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General

osteopoikilosis and fracture healing: the bone quantity–quality paradox—a case report and systematic review with synthesis without meta-analysis

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Introduction

Osteopoikilosis is a rare sclerosing bone dysplasia that may mimic osteoblastic metastases and complicate fracture assessment. Its influence on bone quality, fixation stability, and fracture healing remains unclear.

Objective

To report a tibial plateau fracture in a patient with osteopoikilosis and systematically synthesize published evidence on fracture characteristics, management, and healing outcomes in osteopoikilosis.

Methods

We integrated an index case with a systematic review and synthesis without meta-analysis. The index case involved a 66-year-old woman with a Schatzker type II tibial plateau fracture and incidental osteopoikilosis, evaluated using dual-energy X-ray absorptiometry (DXA), trabecular bone score (TBS), and ^{18}F-NaF PET/CT. A systematic literature search through January 2026 synthesized fracture characteristics and healing outcomes.

Results

In the index case, the fracture occurred within intervening bone, sparing sclerotic lesions. This localization revealed a bone quantity–quality paradox: sclerotic lesions artifactually elevated BMD, whereas low TBS identified underlying systemic fragility. The systematic review (N=11) demonstrated fractures across the axial and appendicular skeletons, including both upper and lower extremities. Management ranged from conservative care to operative fixation with intramedullary nails, locking plates, and headless cannulated screws. Fracture union was consistently achieved, with no reported technical failures or delayed healing.

Conclusion

Osteopoikilosis may mask underlying systemic osteoporosis, as evidenced by fractures occurring in the “spared” bone despite high BMD. TBS serves as a critical diagnostic safeguard to unmask this fragility. Clinically, however, the condition does not compromise biological repair; standard fracture management principles yield excellent outcomes without the need for modified fixation strategies.

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INTRODUCTION

Osteopoikilosis is a rare condition and is considered uncommon, sometimes referred to as "spotted bone disease." It represents a benign sclerosing bone dysplasia and has been reported in approximately 1 in 50,000 individuals.[1,2] The disorder is inherited in an autosomal dominant manner and is associated with loss-of-function mutations in the LEMD3 gene.[3-6] Most patients have no symptoms, and the diagnosis is usually made incidentally when radiographs are obtained for other reasons, such as after minor trauma.[1,7] Radiographically, osteopoikilosis appears as multiple symmetric, well-defined ovoid sclerotic foci clustered around peri-articular regions.[8] Although osteopoikilosis is a benign condition, the radiographic appearance may resemble several other disorders. This similarity becomes a major concern when osteopoikilosis must be differentiated from osteoblastic metastases, as the radiographic patterns can look nearly identical.[9,10] Similar appearances may also be seen in mastocytosis and tuberous sclerosis.[11] If these lesions are seen in older patients, a more complete assessment is often required to confirm that the lesion is benign and more serious conditions need to be ruled out.[10] This step is important, as the alternative diagnoses generally carry higher morbidity. Early recognition of osteopoikilosis may help limit unnecessary investigations and reduce patient anxiety.

Fractures in patients with osteopoikilosis have been reported sporadically, often following low-energy trauma. Nevertheless, whether the underlying sclerosing dysplasia adversely affects fracture healing or fixation stability remains unclear. Studies using Dual-energy X-ray Absorptiometry (DXA) often report normal or even artifactually elevated bone mineral density (BMD), as the dense sclerotic lesions increase the measured density, potentially masking underlying osteopenia or osteoporosis.[4,12] Consequently, relying on BMD alone provides an incomplete assessment of bone strength and fracture risk. The trabecular bone score (TBS), a texture index derived from lumbar spine DXA images, has emerged as a valuable tool for assessing bone microarchitecture independent of BMD; however, its application in osteopoikilosis has not been previously reported.[13] Furthermore, the metabolic activity of these lesions remains a matter of controversy. While traditional bone scintigraphy typically shows no increased uptake, recent reports utilizing advanced imaging such as ^{18}F-sodium fluoride (NaF) PET/CT have demonstrated variable activity, complicating the interpretation of bone turnover in this population.[3,4,14,15]

The objectives of this study were twofold: first, to present a case of an intra-articular tibial plateau fracture in a patient with osteopoikilosis, demonstrating a marked discrepancy between bone quantity and microarchitectural quality ("the quantity-quality paradox"); and second, to systematically review and synthesize the existing literature on fracture characteristics, management, and healing outcomes in patients with osteopoikilosis.

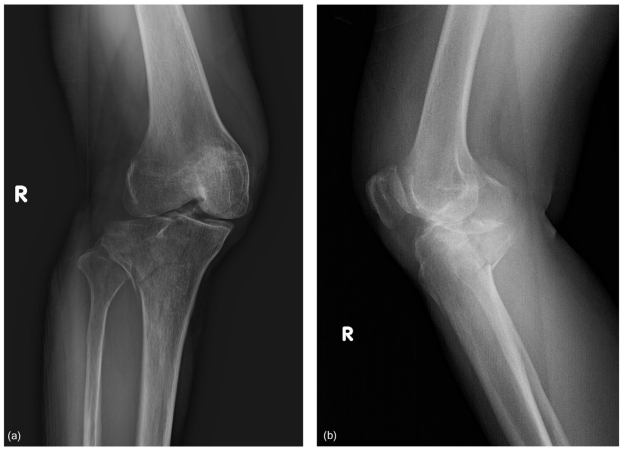

Figure 1. Pre-operative radiographs of the right knee.

(a) Anteroposterior view showing a depressed fracture of the lateral tibial plateau (Schatzker type II).
(b) Lateral view showing the depressed tibial plateau fracture. Note that while osteopoikilosis lesions were prevalent in the pelvis and femurs, the fracture line itself did not traverse a macroscopic sclerotic lesion.

