SYSTEMATIC REVIEW

Bone Mineral Density Changes in Multiple Endocrine Neoplasia Type 1: A Systematic Review and Meta-Analysis of Prevalence and Parathyroidectomy Outcomes

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Abstract

Objectives: This study aimed to analyze the prevalence of osteopenia and osteoporosis in MEN1-related primary hyperparathyroidism (PHPT), examine the impact of parathyroidectomy (PTX) on bone metabolic outcomes, and compare bone density metrics between sporadic and MEN1-related PHPT.

Methods: A systematic review and meta-analysis were conducted in accordance with the guidelines for Meta-Analyses and Systematic Reviews of Observational Studies (MOOSE). We searched PubMed, Web of Science, and Scopus up to June 2024, subsequently screening the articles to identify relevant research. Studies focusing on bone mineral density (BMD), T and Z-scores in patients with MEN1-related conditions were included. Meta-analyses were conducted using random-effects models.

Results: From the initial 2,563 articles, 15 studies were included in the meta-analysis. The pooled prevalence of osteoporosis and osteopenia in patients with MEN1-related PHPT was 45.2% (95% CI: 39.1-51.4%; I2: 16.7%) and 53.3% (95% CI: 44.4-62.0%; I2: 36.15%), respectively. PTX showed no significant impact on BMD in MEN1-related PHPT patients at the lumbar spine (mean difference: -0.054; P-value = 0.092; I2: 0.86%) or femoral neck (mean difference: -0.025; P-value = 0.219; I2: 0.47%). Comparisons of bone density metrics showed that MEN1-related PHPT patients had significantly lower Z-scores at the lumbar spine (mean difference: -0.676; P-value < 0.001; I2: 41.86%), total hip (mean difference: -0.629; P < 0.001; I2: 23.4%), and femoral neck (mean difference: -0.516; P < 0.001; I2 = 38.82%) compared to patients with sporadic PHPT.

Conclusion: Patients with MEN1-related PHPT exhibited a high prevalence of osteopenia and osteoporosis, along with lower BMD metrics compared to those with sporadic PHPT. PTX was not associated with significant changes in BMD among MEN1-related PHPT patients.

Level of evidence: V

Keywords: Bone mineral density, Meta-analysis, Multiple endocrine neoplasia, Primary hyperparathyroidism

Introduction

Multiple endocrine neoplasia (MEN) syndromes are hereditary conditions characterized by the simultaneous development of two or more endocrine tumors.[1] Depending on the affected organs, MEN syndromes are classified into four types: MEN1, MEN2, MEN3, and MEN4.[2] MEN1 is characterized by the presence of two or more of the following: a) parathyroid disorders (primary hyperparathyroidism or PHPT), b) tumors of the anterior pituitary gland, and c) duodenopancreatic neuroendocrine tumors.[3] Among the various endocrine disorders associated with MEN1, PHPT is the most prevalent, typically manifesting by the mid-20s, with nearly all patients showing symptoms by age 50.[4]

Overactivity of the parathyroid glands in patients with

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MEN1-related PHPT predisposes them to complications such as reduced bone mineral density (BMD).[5,6] Studies have demonstrated that patients with MEN1-related PHPT often exhibit lower BMD compared to those with sporadic PHPT, particularly at the femoral neck (FN) and lumbar spine (LS).[7] The reduction in BMD and the increased risk of osteoporotic fractures in individuals with MEN1 are particularly concerning, as these metabolic changes can be observed as early as the third decade of life.[6] Furthermore, MEN1-related PHPT may present with pathological fractures, as evidenced by previous studies.[8,9]

Given the decreased BMD among patients with MEN, the present meta-analysis was conducted to assess bone metabolism outcomes within this population. Specifically, we aimed to determine the prevalence of osteopenia and osteoporosis, investigate the effects of parathyroidectomy (PTX) on MEN1-related PHPT, and compare the bone metabolic characteristics of MEN1-related PHPT with those of sporadic PHPT.

Materials and Methods

This review has been carried out in accordance with the guidelines for Meta-Analyses and Systematic Reviews of Observational Studies (MOOSE).[10] This study was designed accordingly and registered with the PROSPERO International Prospective Register of Systematic Reviews (registration No. CRD42024582930).

