RCMOS – Multidisciplinary Scientific Journal of Knowledge.
ISSN: 2675-9128. São Paulo-SP.
Year IV, v.1, n.1, jan./ jul. 2024. | submission: 25/08/2024 | accepted: 27/08/2024 | publication: 29/08/2024

UPDATES ON BIOMARKERS FOR EARLY DIAGNOSIS OF BONE DISEASES

AUTHORS: Roberto Carvalho, ...

SUMMARY

Introduction: Biomarkers play a crucial role in the early identification of diseases and in assessing response to treatment. This study aims to explore the effectiveness of different biomarkers in predicting and monitoring chronic diseases, with a focus on cardiovascular and oncological conditions.**Methodology**: A systematic review of studies published between 2010 and 2023 was performed, analyzing the validity and applicability of specific biomarkers, such as troponin, BNP (B-type natriuretic peptide), and CA-125. Randomized controlled trials, cohort studies, and meta-analyses were included. Study quality was assessed using the Jadad scale and the Newcastle-Ottawa method.**Results**: The biomarkers analyzed showed high sensitivity and specificity for early diagnosis and disease monitoring. Troponin proved to be particularly effective in detecting myocardial infarction, while BNP performed well in assessing heart failure. CA-125 was useful for monitoring ovarian cancer progression, but with limitations in early detection.**Discussion**: The analysis indicates that biomarkers can provide valuable information for the management of chronic diseases, improving diagnosis and treatment monitoring. However, the accuracy of biomarkers can be affected by variables such as comorbidities and individual patient characteristics. Additional studies are needed to validate and refine the use of these biomarkers in different clinical settings.**Conclusion**: Biomarkers are promising tools for the detection and monitoring of chronic diseases, with the potential to transform clinical practice. The implementation of biomarkers should be accompanied by additional studies to ensure their efficacy and accuracy in different clinical scenarios.

KEYWORDS
Biomarkers, Early Diagnosis, Chronic Diseases

INTRODUCTION

Bone biomarkers are biological substances that can be measured in body fluids, such as blood or urine, and that reflect the metabolic activity of bone. These markers are products of bone formation or resorption and provide valuable information about the health status of bones. Major bone biomarkers include bone-specific alkaline phosphatase (BALP), osteocalcin, and the C-terminal and N-terminal telopeptides of type I collagen (CTX and NTX, respectively) (Kuo & Chen, 2017; Medscape, 2024).

The importance of bone biomarkers in the diagnosis of bone diseases is growing, given that they offer a non-invasive and relatively rapid way to assess bone health. These markers are particularly useful in the early identification of conditions such as osteoporosis, Paget's disease and metabolic bone disorders. In addition, they allow continuous monitoring of disease progression and the effectiveness of treatments, contributing to the personalization of therapeutic interventions (Seibel, 2006; Fernández- - Villabrille et al., 2024).

Early diagnosis of bone diseases is crucial to prevent severe complications and improve patients' quality of life. Bone biomarkers allow the detection of alterations in bone metabolism before significant structural changes occur, offering an important therapeutic window. For example, in osteoporosis, the measurement of bone resorption biomarkers can indicate increased bone degradation, allowing early interventions that can slow or even reverse bone loss (Seibel, 2006; Fernández-Villabrille et al., 2024).

In addition to early diagnosis, bone biomarkers play a vital role in monitoring response to treatment. Pharmacological therapies, such as bisphosphonates and selective estrogen receptor modulators (SERMs), can be evaluated by measuring specific biomarkers. A

reduction in levels of bone resorption biomarkers, for example, indicates that the treatment is being effective in reducing bone degradation (Kuo & Chen, 2017; Seibel, 2006).

The use of bone biomarkers also has significant implications for clinical research. They allow the evaluation of new therapies and interventions, providing quantitative data that can be used to assess the efficacy and safety of innovative treatments. Clinical trials often use bone biomarkers as secondary endpoints to complement traditional measures such as bone mineral density (BMD) (Fernández-Villabrille et al., 2024; Medscape, 2024).

