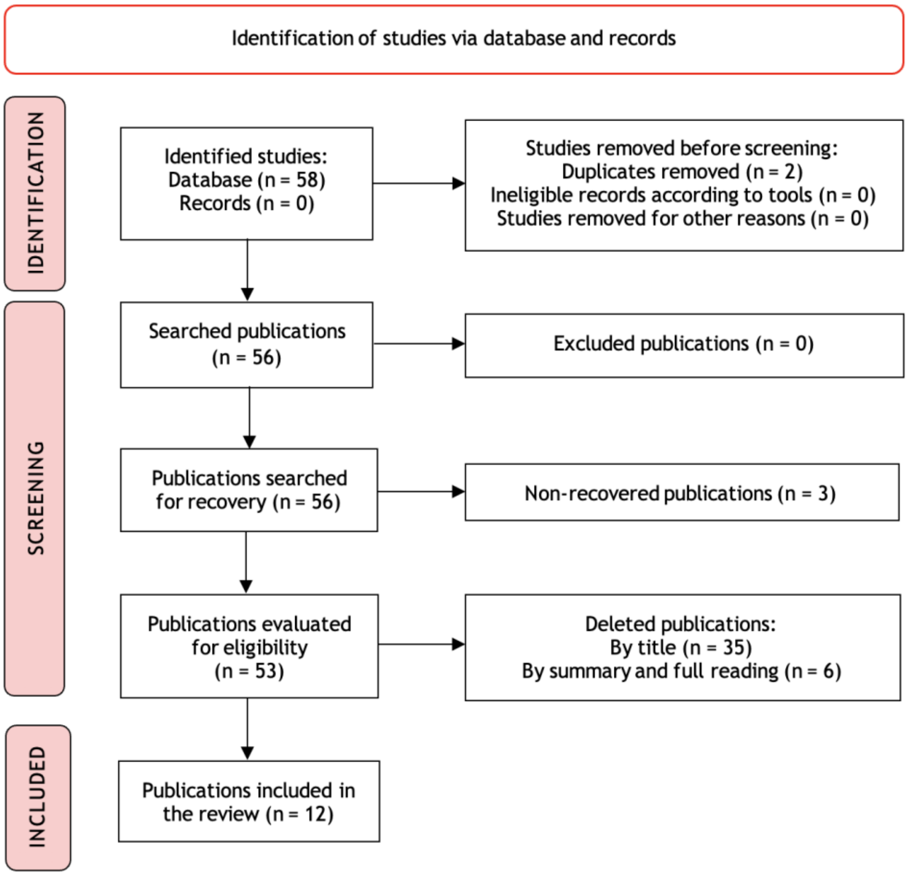

Figure 1 — Bibliographic selection flowchart.

Table 2 — Characteristics of the selected studies.

Author and year of publication	Country	Goals	Clinical applicability
Badri, Salawu , Brow[14] (2019)	UK	Understand the clinical and molecular impact of bone loss in patients undergoing chemotherapy treatment for prostate cancer.	Promotes theoretical foundation and encourages the development of guidelines for screening and prevention of bone loss.
Liuhto et al.[15] (2020)	Finland	To investigate the risk of morbidity in bone metabolism diseases and kidney diseases in 5-year pediatric and juvenile cancer survivors.	Promotes and instigates long-term follow-up care planning, aiming to minimize damage to related organs, it may be possible to reduce adverse effects.
Owen et al.[16] (2016)	Australia	Review guidelines on bone-metabolic adverse effects induced by androgen deprivation therapy.	It summarizes the main guidelines and bone disorders present in patients treated with androgen deprivation therapy and suggests the need for further studies.
Schyrr et al.[17] (2017)	Switzerland	To test whether there is a correlation between osteoporosis and hematopoiesis in stress hematopoiesis before and after adjuvant chemotherapy in the context of a breast cancer cohort.	The study points out an explicit difference in values of neutrophils and thrombocytes in pre- and post-CT patients. This change should be noted in clinical practice to prevent post-CT osteoporosis.
Hellemond et al.[18] (2020)	Germany	To evaluate the relationship between reduced BMD and distant recurrence-free survival (DRFS) and assess the effect of bisphosphonates on DRFS.	After 5 years of follow-up, no association was noted between DRFS and osteopenia or osteoporosis.
Seland et al.[19] (2017)	Norway	To evaluate BMD at six different skeletal sites and investigate	Assessment of BMD is recommended in lymphoma survivors with additional risk

Table 2 — Characteristics of the selected studies (cont.).