Search Strategy

We used three electronic databases: PubMed, Web of Science (WoS), and Scopus. To ensure that we did not overlook any relevant articles, we employed broad keywords. The medical subject heading (MeSH) terms used were "multiple endocrine neoplasia" and "osteoporosis" combined with the following additional search terms using Boolean operators: (osteopor* OR postmenopausal OR osteopen* OR osteopaen* OR fragility OR fracture* OR bone OR dense* OR density OR LBD OR BMD OR FRAX* OR z-score OR t-score).

Eligibility Criteria

The main objective of the present study was to assess the prevalence of osteoporosis and osteopenia in patients with MEN1.

Two additional outcomes were obtained: a comparison of bone mass density metrics (BMD, T-scores, and Z-scores) between patients with MEN1-related hyperparathyroidism and those with sporadic hyperparathyroidism, as well as a pre- and post-parathyroidectomy comparison of bone mass density metrics (including BMD, T-scores, and Z-scores) among patients with MEN1-related PHPT.

For this purpose, we included only observational studies. To assess the prevalence, we included cross-sectional studies, case-series, and cohort studies that reported the prevalence of osteoporosis or osteopenia (outcome) among adults with MEN1-related PHPT (population) at baseline. Furthermore, to evaluate changes in BMD changes before and after PTX, we included cohort studies. In order to compare BMD metrics between sporadic and MEN1-related PHPT, we used observational studies that provided pre-operative reports on BMD profiles.

The exclusion criteria were as follows: (i) articles written in a language other than English and (ii) abstracts of papers presented at conferences, and (iii) non-observational studies, including clinical trials.

Furthermore, the included articles were those published from inception until June 9th, 2024. Moreover, to ensure the inclusion of all relevant articles, those with related findings were manually searched based on their references. Two separate authors (VM and ME) conducted all screening processes.

Selection Process

The selection process for the included studies was conducted systematically and transparently to ensure the reliability of the findings. Initially, we used the MeSH terms and predefined keywords to find relevant articles across three databases. Subsequently, the titles and abstracts of the retrieved articles were screened for initial eligibility based on predetermined criteria; articles that did not meet the inclusion criteria were excluded at this stage. The full texts of the remaining articles were then carefully assessed, and those that reported irrelevant outcomes or were published in languages other than English were excluded from the review. The selection process was conducted by VM and ME, and any discrepancies were resolved through consensus.

Data Extraction

Data extraction in this study was facilitated through the use of a data collection sheet. This sheet included fields for bibliographic information, year of publication, study design and location, sex distribution, age, the studied bone sites, and outcome variables. This method enabled meaningful comparisons and meta-analyses. We assigned serial numbers to the included articles to facilitate the data extraction process. One of the authors reviewed all the included articles and extracted the data accordingly using the data collection sheet. The initial data collection sheet was conducted by VM, followed by a double-check of the records by ME.

Quality Assessment

The Newcastle-Ottawa Scale (NOS) was used in this study to assess the quality of the included studies. The NOS tool evaluates studies based on three main criteria: the selection of study groups, the comparability of the groups, and the exposure or outcome of the study.[11] Two independent reviewers evaluated each paper, and any discrepancies were resolved through discussion. VM and ME conducted the quality assessment.

Data Synthesis

The meta-analysis was performed using Comprehensive Meta-Analysis V2 software. The prevalence and 95% confidence intervals were reported. Moreover, for two-group studies (including comparisons between pre- and post-parathyroidectomy as well as between MEN and sporadic hyperparathyroidism), the differences in means and 95% CI were calculated and reported. We also performed a sensitivity analysis using a leave-one-out approach to assess the impact of each study on the overall effect size. A P-value of less than 0.05 was considered statistically significant. Since the number of included studies in a two-group comparison

was fewer than 10, we did not consider a funnel plot. Publication bias was assessed using Egger's regression test.

Results

As shown in Figure 1, the primary search yielded 2563 articles. After removing duplicate records and excluding articles based on study design, irrelevant subjects, language barriers, and inaccessibility, a total of 15 articles were included in the meta-analysis [Figure 1].