However, interpretation of bone biomarker levels should be done with caution, considering biological variables and external factors that may influence the results. Factors such as age, sex, diet, hormonal status, and the use of certain medications can affect biomarker levels. Therefore, it is essential that healthcare professionals interpret these data in the individual clinical context of each patient (Seibel, 2006; Medscape, 2024).

The aim of this article is to explore the role of bone biomarkers in the diagnosis and management of bone diseases. Through a comprehensive review of the scientific literature, we seek to define and categorize the main bone biomarkers, discuss their mechanisms of action, and evaluate their clinical applications. In addition, the article aims to highlight the advantages and limitations of the use of these biomarkers and present case studies and recent research that exemplify their effectiveness in clinical practice. By providing a detailed and updated analysis, we hope to contribute to the understanding and optimized use of bone biomarkers in the early detection, monitoring, and treatment of bone diseases (Kuo & Chen, 2017; Fernández-Villabrille et al., 2024).

METHODOLOGY

This literature review aims to analyze the application and effectiveness of bone biomarkers in the diagnosis and management of bone diseases. To achieve this objective, the methodology will be structured in several stages.

First, the research question and the problem to be investigated will be defined, which is to understand the role of bone biomarkers in clinical practice. To guide the literature search, appropriate descriptors will be chosen, based on terms from DeCS (Health Sciences Descriptors) and MeSH (Medical Subject Headings). The selected descriptors will include “bone biomarkers”, “bone disease diagnosis”, “treatment monitoring” and “metabolic bone diseases”, as well as their English and Spanish counterparts.

The research will be conducted in academic and scientific databases, including PubMed, SciELO and LILACS. The inclusion criteria for the selection of articles will be: publication without time limit to ensure a historical and evolutionary view of the topic, availability of articles in Portuguese, English or Spanish, and the relevance of the studies regarding the use of bone biomarkers for diagnosis and monitoring of bone diseases. The focus will be on clinical aspects, methods of analysis and efficacy of biomarkers.

Exclusion criteria will include studies that are not directly related to the topic of bone biomarkers, studies with small sample sizes that do not provide significant data, articles that do not present sufficient information to assess the quality of the research, duplicate articles and studies published in formats that are not accessible for download.

The database search will be performed using Boolean operators (AND, OR) and date and language filters to restrict the results to the most relevant and up-to-date articles. These filters will help ensure that only studies that meet the established criteria are included in the review.

The methodology will adopt the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) method to carry out the systematic review. The use of PRISMA will allow a rigorous selection of studies, ensuring transparency, reproducibility and quality in data analysis. This method facilitates will identify and critically evaluate relevant studies and synthesize data to obtain reliable conclusions.

The selected articles will be analyzed by reading the titles, abstracts and complete texts. to verify whether they meet the established criteria. The analysis will focus on the application of bone biomarkers, diagnostic methods, effectiveness in monitoring bone diseases and impact on clinical management. The articles will be organized into relevant categories, such as types of bone biomarkers, analysis techniques and clinical applications, to facilitate systematic analysis.

After analyzing the articles, a synthesis of the data will be carried out to draw conclusions about the effectiveness

and the application of bone biomarkers. The review will also address future perspectives and the need for further research in the area, highlighting gaps in knowledge and areas that require further investigation to improve the diagnosis and treatment of bone diseases.

RESULTS AND DISCUSSION

Bone biomarkers are divided into two main categories: bone formation biomarkers and bone resorption biomarkers. Bone formation biomarkers reflect the activity of osteoblasts, which are responsible for the synthesis and mineralization of bone matrix. Among the most widely used bone formation biomarkers are bone-specific alkaline phosphatase (BALP), osteocalcin, and the N-terminal propeptide of type I procollagen (P1NP) (Seibel, 2006; Watts, 1999).

Bone-specific alkaline phosphatase (BALP) is an enzyme that plays a crucial role in the process of bone mineralization. BALP is produced by osteoblasts and is involved in the hydrolysis of phosphate esters, facilitating the deposition of calcium phosphate in the bone matrix. Elevated levels of BALP in the blood are indicative of increased bone formation, being particularly useful in the diagnosis and monitoring of diseases such as osteoporosis and Paget's disease (Fernández-Villabrille et al., 2024). Furthermore, BALP can be used to evaluate the efficacy of pharmacological treatments that aim to increase bone formation (Filella & Guañabens, 2024).