Author and year of publication	Country	Goals	Clinical applicability
		associations between clinical factors and BMD in lymphoma survivors.	factors such as hypogonadism, disposition, or low body weight.
Sestak et al.[20] (2019)	England	To compare the effect of oral risedronate *versus* placebo in osteopenic women in stratum II who were randomized to anastrozole in the main study.	The results confirm the bone loss associated with anastrozole use and show that anastrozole-induced BMD loss in the spine can be controlled with risedronate treatment.
Park et al.[4] (2019)	USA	Understanding the common classes of chemotherapy drugs and their potential adverse effects on the musculoskeletal system.	Decreased BMD is an adverse effect of chemotherapy regimens, including selective estrogen receptor modulators, aromatase inhibitors, and TCAs used to treat common malignancies and cervical, breast, and prostate cancers.
Bedatsova, Drake[2] (2019)	England	Demonstrate the impact of antineoplastic therapies on the skeleton and available data to limit bone loss and fractures in cancer patients treated with these therapies.	There is well-established evidence that adverse events include increased bone loss and fracture risks. Given these concerns, healthcare professionals and patients must recognize that attention to skeletal health is critical to maintaining quality of life outcomes.
Castaneda et al.[21] (2022)	Spain	Review of the pathophysiology of metabolic bone comorbidity in cancer patients.	There is still limited knowledge about the risk of osteoporosis associated with a wide range of medical and surgical treatments for cancer. In this context, BMD is currently one of the most essential tools for diagnosing and monitoring these patients.
Majithia et al.[22] (2016)	Germany	zoledronic acid can prevent the expected loss of BMD in postmenopausal women with preexisting osteopenia or osteoporosis who were initiating adjuvant letrozole therapy for primary breast cancer.	The 5-year follow-up of this single-arm study supports the notion that BMD loss in women with osteopenia or osteoporosis is stabilized with the simultaneous initiation of two drugs.
Livi et al.[23] (2019)	Italy	ibandronate treatment on bone mineral density (BMD) in osteopenic women using aromatase inhibitors.	Ibandronate compared with placebo improved BMD change in osteopenic women treated with adjuvant AI.

Table 3 — Methodological characteristics of the selected studies.

Reference	Methodology	Level of evidence	Impact Factor (2020)
14	Literature review without meta-analysis with 17 included studies	V	5,163
15	Retrospective cohort with 13,860 people	IV	7.39
16	Literature review without meta-analysis with 5 included studies	V	4,996
17	Retrospective cohort with 143 patients	IV	3.67
18	Randomized clinical trial with 1,860 patients	II	4.62
19	Non-randomized clinical trial with 228 patients	III	3.31
20	Randomized clinical trial with 258 women	II	4.26
4	Literature review without meta-analysis and without specifying the number of studies	V	3.02
2	Literature review without meta-analysis and without specifying the number of studies	V	3,716
21	Literature review without meta-analysis and without specifying the number of studies	V	3,340
22	Prospective cohort with 53 patients	IV	0.49
23	Randomized clinical trial with 561 patients	II	9.162

Table 4 — Quantitative assessment of the studies included in the review.