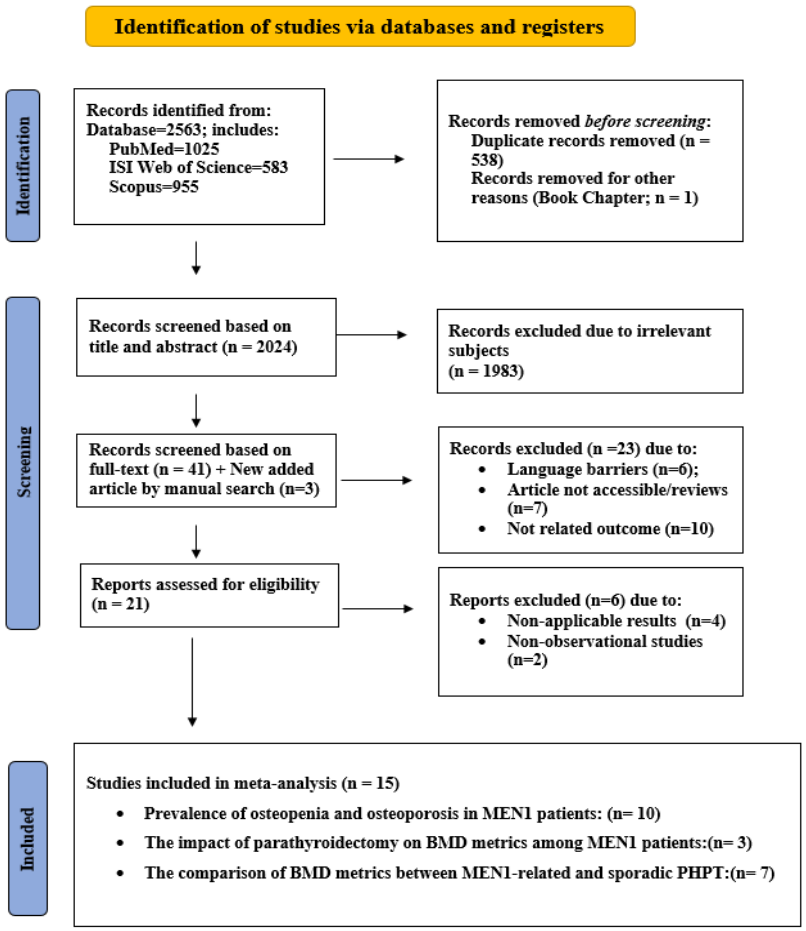

Figure 1. The flow diagram of searches

Study Characteristics

The present meta-analysis included 15 studies conducted between 2008 and 2023, of which 11 were published after 2010. Furthermore, the studies exhibited a balanced geographical distribution, comprising five from Asia, four from Europe, and six from America. The included studies varied in sample sizes, with some involving as few as eight individuals, while others included up to 715 participants. The age range among the studies varied; however, the majority focused on adults aged 30 to 45 years. The sex distribution across the studies revealed that females were the predominant gender in most studies.[5-7,12-18] Different bone sites were studied, including FN, LS, total hip (TH), trochanter, distal one-third radius, and ultra-distal radius; however, some studies did not specify the exact bone site examined.[16,17,19] LS,[5-7,12-15,18,20-23] and femur[1,6,7,12-15,18,20-23] were the predominant bone sites [Table 1].

Quality Assessment

The quality assessment results for the included studies, which employed various study designs, indicated that all studies demonstrated acceptable quality. Four of the cohort studies achieved the maximum score, while six scored 6 out of 9, primarily due to the absence of a control group. The case-control study also recieved a maximum score. Furthermore, all cross-sectional studies earned 6 out of 7 stars, with the exception of the study by Eller-Vainicher et al.,[12] which did not lack the item related to the response rate, as their study achieved a high response rate through consecutive recruitment. The quality assessment highlights the reliability of the evidence base while recognizing certain methodological limitations associated with distinct study designs [Table 2].