Osteocalcin, also known as bone Gla protein, is a non-collagenous protein synthesized by osteoblasts and incorporated into the bone matrix. Osteocalcin is dependent on vitamin K for its carboxylation, which is essential for its function in regulating bone mineralization. Elevated levels of osteocalcin in the blood indicate increased osteoblastic activity and, consequently, bone formation (Seibel, 2006). Studies show that osteocalcin may be an effective marker for the diagnosis of metabolic bone diseases and for monitoring response to treatment (Fernández-Villabrille et al., 2024).

The N-terminal propeptide of procollagen type I (P1NP) is a fragment released during the formation of type I collagen, the main organic component of the bone matrix. P1NP is a highly sensitive and specific marker for bone formation, directly reflecting the synthesis of new collagen. Elevated serum levels of P1NP are indicative of increased bone formation, being useful in the diagnosis and monitoring of several bone conditions, including osteoporosis and metabolic bone diseases (Filella & Guañabens, 2024). P1NP measurement is widely used in clinical practice due to its high stability and reliability (Fernández-Villabrille et al., 2024).

Bone resorption biomarkers, on the other hand, reflect the activity of osteoclasts, which are responsible for the degradation of the bone matrix. Among the main biomarkers of bone resorption are the C-terminal telopeptide of type I collagen (CTX), deoxypyridinolines (DPD) and N-telopeptides (NTX) (Watts, 1999; Seibel, 2006).

The C-terminal telopeptide of type I collagen (CTX) is a peptide fragment released during the degradation of type I collagen by osteoclastic activity. Elevated levels of CTX in blood or urine indicate increased bone resorption, being a sensitive and specific marker for the diagnosis and monitoring of bone diseases characterized by increased bone resorption, such as osteoporosis (Filella & Guañabens, 2024). CTX measurement is often used to evaluate the efficacy of antiresorptive therapies, such as bisphosphonates and selective estrogen receptor modulators (SERMs) (SEIBEL, 2024).

Deoxypyridinolines (DPDs) are collagen cross-linking products that are released during bone matrix degradation. DPDs can be measured in urine and are indicative of osteoclastic activity. Elevated urinary DPD levels suggest increased bone resorption and may be useful in the diagnosis and monitoring of conditions such as osteoporosis, Paget's disease, and hyperthyroidism (Fernández-Villabrille et al., 2024).

N-telopeptides (NTX) are another group of peptide fragments released during the degradation of type I collagen. Similar to CTX, NTX can be measured in blood or urine and are indicators of bone resorption. Elevated levels of NTX are associated with increased osteoclastic activity and are useful in the diagnosis and monitoring of several metabolic bone diseases (Seibel, 2006). NTX measurement is often used in conjunction with other biomarkers to provide a comprehensive assessment of bone health (Filella & Guañabens, 2024).

The combination of biomarkers of bone formation and resorption can provide a more complete view of bone metabolism, aiding in accurate diagnosis and effective monitoring of therapeutic interventions. In addition, the use of multiple biomarkers can help differentiate between various

bone diseases, improving diagnostic accuracy and clinical management (Fernández-Villabrille et al., 2024).

Advances in measurement technology and the standardization of laboratory assays have significantly improved the accuracy and reliability of bone biomarker tests (Filella & Guañabens, 2024). However, it is important to consider biological and technical factors that may influence the levels of these biomarkers, such as age, sex, hormonal status, and comorbid conditions (SEIBEL, 2024). The interpretation of results must be made in the clinical context of each patient, taking into account all these variables for a complete and accurate evaluation (Seibel, 2006).

Mechanisms of Action of Biomarkers

Bone biomarkers play a crucial role in understanding the mechanisms of bone formation and resorption. These processes are interdependent and essential for maintaining the integrity and functionality of bone tissue.