CASE PRESENTATION

A 66-year-old Thai woman presented to the emergency department following a mechanical fall, complaining of acute pain and swelling in her right knee. She had no known underlying medical conditions and no documented family history of skeletal disorders. On physical examination, marked tenderness and joint effusion were observed around the right knee, with limited range of motion secondary to pain. Distal neurovascular examination was unremarkable. Plain radiographs of the right knee demonstrated a depressed fracture of the lateral tibial plateau, consistent with a Schatzker type II injury (Figure 1). As part of the routine trauma evaluation, an anteroposterior pelvic radiograph was obtained, which incidentally revealed multiple small, well-defined, round sclerotic lesions symmetrically distributed within the pelvic bones and proximal femurs (Figure 2). In contrast, the proximal tibia appeared relatively spared, and the fracture line did not traverse any visible sclerotic focus.

The patient was admitted for operative management. Open reduction and internal fixation of the tibial plateau fracture was performed using a locking compression plate and screws. Intraoperatively, adequate screw purchase and construct stability were achieved without technical difficulty. The procedure was completed uneventfully. During the postoperative period, the patient developed acute dyspnea. Computed tomography pulmonary angiography confirmed an acute pulmonary embolism, which was managed with oral anticoagulation. Concurrent computed tomography revealed multiple sclerotic lesions involving the thoracic spine, ribs, and sternum, radiographically resembling osteoblastic metastases (Figure 3). Given the absence of systemic symptoms or known malignancy, further outpatient evaluation was planned.

Subsequent investigations included a whole-abdominal computed tomography scan, which demonstrated no evi-

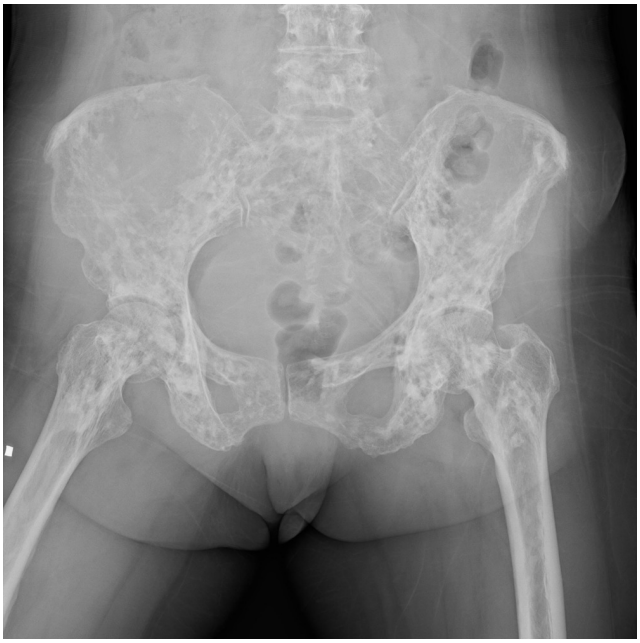

Figure 2. Anteroposterior pelvic radiograph demonstrating numerous symmetric, well-defined sclerotic lesions with peri-articular distribution involving the ilium, sacrum, and proximal femurs, characteristic of osteopoikilosis.

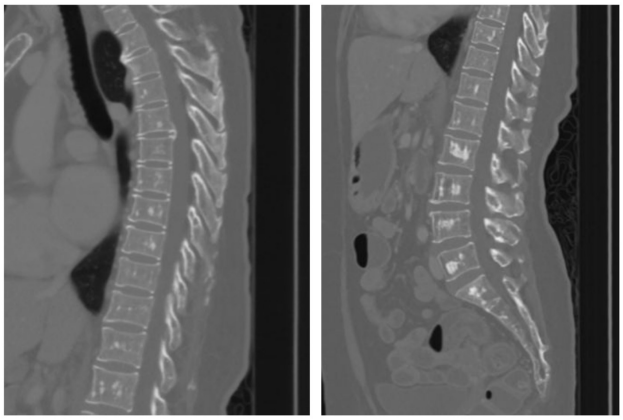

Figure 3. Computed Tomography (CT) of the spine. Sagittal and coronal reconstructions demonstrate multiple discrete, hyperdense sclerotic lesions (bone islands) distributed within the vertebral bodies and posterior elements, without evidence of cortical destruction or soft tissue mass, supporting a benign etiology.

dence of visceral malignancy or lymphadenopathy. Serum tumor markers, including carcinoembryonic antigen (CEA), CA 15-3, CA 125, and CA 19-9, were all within normal limits.

To further characterize skeletal activity, an ^{18}F-NaF PET/CT scan was performed. The study demonstrated mild to intense tracer uptake corresponding to the sclerotic lesions (Figure 4), Serum bone turnover markers were evaluated to assess systemic bone metabolism. C-terminal telopeptide (CTX) was 0.576 ng/mL (reference range for postmenopausal women: 0.177–1.015 ng/mL), and procollagen type 1 N-terminal propeptide (P1NP) was 54.4 ng/mL (reference range: 16.27–73.87 ng/mL). Additional biochemical parameters, including serum calcium, phosphate, alkaline phosphatase, parathyroid hormone, and 25-hydroxyvitamin D, were within normal ranges (Table 1).

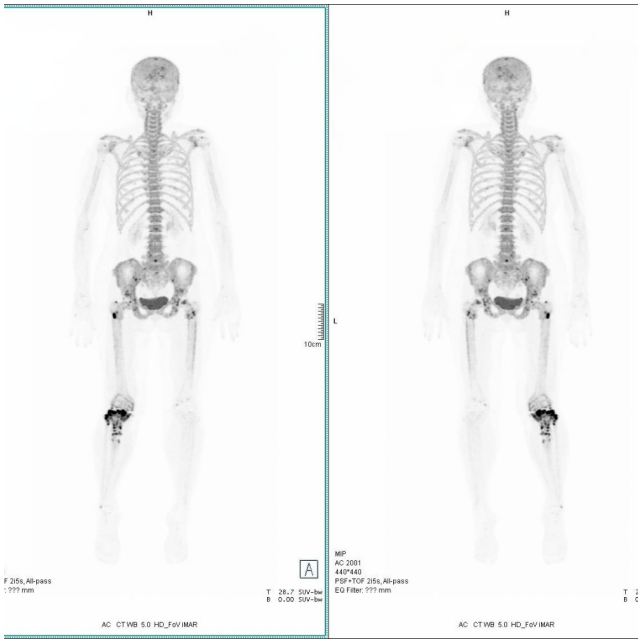

Figure 4. ^{18}F-sodium fluoride (NaF) PET/CT. Axial fused PET/CT image demonstrating mild-to-intense tracer uptake corresponding to sclerotic lesions, indicating focal osteoblastic activity.

