

FERNANDO DELMONTE MOREIRA

**EPIDEMIOLOGIA DOS TUMORES ÓSSEOS DO PÉ E TORNOZELO - UMA REVISÃO
SISTEMÁTICA**

Dissertação apresentada ao Curso de Pós-graduação da Faculdade de Ciências Médicas da Santa Casa de São Paulo para obtenção do Título de Mestre em Ciências da Saúde.

SÃO PAULO

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Área de Concentração: Ciências da Saúde

Orientador: Prof. Dr. Claudio Santili

Coorientador: Prof. Dr. Alex Guedes

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2025

FICHA CATALOGRÁFICA

**Preparada pela Biblioteca Central da
Faculdade de Ciências Médicas da Santa Casa de São Paulo**

Moreira, Fernando Delmonte

Epidemiologia dos tumores ósseos do pé e tornozelo – uma
revisão sistemática. / Fernando Delmonte Moreira. São Paulo, 2025.

Dissertação de Mestrado. Faculdade de Ciências Médicas da
Santa Casa de São Paulo – Curso de Pós-Graduação em Ciências da
Saúde.

Área de Concentração: Ciências da Saúde

Orientador: Cláudio Santili

Coorientador: Alex Guedes

1. Tornozelo 2. Osso e ossos 3. Neoplasia óssea 4. Epidemiologia
5. Pé 6. Revisão sistemática

BC-FCMSCSP/29-25

DEDICATÓRIA

A Deus, que me guia, protege e acompanha todos os dias.

A minha filha Fernanda, fonte de amor, alegria e inspiração.

A minha esposa Kin, pelo amor, companheirismo, compreensão e apoio.

Aos meus pais, Paulo e Elizabeth, grandes exemplos e incentivadores, pelo amor e extrema dedicação, exemplos de retidão, honestidade e caráter.

A todos que me apoiaram nesta jornada.

AGRADECIMENTOS

À Irmandade da Santa Casa de Misericórdia de São Paulo, na pessoa do seu Provedor, o Dr. Vicente Renato Paolillo, pela possibilidade da realização deste trabalho.

À Faculdade de Ciências Médicas da Santa Casa de São Paulo, na pessoa do seu Diretor, o Prof. Dr. Carlos Alberto Herrerias de Campos, pela possibilidade de aprimorar cada vez mais os meus conhecimentos na Medicina com a Pós-Graduação.

Ao Professor Cláudio Santili, Professor Adjunto da Faculdade de Ciências Médicas da Santa Casa de Misericórdia de São Paulo, orientador deste trabalho, pela oportunidade, apoio e possibilidade de compartilhar a sua experiência.

Ao Professor Alex Guedes, Professor Associado e Vice-chefe do Departamento de Cirurgia Experimental e Especialidades Cirúrgicas da Faculdade de Medicina da Bahia - Universidade Federal da Bahia, pioneiro da Oncologia Ortopédica na Bahia, coorientador deste trabalho, pelo exemplo de dedicação, compromisso, profissionalismo, liderança e obstinação pela causa da Ortopedia na Bahia.

Aos amigos, professores e colegas de jornada, pelo incentivo a realização deste trabalho, ensinamentos, pela amizade e confiança.

A todos os acadêmicos, estagiários e residentes com os quais tive o privilégio de conviver, razão maior para seguir lecionando, estudando e me aperfeiçoando.

LISTA DE ABREVIATURAS, SIGLAS E ACRÔNIMOS

CEP HSI-SCMBA ..	COMITÊ DE ÉTICA EM PESQUISA HOSPITAL SANTA IZABEL – SANTA CASA DE MISERICÓRDIA DA BAHIA
COS	CISTO ÓSSEO SIMPLES
NOS	<i>NEWCASTLE-OTTAWA SCALE</i>
OMS	ORGANIZAÇÃO MUNDIAL DA SAÚDE
PRISMA	<i>PREFERRED REPORTING ITEMS FOR SYSTEMATIC REVIEWS AND META-ANALYSES PROTOCOLS</i>
PROSPERO	<i>INTERNATIONAL PROSPECTIVE REGISTER OF SYSTEMATIC REVIEWS</i>
TCGO	TUMOR DE CÉLULAS GIGANTES ÓSSEO

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1. INTRODUÇÃO

Os tumores ósseos que afetam o pé e o tornozelo são raros,¹⁻⁸ representando aproximadamente 1-2% de todas as neoplasias que acometem o esqueleto.⁵ Entretanto, considerando que este segmento anatômico corresponde a apenas 3% da massa corporal, deduz-se que a incidência de neoplasias ósseas é proporcionalmente maior do que a observada em outros sítios.⁷⁻¹⁰ Alguns estudos apontam que as neoplasias de tecidos moles são muito mais frequentes do que as neoplasias ósseas (em torno de 10:1) e os tumores ósseos benignos são pelo menos quatro vezes mais comuns do que os malignos nesta localização.^{1,4,11} Lesões metastáticas (acrometástases) são raras, variando entre 0,01% e 1,3%.² Entretanto, a real incidência destas lesões no pé e tornozelo permanece desconhecida, visto que os dados obtidos na literatura representam a população tratada cirurgicamente.^{9,10}

Neoplasias ósseas situados no pé e tornozelo podem afetar indivíduos de qualquer idade. Os tumores primários benignos parecem ser mais frequentes até a quarta década, enquanto os primários malignos são mais comumente observados em indivíduos mais velhos. Lesões metastáticas são encontradas com mais frequência em pacientes acima dos 60 anos.⁵

Estas lesões tendem a ocorrer predominantemente em indivíduos do sexo masculino,¹² embora esta variável não apresente correlação significativa com o diagnóstico.⁵

O pé e o tornozelo possuem delgada cobertura de tecidos moles, tornando relativamente fácil a inspeção e palpação de tumores situados nesta topografia.^{1,2,5,7,10,13} Além disso, por apresentar múltiplas pequenas articulações, dor e distúrbios funcionais neste segmento são detectados precocemente, tornando

cl clinicamente evidentes até mesmo pequenas lesões⁵ - raramente um tumor permanece despercebido por muito tempo.^{1,13} Apesar disso, o diagnóstico correto é comumente ignorado porque, em muitos casos, estas lesões não são consideradas verdadeiras neoplasias, subestimando-se o seu potencial de risco.⁷ Erros ou atrasos no diagnóstico de tumores localizados no pé e tornozelo são mais comuns do que em outras partes do corpo,⁷ podendo resultar em ressecção inadequada e/ou maior taxa de recorrência.^{1,2,4,5,9,14-16}

Uma suspeita de neoplasia deve sempre ser considerada no diagnóstico diferencial de qualquer aumento de volume persistente ou lesão óssea incerta no pé e tornozelo, buscando garantir o diagnóstico precoce e correto, além do tratamento adequado desta condição.⁷ A avaliação é iniciada com a anamnese, exame físico e exame radiográfico convencional do segmento acometido. Conforme demanda, prossegue-se com o estadiamento local (ressonância magnética contrastada, tomografia computadorizada) e sistêmico (cintilografia óssea, tomografia computadorizada de tórax), finalizado com a realização de uma biópsia.¹⁷⁻¹⁹

O cirurgião ortopédico envolvido no acompanhamento de pacientes portadores de tumores situados no pé e no tornozelo deve estar familiarizado com os critérios necessários ao diagnóstico e estadiamento destas condições.¹⁷⁻²⁰ A peculiar anatomia do tornozelo constitui desafio para a cirurgia de salvamento de membros no contexto da obtenção de margens adequadas.^{2,4,13,21} O tratamento varia de acordo com o tipo histológico, tempo de diagnóstico, comportamento clínico e localização das lesões.¹⁰ Todas as biópsias, procedimentos cirúrgicos e reconstruções devem ser planejados cuidadosamente para evitar contaminação inadvertida e subsequente deiscência de ferida, recorrência local ou reconstrução ineficaz¹² - o tratamento inadequado e incompleto impacta nos resultados oncológicos e funcionais.⁷

Ressecções não planejadas podem atingir até 40-60% de todos os tumores malignos situados nesta topografia e estão associadas a altas taxas de amputações ou recidivas locais.^{7,13,22} Por conta disso, pacientes com suspeita de sarcoma devem ser conduzidos preferencialmente em centros de referência em Oncologia Ortopédica, onde erros diagnósticos e/ou terapêuticos são menos comuns.¹⁴

Devido à raridade e características particulares de apresentação, há poucas evidências a propósito da epidemiologia dos tumores ósseos situados no pé e tornozelo, o que motivou este estudo.

2. OBJETIVO

O objetivo de nossa revisão foi identificar a distribuição destas neoplasias quanto ao tipo histológico, localização anatômica (antepé, médio-pé, retropé e tornozelo), osso afetado, sexo e faixa etária de acometimento.

3. METODOLOGIA

3.1 Registro de protocolo e publicação do protocolo

O protocolo de revisão sistemática foi elaborado sob a orientação do Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols (PRISMA)^{23,24} e registrado no International Prospective Register of Systematic Reviews (PROSPERO) sob o registro CRD42021281687.

3.2. Ética

A aprovação ética não foi necessária para esta revisão sistemática por esta não conter informações privadas sobre os participantes ou violar direitos humanos.

3.3 Critérios para os estudos incluídos na revisão

3.3.1 Tipos de estudos

Estudos epidemiológicos institucionais abordando a casuística geral dos tumores ósseos situados no pé e no tornozelo, sem restrição temporal e independentemente da idade, sexo e etnia dos pacientes.

3.3.2 Critérios de inclusão

Estudos publicados em inglês, português e espanhol.

3.3.3 Critérios de exclusão

Relatos de caso; séries de casos versando sobre tipos histológicos específicos ou que não representem a casuística geral dos tumores ósseos situados no pé e no tornozelo; estudos publicados em outros idiomas que não o inglês, o português e o espanhol.

3.4 Estratégia de busca

As buscas sistemáticas na literatura foram realizadas em janeiro de 2024 nas bases de dados PubMed/MEDLINE, Embase (utilizando Periódicos CAPES) e LILACS, sem restrições temporais na estratégia de busca. No levantamento bibliográfico, adotou-se o vocabulário controlado pelo MeSH, Emtree e termos livres, agrupados e cruzados com os operadores booleanos "OR" e "AND" (**Quadro 1**). As referências dos artigos incluídos foram avaliadas para detectar estudos não identificados nas buscas.

Quadro 1. Estratégia de busca em banco de dados.