Reference	Criteria*												Points	%
	1	2	3	4	5	6	7	8	9	10	11	12		
14	s	s	s	s	No	AT	AT	No	s	s	NI	s	7/10	70
15	s	s	s	s	No	AT	AT	s	s	s	s	s	9/10	90
16	s	s	s	NI	No	AT	AT	No	s	s	NI	s	6/10	60
17	s	s	s	s	No	AT	AT	s	s	s	s	s	9/10	90
18	s	s	s	s	No	s	s	s	s	s	s	s	11/12	91.6
19	s	s	s	s	No	s	s	s	s	s	s	s	11/12	91.6
20	s	s	s	s	No	s	s	s	s	s	s	s	11/12	91.6
4	s	s	NI	s	No	AT	AT	No	s	s	NI	s	6/10	60
2	s	s	NI	s	No	AT	AT	No	s	s	NI	s	6/10	60
21	s	s	NI	s	No	AT	AT	No	s	s	NI	s	6/10	60
22	s	s	s	s	No	AT	AT	s	s	s	NI	s	8/10	80
23	s	s	s	s	No	s	s	s	s	s	s	s	11/12	91.6

* Criteria: 1 = Objective of the study; 2 = Relevant history; 3 = Sample description; 4 = Justification of sample size; 5 = Reliability and Validity of outcome measures; 6 = Description of the intervention; 7 = Contamination and co-intervention; 8 = Statistical significance; 9 = Adequate analysis; 10 = Clinical-Epidemiological Significance; 11 = Dropouts reported; 12 = Appropriate conclusions. *N = No; NA= Not Applicable; NI= Not Informed; Y= Yes. Study classification: ≥70% = Good quality; ≥50% and <70% = Moderate quality; <50% = Poor quality.

defined using T-score below -2.5 standard deviations. In addition, there is the evaluation of the trabecular bone score (TBS), a texture index at the gray level, derived from the DXA images of the lumbar spine, which are related to the bone microarchitecture. A low TBS is directly correlated to an increased risk of fractures. Therefore, the bone composition can be deduced from the T-score and TBS[17,19,23,24].

At the cellular level, osteoporosis presents an unbalanced activity of osteoblasts and osteoclasts. This process increases the resorptive function represented by osteoclasts to the detriment of the renewal of the matrix, which is performed by osteoblasts. Numerous mediators are related to the functioning of the physiological mechanism of bone resorption, formation, and function.However, in cancer patients, there is an imbalance. Osteoclastogenesis has an important mediation role in its functioning through the cytokine receptor activator of nuclear factor *kappa-β* (RANK), its ligand (RANKL), and macrophage colony-stimulating factor (M-CSF). These pathways are significantly modulated by chemotherapy drugs[17,25].

Another critical factor in the genesis of bone matrix dysregulation is the intense presence of cytokines such as IL-1, IL-5, IL-6, IL-7, and TNF-α. Such factors are widely secreted by advanced neoplasms that create a systemic proinflammatory state, contributing to osteoporosis and sarcopenia by stimulating osteoclastogenesis, which is aggravated by bone-depleting chemotherapy drugs[19,25].

Owing to its heterogeneous characteristics, osteoporosis has several risk factors, ranging from non-modifiable risks, such as age, sex, ethnicity, and genetics, to modifiable risk factors, such as the use of glucocorticoids and specific therapy for cancer treatment (aromatase inhibitors, modulators selective estrogen receptor, and androgen deprivation therapy); however, such risk factors also apply to pediatric patients[15,21]. For a better understanding, the discussion was subdivided into the main treatments found and ways of prevention and treatment.

Main drugs used to treat cancer and bone depletion

Selective Estrogen Receptor Modulators (SERMs)

Selective estrogen receptor modulator drugs, such as tamoxifen, are widely used to treat breast cancer in pre and postmenopausal women. Such drugs demonstrate efficacy in controlling tumor cells in breast tissue.

Premenopausal women have greater bone strength than postmenopausal women. However, during treatment with SERMs, there is a blockade of gonadotropin-releasing hormone, which, although this mechanism is effective for treating breast cancer, can lead to a significant reduction in BMD and generate osteoporosis in premenopausal women. This contrasts with another population studied by Smith et al.[26] (2004), who showed that in men with prostate cancer, SERMs present significant protection against bone loss and reduction of fractures[2,4,26].