BMD was performed using dual-energy X-ray absorptiometry (GE Lunar iDXA, GE Healthcare, Madison, WI, USA). Lumbar spine BMD demonstrated a T-score of −0.2 with a Z-score of +1.9, while total hip BMD showed a T-score of 0.5. Trabecular bone score analysis revealed degraded microarchitecture with a value of 1.173 (Figure 5). Based on the characteristic symmetric distribution of sclerotic lesions, absence of malignant findings, and supportive imaging features, a diagnosis of osteopoikilosis was established.

Postoperative rehabilitation was continued according to standard protocols for tibial plateau fractures without modification. At the 2-month follow-up, the patient demonstrated a painless range of motion from 0 to 120 degrees. Radiographs confirmed fracture union with maintained alignment and stable fixation (Figure 6). Full weight-bearing ambulation was subsequently achieved.

METHODS

The study protocol for this systematic review was prospectively registered with the International Prospective Register of Systematic Reviews (PROSPERO; registration number CRD420251272283). The review was conducted and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guide-

Table 1. Laboratory investigations for metabolic bone evaluation and malignancy screening in the index patient

Laboratory Test	Result	Reference Range	Interpretation
Bone & Mineral Metabolism			
Calcium	9.5 mg/dL	8.6 – 10.2	Normal
Phosphorus	3.6 mg/dL	2.5 – 4.5	Normal
Magnesium	2.17 mg/dL	1.6 – 2.4	Normal
Alkaline Phosphatase (ALP)	90 U/L	35 – 105	Normal
25-Hydroxy Vitamin D (Total)	55.6 ng/mL	30 – 100	**Sufficiency**
Bone Turnover Markers			
C-terminal telopeptide (CTX)	0.576 ng/mL	0.177 – 1.015[a]	Within postmenopausal reference range
Procollagen type 1 N-terminal propeptide (P1NP)	54.4 ng/mL	16.27 – 73.87[a]	Within reference range
Secondary Osteoporosis Screen			
TSH	1.30 uIU/mL	0.27 – 4.20	Normal (Euthyroid)
Free T4	1.64 ng/dL	0.93 – 1.70	Normal
Creatinine	0.67 mg/dL	0.5 – 0.9	Normal
eGFR	91.4 mL/min	> 90	Normal
Hematology & Malignancy Screen			
Hemoglobin (Hb)	9.2 g/dL	12.0 – 15.0	**Mild Anemia**
Tumor Markers			No evidence of malignancy
CEA	1.0 ng/mL	< 4.7	Normal
CA 15-3	4.0 ng/mL	< 25	Normal
CA 125	10.5 ng/mL	< 35	Normal
CA 19-9	5.2 ng/mL	< 37	Normal
Serum Protein Electrophoresis	Negative	-	No monoclonal gammopathy
Bone Health Status			
Lumbar spine BMD	T-score −0.2; Z-score +1.9	T-score > -1.0	Preserved BMD
Total hip BMD	T-score 0.5	T-score >-1.0	Preserved BMD
Trabecular Bone Score (TBS)	1.173	Commonly applied category: degraded ≤1.230	**Degraded microarchitecture**

Abbreviations: *TSH,* Thyroid-Stimulating Hormone; *GFR,* Glomerular Filtration Rate; *CEA,* Carcinoembryonic Antigen; *CA,* Cancer Antigen; *BMD,* Bone Mineral Density; *TBS,* Trabecular Bone Score.

[a]*Reference ranges provided for postmenopausal females based on the specific assay used.*

lines and the Synthesis Without Meta-analysis (SWiM) reporting guideline.[16-18] The SWiM approach was applied due to the rarity of osteopoikilosis and the exclusive inclusion of case-based evidence, which precluded quantitative meta-analysis. (Supplementary materials (eMethods 1–2)). Changes to the study protocol are documented in Supplementary materials (eMethods 3).

ETHICAL CONSIDERATIONS

This study was approved by the Human Research Ethics Committee, Chulabhorn Research Institute (IRB No. 121/2568). The requirement for written informed consent was waived by the ethics committee because of the retrospective nature of the study and the use of anonymized data. All patient data were de-identified before analysis, and confidentiality was maintained throughout data collection, analysis, and manuscript preparation.

SEARCH STRATEGY AND STUDY SELECTION

A comprehensive literature search was performed in PubMed/MEDLINE, CINAHL, and Scopus from database inception to January 2026. The search strategy combined Medical Subject Headings (MeSH), database-specific controlled vocabulary (e.g., Emtree), and free-text keywords related to osteopoikilosis and fractures. The primary search terms included: ("osteopoikilosis" OR "spotted bone disease") AND ("fracture" OR "trauma" OR "injury" OR "fracture healing" OR "bone healing").

The complete electronic search strategies for all databases are provided in the Supplementary Materials (eMethods 4). Only articles published in English were considered eligible. Reference lists of all included full-text articles were manually screened to identify additional relevant studies.