Table 1. The characteristics of the included studies

Author/Year/ Reference	Country	Study design	Population	Mean age (mean±SD or median and range)	Sample size, (male/female)	Number of the cases	Bone site	Outcome
Keutgen, 2016 [16]	USA	Cohort	MEN1-related PHPT	31 (15–59) $	30 (11/19)	12	Femur, spine	Prevalence
Wang, 2019 [5]	China	Case-control#	MEN1-related PHPT	38.64 ± 15.25	58 (17/41)	MHPT: 11 SHPT: 47	LS, FN, TH, trochanter	Prevalence, MEN-sporadic comparison,
Lourenco, 2010 [24]	Brazil	Cross-sectional	MEN1-related PHPT	41.6 ± 15.2	36 (18/18)	36	LS, FN, TH, distal 1/3rd radius	Prevalence
Marini, 2021 [15]	Italy	Cohort	MEN1-related PHPT	38.9 ± 16.1	180 (49/131)	MHPT: 53 SHPT: 47	LS, FN, TF	Prevalence, PTX, MEN-sporadic comparison,
Norton, 2008 [19]	USA	Cohort	MEN1-related PHPT	36±2	84 (35/49)	56	NA	Prevalence
Silva, 2016 [6]	USA	Cohort	MEN1-related PHPT	41.5 (14.0–71.0)	118 (38/80)	MHPT: 14 SHPT: 104	LS, TH, FN	Prevalence, PTX, MEN-sporadic comparison
Burgess, 1999 [26]	Australia	Cohort*	MEN1-related PHPT	43.6 ± 2.9	29 (0/29)	29	LS, FN	Prevalence
Lourenco, 2008 [23]	Brazil	Cross-sectional	MEN1-Related and Sporadic PHPT	39.10 ± 16.10	715 (NA)	20	LS, FN, proximal 1/3rd radius	Prevalence
Moyes, 2010[18]	UK	Cohort	MEN1-related PHPT treated with Cinacalcet	20–38	8 (3/5)	8	NA	Prevalence
Kann, 2012 [21]	Germany	Cohort	MEN1-related PHPT	46 ± 12 (23-67)	23 (13/10)	23	Total BMD	Prevalence
Coutinho, 2010 [22]	Brazil	Cohort*	MEN1-related PHPT	40.4 ± 10.9	16 (10/6)	16	LS, FN, TF, distal 1/3rd radius, ultra distal radius	PTX
Eller-Vainicher, 2009 [12]	Italy	Cross-sectional	MEN1-Related and Sporadic PHPT	44.2 ± 16.1	533 (113/420)	MHPT: 64 SHPT: 469	LS, FN	MEN-sporadic comparison,
Mathew, 2023 [25]	India	Cross-sectional	MEN1-Related and Sporadic PHPT	35.1 ± 8.7 (17–49)	274 (N/A)	MHPT: 22 SHPT: 202	LS, FN, distal 1/3rd radius	MEN-sporadic comparison,
Song, 2023 [20]	China	Cohort**	MEN1-Related and Sporadic PHPT	43.5 (31.5, 52.0) $	480 (155/325)	MHPT: 86 SHPT: 86	LS, TH, FN	MEN-sporadic comparison,
Kong, 2016 [17]	China	Cohort**	MEN1-Related and Sporadic PHPT	45.0±14.0	209 (61/148)	MHPT: 40 SHPT: 169	LS, FN	MEN-sporadic comparison

The reporting of age was heterogeneous in different studies; some reported age at first surgery, others at first hospital visit or diagnosis. Also, the age column only reports the mean or median age of the MEN1 patients. Regarding the bone site, some studies did not mention their assessed bone site, identified as not available (NA).

Abbreviations: PHPT: primary hyperparathyroidism; MHPT: MEN1-related hyperparathyroidism; SHPT: sporadic hyperparathyroidism

The data extracted from this study were all obtained from only the case group, which consisted of 11 MHPT and 47 SPHT patients.
$ The study reported an interquartile range (IQR) for the age range of the participants.
* These studies were reported as case series originally but were cohort studies in nature.
** These studies were cohort, but the extracted data were reported at baseline.

The data for MEN1 vs sporadic comparison extracted from cross-sectional or cohort studies were reported at baseline in these studies.