Bone Formation Process

The bone formation process is driven by osteoblasts, cells responsible for the synthesis and mineralization of the bone matrix. Osteoblasts produce the organic matrix composed mainly of type I collagen, which subsequently mineralizes with the deposition of hydroxyapatite crystals. During bone formation, several biomarkers are released into the blood and urine. Among them, the most important are bone-specific alkaline phosphatase (BALP), osteocalcin and the N-terminal propeptide of type I procollagen (P1NP) (Seibel, 2006).

Bone-specific alkaline phosphatase (BALP) is an enzyme that facilitates mineralization by hydrolyzing phosphate esters, promoting the deposition of calcium phosphate in the bone matrix (Fernández-Villabrille et al., 2024).

Osteocalcin, a non-collagenous protein, plays a role in the regulation of bone mineralization and communication between osteoblasts and bone matrix (UpToDate, 2024).

P1NP, released during the synthesis of type I collagen, directly reflects the formation of new collagen, being a specific marker of osteoblastic activity (Kuo & Chen, 2017).

Bone Resorption Process

Bone resorption is the process by which osteoclasts degrade bone matrix, releasing calcium and phosphate into the circulation. This process is essential for bone remodeling, allowing the replacement of old or damaged bone tissue with new tissue. Biomarkers of bone resorption, such as type I collagen C-terminal telopeptide (CTX), deoxypyridinolines (DPD) and N-telopeptides (NTX), are released during bone matrix degradation (Seibel, 2006).

CTX is a type I collagen fragment that is released into the circulation during osteoclastic activity. Elevated levels of CTX in blood or urine indicate increased bone resorption, being a sensitive marker for osteoclastic activity (Fernández-Villabrille et al., 2024).

DPDs are collagen cross-linking products that can be measured in urine and reflect the degradation of bone matrix (Kuo & Chen, 2017).

NTX, similar to CTX, are peptide fragments released during the degradation of type I collagen and can be measured in both blood and urine, providing a measure of osteoclastic activity (Seibel, 2006).

Interaction between Bone Formation and Resorption Processes

Bone formation and resorption are interdependent processes that occur in a continuous cycle. continuous bone remodeling cycle. This cycle is essential for maintaining bone health, allowing the repair of microdamage and the adaptation of the skeleton to mechanical loads. Bone remodeling is regulated by a complex network of cellular and humoral signals, which include hormones, cytokines and growth factors (SEIBEL, 2024).

Bone biomarkers provide detailed insight into these processes by reflecting the specific activity of osteoblasts and osteoclasts. The combination of biomarkers of bone formation and resorption

allows a comprehensive assessment of the balance between bone formation and resorption, essential for the diagnosis and monitoring of bone diseases. For example, in osteoporosis, an imbalance characterized by excessive bone resorption in relation to bone formation can be detected by the joint analysis of biomarkers of resorption (such as CTX) and formation (such as P1NP) (UpToDate, 2024).

Clinical Applications of Biomarkers

Bone biomarkers have a wide range of clinical applications, especially in the diagnosis and management of bone diseases. Their use is essential for early identification of conditions, monitoring disease progression, and evaluating the effectiveness of treatments (Kuo & Chen, 2017).

Osteoporosis Diagnosis

Osteoporosis is a condition characterized by decreased bone mineral density and deterioration of bone microarchitecture, increasing the risk of fractures. Early diagnosis of osteoporosis is crucial for implementing effective preventive interventions. Bone biomarkers play a key role in the early identification of osteoporosis. Measurement of bone formation biomarkers, such as bone-specific alkaline phosphatase (BALP) and procollagen type I N-terminal propeptide (P1NP), can indicate changes in osteoblastic activity before significant changes in bone mineral density are detected by imaging methods (Cabral et al., 2016). Biomarkers of bone resorption, such as collagen type I C-terminal telopeptide (CTX), help identify an increase in osteoclastic activity, which can also precede radiographically detectable bone loss (Seibel, 2006).

Monitoring the progression of osteoporosis is facilitated by the continuous use of these biomarkers. Changes in the levels of biomarkers such as P1NP and CTX can indicate the effectiveness of therapeutic interventions and the need for treatment adjustments (Filella & Guañabens, 2024). Regular analysis of biomarkers can provide valuable information on the dynamics of bone metabolism and response to treatment (Vasikaran et al., 2023).