Aromatase inhibitor (AI)

AIs are mainly used as standard adjuvant treatment for postmenopausal women with hormone receptor-positive breast cancer because cancers that require estrogen respond to slower growth with low levels of this hormone[20,26].

In premenopausal women, bone mass is regulated by estradiol levels, inhibiting the formation of osteoclasts and reducing bone remodeling. AIs can suppress endogenous estradiol levels by inhibiting the aromatase enzyme, which converts androgens to estrogens in soft tissues, especially fat. During treatment, there are prolonged and sustained reductions in these estradiol levels, resulting in rapid bone loss, an increase in cortical porosity, and trabecular deterioration, contributing to an increased risk of BMD loss and, therefore, fractures. The most commonly reported musculoskeletal symptoms during AI treatment are arthralgia, bone pain, tendonitis, tendinopathies, carpal tunnel syndrome, trigger finger, and joint stiffness[2,4,20].

Therapies that reduce endogenous estradiol levels have systematically demonstrated superior clinical efficacy in hormone-responsive breast cancer. Therefore, adjuvant therapies with AIs are considered the first line when used in breast cancer compared with SERMs. However, AIs present additional bone loss and increased risk of fractures in postmenopausal women by further reducing low estradiol levels. According to several studies, treatment with AI results in a more significant decline in BMD in the hip and spine than SERMs[2].

Antiresorptive agents have gained prominence in pharmacological therapy to reduce bone loss induced by AIs because an increase in osteoclast activity occurs when estradiol levels are supressed[2,4].

Androgen deprivation therapy (ADT)

Androgen deprivation therapy has become an established form of treatment for prostate cancer of various stages: men who have metastasized or have progressed, who have received radical radiotherapy for localized or locally advanced disease, and those whoprogress with the disease and are not suitable for radical treatment[4,14].

Treatment based on hormone deprivation reduces testosterone levels to 20% below baseline after 2 to 4 weeks. Therefore, these patients experience rapid losses in BMD, which can be detected 6 to 9 months after starting treatment. It is estimated that there is 5to 10-fold increase in the rate of bone loss at all skeletal sites. Fragility fractures appear in up to 20% of patients in the first 5 years, and the risk of osteoporosis increases from 10% to 40% to 80% after 10 years of exposure to ADT, in addition to the fact that 35% of patients suffer skeletal fractures. It is worth mentioning that ADT also affects the muscles; thus, sarcopenia is evident with rapid loss of muscle mass and increased risk of falls in these patients[4,21,23].

Furthermore, studies have shown that, even before starting ADT, men with prostate cancer have a higher incidence of osteoporosis and osteopenia than those without the disease. Thus, after starting ADT, men at increased risk of skeletal complications developed more fractures[14].

Glucocorticoids

Another widely used class is glucocorticoids. Such drugs promote decreased calcium reabsorption, inhibition of the osteoformation pathway, and increased RANKL levels, which are essential for pathological fractures[25.]

Glucocorticoid-mediated bone loss is based on its direct effects on mature osteoblasts. This drug increases the apoptosis rate of osteocytes and osteoblasts, initially increasing the lifespan of osteoclasts and decreasing osteoclastogenesis, thus suppressing the osteoblastic activity. Furthermore, glucocorticoids reduce intestinal calcium absorption, increase urinary calcium losses, induce hypogonadism, and produce proximal muscle weakness[2,14].

As a result, there is harm to bone health due to the induction of bone mineral loss and an increased risk of falls and fractures, making it necessary to approach it with anti-resorptive and anabolic therapy[2]. The mechanisms of bone loss promoted by the specific therapies discussed in this article are represented in Figure 2.

Bone density assessment

Although highly specific, DXA assessment of BMD has low sensitivity for predicting fragility fractures occurring in individuals without a diagnosis of osteoporosis, as several other factors contribute to fracture risk, including advanced age, sex, risk of falls, history of previous fractures, family history of fractures, and other lifestyle factors. However, this test remains the gold standard for assessing BMD in the population[14,28].