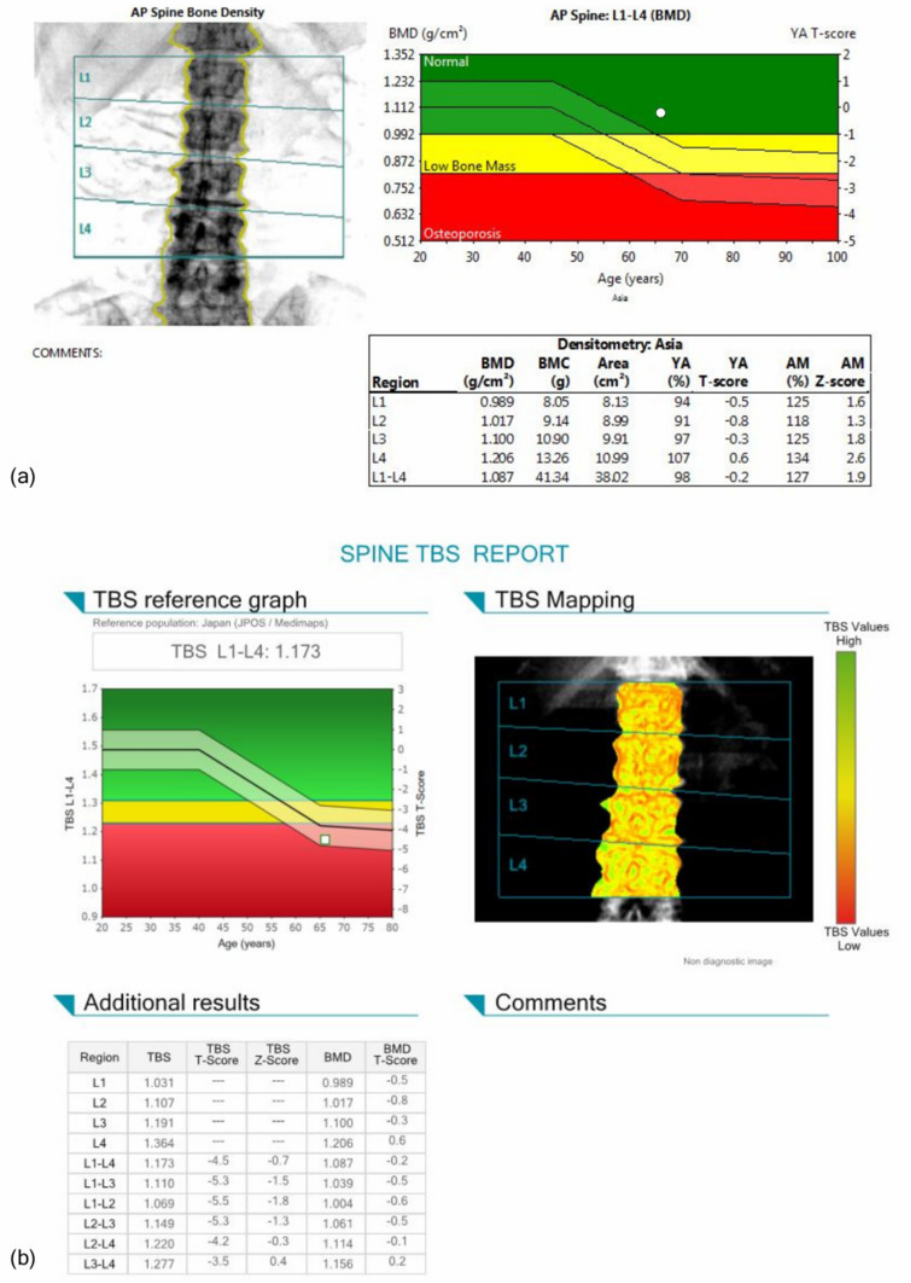

Figure 5. Bone quantity–quality discordance in osteopoikilosis.

(a) Lumbar spine DXA showing a normal areal BMD (T-score −0.2), potentially influenced by sclerotic lesions.
(b) Corresponding trabecular bone score (TBS) analysis demonstrating degraded trabecular microarchitecture (TBS 1.173), highlighting a bone quantity–quality paradox.

All retrieved records were uploaded to a web-based platform for study management. Duplicate records were removed prior to screening. Titles and abstracts were initially screened by one reviewer (NC) and independently verified by a second reviewer (RS). Full-text articles were subsequently assessed for eligibility by the same reviewers. Disagreements were resolved through discussion and consensus.

ELIGIBILITY CRITERIA

Detailed inclusion and exclusion criteria are presented in Supplementary Materials (eTable 1). Briefly, studies were eligible if they: (i) reported human patients of any age or sex with a confirmed diagnosis of osteopoikilosis based on radiographic, clinical, or genetic findings; (ii) described one or more skeletal fractures; (iii) provided information on fracture management and/or healing outcomes; and (iv) were published as full-text articles in English. Eligible studies were screened for applicability to the review question using the ROBINS-E framework.[19] (Supplementary materials eTable 2 & 3)

Studies were excluded if they lacked fracture-related clinical details, provided insufficient information to confirm the diagnosis of osteopoikilosis, or did not present original patient-level data. Review articles, systematic reviews, editorials, conference abstracts, and publications without accessible full text were also excluded.

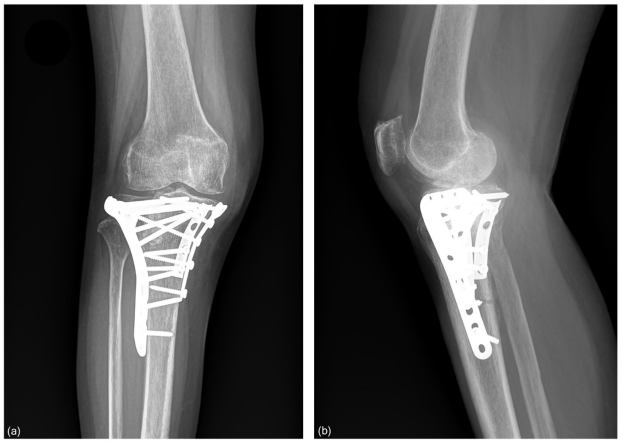

Figure 6. Post-operative radiographs of the right knee at 2-month follow-up demonstrating solid fracture union with bridging callus formation, maintained alignment, stable implant position, and no evidence of loosening or failure.