	PubMed	Embase	LILACS
#1	"Ossos do Pé"[Malha]	mh: "Ossos do pé"	mh: "Ossos do pé"
#2	"Ossos Metatarsais"[Malha]	mh:"Ossos Metatarsais"	mh:"Ossos Metatarsais"
#3	Metatars*[título/resumo]	Metatars\$	Metatars\$
#4	"Ossos do Tarso"[Malha]	mh:"Osso do Tarso"	mh:"Osso do Tarso"
#5	"Osso Cuneiforme"[Título/Resumo]	"Osso cuneiforme"	"Osso cuneiforme"
#6	"Osso Cubóide"[Título/Resumo]	"Osso Cubóide"	"Osso Cubóide"
#7	"Ossos do Tarso/anatomia e histologia"[Malha]	mh:"Ossos do Tarso/AH"	mh:"Ossos do Tarso/AH"
#8	"Calcâneo" [Eu]	mh:"Calcâneo"	mh:"Calcâneo"
#9	"Heel Bone"[Título/Resumo]	"Osso do calcanhar"	"Osso do calcanhar"

#10	"Calcâneo/anatomia e histologia"[Malha]	mh:"Calcâneo / AH"	mh:"Calcâneo / AH"
#11	"Talus"[Malha]	mh:"Talus"	mh:"Talus"
#12	"Falanges dos dedos dos pés" [Malha]	mh: "Falanges dos dedos dos pés"	mh: "Falanges dos dedos dos pés"
#13	"Falanges dos dedos dos pés/anatomia e histologia"[Malha]	mh:"Falanges dos dedos dos pés/AH"	mh:"Falanges dos dedos dos pés/AH"
#14	"Tornozelo" [Malha]	mh:"Tornozelo"	mh:"Tornozelo"
#15	"Hálux" [Malha]	mh: "Hálux"	mh: "Hálux"
#16	# 1 OU # 2 OU # 3 OU # 4 OU # 5 OU # 6 OU # 7 OU # 8 OU # 9 OU # 10 OU # 11 OU # 12 OU # 13 OU # 14 OU # 15	# 1 OU # 2 OU # 3 OU # 4 OU # 5 OU # 6 OU # 7 OU # 8 OU # 9 OU # 10 OU # 11 OU # 12 OU # 13 OU # 14 OU # 15	# 1 OU # 2 OU # 3 OU # 4 OU # 5 OU # 6 OU # 7 OU # 8 OU # 9 OU # 10 OU # 11 OU # 12 OU # 13 OU # 14 OU # 15
#17	"Neoplasias"[Malha]	mh:"Neoplasias"	mh:"Neoplasias"
#18	Neoplasia*[Título/Resumo]	Neoplasia\$	Neoplasia\$
#19	"Neoplasias Ósseas" [Malha]	mh:"Neoplasias Ósseas"	mh:"Neoplasias Ósseas"
#20	Tumor*[Título/Resumo]	Tumor\$	Tumor\$
#21	Maligno*[Título/Resumo]	Maligno\$	Maligno\$
#22	Neoplasia Benigna*[Título/Resumo]	Neoplasia benigna\$	Neoplasia benigna\$
#23	"Câncer ósseo"[Título/Resumo]	"Câncer ósseo"	"Câncer ósseo"
#24	# 17 OU # 18 OU # 19 OU # 20 OU # 21 OU # 22 OU # 23	# 17 OU # 18 OU # 19 OU # 20 OU # 21 OU # 22 OU # 23	# 17 OU # 18 OU # 19 OU # 20 OU # 21 OU # 22 OU # 23
#25	#16 E #24	#16 E 24	#16 E 24

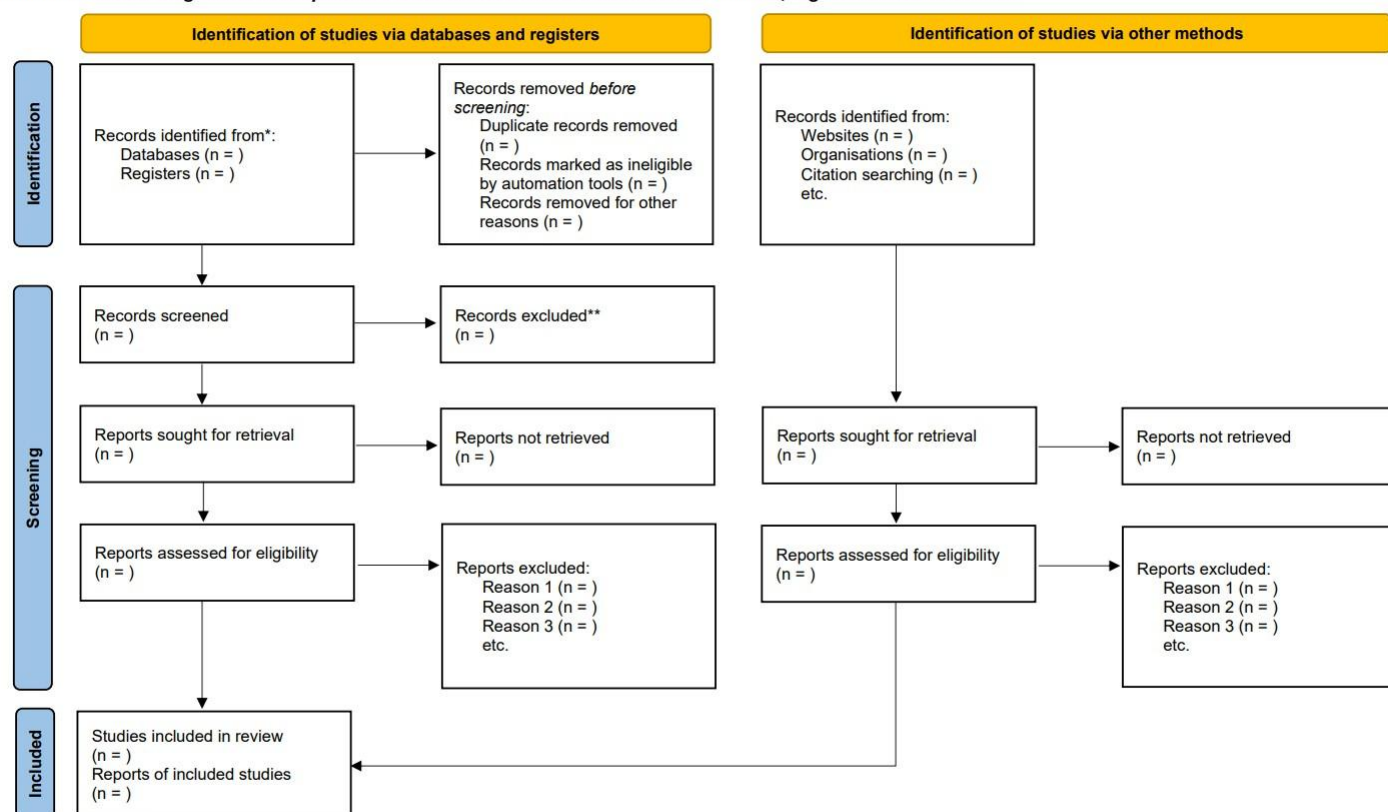
3.5 Triagem e extração de dados

Um dos pesquisadores conduziu a pesquisa nos bancos de dados, exportou os resultados para o programa de gerenciamento de seleção de domínio da web *Rayyan*: *Rayyan Qatar Computing Research Institute* (Rayyan QCRI) e removeu duplicatas. Em seguida, dois avaliadores selecionaram os artigos de forma

independente por títulos e resumos, identificando os estudos elegíveis para leitura completa. Todos os procedimentos de seleção foram baseados no fluxograma PRISMA.²⁴(**Figura 1**) Nos casos de divergência, os avaliadores discutiram a inclusão. Se nenhum acordo fosse alcançado, um terceiro avaliador fazia o desempate.

Figura 1. Fluxograma PRISMA 2020 para novas revisões sistemáticas que incluiu buscas em bases de dados, registros e outras fontes.

PRISMA 2020 flow diagram for new systematic reviews which included searches of databases, registers and other sources



*Consider, if feasible to do so, reporting the number of records identified from each database or register searched (rather than the total number across all databases/registers).

**If automation tools were used, indicate how many records were excluded by a human and how many were excluded by automation tools.

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n7 doi: 10.1136/bmj.n71. For more information, visit: <http://www.prisma-statement.org/>

Os dados foram extraídos usando o Microsoft® Excel® (Microsoft Corporation, 2019). Para evitar vieses nas extrações, dois avaliadores as realizaram de forma independente. A partir dos estudos selecionados foram extraídas informações sobre tipos histológicos, atualizados de acordo com a última edição da

classificação da Organização Mundial da Saúde (OMS), publicada em 2020,²⁵ região anatômica acometida (antepé, médio-pé, retropé e tornozelo, segundo a classificação de Ruggieri et al., adaptada por Toepfer et al.),^{11,15} osso afetado, sexo e faixa etária (<20 anos, 20-59 anos e ≥60 anos) dos pacientes.

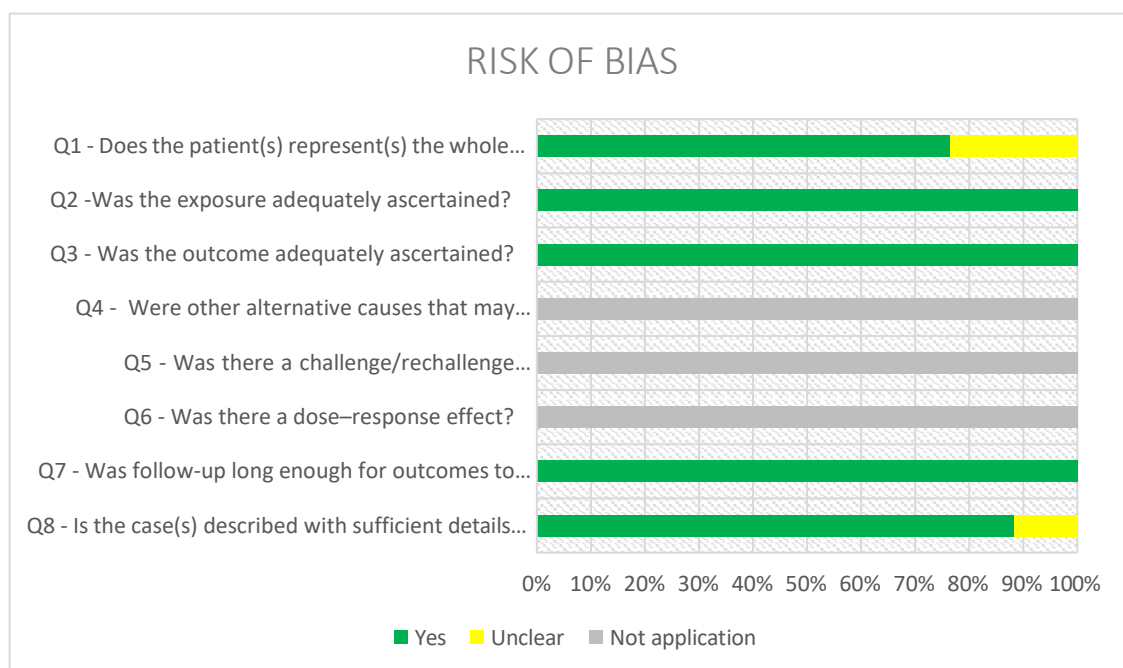
3.5.1 Tratamento dos dados em falta

Nas situações em que os dados oriundos de estudos potenciais estavam ausentes, insuficientes ou vagos, tentamos entrar em contato com os autores correspondentes para recuperar os dados necessários por e-mail. Os estudos foram excluídos nos casos em que dados relevantes não puderam ser obtidos usando esta abordagem.

3.6 Avaliação do risco de enviesamento (qualidade)

Dois autores avaliaram de forma independente o risco de viés nos estudos selecionados utilizando a ferramenta proposta por Murad et al. (2018)²⁶ (**Figura 2**), desenvolvida para avaliar a qualidade metodológica e síntese de séries e relatos de casos, instrumento derivado da *Newcastle-Ottawa Scale* (NOS), exceto por duas questões não relevantes para nossa revisão ("Houve um fenômeno de desafio/redesafio?" e "Houve um efeito dose-resposta?").

Figura 2. Avaliação do risco de viés dos estudos incluídos.



3.7. Análise estatística

3.7.1 Análise e tratamento dos dados

Foi realizada síntese descritiva dos resultados dos estudos incluídos, estruturada em torno dos tipos histológicos,²⁵ região anatômica acometida,^{10,15} osso afetado, sexo e faixa etária dos pacientes.

3.7.2 Análise de subgrupos ou subconjuntos

Realizamos análise de subgrupos estruturada em torno das informações sobre tipos histológicos,²⁵ região anatômica acometida,^{10,15} osso afetado, sexo e faixa etária dos pacientes.

4. RESULTADOS

Artigo

Epidemiology of bone tumors of the foot and ankle – A systematic review

Running Title: Epidemiology of bone tumors of the foot and ankle

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Acknowledgments

Not applicable.

Declaration of conflicting interest

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding statement

The authors received no financial support for the research, authorship, and/or publication of this article.

Ethical approval and consent to participate

The study protocol was registered with the International Prospective Register of Systematic Reviews (PROSPERO), registration number CRD42021281687. This systematic review was exempt from research ethics committee approval as it did not involve private information from participants or any potential violation of human rights.

Consent for publication

Not applicable.

Data availability statement

All relevant data are within the paper.

Author contributions

All authors declare that they participated in the research that led to the manuscript, read and approved the text, tables, and figures submitted.