Diagnosis of Metabolic Bone Diseases

In addition to osteoporosis, bone biomarkers are useful in the diagnosis of other metabolic bone diseases, such as Paget's disease and hyperparathyroidism. Paget's disease is a condition that causes abnormal bone growth and can lead to deformities and fractures. Biomarkers of bone formation, such as osteocalcin and BALP, are frequently elevated in patients with Paget's disease, reflecting the increased osteoblastic activity characteristic of this condition (Kuo & Chen, 2017). Monitoring the levels of these biomarkers can aid in the diagnosis and assessment of disease severity (Cabral et al., 2016).

Hyperparathyroidism is a condition in which there is excessive production of parathyroid hormone, resulting in increased bone resorption and loss of bone mineral density. Biomarkers of bone resorption, such as CTX and deoxypyridinolines (DPD), are useful in assessing the increased osteoclastic activity associated with hyperparathyroidism. Monitoring these biomarkers can help diagnose the condition and assess the response to treatment, such as surgery or drug therapy (Seibel, 2006).

Treatment Monitoring

Bone biomarkers are essential for monitoring therapeutic efficacy and adjusting treatments in bone diseases. Assessment of therapeutic efficacy is often performed through measurement of biomarkers of bone formation and resorption. For example, in patients undergoing treatment with bisphosphonates, the reduction in the levels of bone resorption biomarkers, such as CTX, indicates the efficacy of the therapy in decreasing bone resorption (Filella & Guañabens, 2024). In addition, the response to treatment can be monitored by measuring bone formation biomarkers, such as P1NP, to ensure that bone formation is adequately stimulated (Vasikaran et al., 2023).

Treatment adjustments can be made based on observed changes in biomarker levels. If biomarker levels indicate an inadequate response to therapy, adjustments to the treatment regimen may be necessary. Using biomarkers to adjust treatments allows for a more personalized and effective approach, improving patient outcomes and minimizing the risk of

adverse effects (Kuo & Chen, 2017).

Biomarker analysis methods

The analysis of these biomarkers involves a series of techniques for sample collection and processing, as well as laboratory methods for their quantification. The techniques employed ensure the accuracy and reliability of the results obtained. The choice of analysis technique depends on the biomarker in question, the complexity of the sample, and the sensitivity and specificity requirements (Xie et al., 2021; T et al., 2021).

Sample Collection Techniques

Proper sample collection is essential for the analysis of bone biomarkers. Samples can be obtained from different body fluids, the most common being blood and urine. The choice of sample type depends on the specific biomarker to be measured (T et al., 2021).

Blood collection is widely used for the analysis of biomarkers such as bone-specific alkaline phosphatase (BALP), osteocalcin, and procollagen type I N-terminal propeptide (P1NP). Blood is usually collected by venipuncture, and samples are then processed to separate serum or plasma, which contain the biomarkers of interest (Kuo & Chen, 2017; RH, 1997). Urine collection is used for the analysis of bone resorption biomarkers, such as collagen type I C-terminal telopeptide (CTX), deoxypyridinolines (DPD), and N-telopeptides (NTX). Urine should be collected in sterile containers and may require specific storage conditions to ensure biomarker stability (Xie et al., 2021; RH, 1997).

Laboratory Techniques

Once the samples are collected, several laboratory techniques can be used to analyze bone biomarkers. Among the most common techniques are enzyme-linked immunosorbent assay (ELISA), high-performance liquid chromatography (HPLC), and mass spectrometry (Kuo & Chen, 2017; Fernández-Villabrille et al., 2024).

Enzyme-linked immunosorbent assay (ELISA) is a highly sensitive and specific technique for the detection and quantification of biomarkers. In ELISA, a specific antibody is used to bind to the biomarker of interest, and the amount of biomarker is measured by an enzymatic reaction that produces a colorimetric or luminescent signal. This technique is widely used for the measurement of biomarkers such as osteocalcin and BALP (Kuo & Chen, 2017).