DATA EXTRACTION AND QUALITY ASSESSMENT

Data extraction was performed using a predefined and piloted extraction form. Extracted variables included author and year of publication, patient demographics (age and sex), fracture site and characteristics, mechanism of injury, method of fracture management (operative or non-operative), and reported fracture healing outcomes, including time to union and complications when available.

Data extraction was conducted independently by one reviewer (PT) and subsequently checked for accuracy and completeness by a second reviewer (NC). Any discrepancies were resolved through discussion and consensus. All included studies were appraised for methodological quality using a modified version of the Newcastle–Ottawa Scale (NOS) by two reviewers (RS and NC).[20]

Because all included studies consisted of case reports or small case series without comparator groups, several domains of the original Newcastle–Ottawa Scale (NOS) which was developed for non-randomized comparative studies were not applicable.

To ensure an appropriate and transparent assessment of methodological quality, a modified NOS framework tailored for descriptive clinical reports was applied, consistent with prior systematic reviews of rare diseases and fracture case literature [20]. This modified framework focused on four domains: clarity of osteopoikilosis diagnosis, adequacy of fracture characterization, reliability of management reporting, and documentation of clinical and radiographic healing outcomes. In accordance with the SWiM guideline, this qualitative assessment was used to contextualize the robustness of the evidence and inform interpretation, rather than as a criterion for study exclusion. Full methodological details are provided in Supplementary Materials (eMethods 5).

DATA SYNTHESIS

Given the rarity of osteopoikilosis and the exclusive inclusion of case reports and small case series, quantitative meta-analysis was not feasible. Data were therefore synthesized using a structured qualitative approach in accordance with the SWiM reporting guideline.

Included studies were synthesized at the level of individual clinical cases. When multiple publications described the same patient, cases were identified through cross-referencing of demographic, clinical, and radiographic information and were synthesized as a single case to avoid double-counting.

For descriptive comparison, cases were grouped according to fracture location (axial skeleton, upper extremity, or lower extremity) and method of management (operative versus non-operative). All cases were assigned equal weight, as no comparative or longitudinal data were available. The rationale for these groupings is provided in Supplementary Materials (eMethods 6).

Outcomes of interest included fracture union, time to union when reported, and the occurrence of complications such as delayed union, nonunion, implant failure, or compromised fixation stability. Clinical heterogeneity was explored descriptively by examining variations in patient characteristics, fracture patterns, and treatment strategies. No formal statistical assessment of heterogeneity was performed.

Given the descriptive nature and low level of the available evidence, findings were interpreted as hypothesis-generating rather than confirmatory. Results are presented in a structured narrative format and summarized in Table 2 to enhance transparency and reproducibility.

RESULTS

SEARCH RESULTS

A PRISMA flow diagram (Figure 7) reports our screening process. In summary, the systematic literature search identified a total of 94 records from electronic databases, including PubMed/MEDLINE (n = 20), CINAHL (n = 16), and Scopus (n = 58). After removal of duplicate records (n = 28), 66 records remained for title and abstract screening, of which 50 were excluded for not meeting the eligibility criteria. Sixteen reports were sought for full-text retrieval and all were successfully obtained and assessed for eligibility. During full-text review, seven studies were excluded, including three reports that did not provide fracture-related clinical information and four reports that were not published in English.[10,29-34] As a result, nine studies identified through database searching met the predefined inclusion criteria.[1-3,21,24-28]

In addition, two reports were identified through other sources. Both were retrieved and assessed for eligibility and met the inclusion criteria.[22,23] Consequently, a total of eleven studies were included in the final qualitative synthesis.

Table 2. Summary of reported fracture cases in patients with osteopoikilosis included in the qualitative synthesis (SWiM), stratified by anatomical location and treatment modality

Author (Year)	Age	Sex	Fracture Site	Treatment	Healing Outcome / Time to Union	Quality rating[a] (Modified NOS)
Axial skeletal						
Gurcan[21] 2012	26	F	C5 vertebra (with spondylolisthesis)	Surgical stabilization	Neurological recovery (AIS-B to AIS-C); Stable at 1 year	High
Upper Extremity Fractures						
Du Mortier[3] 2014	37	M	Proximal humerus	Conservative	Callus at 6 weeks, Union at 3 months	High
Khattak[22] 2012 Ali[23] 2017[b,]	33	M	Olecranon	ORIF (Tension band wiring)	Uneventful healing	Moderate
Liu[24] 2024	34	M	Distal radius	Surgical fixation	Satisfactory healing	Moderate
Pollen[25] 1968	21	F	Thumb metacarpal (Bennett's fracture)	Conservative (Manipulation & Plaster)	Fracture united in 4 weeks; subluxation corrected	High
Spiezia[26] 2025	17	M	Index finger (Proximal phalanx)	Surgical repair	Resolution confirmed at 4 months	High
Lower Extremity Fracture (Weight-bearing)						
Buyukbebeci[27] 2005	25	M	Subtrochanteric femur	Conservative (Skeletal traction)	Callus at 4 weeks, Union at 26 weeks	High
Ye[2] 2017	17	M	Femoral shaft	Surgical (Intramedullary nailing)	Callus at 1 month, Union at 3 months	High
Bansal[1] 2013	34	M	Distal tibia (Pilon type I)	ORIF (Plate osteosynthesis)	Union at 12 weeks	High
Ogalde-Bravo[28] 2026	21	M	Ankle (Medial malleolus)	ORIF (Cannulated screws)	Return to work at 5 weeks, last follow-up at 17 months; no pain, normal function	High
Current Case Suwanaratana 2025	66	F	Tibial Plateau (Schatzker II)	ORIF (Plate osteosynthesis)	Union at 2 months	High

Abbreviations: *NOS* Newcastle–Ottawa Scale (modified for case-based evidence), *AIS* American Spinal Injury Association Impairment Scale, *ORIF* Open reduction and internal fixation.