Foot & Ankle International

Epidemiology of bone tumors of the foot and ankle – A systematic review

Journal:	<i>Foot & Ankle International</i>
Manuscript ID	Draft
Manuscript Type:	Contemporary Review
Keywords:	Foot, Ankle, Bone, Bone Neoplasms, Epidemiology, Systematic Review
STRUCTURED ABSTRACT (Limit 300 words) Background, Methods, Results & Conclusion:	

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1 **Epidemiology of bone tumors of the foot and ankle – A systematic review**

2

3 **Running Title: Epidemiology of bone tumors of the foot and ankle**

4

5 **ABSTRACT**

6 **Background:** Bone tumors of the foot and ankle account for 1% to 2% of all skeletal

7 neoplasms. Our review aimed to determine their distribution according to histological

8 type, anatomical site, affected bone, patient sex, and age group. **Methods:** We

9 reviewed institutional epidemiological studies focusing on bone tumors of the foot

10 and ankle. Our selection process adhered to the PRISMA guidelines. We provide a

11 descriptive synthesis of the results from the included studies, along with subgroup

12 analyses. **Results:** We included 17 studies, totaling 2438 tumors (70.7% benign,

13 11.0% intermediate, and 18.3% malignant). The most frequent benign tumors were

14 enchondroma, osteoid osteoma, and simple bone cysts. Among intermediate tumors,

15 giant cell tumor of bone and osteoblastoma were most common, while

16 chondrosarcoma, Ewing’s sarcoma, and osteosarcoma were the most frequent

17 malignant tumors. The hindfoot was the most affected segment, followed by the

18 forefoot, midfoot, and ankle. The calcaneus was the bone most affected by both

19 benign and malignant tumors, whereas the metatarsals were the most frequent site for

20 intermediate tumors. There was a slight predominance in men (55.6%). Benign

21 tumors were more prevalent in individuals under 20 years of age, while intermediate

22 and malignant tumors were more common between the ages of 20 and 59. All tumors

23 in individuals aged 60 years and older were malignant. **Conclusion:** Despite the

24 challenge of data heterogeneity across the included studies for absolute comparisons,

25 the consistent findings of this review provide valuable insights into the epidemiology

26 of bone tumors of the foot and ankle.

27 **Keywords:** Foot; Ankle; Bone; Bone Neoplasms; Epidemiology; Systematic Review.

28 INTRODUCTION

29 Bone tumors located in the foot and ankle are uncommon,¹⁻⁸ accounting for
30 1% to 2% of all skeletal tumors.⁵ Interestingly, its occurrence is proportionally higher
31 compared to other anatomical segments, since the foot and ankle represent only about
32 3% of the total body mass.⁷⁻¹⁰

33 Bone tumors of the foot and ankle can affect people of all ages. Primary
34 benign neoplasms are most often seen in individuals up to the fourth decade of life,
35 while primary malignant neoplasms are more common in older adults. In addition,
36 these tumors seem to occur more frequently in men,^{11,12} although gender is not a
37 strong indicator of the specific diagnosis.⁵

38 The thin layer of soft tissue over the foot and ankle facilitates the clinical
39 diagnosis of tumors,^{1,2,5,7,10,13} making even minor lesions noticeable.⁵ However,
40 tumors in this region can sometimes be misdiagnosed.^{1,13} This is usually because these
41 lesions are not considered true neoplasms, resulting in an underestimation of their
42 potential severity.⁷ Consequently, diagnostic errors or delays for foot and ankle
43 tumors are more frequent than in other parts of the body,⁷ and can lead to inadequate
44 surgical removal and a higher likelihood of recurrence.^{1,2,4,5,9,14-16}

45 Orthopedic surgeons managing patients with bone tumors of the foot and
46 ankle must possess a comprehensive understanding of the diagnostic and staging
47 criteria for these intricate cases.¹⁷⁻²⁰ The unique anatomical challenges of the ankle
48 further complicate limb-sparing surgery, particularly in achieving sufficient surgical
49 margins.^{2,4,13,21} Unplanned resections, occurring in a considerable percentage (40% to
50 60%) of malignant foot and ankle tumors, are associated with elevated amputation and
51 local recurrence rates.^{7,13,22}

52 Given the rarity and distinct presentation of bone tumors of the foot and
53 ankle, epidemiological data remain limited. Therefore, the primary objective of this
54 review was to determine the distribution of these neoplasms according to histological

55 type, anatomical site (forefoot, midfoot, hindfoot, and ankle), affected bone, patient
56 sex, and age group.

57

58 **METHODS**

59 This review was conducted in accordance with the Preferred Reporting Items
60 for Systematic Reviews and Meta-Analyses (PRISMA) statement.^{23,24} The study
61 protocol was registered with the International Prospective Register of Systematic
62 Reviews (PROSPERO).

63 This systematic review was exempt from research ethics committee approval
64 as it did not involve private information from participants or any potential violation of
65 human rights.

66

67 **Search strategy**

68 We searched MEDLINE/PubMed, Embase, and Latin American and
69 Caribbean Health Sciences Literature (LILACS) databases for articles published from
70 database inception to January 2024. No publication date or language restrictions were
71 imposed. The search strategy combined MeSH keywords, Emtree terms, and
72 uncontrolled terms using the Boolean operators "OR" and "AND". We also scanned
73 the reference lists of the included studies to detect potentially relevant studies not
74 identified by the previous search strategies.

75

76 **Eligibility criteria**

77 Studies eligible for inclusion in this review were institutional
78 epidemiological studies published in English, Portuguese, or Spanish that focused on
79 bone tumors of the foot and ankle and enrolled patients of any age, sex, or ethnicity.
80 Case reports and case series that focused on specific histological types of bone tumors
81 or did not represent the overall range of bone tumors occurring in the foot and ankle

as well as studies published in languages other than English, Portuguese, or Spanish were excluded.

Screening and data extraction

One reviewer (CLSL) exported the results of the database searches into Rayyan Qatar Computing Research Institute (Rayyan QCRI) software and removed duplicates. Two reviewers (BGB and AALG) independently screened titles and abstracts and then assessed the full texts of all potential studies for inclusion. Any disagreements between reviewers were resolved through discussion. If a consensus was not reached, a third independent reviewer (FDM) was consulted.

To ensure unbiased data extraction, two reviewers (CS and AG) independently extracted data using a standardized Excel spreadsheet (Microsoft Corporation, 2019). Data extracted included histological type, updated according to the 2020 World Health Organization (WHO) classification,²⁵ anatomical site (forefoot, midfoot, hindfoot, and ankle), affected bone, patient sex, and age group (< 20 years, 20-59 years, and $\geq$ 60 years).

When information from potential studies was missing, insufficient, or vague, we attempted to contact the corresponding authors via email to obtain the necessary data. Ultimately, studies were excluded if the relevant data could not be obtained through this process.

Risk of bias (quality) assessment

For the selected studies, two reviewers (FDM and CLSL) independently assessed the risk of bias using the tool developed by Murad et al.²⁶ This tool, based on the Newcastle-Ottawa Scale (NOS), was designed to assess the methodological quality of case series and case reports and synthesize their results. It comprises eight questions across four domains: selection (Q1), ascertainment (Q2 and Q3), causality

(Q4-Q7), and reporting (Q8). We excluded three questions from this tool that were not applicable to our review: “Were other alternative causes that may explain the observation ruled out?” (Q4), “Was there a challenge/rechallenge phenomenon?” (Q5), and “Was there a dose-response effect?” (Q6).

Data analysis

We provide a descriptive synthesis of the results from the included studies. Additionally, we conducted structured subgroup analyses based on histological type, anatomical site, the specific bone affected, patient sex, and age group. Due to the inability to subset for homogeneity, a meta-analysis was not feasible.

RESULTS

The initial search identified 8578 records, 6835 of which remained after removing duplicates. Following title and abstract screening, 159 studies (2.32%) were considered potentially eligible and were sought for full-text retrieval. The full texts of three potentially eligible studies could not be retrieved, resulting in 156 studies being retrieved for full-text review. Of these, 15 (0.21%) met the inclusion criteria. Another two full-text articles identified through citation searching were deemed eligible, bringing the total number of studies included in this review to 17.^{1,2,4,5,7,10,12,13,15,21,22,27-32} The study selection process is detailed in Figure 1.

Characteristics of included studies

Table 1 provides a summary of the included studies, outlining the characteristics of each study sample. All studies included in this review were retrospective, with follow-up periods ranging from 9 to 84 years, encompassing a total of 2438 bone tumors of the foot and ankle.

Risk of bias (quality) assessment

The findings from our risk of bias assessment, using the tool developed by Murad et al.,²⁶ are shown in Figure 2. For the domain of selection (Q1), our analysis indicated an unclear risk of bias in 24% (4/17) of the included studies. For the domain of ascertainment (Q2 and Q3), we observed a low risk of bias across all the studies. In the domain of causality (Q4-Q7), questions Q4, Q5, and Q6 were not applicable to our review as they focused on adverse drug events. For the remaining question in this domain (Q7), all studies demonstrated a low risk of bias. For the domain of reporting (Q8), we identified an unclear risk of bias in 12% (2/17) of the included studies.

Histological types

Of the 2438 bone tumors, 1722 (70.7%) were classified as benign, 269 (11.0%) as intermediate, and 447 (18.3%) as malignant (Table 2).

The most frequent benign tumors were enchondroma (n = 317; 18.4%), osteoid osteoma (n = 297; 17.2%), and simple bone cyst (SBC) (n = 280; 16.3%). Among intermediate tumors, giant cell tumor of bone (GCTB) (n = 169; 62.8%), osteoblastoma (n = 91; 33.8%), and desmoplastic fibroma (n = 5; 1.9%) were most common. For primary malignant tumors, the most frequent types were chondrosarcoma (n = 118; 26.4%), Ewing's sarcoma (n = 105; 23.5%), and osteosarcoma (n = 91; 20.3%).

Anatomical sites

Regarding the 1819 tumors with described anatomical sites, the hindfoot was the most affected segment, accounting for 829 cases (45.6%), followed by forefoot in 552 cases (30.3%), midfoot in 305 cases (16.8%), and ankle in 133 cases (7.3%) (Table 3).

When examining the 1286 benign tumors, the hindfoot was also the most common site (n = 573; 44.6%), followed by forefoot (n = 434; 33.7%), midfoot (n = 190; 14.8%), and ankle (n = 89; 6.9%). Among the 217 intermediate tumors, the hindfoot was the most frequent location (n = 101; 46.5%), followed by midfoot (n = 48; 22.1%), forefoot (n = 55; 25.3%), and ankle (n = 13; 6.0%). In the 316 malignant tumors, the hindfoot was the most affected region (n = 155; 49.1%), followed by forefoot (n = 63; 19.9%), midfoot (n = 67; 21.2%), and ankle (n = 31; 9.8%).

Affected bones

Regarding the 589 tumors where the specific bone affected was identified, the calcaneus was the most frequently involved bone, accounting for 186 cases (31.9%), followed by metatarsals in 141 cases (23.9%) and phalanges in 127 cases (21.6%). The tibia and fibula were the least commonly affected, with 7 cases (1.2%) and 1 case (0.2%), respectively (Table 4).

When examining the 357 benign tumors, the calcaneus was also the most commonly affected bone (n = 125; 35.0%), followed by phalanges (n = 99; 27.7%) talus (n = 62; 17.4%), metatarsals (n = 62; 17.4%), navicular (n = 3; 0.8%), cuboid (n = 3; 0.8%), tibia (n = 2; 0.6%), and fibula (n = 1; 0.3%). We did not identify any benign bone tumors in the cuneiform bones.

Among the 123 intermediate tumors, the metatarsals were the most frequently affected bones (n = 40; 32.5%), followed by talus (n = 23; 18.7%), calcaneus (n = 21; 17.1%), phalanges (n = 20; 16.3%), cuneiform bones (n = 8; 6.5%), navicular (n = 6; 4.9%), and cuboid (n = 5; 4.0%). We found no intermediate bone tumors in tibia or fibula.