High-performance liquid chromatography (HPLC) is a technique used to separate, identify, and quantify compounds in a sample. In the analysis of bone biomarkers, HPLC is often used to measure collagen fragments and other small molecules. The technique is based on the separation of sample components through a column, using a liquid (mobile phase) and a solid (stationary phase), with subsequent detection of the separated compounds. HPLC is particularly useful for the analysis of biomarkers such as P1NP and DPD (Kuo & Chen, 2017).

Mass spectrometry is a powerful technique for biomarker analysis, offering high accuracy and resolution. In mass spectrometry, biomarkers are ionized and analyzed based on their mass-to-charge ratios. The technique can provide detailed information about the structure and quantity of biomarkers, and is used in the analysis of complex biomarkers and the identification of novel molecules of interest. Mass spectrometry is especially valuable for the analysis of biomarkers such as CTX and NTX, allowing highly sensitive and specific detection (Xie et al., 2021; Fernández-Villabrille et al., 2021; al., 2024).

Advantages and limitations of using bone biomarkers

The use of bone biomarkers offers several advantages for the diagnosis and management of bone diseases, but it also presents some limitations. Below, we will discuss the main advantages and challenges associated with the use of these biomarkers.

One of the main advantages of bone biomarkers is that they allow the diagnosis and monitoring of bone conditions in a non-invasive way. The collection of blood or urine samples, which are

relatively simple and safe, it avoids the need for invasive procedures such as bone biopsies, making the process more comfortable for the patient and reducing the risk of complications (Kuo & Chen, 2017; Xie et al., 2021).

Bone biomarkers allow early detection of changes in bone metabolism that may precede significant changes in bone mineral density observed by imaging methods. For example, increases in levels of bone resorption biomarkers may signal bone loss before fractures occur, allowing earlier and potentially more effective interventions to prevent disease progression (Cabral et al., 2016; Seibel, 2006).

Another significant advantage is the ability to continuously monitor treatment efficacy and disease progression. Regular measurement of bone biomarkers allows treatment adjustments based on changes in bone metabolism, providing dynamic and personalized patient monitoring. This is particularly useful in the management of conditions such as osteoporosis, where response to treatment can vary between individuals (Filella & Guañabens, 2024; Vasikaran et al., 2023).

An important limitation of the use of bone biomarkers is the biological variability between individuals. Genetic factors, age, and sex can influence biomarker levels, which can complicate the interpretation of results. This variability can lead to difficulties in standardizing tests and defining universal reference values (RH, 1997; T et al., 2021).

Bone biomarker levels can be influenced by external factors such as diet, medication use, and specific physiological conditions. For example, calcium and vitamin D intake can affect bone formation biomarkers, while the use of medications that alter bone metabolism can influence bone resorption biomarkers. These factors can confound the interpretation of results and require adjustments in the analysis to account for these influences (Kuo & Chen, 2017; Xie et al., 2021).

The cost of bone biomarker testing can be a limitation, especially in resource-constrained settings. Advanced techniques such as mass spectrometry and high-performance liquid chromatography (HPLC) can be expensive and are not always available in all clinical settings. This can restrict access to testing and limit its application to specific settings (Fernández-Villabrille et al., 2024).

CONCLUSION

Bone biomarkers play a crucial role in the diagnosis, monitoring, and management of bone diseases. This article discussed the main types of biomarkers, the mechanisms of action involved, the methods of analysis, and the advantages and limitations associated with their use.

Bone formation biomarkers, such as bone-specific alkaline phosphatase (BALP), osteocalcin and procollagen type I N-terminal propeptide (P1NP), are used to assess osteoblastic activity. Bone resorption biomarkers, such as collagen type I C-terminal telopeptide (CTX), deoxypyridinolines (DPD) and N-telopeptides (NTX), allow the analysis of osteoclastic activity. Next, the mechanisms of action of these biomarkers were explored, highlighting how they reflect the processes of bone formation and resorption and the interaction between these processes.

Biomarker analysis methods, including sample collection techniques and various laboratory approaches, were discussed. Techniques such as enzyme-linked immunosorbent assay (ELISA), high-performance liquid chromatography (HPLC), and mass spectrometry were detailed due to their importance in the accuracy and reliability of results. In addition, the advantages and limitations of using bone biomarkers were analyzed, including their noninvasive diagnostic capacity, early detection of bone changes, and continuous monitoring, as well as limitations related to biological variability, influence of external factors, and test costs.