[a] Study quality categories were used to contextualize findings within the qualitative synthesis and were not used for statistical weighting.

[b] Khattak et al. (2012) and Ali (2017) describe the same clinical case and were synthesized as a single patient.

STUDY CHARACTERISTICS

The eleven included articles provided data on ten unique patients from the literature. When combined with the present case, a total of eleven patients were included in the qualitative synthesis. The cohort comprised nine male and two female patients. Age at presentation ranged from 17 to 66 years. In all cases, osteopoikilosis was identified incidentally during radiographic evaluation following traumatic injury, which ranged from low-energy falls to high-energy trauma. Cross-referencing of demographic and radiographic data revealed that two publications described the same clinical case; these reports were therefore synthesized as a single patient to prevent double-counting.[22,23]

Fractures predominantly involved the appendicular skeleton, although axial involvement was also reported. Injuries of the lower extremity included femoral shaft fracture, subtrochanteric femoral fracture, comminuted tibial pilon fracture, and medial malleolus fracture. Injury of the axial skeleton included a cervical spine fracture associated with spondylolisthesis. Upper extremity fractures involved the proximal humerus, olecranon, distal radius, and small bones of the hand, including metacarpal and phalangeal fractures. The present case represents an intra-articular fracture of the tibial plateau.

QUALITY ASSESSMENT

Using the modified NOS, eight studies were found to be of high quality (4–5 stars) and two cases were of moderate quality (3 stars). Moderate-quality cases primarily lacked documentation of time to fracture union or had insufficient

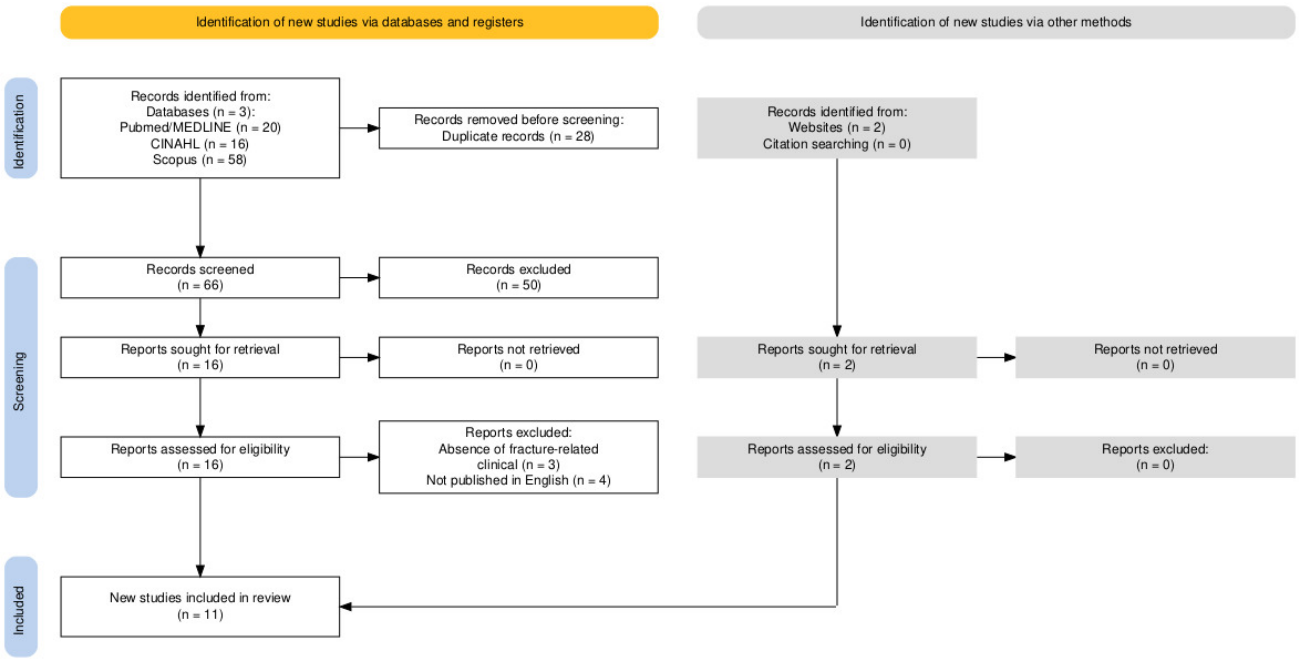

Figure 7. PRISMA flow diagram illustrating the study selection process. A total of 94 records were identified through database searching, including PubMed/MEDLINE (n = 20), CINAHL (n = 16), and Scopus (n = 58). After removal of duplicates, 66 records were screened by title and abstract. Sixteen reports were assessed for full-text eligibility, of which seven were excluded. In addition, two reports identified through other sources met the inclusion criteria. Ultimately, eleven studies were included in the qualitative synthesis. Duplicate publications describing the same patient were identified and synthesized as a single clinical case.

follow-up duration to confirm definitive healing.[22-24] Detailed domain-level scoring and scale modifications are presented in Supplementary information (eTable 4).

SWIM ANALYSIS

Across all included cases, standard orthopedic management principles were consistently applied, adhering to established trauma protocols regardless of the underlying sclerosing bone dysplasia. Therapeutic decisions were dictated primarily by fracture personality, anatomical location, and mechanical stability, rather than the presence of osteopoikilosis.