In the 109 malignant tumors, the calcaneus was the most affected bone (n = 40; 36.7%), followed by metatarsals (n = 39; 35.8%), talus (n = 8; 7.3%),

phalanges (n = 8; 7.3%), tibia (n = 7; 6.4%), cuboid (n = 5; 4.6%), and cuneiform bones (n = 2; 1.8%). We did not identify any malignant tumors in fibula or navicular.

Patient sex

Regarding the 968 tumors identified by sex, 538 (55.6%) were found in males and 430 (44.4%) in females. Specifically, among the 678 benign bone tumors, 383 (56.5%) occurred in males. For the 125 intermediate bone tumors, 65 (52.0%) were found in males, while among the 165 malignant bone tumors, 104 (63.0%) affected males (Table 5).

Age groups

In the selected studies where the age group was identified, a total of 113 tumors were categorized. Most benign bone tumors occurred in individuals under 20 years of age (n = 36; 55.4%). Intermediate bone tumors most frequently affected individuals aged 20 to 59 years (n = 11; 91.7%). Malignant bone tumors also occurred more frequently between the ages of 20 and 59 (n = 22; 61.1%). All bone tumors diagnosed in individuals over 60 years of age were malignant (n = 7; 100%) (Table 6).

DISCUSSION

The present study sought to establish representative epidemiological data for all categories of bone tumors located in the foot and ankle. We analyzed a total of 2438 bone tumors across 33 distinct histological types, classified according to the 2020 WHO criteria.²⁵ To the best of our knowledge, there are no published systematic reviews specifically detailing the epidemiological characteristics of bone tumors of the foot and ankle.

To uphold the methodological rigor of this review and minimize selection bias, we limited our inclusion criteria to institutional epidemiological studies

216 encompassing all types of bone tumors of the foot and ankle. We believe that this
217 strategy allows for a more accurate representation of the true distribution of these
218 neoplasms.

219 In our analysis of 2438 bone tumors, we found that 1722 (70.7%) were
220 benign, 269 (11.0%) were intermediate, and 447 (18.3%) were malignant. The higher
221 incidence of benign tumors compared to malignant ones in the foot and ankle aligns
222 with existing literature. Prior research, such as the studies by Ruggieri et al.¹⁵ and
223 Toepfer et al.,¹⁰ reported similar benign tumor percentages (75.4% and 80.0%,
224 respectively). Conversely, Ozdemir et al.,¹ Özer et al.,⁵ and Delgado Cedillo et al.³²
225 observed higher percentages (87.5%, 85.4%, and 90.4%, respectively), while Casadei
226 et al.²⁷ and Murari et al.²⁸ found lower percentages (60.7% and 51.8%, respectively).
227 Notably, none of these earlier studies included a separate category for intermediate
228 tumors, classifying them within the benign group, even though the WHO had already
229 introduced this distinct category in the 2002 third edition of its classification.³³ Our
230 study identified 11.0% as intermediate. This figure is consistent with the 11.3%
231 reported by both Casadei et al.²⁷ and Bakotic and Huvos,³⁰ while Ozdemir et al.,¹ Özer
232 et al.,⁵ and Ruggieri et al.¹⁵ reported slightly lower rates (7.8%, 7.6%, and 8.0%,
233 respectively). Regarding malignant tumors, our sample's rate of 18.3% is comparable
234 to that of Murari et al.²⁸ (16.5%) and Ruggieri et al.¹⁵ (16.6%). However, it was lower
235 than the percentages found by Casadei et al.²⁷ (28.0%) and Bakotic and Huvos³⁰
236 (47.2%), and higher than those reported by Ozdemir et al.¹ (4.7%), Özer et al.⁵
237 (6.6%), and Delgado Cedillo et al.³² (1.2%).

238 In our sample of benign bone tumors, enchondroma was the most prevalent
239 (18.4%), closely followed by osteoid osteoma (17.2%) and SBC (16.3%). It is
240 interesting to note that, although the percentages are different, the order of frequency
241 we observed (enchondroma > osteoid osteoma) aligns with the largest study included
242 in our review.¹⁵ Other studies with relevant sample sizes presented varying sequences:

Toepfer et al.¹⁰ found SBC as the most frequent, followed by enchondroma and osteochondroma; Murari et al.²⁸ observed chondromyxoid fibroma as the most common, followed by SBC and chondroblastoma; and Casadei et al.²⁷ identified osteoid osteoma as the most common, followed by SBC and enchondroma.

Regarding intermediate tumors in our sample, GCTB was the most common (62.8%), followed by osteoblastoma (33.8%). This order is consistent with the findings of Ruggieri et al.,¹⁵ Murari et al.,²⁸ and Toepfer et al.,¹⁰ although the proportions differed. Notably, Casadei et al.²⁷ reported an equal number of cases for these two neoplasms.

Our analysis of malignant tumors revealed chondrosarcoma (26.4%) as the most frequent, followed by Ewing's sarcoma (23.5%) and osteosarcoma (20.3%). These findings are supported by the study of Özer et al.,⁵ who also identified chondrosarcoma as the most common malignant tumor, although at a considerably higher rate (63%), with Ewing's sarcoma and osteosarcoma each representing 18% of cases.

In our analysis of 1819 bone tumors with reported anatomical sites, the hindfoot was the most frequently affected area, representing nearly half of the cases, followed by the forefoot, midfoot, and ankle. These findings align with the study conducted by Casadei et al.,²⁷ who also identified the hindfoot as the primary site, followed by the forefoot and midfoot, for both benign and malignant bone tumors. However, other studies have presented different frequency sequences. Toepfer et al.¹⁰ reported a sequence of hindfoot, ankle, forefoot, and midfoot, while Murari et al.²⁸ observed the highest incidence in the forefoot, followed by hindfoot and midfoot.

When examining the specific bones involved in a subset of 583 tumors with this information available, the calcaneus was the most affected bone (31.9%). This predominance was consistent across both benign (35.0%) and malignant tumors (36.7%). Conversely, intermediate tumors were most often located in metatarsals

(32.5%). Our observation of calcaneus being the most prevalent site is consistent with the findings of Ozdemir et al.,¹ who reported this location in 33.0% of cases. It is worth mentioning, however, that Murari et al.²⁸ found a higher incidence of tumors in metatarsals (35.2%).

Regarding the sex of the affected patients in the studies where this information was available, our analysis revealed a male predominance, accounting for 55.6% of cases. This trend aligns with observations in the studies by Toepfer et al.¹⁰ (61.5% male) and Murari et al.²⁸ (61.4% male). Within our sample, we found the following distribution across different tumor types: (a) benign tumors occurred in 56.5% of men; (b) intermediate tumors affected 52% of males; and (c) malignant tumors showed a considerably higher incidence in males, with 63% of cases. These findings are consistent with previous studies. Toepfer et al.¹⁰ reported that, of 231 benign bone tumors, 59.7% occurred in men; of 35 malignant bone tumors, 57.1% affected males. Similarly, Murari et al.²⁸ found that, among 208 benign bone tumors, 62.5% occurred in men, while of the 41 malignant bone tumors, 56.1% affected men.

In our review, less than 5% of the included studies provided information on patient age. However, in those studies that did, bone tumors were most diagnosed in individuals aged 20 to 59 years, followed by those under 20 years and those 60 years or older. Benign tumors were most prevalent in individuals under 20 years (84.1% of cases) and in those aged 20 to 59 years (64.5% of cases). Conversely, malignant tumors showed an inverse pattern, representing 100% of tumors in the 60 years or older age group, 35.48% in the 20 to 59 years group, and 15.90% in the under 20 years group. Notably, Kinoshita et al.²⁹ did not identify malignant bone tumors in patients under 50 years of age, and half of the tumors in patients over 50 years of age were malignant. Toepfer et al.¹⁰ also observed an increasing frequency of malignant bone tumors with advancing age.

Limitations of this systematic review include considerable heterogeneity among the included studies, particularly in the various data collection methods, varying durations of patient follow-up, and different tumor classification criteria, as well as incomplete data that restricted more comprehensive analyses. It is important to consider that our analysis focused on surgically treated tumors with confirmed histological diagnoses, which may limit the applicability of our findings to other contexts. In addition, a considerable portion of the studies come from Europe, which may affect the generalization of our results to populations in other regions, where genetic, environmental, and health system differences may exist and have not been accounted for.

CONCLUSION

This systematic review provides a comprehensive characterization of bone tumors occurring in the foot and ankle. Our analysis encompasses histological type, anatomical site, the specific bone involved, patient sex, and age group.

While acknowledging the challenge of data heterogeneity across the included studies for absolute comparisons, the consistency of our findings provide valuable insights into the epidemiology of bone tumors of the foot and ankle.

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FIGURE LEGENDS

Figure 1. Flow diagram of study selection.

Figure 2. Assessment of risk of bias using the tool developed by Murad et al.²⁶

Color for online version only.

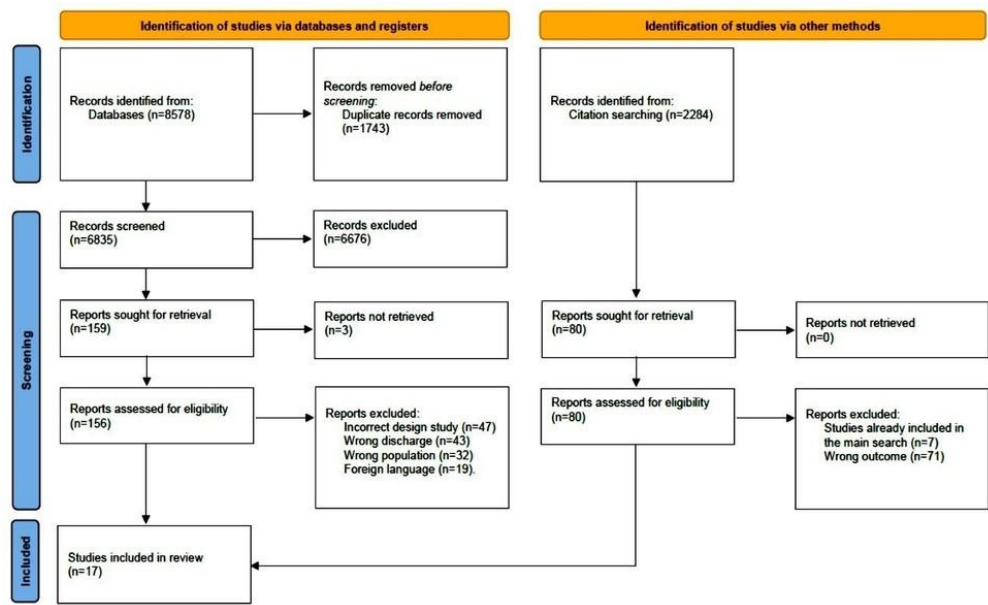


Figure 1. Flow diagram of study selection.

41x25mm (600 x 600 DPI)

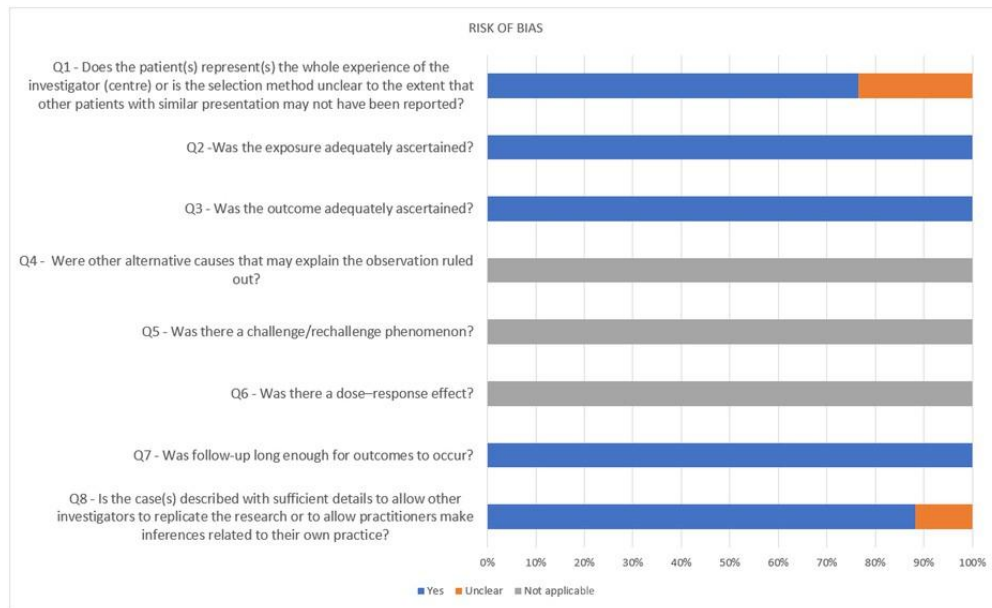


Figure 2. Assessment of risk of bias using the tool developed by Murad et al.²⁶

39x24mm (600 x 600 DPI)

Table 1. General characteristics of the included studies.