Table 2. Quality assessment for the included studies according to the NOS

NOS for Cohort studies

Study	Selection				Comparability		Outcome			Overall Score
	Representativeness of the cohort	*Selection of non-exposed cohort*	*Ascertainment of exposure*	*Absence of outcome of interest at baseline*	*Control for the main factor*	*Control for additional factors*	*Assessment of outcome*	*Long enough follow-up*	*Adequacy of follow up of cohorts*	
Kann et al. (2012)	*	-	*	*	-	-	*	*	*	6/9
Silva et al. (2016)	*	*	*	*	*	*	*	*	*	9/9
Marini et al. (2021)	*	*	*	*	*	*	*	*	*	9/9
Norton et al. (2008)	*	-	*	*	-	-	*	*	*	6/9
Song et al. (2024)	*	*	*	*	*	*	*	*	*	9/9
Moyes et al. (2010)	*	-	*	*	-	-	*	*	*	6/9
Keutgen et al. (2016)	*	-	*	*	-	-	*	*	*	6/9
Kong et al. (2016)	*	*	*	*	*	*	*	*	*	9/9
Burgess et al.1999	*	-	*	*	-	-	*	*	*	6/9
Coutinho et al. 2010	*	-	*	*	-	-	*	*	*	6/9

NOS for Case Control studies

Study	Selection				Comparability		Exposure			Overall Score
	Adequate Case definition	*Representativeness of the cases*	*Selection of Controls*	*Definition of Controls*	*Control for the main factor*	*Control for additional factors*	*Ascertainment of exposure*	*Same method of ascertainment for cases and controls*	*Non-Response rate*	
Wang et al. (2019)	*	*	*	*	*	*	*	*	*	9/9

NOS for Cross-sectional studies

Study	Selection			Comparability		Outcome		Overall Score
	Representativeness of the sample	*Satisfactory response rate*	*Ascertainment of the exposure*	*Control for the main factor*	*Control for additional factors*	*Assessment of the outcome*	*Appropriateness of the statistical tests*	
Lourenco et al. (2008)	*	-	*	*	*	*	*	6/7
Lourenco et al. (2010)	*	-	*	*	*	*	*	6/7
Eller-Vainicher et al. (2009)	*	*	*	*	*	*	*	7/7
Mathew et al. (2023)	*	-	*	*	*	*	*	6/7

The studies by Burgess et al. and Coutinho et al. were basically case series but cohort studies in nature.

Prevalence of Osteopenia and Osteoporosis

Among the studies included in the analysis, five reported relevant findings regarding the prevalence of osteopenia, while ten addressed the prevalence of osteoporosis. Overall, the analysis showed that the prevalence rates for osteoporosis and osteopenia were 45.2% (confidence interval = 39.1-51.4%; I^2 = 16.7%, P-value = 0.28) and 53.3% (confidence interval = 44.4-62%; I^2 = 36.15%, P-value = 0.18), respectively [Figure 2]. Lourenco et al.[22] reported the highest prevalence of osteopenia at 78.6%, while the highest prevalence of osteoporosis was reported by Moyes et al.[16] at 62.5%.