Other tools have validation for assessing fracture risk, such as FRAX®, which calculates the 10-year probability of a major osteoporotic fracture and a hip fracture and has been approved by the Food and Drug Administration and National Institute for Clinical Excellence[14].

Prevention and treatment

Because of damage to the bone matrix after chemotherapy, it is essential to use measures to prevent and treat these complications.From these perspectives, one can mention calcium and vitamin D supplementation, frequent physical exercise, use of drug therapy, such as bisphosphonates, parathyroid hormone agonists, RANKL inhibitors, tamoxifen (in menopausal women), and even clinical treatment and surgery for fractures[4]. From this perspective, the importance of assessing BMD using DXA is urgent[14].

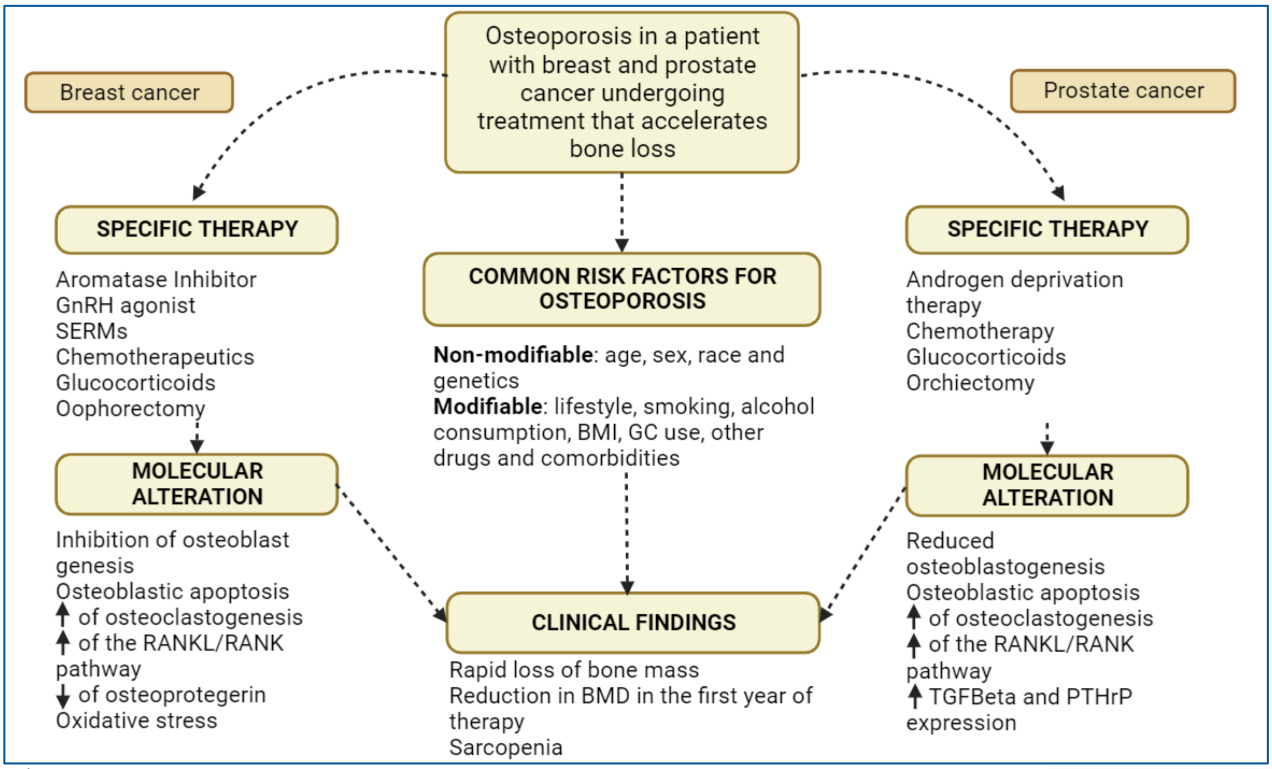

Figure 2 — Risk factors and pathophysiological mechanisms for osteoporosis in cancer patients. Bone mineral density (BMD), Body mass index (BMI), Glucocorticoids (GC*),* Parathyroid hormone-related protein (*PTHrP),* and transforming growth factor beta (*TGFB).* Developed with the *software BioRender*.