Study (year)	Country	Follow-up	Bone Tumors*				Sex		Location			
			n	Benign	Intermediate	Malignant	Male	Female	Forefoot	Midfoot	Hindfoot	Ankle
Murari et al. ²⁸ (1989)	USA	16 years	249	129 (51.8%)	79 (31.7%)	41 (16.5%)	153	96	129	39	81	NR
Casadei et al. ²⁷ (1991)	Italy	84 years	247	150 (60.7%)	28 (11.3%)	69 (28.0%)	NR	NR	76	26	134	NR
Chou and Malawer ¹² (1994)	USA	14 years	14	5 (35.7%)	1 (7.1%)	8 (57.2%)	12	2	2	2	2	7
Sarkar et al. ³¹ (1996)	German	13 years	23	12 (52.2%)	4 (17.4%)	7 (30.4%)	13	10	8	3	10	1
Ozdemir et al. ¹ (1997)	Turkey	10 years	128	112 (87.5%)	10 (7.8%)	6 (4.7%)	#	#	#	#	#	#
Bakotic and Huvos ²⁸ (2001)	USA	15 years	142	59 (41.5%)	16 (11.3%)	67 (47.2%)	70	72	#	#	#	#
Kinoshita et al. ²⁹ (2002)	Japan	26 years	35	32 (91.4%)	0 (0.0%)	3 (8.6%)	18	17	22	1	12	NR
Chou et al. ² (2009)	USA	20 years	64	31 (48.4%)	16 (25.0%)	17 (26.6%)	#	#	#	#	#	#
Azevedo et al. ⁴ (2013)	Portugal	10 years	9	4 (44.5%)	3 (33.3%)	2 (22.2%)	6	3	4	1	#	4
Ruggieri et al. ¹⁵ (2014)	Italy	17 years	849	640 (75.4%)	68 (8.0%)	141 (16.6%)	NR	NR	NR	NR	NR	NR
Özer et al. ⁵ (2017)	Turkey	30 years	157	134 (85.4%)	12 (7.6%)	11 (7.0%)	#	#	#	#	#	#
Delgado Cedillo et al. ³² (2017)	Mexico	9 years	83	75 (90.4%)	7 (8.4%)	1 (1.2%)	#	#	#	#	#	#
Murahashi et al. ²² (2021)	Japan	22 years	23	21 (91.3%)	0 (0.0%)	2 (8.7%)	14	11	11	1	6	7
Toepfer et al. ¹⁰ (2018)	Germany and Switzerland	18 years	265	212 (80.0%)	18 (6.8%)	35 (13.2%)	163	102	53	39	104	69
Karadeniz et al. ⁷ (2022)	Turkey	17 years	55	35 (63.7%)	2 (3.6%)	18 (32.7%)	#	#	#	#	#	#
Oliveira et al. ¹³ (2022)	Brazil	30 years	48	30 (62.5%)	4 (8.3%)	14 (29.2%)	#	#	NR	NR	NR	48
Kokubu et al. ²¹ (2022)	Japan	12 years	47	41 (87.2%)	1 (2.1%)	5 (10.6%)	#	#	#	#	#	#

n, sample size; #, unable to extract; NR, not reported. *According to the 2020 World Health Organization (WHO) classification of bone tumors.

Table 2. List of bone tumors of the foot and ankle reported in the included studies.

Benign bone tumors	k	n	%
Enchondroma	12	317	18.4%
Osteoid osteoma	12	297	17.2%
Simple bone cyst	15	280	16.3%
Osteochondroma	16	243	14.1%
Aneurysmal bone cyst	11	128	7.4%
Chondroblastoma	13	95	5.5%
Bizarre parosteal osteochondromatous proliferation	2	81	4.7%
Chondromyxoid fibroma	8	59	3.4%
Lipoma	10	57	3.3%
Subungual exostosis	5	54	3.1%
Non-ossifying fibroma	6	51	2.9%
Periosteal chondroma	4	34	2.0%
Hemangioma	5	13	0.8%
Fibrous dysplasia	7	9	0.5%
Osteofibrous dysplasia	1	2	0.1%
Osteoma	2	2	0.1%
Overall		1722	100.0%
Intermediate bone tumors	k	n	%
Giant cell tumor of bone	13	169	62.8%
Osteoblastoma	11	91	33.8%
Desmoplastic fibroma	3	5	1.9%
Langerhans cell histiocytosis	3	4	1.5%
Overall		269	100.0%
Malignant bone tumors	k	n	%
Chondrosarcoma	14	118	26.4%
Ewing's sarcoma	9	105	23.5%
Osteosarcoma	15	91	20.3%
Bone metastases	10	40	8.9%
Epithelioid hemangioendothelioma	5	40	8.9%
Fibrosarcoma	7	21	4.7%
Lymphoma	3	11	2.5%
Pleomorphic sarcoma, undifferentiated	3	8	1.8%
Plasmacytoma	2	4	0.9%
Giant cell tumor of bone, malignant	1	4	0.9%
Leiomyosarcoma	1	2	0.4%
Angiosarcoma	2	2	0.4%
Adamantinoma	1	1	0.2%
Overall		447	100.0%

k, number of studies in which the tumor was described; n, sample size.

Table 3. Type of tumor *versus* anatomical site (affected foot region).

Benign bone tumors	k	n	Forefoot	Midfoot	Hindfoot	Ankle
Enchondroma	5	277	154	97	22	4
Osteoid osteoma	7	261	35	22	196	8
Simple bone cyst	9	187	10	6	161	10
Osteochondroma	8	138	60	23	32	23
Aneurysmal bone cyst	7	97	5	27	52	13
Bizarre parosteal osteochondromatous proliferation	1	78	77	1	0	0
Chondroblastoma	7	72	3	7	61	1
Chondromyxoid fibroma	4	51	35	1	14	1
Periosteal chondroma	4	34	27	4	2	1
Lipoma	5	31	1	0	30	0
Non-ossifying fibroma	2	23	0	0	0	23
Subungual exostosis	2	22	22	0	0	0
Fibrous dysplasia	4	6	0	2	1	3
Hemangioma	3	6	3	0	2	1
Osteoma	2	2	2	0	0	0
Osteofibrous dysplasia	1	1	0	0	0	1
Overall		1286	434	190	573	89
Intermediate bone tumors	k	n	Forefoot	Midfoot	Hindfoot	Ankle
Giant cell tumor of bone	8	133	31	36	54	12
Osteoblastoma	7	78	23	11	44	0
Langerhans cell histiocytosis	3	4	1	1	1	1
Desmoplastic fibroma	2	2	0	0	2	0
Overall		217	55	48	101	13
Malignant bone tumors	k	n	Forefoot	Midfoot	Hindfoot	Ankle
Chondrosarcoma	9	90	25	21	36	8
Ewing's sarcoma	7	77	13	20	39	5
Osteosarcoma	10	61	9	7	32	13
Epithelioid hemangioendothelioma	4	32	6	11	14	1
Fibrosarcoma	5	17	2	2	12	1
Bone metastases	6	13	2	3	5	3
Lymphoma	2	10	1	0	9	0
Pleomorphic sarcoma, undifferentiated	2	5	2	0	3	0
Plasmacytoma	2	4	0	3	1	0
Giant cell tumor of bone, malignant	1	4	3	0	1	0
Leiomyosarcoma	1	2	0	0	2	0
Angiosarcoma	1	1	0	0	1	0
Overall		316	63	67	155	31

k, number of studies in which the tumor was described; n, sample size.

Table 4. Type of tumor versus affected bone.

Benign bone tumors	k	n	Tibia	Fibula	Talus	Calcaneus	Navicular	Cuboid	Cuneiform bones	Metatarsals	Phalanges
Osteoid osteoma	4	74	0	0	41	10	0	0	0	5	18
Simple bone cyst	5	72	0	0	4	61	0	0	0	7	0
Chondromyxoid fibroma	3	49	0	0	2	11	1	0	0	19	16
Osteochondroma	8	35	0	0	0	7	0	0	0	11	17
Chondroblastoma	3	29	0	0	7	18	0	1	0	3	0
Periosteal chondroma	3	25	0	0	1	0	1	0	0	6	17
Subungual exostosis	2	22	0	0	0	0	0	0	0	0	22
Aneurysmal bone cyst	4	20	2	1	6	6	0	1	0	3	1
Enchondroma	2	14	0	0	0	3	0	0	0	3	8
Lipoma	3	9	0	0	0	8	0	0	0	1	0
Hemangioma	2	4	0	0	0	1	0	0	0	3	0
Fibrous dysplasia	2	3	0	0	1	0	1	1	0	0	0
Osteoma	1	1	0	0	0	0	0	0	0	1	0
Overall		357	2	1	62	125	3	3	0	62	99
Intermediate bone tumors	k	n	Tibia	Fibula	Talus	Calcaneus	Navicular	Cuboid	Cuneiform bones	Metatarsals	Phalanges
Giant cell tumor of bone	5	66	0	0	5	14	4	5	7	23	8
Osteblastoma	5	50	0	0	18	6	2	0	1	11	12
Desmoplastic fibroma	1	4	0	0	0	1	0	0	0	3	0
Langerhans cell histiocytosis	1	3	0	0	0	0	0	0	0	3	0
Overall		123	0	0	23	21	6	5	8	40	20
Malignant bone tumors	k	n	Tibia	Fibula	Talus	Calcaneus	Navicular	Cuboid	Cuneiform bones	Metatarsals	Phalanges
Chondrosarcoma	4	40	2	0	2	13	0	4	1	15	3
Ewing's sarcoma	4	24	0	0	1	10	0	0	1	11	1
Osteosarcoma	5	21	2	0	3	7	0	0	0	6	3
Fibrosarcoma	3	7	1	0	0	5	0	0	0	1	0

Pleomorphic sarcoma, undifferentiated	2	5	0	0	1	2	0	0	0	1	1
Giant cell tumor of bone, malignant	1	4	0	0	0	1	0	0	0	3	0
Bone metastases	2	3	2	0	0	0	0	1	0	0	0
Epithelioid hemangioendothelioma	2	2	0	0	0	0	0	0	0	2	0
Angiosarcoma	1	1	0	0	1	0	0	0	0	0	0
Plasmacytoma	1	1	0	0	0	1	0	0	0	0	0
Lymphoma	1	1	0	0	0	1	0	0	0	0	0
Overall		12	7	0	8	40	0	5	2	39	8

k, number of studies in which the tumor was described; n, sample size.

Table 5. Type of tumor *versus* patient sex.