1. SURGICAL MANAGEMENT

Operative treatment was the predominant management strategy, particularly for unstable fractures involving weight-bearing extremities or the axial skeleton. In the lower extremity, intramedullary nailing was used successfully for a femoral shaft fracture in an adolescent patient, resulting in fracture union without reported complications.[2] Peri-articular fractures were managed with plate osteosynthesis, including a comminuted distal tibial pilon fracture treated with open reduction and internal fixation, with satisfactory alignment and healing.[1] More recently, successful fixation of a medial malleolus fracture using headless cannulated screws was reported, with full functional recovery at 17 months and no complications.[28] The present case was managed with locked plate fixation of a tibial plateau fracture, with stable fixation achieved.

In the axial skeleton, posterior spinal instrumentation was performed for a cervical spine injury associated with C5 spondylolisthesis, resulting in neurological recovery and maintained spinal stability.[21] In the upper extremity, operative fixation was performed for fractures requiring anatomical restoration or early mobilization, including tension band wiring for olecranon fracture and surgical fixation for distal radius and proximal phalanx fractures.[22-24, 26] Across all surgically treated cases, no intraoperative difficulties related to drilling or screw insertion through sclerotic lesions were reported. No cases of implant loosening or hardware failure were documented.

2. CONSERVATIVE MANAGEMENT

Non-operative management was applied to stable fracture patterns and resulted in favorable outcomes. A subtrochanteric femoral fracture was managed with skeletal traction, demonstrating callus formation at 4 weeks and complete radiographic union by 26 weeks.[27] In the upper extremity, immobilization was sufficient for fractures of the proximal humerus and thumb metacarpal fracture-dislocations.[3,25] These cases suggest that natural fracture healing cascades, including hematoma organization, callus formation, and remodeling, proceed normally in osteopoikilosis bone.

3. HEALING OUTCOMES AND COMPLICATIONS

Fracture union was achieved in all reported cases managed either surgically or conservatively. When reported, time to

union ranged from 8 to 26 weeks. No cases of delayed union, nonunion, refracture, implant failure, or compromised fixation stability were documented. This systematic review provides consistent descriptive evidence that osteopoikilosis, despite its striking radiographic appearance and microarchitectural abnormalities, does not adversely affect fracture healing potential or clinical outcomes.

DISCUSSION

This study provides novel insights into the relationship between bone density, bone quality, and fracture healing in osteopoikilosis. By integrating a detailed case report with a systematic synthesis of the existing literature, we demonstrate two key findings: first, that increased bone density in osteopoikilosis may coexist with impaired bone microarchitecture, reflecting a bone quantity–quality paradox; and second, that despite this apparent discrepancy, fracture healing outcomes in osteopoikilotic patients appear comparable to those observed in the general population when standard treatment principles are applied.

The distinction between osteopoikilosis and osteoblastic metastases remains a major diagnostic challenge, particularly in the trauma setting where fractures may be misconstrued as pathological.[9,35] As illustrated in our case, the radiographic appearance of multiple, well-defined, ovoid sclerotic foci can be alarming. Unlike metastases, which are typically asymmetric and favor the axial skeleton, osteopoikilosis lesions display strict bilateral symmetry and a predilection for peri-articular regions, while sparing the skull and ribs.[8,36] Furthermore, these lesions are usually uniform and lack cortical destruction or periosteal reaction.[3,14] Recognition of this characteristic "spotted bone" pattern allows clinicians to confidently exclude malignancy and proceed with standard trauma management without unnecessary oncologic investigations.[1,37]

In the present case, conventional DXA demonstrated normal to increased areal BMD, whereas TBS revealed degraded trabecular microarchitecture, highlighting a clear dissociation between bone quantity and bone quality. This finding underscores the limitation of DXA-derived BMD as a surrogate for skeletal strength and suggests that sclerotic bone lesions may disproportionately inflate areal density without conferring a corresponding biomechanical advantage. To our knowledge, this is the first report to demonstrate such discordance in osteopoikilosis using TBS.

This observation is consistent with mechanistic evidence from other sclerosing bone dysplasias, particularly Buschke–Ollendorff syndrome, in which elevated areal BMD has been attributed to focal endocortical thickening rather than generalized improvements in structural bone strength.[4] Similar measurement artefacts have been described in conditions characterized by focal sclerosis, such as degenerative joint disease, where increased BMD may obscure underlying skeletal fragility.[38] In this context, adjunctive assessment of bone microarchitecture is clinically relevant, as TBS has been shown to predict fracture risk independently of BMD and to improve risk stratification in secondary osteoporosis.[39] While standard fracture management principles remain applicable regardless of TBS, its clinical value lies in preventing false reassurance when BMD appears normal or elevated. TBS therefore serves as a diagnostic safeguard that unmasks microarchitectural degradation obscured by conventional DXA, supporting appropriate long-term skeletal risk counseling.[40]

A parallel consideration concerns the metabolic behavior of osteopoikilosis lesions on nuclear imaging. Historically, these lesions have been described as scintigraphically inert on conventional Tc-99m MDP bone scans.[3,23] However, this characterization may reflect the limited sensitivity of older planar imaging rather than true metabolic quiescence. Prior reports have documented increased radionuclide uptake in selected cases, attributed to active osseous remodeling.[41,42] Similar findings have been reported in bone islands, which are histologically identical to osteopoikilosis lesions, particularly when lesions are large or enlarging.[43,44]

In our case, ^{18}F-NaF PET/CT demonstrated focal tracer uptake corresponding to sclerotic lesions. This modality provides superior sensitivity and spatial resolution compared with conventional scintigraphy, enabling detection of subtle osteoblastic activity.[45] Similar uptake patterns have recently been reported in other sclerosing bone dysplasias.[4] Although the clinical implications of this metabolic activity remain uncertain, it may reflect low-grade remodeling at the margins of sclerotic foci, potentially contributing to preserved fracture healing capacity despite altered bone architecture.