Calcium, vitamin D supplementation and physical exercise

Behavioral measures that can be taken to avoid bone loss after cancer chemotherapy include lifestyle changes such as strategies to prevent weight gain, increased physical activity, cessation of conditions such as alcoholism and smoking, and high dietary calcium intake[16].

Calcium and vitamin D supplementation in men undergoing androgen deprivation treatment for prostate cancer is controversial because they have a higher fracture risk. To date, no study has evaluated the risk-benefit ratio of this therapy in this group. On the other hand, the currently recommended doses of calcium and vitamin D supplementation for the prevention of osteoporosis are inadequate in preventing the loss of bone density in this group. Still, it should always be carried out to manage the clinical condition better[16,25].

Use of bisphosphonates and denosumab

Bisphosphonates, in addition to vitamin D and calcium supplementation, are essential for the treatment of osteoporosis. In addition to preventing bone loss and fractures, the use of this class in an adjuvant setting has improved bone loss prevention results in postmenopausal breast cancer patients[18,29].

The Early Breast Meta-analysis Cancer Trialists Collaborative Group[30] (2015) showed significant improvements in groups using bisphosphonates, driven by reduced bone recurrences, reduced mortality from breast cancer, and improved patients' health-related quality of life.

The study by Majithia et al. (2015)[22] followed up for 5 years and investigated the use of zoledronic acid, a bisphosphonate, in the treatment of osteopenia and osteoporosis in women with breast cancer undergoing treatment with an adjuvant aromatase inhibitor. The results demonstrated a significant benefit in reducing bone loss, making it an effective and safe treatment for preventing bone changes in women with early-stage breast cancer.

The use of bisphosphonates demonstrated a benefit in reducing the loss of BMD among patients with prostate cancer undergoing androgen deprivation therapy, according to the RADAR study[30], significantly preventing fractures and osteoporosis without causing important side effects[14].

Denosumab is a drug that provides a significant increase in BMD and a decrease in the incidence of new fractures. Currently, denosumab is the only agent regulated for the treatment of bone loss in men with prostate cancer treated with androgen deprivation therapy[14,31]. One of the most important studies is a large randomized clinical trial[32], in which 1,468 patients were randomized to receive monthly medication injections at 60 mg subcutaneously for 3 years. Their results demonstrated a significant increase in BMD and patients' quality of life after the procedure.

Selective Estrogen Receptor Modulators (SERMs)

Selective estrogen receptor modulators have been investigated in men receiving antiandrogen therapy and their role in preventing BMD loss. This study showed that this drug class promotes increased BMD and significantly reduces fracture risk. However, there is an increased risk of thromboembolic events, making it necessary to balance the indications and personal risk factors for each patient[14,31,32].

This review has some limitations. The established time limit and language restrictions may have influenced the final number of articles selected for the study, and gray literature and preprints were not considered. Furthermore, most of the evidence gathered was classified as LE V, considering a literature review without meta-analysis and often without classifying the methodological quality of the selected studies. To this end, we recommend new, well-designed studies with greater robustness (LE I, II, III) to strongly guide clinical practice recommendations. However, this review highlights the need to prevent and promote bone health in patients undergoing antineoplastic treatment; therefore, DXA is recommended in patients undergoing anticancer treatment.

CONCLUSION

The scientific community faces one of its biggest Several factors contribute to the pathophysiological mechanism of cancer in adults, ranging from hereditary genetic conditions to exposure to carcinogens, such as irradiation, air pollution, sedentary lifestyle, and intrinsic conditions, such as obesity, diabetes, and habitual risk behaviors for cancer. Therefore, people at the highest risk of developing cancer are also at the highest risk of developing osteopenia and osteoporosis when the process is already established and undergoing antineoplastic treatment due to shared risk factors.

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