Benign bone tumors	<i>k</i>	<i>n</i>	Male	Female
Simple bone cyst	7	262	155	107
Osteochondroma	6	85	44	41
Enchondroma	5	71	41	30
Chondromyxoid fibroma	4	46	25	21
Aneurysmal bone cyst	4	40	21	19
Chondroblastoma	5	38	28	10
Subungual exostosis	2	32	5	27
Lipoma	5	31	19	12
Osteoid osteoma	4	30	24	6
Non-ossifying fibroma	2	14	7	7
Periosteal chondroma	3	13	6	7
Hemangioma	3	8	4	4
Fibrous dysplasia	2	3	1	2
Bizarre parosteal osteochondromatous proliferation	1	3	3	0
Osteoma	2	2	0	2
Overall		678	383	295
Intermediate bone tumors	<i>k</i>	<i>n</i>	Male	Female
Giant cell tumor of bone	5	79	40	39
Osteoblastoma	5	42	22	20
Desmoplastic fibroma	2	4	3	1
Overall		125	65	60
Malignant bone tumors	<i>k</i>	<i>n</i>	Male	Female
Chondrosarcoma	7	57	39	18
Osteosarcoma	6	31	16	15
Ewing's sarcoma	4	29	20	9
Bone metastases	4	19	9	10
Epithelioid hemangioendothelioma	2	9	5	4
Fibrosarcoma	2	7	5	2
Malignant giant cell tumor of bone	1	4	3	1
Pleomorphic sarcoma, undifferentiated	3	4	3	1
Leiomyosarcoma	1	2	1	1
Plasmacytoma	1	1	1	0
Angiosarcoma	1	1	1	0
Lymphoma	1	1	1	0
Overall		165	104	61

k, number of studies in which the tumor was described; *n*, sample size.

Table 6. Type of tumor *versus* age group.

Benign bone tumors	k	n	< 20 yrs	20-59 yrs	≥ 60 yrs
Osteochondroma	3	18	13	5	0
Simple bone cyst	4	14	8	6	0
Aneurysmal bone cyst	3	12	10	2	0
Enchondroma	1	7	0	7	0
Chondroblastoma	2	3	1	2	0
Lipoma	3	3	1	2	0
Osteoid osteoma	2	2	2	0	0
Osteoma	2	2	0	2	0
Fibrous dysplasia	1	2	1	1	0
Chondromyxoid fibroma	1	1	0	1	0
Periosteal chondroma	1	1	0	1	0
Overall		65	36	29	0
Intermediate bone tumors	k	n	< 20 yrs	20-59 yrs	≥ 60 yrs
Giant cell tumor of bone	2	6	0	6	0
Osteoblastoma	3	4	0	4	0
Desmoplastic fibroma	1	1	0	1	0
Langerhans cell histiocytosis	1	1	1	0	0
Overall		12	1	11	0
Malignant bone tumors	k	n	< 20 yrs	20-59 yrs	≥ 60 yrs
Osteosarcoma	5	7	4	2	1
Chondrosarcoma	4	6	0	5	1
Pleomorphic sarcoma, undifferentiated	3	4	1	2	1
Giant cell tumor of bone, malignant	1	4	0	4	0
Fibrosarcoma	2	4	0	2	2
Ewing's sarcoma	2	3	1	2	0
Bone metastases	2	2	0	1	1
Leiomyosarcoma	1	2	0	2	0
Epithelioid hemangioendothelioma	1	1	0	1	0
Plasmacytoma	1	1	0	1	0
Lymphoma	1	1	0	0	1
Angiosarcoma	1	1	1	0	0
Overall		36	7	22	7

k, number of studies in which the tumor was described; n, sample size; yrs, years old.



PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	Page 1
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	Page 1
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	Page 2
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	Pages 2,3
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	Pages 3,4
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	Page 3
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	Pages 3,4
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	Page 4
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	Page 4
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	Page 4
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	Page 4
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	Pages 4,5
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	NA
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	Pages 3,4
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	Page 4,5
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	Page 5
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	Page 5
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	NA
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	NA
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	Pages 4,5
Certainty	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	NA

5. DISCUSSÃO

O objetivo deste estudo foi identificar dados epidemiológicos representativos para todos os tipos de tumores ósseos situados no pé e tornozelo. Os estudos que atenderam aos critérios de inclusão englobaram total de 2.438 tumores ósseos, agrupados em 33 tipos histológicos diferentes, de acordo com a última edição da classificação da OMS,²⁵ sendo 16 benignos, quatro intermediários e 13 malignos. Até onde sabemos, não há, na literatura, revisão sistemática caracterizando o perfil epidemiológico dos tumores situados no pé e tornozelo.

Para garantir a qualidade metodológica da revisão, buscando evitar viés de seleção, optamos por incluir apenas estudos epidemiológicos institucionais que abarcassem todos os tipos de tumores ósseos situados no pé e no tornozelo, buscando reproduzir a realidade da distribuição destas neoplasias.

Na nossa casuística, 1.722 tumores (70,7%) foram classificados como benignos, 269 (11,0%) como intermediários, e 447 (18,3%) como malignos. A predominância dos tumores benignos sobre os malignos no pé e tornozelo é consistente com a literatura existente. Ruggieri et al.¹⁵ (n=849) e Toepfer et al.¹⁰ (n=265) relataram achados similares à de nossa revisão, apresentando percentuais de tumores benignos respectivamente de 75,4% e 80,0%, enquanto Ozdemir et al.¹ (n=128), Özer et al.⁵ (n=157) e Delgado Cedillo et al.³² (n=83) detectaram percentuais maiores (respectivamente 87,5%, 85,4% e 90,4%) e Casadei et al.²⁷ (n=247) e Murari et al.²⁸ (n=249) identificaram percentuais menores (respectivamente 60,7% e 51,8%). Nenhum dos estudos incluídos apresentou extrato de tumores intermediários em suas amostragens, agrupando-os todos como benignos, muito embora esta categoria de tumores tenha sido incluída na classificação de tumores ósseos da OMS desde a sua

3.^a edição, publicada em 2002³³ - coube a nós estratificar a amostra, identificando e apartando os tumores benignos dos intermediários – obtivemos percentual de 11,0% de tumores intermediários, achado similar aos estudos de Casadei et al.²⁷ (n=247) e Bakotic et al.³⁰ (n=242) com percentual de 11,3% cada, enquanto Ozdemir et al.¹, Özer et al.⁵ e Ruggieri et al.¹⁵ identificaram percentuais pouco menores (respectivamente de 7,8%, 7,6% e 8,0%). Os estudos de Chou et al.¹² (n=14) e Bakotic et al.³⁰ (n=142) foram os únicos que identificaram maior percentual de tumores malignos; nossa casuística (18,3%) foi similar à encontrada nos estudos de Murari et al.²⁸ (16,5%) e Ruggieri et al.¹⁵ (16,6%), porém inferior à detectada nos estudos de Casadei et al.²⁷ (28,0%) e Bakotic et al.³⁰ (47,2%) e superior à de Ozdemir et al.¹ (4,7%), Özer et al.⁵ (6,6%) e Delgado Cedillo et al.³² (1,2%).

Entre os tumores ósseos benignos, o mais comum foi o encondroma (n=317; 18,4%), seguido pelo osteoma osteoide (n=297; 17,2%) e o COS (n=280; 16,3%). Estes achados, embora diferentes em termos percentuais, foram similares aos observados no maior estudo selecionado nesta revisão,¹⁵ que identificou os encondromas (37,0%) como os tumores benignos mais comuns, seguidos pelo osteoma osteoide (19,4%), divergindo quanto ao terceiro tumor mais comum, a proliferação osteocondromatosa parosteal bizarra (9,2%). Na sequência dos estudos com maior casuística, Toepfer et al.¹⁰ identificaram o COS, seguidos pelo encondroma e o osteocondroma como os tumores ósseos benignos mais frequentes, enquanto Murari et al.²⁸ observaram a sequência fibroma condromixoide>COS>condroblastoma e Casadei et al.²⁷ identificaram a sequência osteoma osteoide>COS>encondroma.

Em nossa casuística, dentre os tumores intermediários, os mais frequentes foram o TCGO (n=169; 62,8%) e o osteoblastoma (n=91; 33,8%), sequência similar (porém apresentando percentuais diferentes) às identificadas nos estudos de Ruggieri

et al.¹⁵, Murari et al.²⁸ e Toepfer et al.¹⁰. No estudo de Casadei et al.²⁷ observou-se empate no número destas neoplasias.

Identificamos que os tumores malignos mais frequentes foram, na ordem, condrossarcoma (n=118; 26,4%), sarcoma de Ewing (n=105; 23,5%) e osteossarcoma (n=91; 20,3%), achados corroborados pelo estudo de Özer et al.,⁵ que identificaram como mais frequente o condrossarcoma, embora em percentual muito maior (63%), seguido pelo sarcoma de Ewing e o osteossarcoma (cada um representando 18% dos casos).

Dentre os estudos incluídos, o segmento anatômico acometido foi reportado em 1.819 tumores. O retopé foi acometido em quase metade dos casos, seguido pelo antepé, médio-pé e tornozelo, corroborando os achados de Casadei et al.,²⁷ que reportaram o retopé, seguido pelo antepé e médio-pé como os segmentos mais comumente mais acometidos por tumores ósseos benignos e malignos; divergindo desta sequência, temos os estudos de Toepfer et al.¹⁰ (retopé>tornozelo>antepé>médio-pé) e de Murari et al.²⁸ (antepé>retopé>médio-pé).

Nos estudos incluídos em nossa revisão, apenas 583 tumores tiveram o osso acometido identificado. O calcâneo foi osso mais afetado (n=186, 31,9%), tanto pelos tumores benignos (n=125, 35,0%) quanto pelos malignos (n=40, 36,7%), enquanto os tumores intermediários foram encontrados mais frequentemente nos metatarsos (n=40, 32,5%). Nossos achados foram similares aos de Ozdemir et al.,¹ que identificaram o calcâneo como sítio afetado em 33,0% dos casos. Murari et al.²⁸, entretanto, observaram maior incidência (35,2%) de tumores situados nos metatarsos.

Quanto ao sexo afetado, nos estudos em que este dado foi identificado, observamos predominância do sexo masculino, correspondendo a 55,6% (n=538); o sexo feminino foi afetado em 44,4% (n=430) dos casos – esta ascendência também

foi identificada nos estudos de Toepfer et al.¹⁰ (61,5%) e de Murari et al.²⁸ (61,4%). Em nossa casuística: (i) o sexo masculino foi afetado em 56,5% (n=383) e o feminino em 43,5% (n=295) dos tumores benignos; (ii) o sexo masculino foi afetado em 52% (n=65) e o feminino em 48% (n=60) dos tumores intermediários; e, (iii) a incidência de tumores malignos foi consideravelmente maior no sexo masculino, afetado em 63% (n=104) e o feminino em 37% (n=61) dos casos. Outros estudos identificaram achados similares: dentre 231 tumores ósseos benignos descritos em seu estudo, Toepfer et al.¹⁰ identificaram 138 (59,7%) acometendo homens e 93 (40,3%) afetando mulheres; dos 35 tumores ósseos malignos, 20 (57,1%) afetaram o sexo masculino e 15 (42,9%), o feminino. Murari et al.²⁸ relataram 208 tumores ósseos benignos, 130 (62,5%) afetando homens e 78 (37,5%), mulheres; dentre os 41 tumores ósseos malignos, 56,1% (n=23) afetaram homens e 43,9% (n=18), mulheres.

Menos de 5% de nossa casuística continha informações a propósito da idade de acometimento dos pacientes. Nos estudos em que este dado foi descrito, os tumores foram mais frequentemente detectados na faixa intermediária (20-59 anos), seguida pelas faixas etárias <20 anos e ≥60 anos. Os tumores benignos predominaram nas faixas <20 anos (84,1% dos casos) e 20-59 anos (64,5% dos casos), achado inverso aos dos tumores malignos, que corresponderam a 100% dos tumores na faixa ≥60 anos, 35,48% na faixa 20-59 anos e 15,90% na faixa <20 anos. Kinoshita et al.,²⁹ em sua casuística, não identificaram tumores ósseos malignos nos pacientes <50 anos; metade dos tumores descritos nos pacientes >50 anos eram malignos. Toepfer et al.¹⁰ também observaram aumento na frequência de tumores ósseos malignos com o avançar da idade.

Este estudo apresenta limitações que demandam destaque. Em primeiro lugar, a heterogeneidade entre os estudos incluídos, especialmente no que diz

respeito aos métodos de coleta de dados, seguimento e classificação dos tumores, que pode introduzir vieses; muitos artigos apresentavam dados incompletos, dificultando análises mais abrangentes. Outra limitação é que nossa casuística diz respeito apenas a tumores ósseos tratados cirurgicamente, definindo o diagnóstico histológico. Outro aspecto digno de nota é que a maior parte das informações disponíveis provém de estudos realizados em países europeus, o que pode limitar a generalização dos resultados para populações de outras regiões, considerando possíveis variações genéticas, ambientais e aquelas relacionadas aos sistemas de saúde. Adicionalmente, centros oncológicos de grande relevância mundial frequentemente coletam dados epidemiológicos representativos, mas nem sempre publicam essas informações nas bases de dados analisadas; a exclusão de fontes não publicadas pode ter restrito o escopo de nossa análise.