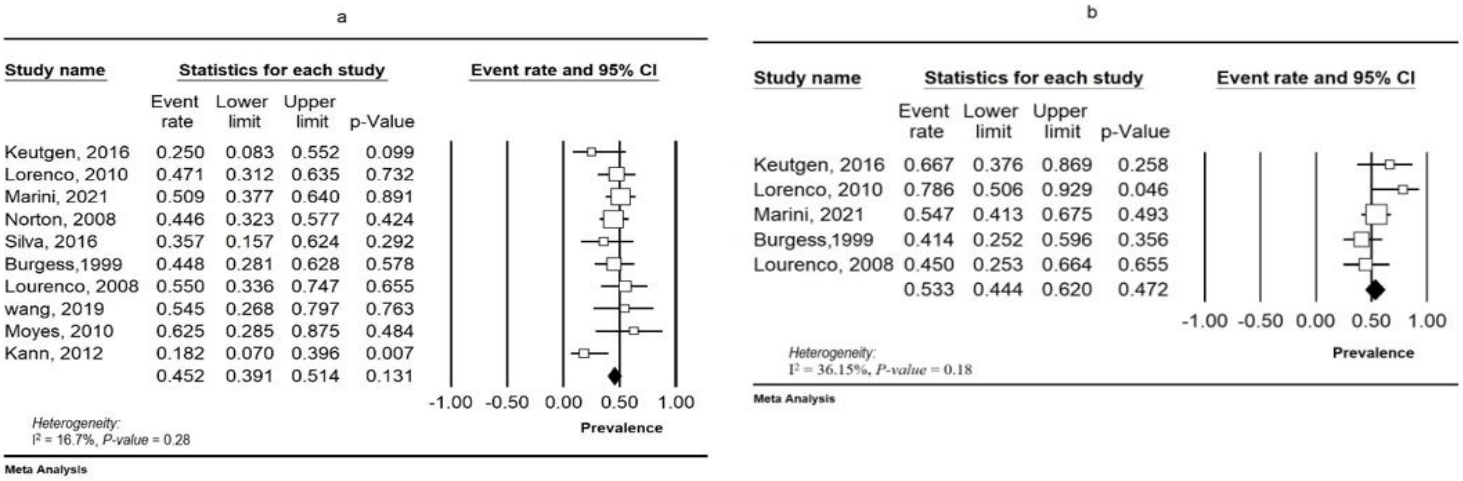

Figure 2. Meta-analysis of event rates and 95% confidence intervals for studies on a) osteoporosis (I2 = 16.7%, P-value = 0.28) and b) osteopenia (I2 = 36.15%, P-value = 0.18) in MEN1-related PHPT

Comparison of MEN1-Related PHPT with Sporadic PHPT

In the analysis comparing MEN1-related PHPT with sporadic PHPT patients, sufficient data were available for three bone sites (LS, TH, and FN) regarding Z-scores, and two sites (LS and FN) concerning T-scores and BMD. The analyses showed that the Z-scores of the two groups were significantly different at the LS (mean difference = -0.676; 95% CI = -0.884 to -0.469; P-value < 0.001; I^2 = 41.86%, P-value = 0.12), TH (mean difference = -0.629; 95% CI = -0.879 to -0.379; P-value < 0.001; I^2 = 23.4%, P-value = 0.27), and FN (mean difference = -0.516; 95% CI = -0.692 to -0.34; P-value < 0.001; I^2 = 38.82%, P-value = 0.14). However, comparisons of T-scores and BMD between the groups did not show significant differences [Table 3].

Effect of Parathyroidectomy on BMD

The analysis of the effects of parathyroidectomy on bone metabolism metrics was based on LS and FN BMD measurements from three studies. The results showed that parathyroidectomy did not lead to significantly different BMD values in LS (mean difference = -0.054, 95% CI = -0.116 to 0.009, P-value = 0.092; I^2 = 0.86%, P-value < 0.001) or the FN (mean difference = -0.025; 95% CI = -0.064 to 0.015, P-value = 0.219; I^2 = 0.47%, P-value < 0.001) [Table 3].

Table 3. The detailed report of the analysis between MEN1-related PHPT vs. sporadic PHPT and before vs. after parathyroidectomy BMD findings

			Number of included studies	Mean (95%CI)	P-value within group	Heterogeneity		
						I2 (%)	p-value	Model
MEN1-related PHPT vs. sporadic PHPT	*Z-score*	***LS***	6	-0.676* (-0.884, -0.469)	<0.001	41.86	0.12	Fixed
		TH	3	-0.629* (-0.879, -0.379)	<0.001	23.4	0.27	Fixed
		FN	6	-0.516* (-0.692, -0.34)	<0.001	38.82	0.14	Fixed
	T-score	***LS***	4	0.052 (-0.589, 0.693)	0.875	80.92	0.001	Random
		FN	4	-0.030* (-0.491, 0.431)	0.9	79.67	0.002	Random
	BMD (g/cm2)	***LS***	3	-0.026* (-0.115, 0.063)	0.57	82.4	0.003	Random
		FN	3	-0.001* (-0.041, 0.038)	0.947	40.52	0.18	Fixed
Before vs. after parathyroidectomy	*BMD (g/cm2)*	***LS***	3	-0.054** (-0.116, 0.009)	0.092	0.86	<0.001	Fixed
		FN	3	-0.025** (-0.064, 0.015)	0.219	0.47	<0.001	Fixed

MEN1: multiple endocrine type 1; PHPT: primary hyperparathyroidism; LS: lumbar spine; TH: total hip; FN: femoral neck
The subgroup analysis was conducted only when at least 3 studies had related findings.
* The negative mean indicates a lower Z-score for MEN1-related PHPT compared to sporadic PHPT.
** The negative mean indicates a lower Z-score after parathyroidectomy compared to before surgery.