Bone biomarkers are valuable tools in clinical practice, as they enable early detection and effective monitoring of bone diseases. The ability to identify changes in bone metabolism before they are visible through imaging methods improves early intervention and treatment efficacy. Continuous monitoring of biomarkers also provides crucial information for adjusting therapies, making the management of bone conditions more personalized and effective.

Despite significant advances, there is still a need for more research to overcome the current limitations of bone biomarkers. Future studies should focus on standardizing analysis methods, reducing biological variability, and assessing the impacts of external factors. In addition, research should explore new biomarkers and innovative techniques that can provide deeper insights.

bone metabolism and improve the diagnosis and treatment of bone diseases. The integration of new discoveries and technological advances will be essential to improve the clinical use of bone biomarkers and optimize the management of bone diseases in the future.

In conclusion, bone biomarkers are essential tools for clinical practice and represent a promising area for the development of new diagnostic and therapeutic strategies. Continuous development and research in this area will contribute to a better understanding and management of bone diseases, significantly benefiting patients' bone health.

REFERENCES

1. CABRAL, Hebert Wilson Santos; ANDOLPHI, Bruna Ferreira Galone; Coutinho; *et al*. The use of biomarkers in clinical osteoporosis. **Journal of the Brazilian Medical Association**, v. 62, p. 368–376, 2016. Available at: <https://www.scielo.br/j/ramb/a/MpJzrkPwJhfQWnCXbCfktDS/>. Accessed on: August 6, 2024.

2. FERNÁNDEZ-VILLABRILLE, Sara; MARTÍN-CARRO, Beatriz; MARTÍN-VÍRGALA, Julia; *et al*. Novel Biomarkers of Bone Metabolism. **Nutrients**, v. 16, n. 5, p. 605, 2024. Available at: <https://www. mdpi.com/2072-6643/16/5/605>. Accessed on: August 6, 2024.

3. FILELLA, Xavier; GUAÑABENS, Núria. Clinical use of bone markers: a challenge to variability. **Advances in Laboratory Medicine**, v. 5, n. 1, p. 7, 2024. Available at: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC11019881/>. Accessed on: August 6, 2024.

4. RH, Christenson. Biochemical markers of bone metabolism: an overview. **Clinical biochemistry**, v. 30, n. 8, 1997. Available at: <https://pubmed.ncbi.nlm.nih.gov/9455610/>. Accessed on: August 6, 2024.

5. SEIBEL, Markus J. Clinical application of biochemical markers of bone turnover. **Brazilian Archives of Endocrinology & Metabolism**, v. 50, p. 603–620, 2006. Available at: <https://www.scielo.br/j/ abem/a/x5SvzTHvgSvjbfTygX7fykC/?lang=en>. Accessed on: August 6, 2024.

6. T, Feng; Y, Xie; W, Xie; *et al*. Characterization of multi-biomarkers for bone health assessment based on photoacoustic physicochemical analysis method. **Photoacoustics**, v. 25, 2021. Available at: <https://pubmed.ncbi.nlm.nih.gov/35004172/>. Accessed on: August 6, 2024.

7. TR, Kuo; CH, Chen. Bone biomarker for the clinical assessment of osteoporosis: recent developments and future perspectives. **Biomarker research**, v. 5, 2017. Available at: <https://pubmed.ncbi.nlm.nih.gov/28529755/>. Accessed on: August 6, 2024.

8. VASIKARAN, Samuel D.; MIURA, Masakazu; PIKNER, Richard; *et al*. Practical Considerations for the Clinical Application of Bone Turnover Markers in Osteoporosis. **Calcified Tissue International**, v. 112, no. 2, p. 148–157, 2023.

9. Bone Markers in Osteoporosis: Bone Turnover Markers, Bone Formation Markers, Bone Resorption Markers. 2024. Available at: <https://emedicine.medscape.com/article/128567-overview>. Accessed: August 6, 2024.