6. CONSIDERAÇÕES FINAIS

Esta revisão sistemática forneceu caracterização abrangente dos tumores ósseos do pé e tornozelo, abordando o tipo histológico, localização anatômica, osso acometido, sexo e faixa etária de acometimento.

Foram incluídos 17 estudos, perfazendo 2.438 tumores, 70,7% benignos, 11,0% intermediários e 18,3% malignos. Os tumores benignos mais frequentes foram encondroma, osteoma osteoide e COS; os tumores intermediários mais comuns foram TCGO e osteblastoma; os tumores malignos mais frequentes foram condrossarcoma, sarcoma de Ewing e osteossarcoma.

O retropé foi o segmento mais acometido (n=829; 45,6%), seguido pelo antepé (n=552; 30,3%), médio-pé (n=305; 16,8%) e tornozelo (n=133; 7,3%)

O calcâneo foi o osso mais acometido entre os tumores benignos (35,0%) e malignos (36,7%), enquanto os metatarsos (32,5%) constituíram o sítio mais frequente de tumores intermediários.

Houve predominância do sexo masculino (55,6%), ainda maior nos casos de tumores malignos (63%).

Tumores benignos foram mais frequentes em indivíduos <20 anos; tumores intermediários e malignos predominaram entre 20-59 anos; todos os tumores diagnosticados em indivíduos ≥60 anos foram malignos.

Embora a heterogeneidade das informações obtidas a partir dos estudos tenha constituído desafio para comparações absolutas, os achados desta revisão foram consistentes, possibilitando maior compreensão sobre a epidemiologia dos tumores ósseos situados no pé e tornozelo.

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1. ANEXOS

Anexo 1. Submissão à revista *Foot & Ankle International*.

05/06/2025, 13:36

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Manuscript ID

FAI-25-0427

Title

Epidemiology of bone tumors of the foot and ankle – A systematic review

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Anexo 2. Normas de publicação da revista *Foot & Ankle International*.

Please read the guidelines below then [submit your manuscript here](#).

Hide all

Key information

Foot & Ankle International (FAI) welcomes articles that contribute to orthopaedic science as it relates to the foot and ankle. Articles are welcome from all countries and all sources under the following conditions:

- Articles are accepted only for exclusive publication in *Foot & Ankle International*.
- Publication does NOT constitute official endorsement of opinions presented in articles.
- Published articles and illustrations become the property of *Foot & Ankle International*.
- Manuscripts not prepared according to the instructions below will be returned.

What We Publish

1. Clinical and Biomedical Scientific Manuscripts
2. Short Scientific Reports
3. Systematic Review/Meta-Analyses
4. Contemporary Reviews
5. Letters to the Editor

What We Do Not Publish

1. Case Reports
2. Technique Tips
3. Language/country specific translations of outcome instruments.
4. Bibliometric papers
5. Qualitative or mixed methods research
6. "Learning curve" Manuscripts
7. Large Language Models (LLM) evaluations

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NIH and Wellcome Trust-Funded Submissions

Authors should check the box at submission if a manuscript was funded by NIH or Wellcome Trust. If the article is accepted to *FAI*, the article will be automatically deposited to PubMed Central (PMC). This service previously cost \$3,000 and was only available after the print publication of the article. It is now completely free and the article will be deposited automatically within 6 months for Wellcome Trust and 12 months for NIH.

Preparing your manuscript for submission

Your article must be within the scope of the journal and be of sufficient quality. If not, it will not be reviewed. Please read the journal’s [Aims and Scope](#) to see if your article is appropriate.

The manuscript must be your original work, you must have the rights to the work, and you must have obtained and be able to supply all necessary permissions for the reproduction of any copyright works not owned by you, including figures, illustrations, tables, lengthy quotations, or other material previously published elsewhere.

Preparing Manuscript

Manuscript Body

Manuscripts should be organized in the following order: Title, Abstract, Level of Evidence (Clinical Research) / Clinical Relevance (Basic Science), Keywords, Introduction, Methods, Results, Discussion, Conclusion, References.

Introduction

Establish relevance of question

- Why is study important?
- Why is question interesting or controversial?
- What is the gap in the literature you're filling?
- Do not repeat the same in the Discussion

Methods

The Methods section must define the period during which the study was conducted, the specific criteria for inclusion and exclusion of patients, and the duration of follow-up. For retrospective studies, all patients who meet the inclusion/exclusion criteria in the specified time period should form the study population and the reasons for any additional exclusions should be reported (i.e. death, loss to follow-up, study withdrawal, etc.).

Provide enough details to replicate your procedures. In particular, surgical techniques must be described well enough so another surgeon can reproduce the procedure.

Considerations for the Statistical Analysis section

Please refer to the Author Guidelines at JAMA Network "Statistical Methods and Data Presentation" section

at <https://jamanetwork.com/journals/jamanetworkopen/pages/instructions-for-authors#Ref1> for a detailed set of specifications and principles that FAI and FAO are aiming to achieve in the submissions. Furthermore, FAI and FAO endorse the guidelines (as mentioned in the above JAMA Network link) in the publication '*Reporting statistical information in medical journal articles*' by Cummings and Rivara (2003). [Cummings P, Rivara FP. Reporting statistical information in medical journal articles. *Arch Pediatr Adolesc Med*. 2003;157(4):321-324. [doi:10.1001/archpedi.157.4.321](https://doi.org/10.1001/archpedi.157.4.321).]

Briefly, the Statistical Analysis section must describe:

- Whether the analysis is framed as exploratory or hypothesis-testing (see JAMA source above for explanation)
- All analyses performed in the study including demographic and sample characteristics for the study population and any comparative groups (e.g. group means, standard deviations).
- How missing data was treated (e.g. imputation, excluded from analyses)
- If performed, correction for multiple hypothesis testing (e.g. Bonferroni) and how it is expressed in the Results

- The software used for analysis

STATISTICAL SAMPLE SIZE CALCULATION GUIDELINES

With regard to sample size for a study, we recommend:

1. Inclusion in methodology: In general, research submissions should detail their sample size calculation in the methods section and specify whether it was performed *a priori* or *post hoc*. In certain contexts, this may not be necessary, including exploratory or descriptive studies, pilot studies, quality improvement initiatives, and qualitative research studies. The study research question and objectives should be framed accordingly, and the sample size should be sufficient to provide meaningful insights. Please consult the JAMA Network source above for further detail regarding which types of studies require *a priori* and *post hoc* power analyses.
2. Acknowledging absence of an *a priori* calculation: If an *a priori* sample size calculation was not conducted, this omission should be highlighted in the discussion as a methodological weakness. As noted above, authors should supply in tables sufficient aggregated results (eg, group means and sample sizes) for readers to independently perform a post-hoc power analysis.
3. Addressing underpowered studies: If a sample size calculation indicates a study is underpowered, this should be mentioned in the study limitations along with details regarding the necessary number of subjects to ensure the research has adequate power.

These recommendations aim to enhance the transparency and reliability of research through careful consideration of sample size and power analysis.

We recommend that authors use the following UCSF "sample size and power calculation" web page: <https://data.ucsf.edu/research/sample-size>.

Reporting and Discussion of Results

- Ninety-five percent confidence intervals must be calculated for point estimates (e.g. hazard ratios, odds ratios) whenever the results of survivorship or logistic regression analysis are given in the text or in graphs. Authors are encouraged to use 95% confidence intervals in addition to or instead of standard deviations when reporting results. If presenting confidence intervals other than 95% (e.g., 90%), this decision must be justified.
- The statement that "no significant difference was found between two groups" cannot be made unless an *a priori* power analysis was performed and the value of alpha or beta is reported. In most cases, a sufficient number of patients (depending on the group differences in the main outcome, which can be expressed as an effect size) with the conventional $\alpha=0.05$ with power=0.80, and often more, in each group is required to make such a statement. If no such power study was done and sufficient sample is not present, the author must state: "With the numbers available, no significant difference could be detected."

- The term 'significant' should only be used to describe statistical significance and should be reported along with a *P* value.

The word "correlation" requires reporting of the Pearson correlation coefficient (*r*) or Spearman rank correlation (*r_s*) (when assumptions of parametric analysis are not met).

Results

Provide a detailed report on the data obtained during the study

General outline for clinical studies:

- Paragraph(s) 1
 - Demographics, baseline characteristics (Table(s) 1)
 - Participant flow (FIGURE 1)
- Paragraph(s) 2
 - What did you find in terms of Primary Objective? (Table/Figure 2)
- Paragraph(s) 3
 - What did you find in terms of secondary objectives?
- Paragraph(s) 4
 - Sensitivity analyses, exploratory aims

Tables and text should complement each other, not repeat each other.

- Summarize key point in text, then refer to table.
- If table can be summarized in 1 sentence, delete the table.

Discussion

Paragraph 1: General summary statement of primary aim. Do not paste in all results. Results should be in Results and not appear first in Discussion!

Paragraph(s) 2: How do results fit with current literature?

- What are differences between this study and others?
- Speculate on why your findings differ.
- Summarize directions of the literature, not each and every manuscript.
- Reference source documents when possible.
- Claims of priority ("This is the first...") must be backed up.

Paragraph(s) 3

- Balanced (humble) analysis of strengths and limitations

- If study is underpowered, the discussion should specify how many subjects needed to ensure the research has adequate power.
- Generalizability
- Subjects: All patients vs Women only, Men only
- Geography/Culture: Women in Rio vs Women in Alaska Setting: Tertiary Center/Expert Surgeon vs Generalist

Conclusion

Paragraph 4

- Implications of the Findings
- Possible mechanisms
- What is the meaning for:
 - Patients
 - Providers

Legends

All artwork (figures and tables) submitted must have text included here, listed in order. Explain what each illustration shows rather than simply defining it. Give the amount of magnification of all photomicrographs. Define all arrows and other such indicators appearing, when necessary. If an illustration is of a patient who is identified by a case number in the text or table, include that case number in the legend. If a piece of artwork has been published elsewhere prior to this article and permission to include it has been granted, include proper attribution in the figure legend here.

Reporting Guidelines Checklist

All full-length original clinical submissions require a checklist to be completed. The following checklists should be completed and submitted for these types of study:

- Randomized Control Trial: [CONSORT 2010](#)
- Observational Studies: [STROBE fillable form](#) (or [here](#))
- Systematic Reviews/Meta-analysis of Observational Studies: [MOOSE](#)
- Systematic Reviews/Meta-analysis of RCTs: [PRISMA 2020](#)

What We Publish

Type of Article	Number of Words: Manuscript	Number of Words: Abstract	Figures	Tables	References
Clinical or Biomedical Scientific Manuscript	3,000	300	8	4	No limit
Short Scientific Report	1,200	225	3 total figures &/or tables	3 total figures &/or tables	10
Systematic Review / Meta-Analysis	3,000	250	4	4	No limit
Contemporary Review	4,000	n/a	10	3	No limit
Letter to the Editor	400	n/a	1 total figure or table	1 total figure or table	5

Short Scientific Report

Short scientific reports are suitable for the presentation of research that presents preliminary data on novel treatments, extends previously published research including the reporting of additional controls, confirmatory results in other settings or even patients from the same cohort. Authors must clearly acknowledge any work upon which they are building, both published and unpublished. The Editor may ask authors to convert a full-length submission to a Short Scientific Report for the purposes of publication. Reviews, case reports, and technique tips are not considered for publication under this category.

Briefly summarize the results of original data. Each short scientific report is considered a scientific publication; authors must meet all requirements regarding responsible conduct of research (eg., appropriate IRB approval, data integrity, data retention).