Sensitivity Analysis

We conducted a sensitivity analysis of the results, which led to altered findings in two cases. By excluding the study by Song et al., [18] the results of the TH Z-score became statistically insignificant. Furthermore, after excluding the same study, the LS T-score results showed significantly lower Z-scores for the sporadic PHPT patients, in contrast to the results obtained prior to the sensitivity analysis [Figure 3]. Other findings remained unaffected by the sensitivity analysis.

Publication Bias

Egger's test indicated no evidence of publication bias for the prevalence of osteoporosis (P-value = 0.40) and osteopenia (P-value = 0.36) among MEN individuals.

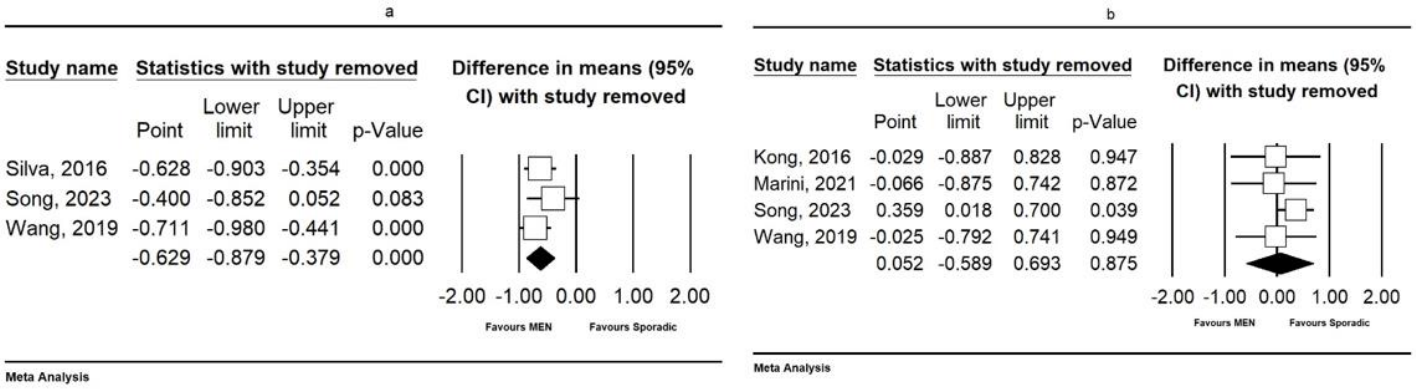

Figure 3. The results of sensitivity analysis on the studies that compared the bone density metrics of MEN1-Related PHPT with Sporadic PHPT; as can be seen, with the exclusion of the study by Song et al. (2023) the results of TH Z-score are no longer significant (a). Furthermore, by excluding the same article, the results of LS T-score become significant towards sporadic PHPT patients (b)

Discussion

The present study conducted a meta-analysis of the bone metabolism characteristics in patients with MEN-related PHPT. This meta-analysis showed that the prevalence of osteoporosis and osteopenia among the included studies was 45.2% and 53.3%, respectively. Furthermore, the Z-scores of MEN-related PHPT patients were significantly different from those of sporadic PHPT patients, whereas the T-scores and BMD did not show significant differences. Furthermore, this study showed that parathyroidectomy is not associated with significant changes in the bone metabolism profile of MEN1-related patients.

PHPT is prevalent among patients with MEN; in fact, it is often the initial presentation in most cases.[24] When compared to sporadic PHPT, MEN-related PHPT exhibits distinct characteristics, including an earlier age of onset and equal distribution between sexes.[25] However, it is important to note that index cases can remain undiagnosed for years, resulting in a later age at diagnosis and an increased risk of complications.