Systemic metabolic evaluation further supports the concept that osteopoikilosis represents a localized skeletal process rather than a generalized high-turnover disorder. While ^{18}F-NaF PET/CT reflects site-specific osteoblastic activity, serum markers such as CTX and P1NP indicate global skeletal turnover.[45,46] In contrast to disorders such as Paget's disease, our patient demonstrated normal systemic bone turnover despite focal metabolic activity on imaging.[47] This dissociation reinforces the benign nature of osteopoikilosis and supports confident diagnosis without invasive biopsy when characteristic imaging features and normal biochemical markers are present.

In this case, the fracture line did not propagate through a macroscopic sclerotic lesion. This finding argues against a localized stress-riser effect created by dense bone islands and instead suggests that fracture initiation occurred within the intervening bone. Such localization supports the concept that the radiographically "spared" bone may represent the biomechanically weakest compartment, despite the presence of dense sclerotic lesions elsewhere. This observation aligns with the degraded microarchitecture identified by TBS and further illustrates the discrepancy between apparent bone density and true skeletal strength.

Importantly, impaired bone microarchitecture, as suggested by low TBS, does not necessarily translate into impaired fracture healing, underscoring the distinction between fracture susceptibility and fracture repair capacity.

Our systematic synthesis of 11 cases provides additional insight into the clinical behavior of fractures in this population. Fractures occurred across a wide age range, from ado-

lescence to late adulthood, reflecting the typically incidental nature of osteopoikilosis until trauma prompts imaging. Although the condition affects both sexes equally, a male predominance was observed among reported fracture cases, likely reflecting trauma-exposure or reporting bias rather than biological susceptibility.[1,21,24] Fracture distribution was broad, involving weight-bearing bones of the lower extremity, the axial skeleton, and the upper extremity.[25-27] Importantly, all fractures were associated with identifiable trauma, and no spontaneous or insufficiency fractures were reported, suggesting that osteopoikilosis does not predispose to failure under physiological loading conditions.

Across the available literature, fractures were managed using conventional orthopedic principles. Both operative and non-operative strategies resulted in consistent fracture union, with no reported cases of delayed union, nonunion, implant failure, or compromised fixation stability. To our knowledge, this represents the first systematic review using a structured SWiM approach to specifically evaluate fracture healing outcomes in osteopoikilosis. Despite the low level of evidence, the consistency of favorable healing across fracture types and treatment modalities are noteworthy.

From a surgical perspective, concerns regarding fixation stability in sclerotic bone are understandable. However, existing evidence is reassuring. Standard implants and instrumentation were successfully applied across all reported cases without the need for modified techniques. Intramedullary nailing, plate osteosynthesis, and screw fixation were all effective across various anatomical regions.[1,2,24,28] Even in complex scenarios such as cervical spine instrumentation or small bone fixation in the hand, no technical complications related to the bone density were reported.[21,26] Our intra-operative findings were concordant, as increased tactile resistance during drilling did not compromise screw insertion or construct stability. These observations support the continued application of standard AO fixation principles in patients with osteopoikilosis.

Conservative management was similarly effective for stable fracture patterns. Reported cases demonstrated normal callus formation and union timelines comparable to those expected in the general population.[25,27] This suggests that the biological cascade of fracture repair, including hematoma formation, callus development, and remodeling, remains intact despite the presence of multiple bone islands. Together, these findings indicate preserved healing capacity despite altered microarchitecture.

Taken together, our findings suggest that although osteopoikilosis alters bone density measurements and microarchitectural appearance, it does not impair the biological capacity for fracture repair. Clinicians should exercise caution when interpreting BMD in this population, as elevated values may not reflect true skeletal strength. Adjunctive tools such as TBS or functional imaging may provide complementary insight in selected cases. Importantly, current evidence does not support deviation from standard fracture management strategies.

The strengths of this study include its integrated design, combining advanced imaging with a systematically conducted qualitative synthesis using SWiM methodology. This approach allows a comprehensive understanding of osteopoikilosis that bridges metabolic bone assessment and practical orthopedic decision-making. To our knowledge, this is the first report to document a bone quantity–quality paradox using TBS in a fracture patient with this condition.

Several limitations should be acknowledged. The systematic review was restricted to case reports and small case series, reflecting the rarity of osteopoikilosis and limiting the level of evidence. Publication bias and heterogeneous outcome reporting are likely. In addition, bone microarchitecture was assessed using TBS, an indirect textural index that has not been specifically validated in sclerosing bone dysplasias. Although high-resolution peripheral quantitative computed tomography would provide direct volumetric assessment, its limited availability and higher radiation exposure precluded its use. Accordingly, these findings should be interpreted as hypothesis-generating rather than definitive.

CONCLUSION

This study elucidates the bone quantity–quality paradox in osteopoikilosis, demonstrating that sclerotic lesions can mask underlying systemic fragility in the intervening bone. We highlight the utility of TBS as a diagnostic safeguard to prevent false reassurance from artifactually elevated BMD. Furthermore, systematic synthesis confirms that despite this microarchitectural impairment, fracture healing capacity is preserved, validating the continued application of standard orthopedic management principles in this rare condition.

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AUTHOR CONTRIBUTIONS

- **Rathapoom Suwanaratana**: Investigation; Case data acquisition; Data curation; Literature screening; Writing – review & editing; Critical revision of the manuscript for important intellectual content
- **Pichaya Thanindratarn:** Data curation; Literature screening; Validation of extracted data; Writing – review & editing
- **Nuttawut Chanalithichai:** Conceptualization; Study design; Methodology; Investigation; Data curation; Formal analysis; Literature search and systematic review; Data synthesis; Visualization; Writing – original draft; Writing – review & editing; Supervision

All authors approved the final version of the manuscript and agree to be accountable for all aspects of the work.

CONFLICTS OF INTEREST

Rathapoom Suwanaratana, Pichaya Thanindratarn, and Nuttawut Chanalithichai declare that they have no conflict of interest.

DATA AVAILABILITY

All data generated or analyzed during this study are included in this published article and its supplementary materials.

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SUPPLEMENTARY MATERIALS

Supplementary Data

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