Short scientific reports are limited to 1200 words with 3 figures and/or tables (not counting the title page, abstract, references, or legends). We allow a maximum of 10 highly relevant references. Online supplementary materials are permitted. Abstracts are limited to 225 words and include Background, Methods, Results, and Conclusion. The text body should include the following truncated sections: Introduction, Methods, Results, Discussion/Conclusion with enough detail or appropriate references to help others reproduce the investigation. Include Clinical Relevance for basic-science articles or Level of Evidence for clinical research articles. Keywords should describe the information contained in the paper, including any terms unique to the paper's subject.

Scientific Manuscripts

Maximum Limits:

Text Body: 3,000 words, Abstract: 300 words, 4 Tables, 8 Figures

Total Ankle Arthroplasty (TAA) Manuscripts

1. TAA manuscripts must have a minimum of two-year follow-up for all patients in the study. Complications or implant issues can be reported with shorter follow-up. All repeat surgeries must be documented for all time points from the time of the index TAA.
2. Repeat surgery can be reported individually or as a series of events. The authors should outline which method was used.
3. Non-surgical complications (such as DVT, pulmonary embolism or infection treated by antibiotics) should be documented.
4. The template below should be used as a **guide** for authors in reporting complications resulting in reoperation(s). This is based on the COFAS Ankle Arthritis Study Group coding system for reporting reoperations. Overlap will occur for some of these categories as individual patients may have had more than one re-operation. The intent is to distinguish between different types of complications resulting in reoperation (instead of simply reporting that a certain number of patients in a study had re-operations).
 1. No reoperation
 2. Hardware removal related to TAA (e.g. medial malleolus screw(s), fibular plate)
 3. Subsequent operative treatment related to TAA but not involving TAA components
(e.g. osteotomy, fusion of other joint(s) of the foot, ligament repair/reconstruction)
 4. Operative treatment of periprosthetic fracture(s)
 1. At the time of the index procedure
 2. After the index procedure
 5. Debridement of gutter or heterotopic ossification with retention of components
 6. Polyethylene liner exchange for polyethylene wear or fracture
 7. Operative treatment of postoperative arthrofibrosis
(e.g. joint debridement +/- capsulotomy, Achilles lengthening, PE liner exchange)
 8. Debridement +/- grafting of osteolytic cyst(s)
(with retention of metal components +/- polyethylene exchange)
 9. Operative treatment of superficial infection or incision problem
(e.g. I & D, secondary closure)

10. Operative treatment of deep infection requiring debridement
(+/- polyethylene liner exchange but NOT removal of metal components)
11. Deep Infection requiring removal of ALL components
 1. One stage TAA revision to TAA
 2. Two stage TAA revision to TAA
 3. Conversion to “long term” cement spacer
 4. Conversion to arthrodesis
12. Revision of metal components because of implant failure
(e.g. aseptic loosening, subsidence, malposition, implant fracture --- not for infection)
 1. Tibia
 2. Talus
 3. Both tibia and talus revised to TAA
 4. Removal of components and conversion to arthrodesis
13. Amputation related to complications from TAA
State reason(s): pain, infection, vascular compromise, failed prior treatments, patient choice, etc.

Randomized Controlled Trials (RCTs)

Randomized Controlled Trials (RCTs) must be prospectively registered in a publicly searchable clinical trials registry before considering review for publication from 1 January, 2020. RCTs, which started after the date of electronic publication of the editorial policy for *Foot & Ankle International (FAI)* in the transition period in 2019, as well as RCTs with satisfactory evidence of starting before electronic publication of the editorial policy for *FAI*, shall be allowed retrospective registration in a publicly searchable clinical trials registry prior to review and potential publication. The Editorial Board, however, will reserve the right to make rare exceptions in the event of unusual studies in extenuating circumstances following guidance from the Editor in Chief with an explanatory note from the authors regarding the reasons and an Editorial note for the exception, published as a foot note to the article.

Biomechanical Scientific Manuscripts

Submit biomechanical manuscripts under Basic Science and include a Clinical Relevance statement with abstract.

- **Biomechanical Models:** All biomedical science models should represent clinically relevant and realistic situations. With biomechanical studies, in particular, the editors strongly discourage the use of surrogate Bone models (e.g., Sawbones) except as detailed below:

1. Method development for biomechanical testing using actual bone.
2. Determining mechanical properties and/or mechanical performance of an implant that exclude the mechanical properties and/or mechanical performance of the implant-sawbones interface.
3. Determining mechanical properties and/or mechanical performance of different implant-bone constructs with anatomically (geometrically) representative sawbones models that are validated for mechanical properties and implant-bone interface properties.
4. Bone anatomy related geometric studies (e.g., osteotomy correction, surgical navigation registration, certain imaging investigations)

In addition, other biomechanical studies have been published periodically that have inaccurate models to represent clinical reality. For example, an Achilles transection model is very different from a clinical rupture with significant shredding of tissue at the rupture site. In this case, investigators try to simulate an Achilles tendon rupture more validly (i.e., some degree of shredding at the damaged tendon site) so the findings can mirror clinically relevant and realistic situations.

Meta-analysis / Systematic Review

Submit meta-analysis / systematic reviews under clinical research. Do not include Level of Evidence with the abstract.

Systematic reviews and meta-analysis techniques are used to review and pool data obtained from high quality studies usually with Level I or II evidence. These techniques require determination of a specific health care question, selection of studies which meet research methodology and quality standards, and then application of rigorous methodology to minimize error, bias, and inaccurate or misleading conclusions. It is recommended that authors have or obtain expertise in these types of studies and plan their methodology accordingly. Working with an experienced librarian and statistician with specialized skills is highly recommended. Studies which conclude that the quality of existing literature is not adequate (poor) and that more studies are needed, provide little useful information to the reader and will seldom be accepted for publication.

Contemporary Reviews

A Contemporary Review serves to educate the readership about conditions and/or procedures. Covered topics typically have a narrow focus or describe new procedures associated with limited clinical evidence. Word count is 4000 words excluding references. Do not include abstract or Level of Evidence.

Authors can contact the Senior Editor for Contemporary Reviews, Christopher P. Chiodo, MD, to find out if *FAI* or *FAO* have recently published a review article on that topic, if there is a similar submission in progress or if the subject matter is considered in scope for the journals. Email Dr. Chiodo at ContemporaryReviews@aofas.org (cc: FAIjournal@aofas.org) to inquire about your idea.

Submit completed papers directly to the journal at <https://mc.manuscriptcentral.com/faj>. All submitted Contemporary Review Articles will be considered by the Contemporary Review Editors

Format of a Contemporary Review

1. Introduction. Present a brief overview and purpose statement - Why is this condition worthy of a review?
2. Background of the condition(s). Summarize relevant background information. This may include a historical survey, basic science, pertinent clinical studies, and current controversies related to the condition.
3. Presentation. Briefly describe the typical clinical presentation of the condition(s).
 - a. history
 - b. physical examination
 - c. radiographic/imaging and laboratory findings
4. Treatment. Describe both non-operative and operative treatment options.
 - a. This section can be divided into subsections (e.g. addressing a treatment option or set of treatment options). Each subsection should then be comprised of one or more paragraphs. The introductory topic sentence(s) of each subsection should neatly frame the issue. When possible, this should be a specific, direct query that begs an affirmative or negative response. Sometimes the issue is framed with a broad, generalized question that is then broken with specific details in a succession of paragraphs.
5. Complications. If applicable, describe the relevant and most common complications associated with a surgical procedure or non-operative treatment.
6. Authors' preferred method of treatment (optional). If applicable, this section can include your preferred treatment for a described condition. Please make sure to include your rationale and include any technique tips that you feel may help the reader.
7. Summary of the Main Points. Include four to eight main points of your manuscript. These may include treatment options with a growing body of evidence in the literature. Significant, unresolved controversies may be included with a brief discussion of the opposing viewpoints.

8. References. Alphabetical and as formatted per *Foot & Ankle International* guidelines. Try to use only recent or essential references.
9. Figures and Legends: A key feature of the Contemporary Reviews is to illustrate anatomic pathology, key imaging findings and surgical technique.
 - a. Maximum Number of Tables: 3
 - b. Maximum Number of Figures: 10

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Letters may have no more than 3 authors. The text should include the full name, academic degrees, and a single institutional affiliation for each author and the email address for the corresponding author.

Letters discussing an article in this journal should be submitted within 4 months of publication of the article in print. Letters received after 4 months will rarely be considered. Letters should not exceed 400 words of text, one (1) figure or table and 5 references (including a required citation to the related article). All data presented must be fully citable and cited in the supporting reference list (unpublished data must not be described in the letter).

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Language/country specific translations of outcome instruments

The Editorial Board has decided not to publish any additional language/country specific translations of outcome instruments. While the methodology is important within the specific country or for the language of interest, it is not germane to the other countries of our international audience. Please submit directly to [Foot & Ankle Orthopaedics](#).

Bibliometric papers

Bibliometric methods are used to help estimate how much influence or impact a selected research article or individual researcher has had on the wider research community. It usually does this by counting the number of times an article is cited after it is published. These analyses can be used to track researcher output and impact related tenure, promotion and grant funding decisions. Their utility to the readership of *Foot & Ankle International* is minimal at best. For this reason *FAI* and *FAO* will not publish bibliometric papers.

Qualitative or mixed methods research

Although qualitative or mixed methods research can influence the direction of research or trial design, the AOFAS journals are generally focused on nearer term impact. Neither our peer reviewer pool nor our restrictions on word count are aligned with publishing qualitative or mixed methods research at *FAI* or *FAO*.

“Learning curve” Manuscripts

Orthopaedic “learning curve” papers deal with the attainment of proficiency in new surgical techniques or implants. The development of psychomotor surgical skills is a complex educational process, poorly measured by surgical time or predefined benchmark skills as indirect measures of proficiency. The generalizability of such data is also poor, inadequately reflecting care by all surgeons in various settings. Learning curve papers thus offer little to the readership of *FAI* and *FAO* and therefore will not be considered for publication.

Large Language Models (LLM) evaluations

Submissions evaluating Large Language Models (LLMs) such as ChatGPT, Claude, or Perplexity and their ability to answer patient questions about orthopaedic conditions will only be considered for publication in *Foot & Ankle Orthopaedics (FAO)*, rather than *Foot & Ankle International (FAI)*, which prioritizes hypothesis-driven clinical research.

AOFAS Clinical Rating Systems – Do Not Use

We do not accept papers that rely primarily on the AOFAS Clinical Rating systems to assess patient outcomes from treatments. As stated in the 2011 AOFAS Position Statement Regarding the Future of the AOFAS Clinical Rating Systems and further emphasized in the 2014 AOFAS Position Statement Regarding Patient-Reported Outcome Measures, scores from the AOFAS Clinical Scoring Systems have not been found to be valid or reliable.

Pinsker E, Daniels TR. AOFAS Position Statement Regarding the Future of the AOFAS Clinical Rating Systems. *Foot & Ankle International*. 2011;32(9):841-842. doi:10.3113/FAI.2011.0841

Kitaoka HB, Meeker JE, Phisitkul P, Adams SB, Kaplan JR, Wagner E. AOFAS Position Statement Regarding Patient-Reported Outcome Measures. Foot & Ankle International. 2018;39(12):1389-1393. doi:10.1177/1071100718809066

Language to communicate specific regions and motions of the foot and ankle

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The average age was 46 (range, 38-74) years.
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J Bone Joint Surg Am, 2015 Jan 07; 97 (1): 1-

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Anexo 3. Declaração CEP HSI-SCMBA.

DECLARAÇÃO

Declaro, para os devidos fins, que, de acordo com normas regimentais da Comissão Nacional de Ética em Pesquisa envolvendo Seres Humanos (CONEP) do Ministério da Saúde (Resolução 510/16 do CNS/MS), a pesquisa intitulada “Epidemiologia dos tumores ósseos do pé e tornozelo - Uma revisão sistemática”, de autoria do Pesquisador Fernando Delmonte Moreira, não é passível de apreciação ética pelo Sistema CEP/CONEP:

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- (...)

Diante do exposto, colocamo-nos à disposição para quaisquer outros esclarecimentos.

Salvador, 08 de junho de 2025.

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