Regarding the prevalence of osteopenia or osteoporosis, the majority of studies did not identify the exact bone sites used for diagnosis, [4-7,15,16,19]. In contrast, three studies provided detailed reports on osteopenia and osteoporosis defined based on different sites.[7,21,22] Accordingly, when the FN was used for diagnosis, all three studies yielded a higher prevalence of osteopenia compared to the LS (41.3% vs. 34.4, 45% vs. 20%, and 46.7% vs. 13.3, respectively). However, among these studies, only Burgess et al.[7] showed a higher prevalence of osteoporosis with FN compared to LS as the assessed bone site. Additionally, the TH yielded the highest rate of osteopenia at 78.6% compared to other bone sites.[22] On the other hand, we excluded the study by Lambert et al.,[26] which reported that all six study subjects had either osteopenia or osteoporosis, as the subjects were not reported separately for these conditions. We also excluded the study by Figueiredo et al.[27] because their criteria for reporting reduced bone density did not align with those of the included studies.

Seven studies evaluated the BMD profiles of patients with MEN-related PHPT and those with sporadic PHPT.[5,6,12,14,15,18,23] This meta-analysis showed a significant difference between the Z-scores of MEN1-related and sporadic PHPT patients. This finding is clinically important for PHPT patients who are candidates for parathyroidectomy, as distinguishing between MEN-related and sporadic PHPT influences treatment decisions. Thus, genetic testing is essential for diagnosing MEN1, particulrly when there is no clinical evidence of the disease, such as the clinical features of MEN1 or a family history in individuals with isolated PHPT.[28] The surgical trend for MEN1-related PHPT is shifting towards less invasive techniques (i.e., focal or unilateral approaches) facilitated by the development of new localization devices that allow for intraoperative PTH sampling. However, these surgical methods carry the risk of overlooking a multiglandular disease, which may lead to a failure to diagnoseMEN1 as the underlying cause.[29] Nevertheless, it should be noted that even in cases involving MEN patients, single-gland adenoma remains the most common form in MEN2.[30] To identify individuals who may warrant suspension of MEN1 syndrome and consider possible genetic testing, Eller-Vainicher et al. proposed that a

normal PTH level combined with an age of less than 50 should raise concern.[12]

Silva et al., Marini et al., and Coutinho et al.[6,15,20] were available studies on the effects of parathyroidectomy on the BMD of MEN1 patients. It should be noted that the studies by Burgess et al.[7] and Kann et al.[19] were excluded from the analysis because they categorized their patients into controlled and uncontrolled PHPT, which did not align with the other studies. Our analysis focused on subgroups with at least three studies that provided corresponding results, yielding findings only on LS and FN BMD, none of which were statistically significant [Table 3]. All included studies evaluated BMD at least 12 months after parathyroidectomy, and only the study by Coutinho et al. reported significant improvements; this could be explained by possible differences in the surgical techniques employed across these studies (adenectomy versus parathyroidectomy). Furthermore, although the meta-analysis revealed that the LS and FN BMD of MEN1-related PHPT patients did not significantly change after PTX, some other findings should be highlighted while reviewing the included studies. For instance, Coutinho et al.[20] showed that LS, FN, and TF T- and Z-scores significantly changed after the surgery. Furthermore, Silva et al.[6] reported that the LS Z-score of these patients significantly changed after PTX. However, we could not include these results in the meta-analysis due to insufficient related articles (e.g., in the case of LS Z-score changes after PTX, only two were available). Notably, only one study compared the mean changes in BMD before and after parathyroidectomy between MEN1-related and sporadic PHPT patients. Silva et al.[6] assessed three bone sites (LS as a trabecular bone, TH as a combination of cortical and trabecular bone, and FN as a cortical bone), none of which showed significant differences between the two groups. However, the authors highlighted the need for longer follow-ups for a more robust conclusion.

Conclusion

This study showed a high prevalence of bone density loss in MEN1-related PHPT patients. Furthermore, the results showed that the Z-score was significantly lower in MEN1-related PHPT patients compared to sporadic PHPT patients. Finally, this meta-analysis showed no significant differences in the changes in BMD of patients after parathyroidectomy.

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Declaration of Informed Consent: The present study was a meta-analysis that included no no information (names, initials, hospital identification numbers, or photographs) that can be used to identify patients.

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