Review Article

Periosteal Manifestations of Osteomyelitis and Arthritis on Ultrasound: A Systematic Review

Palapun Waitayangkoon[1]*, Pablo Weilg-Espejo[2], Eugene Y. Kissin[2]

[1]Department of Medicine, MetroWest Medical Center, Tufts University School of Medicine, Framingham, MA, USA, [2]Department of Medicine, Boston University School of Medicine, Boston, MA, USA

Abstract

Ultrasound (US) can visualize the periosteal changes in the early stage compared to radiography. In this review, we studied periosteal manifestations on US and assessed their diagnostic utility for osteomyelitis (OM) and arthritis. We included articles that studied ultrasonographic findings of periosteal changes in OM and arthropathies with aims to systematically review periosteal manifestations of each condition and summarize diagnostic values of each finding. A total of 13 articles were included in the systematic review. Of these, 10 articles are on OM, 3 articles are on psoriatic arthritis (PsA), 1 article is on rheumatoid arthritis (RA), and 1 article is on gouty arthritis (GA). In OM, subperiosteal fluid/subperiosteal collection (SF/SC) was detected in 32%–76% within 72 h after presentation. Periosteal reaction (PR) was seen after day 4 and the sensitivity on US ranges from 33% to 100%. In PsA, PR was seen near 16%–59% in active PsA joints. Periosteal changes are rarely detected in RA joints. Small hyperechoic spots were seen in 87.5% of GA. SF/SC may be seen on US as the earliest sign followed by PR for OM. PR is more specific in PsA than RA. Further investigations on periosteal abnormalities on US are warranted to confirm our findings.

Keywords: Arthritis, osteomyelitis, periosteum, ultrasound

Introduction

Ultrasound (US) use as a diagnostic modality for the musculoskeletal system has expanded over the last decade due to its feasibility, cost-effectiveness, and lack of radiation exposure.[1] It is commonly used to evaluate the superficial structures such as muscles, tendons, and ligaments but cannot image structures deep to cortical bone. Periosteum is a dense fibrous membrane covering the bone surfaces that can be visualized on US superficial to bone cortex.[2] It is normally thick and apparent in children, then becomes thinner with age in healthy adults and can no longer be normally visualized on radiographs.[3]

With its osteoblastic differentiation potential, periosteum becomes ossified and radiographically visible when the underlying cortical bone is injured.[4] This phenomenon is called periosteal reaction (PR).[5] Several conditions, including local infections, inflammation, trauma, tumors, as well as systemic disorders, can stimulate periosteum to produce new bone. PR is the general term used to refer to periostitis, periosteal thickening (PT), and periosteal elevation (PE). It usually takes at least 10 days following the insults until PR becomes well-visualized on radiography.[6] Computed tomography can detect ossified periosteum at an earlier stage, while early nonossified periosteum is only visualized by US and magnetic resonance imaging (MRI).[7,8] As opposed to MRI, performing US in ambulatory and point-of-care settings is much more convenient and practical.

We aim to systematically review studies regarding periosteal manifestations visualized on US to assess its diagnostic utility for such conditions.

Materials and Methods

We conducted a scoping review to identify an overview of the available information regarding imaging findings of PR in the medical literature. We then developed population, intervention,

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Address for correspondence: Dr. Palapun Waitayangkoon, Department of Medicine, MetroWest Medical Center, Tufts University School of Medicine, Framingham, MA, USA. E-mail: palapun@gmail.com

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comparison, and outcome (PICO) questions and search terms based on this information.

Design

This systematic review has been carried out following the recommendations of the preferred reporting items for systematic reviews and meta-analysis statement and guidelines for systematic reviews.

Eligibility criteria

The inclusion criteria were made following the selection protocol based on the PICO questions. All types of studies examining the general human population were included. Any study that recruited people with osteomyelitis (OM) and arthropathies of any kind with periosteal involvement and looked at the US findings was selected for the inclusion in the systematic review. The exclusion criteria were case reports and articles for which US was not utilized as a diagnostic modality or periosteum lesions were not described. Articles published before 2000 were excluded due to the evolution of US technology since then. Articles in the abstract form only were also excluded.

Search strategy

Potentially eligible studies identified from publications indexed in Medline and Embase from inception to August 2022 were independently searched by two investigators (PW, PWE). Search terms were derived from terms related to "periosteum" and "echography" and "arthropathy." The detailed search strategy is described in Supplementary Material 1. There were no design or language limitations applied to the search strategy. Relevant articles in languages other than English were translated by Google Translate or other formal methods if required.

Primary outcomes and secondary outcomes

The primary outcome of this review was to gather information regarding the periosteal changes on US for each condition. Our secondary outcomes were the test characteristics of each finding: Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV), inter-and intra-rater reliability, and to statistically combine the results from included studies.

Data collection and extraction

Two authors (PW, PWE) identified potentially eligible studies by careful and critical reading according to the research protocols independently, and then compared the data extraction [Figure 1]. Any discrepancies were resolved by discussion with the senior investigator (EK). A standardized collection form to record the information of the included research was used with the following variables: Authors, publication year, country of the study, study design, study population, medical diagnosis, and periosteum-related US findings including test characteristics (if available).

Methodological quality

A final analysis was carried out independently by two researchers (PW, PWE) to assess the methodological quality of the full texts that met the eligibility criteria. The quality of each study was assessed using the Joanna Briggs Institute (JBI)

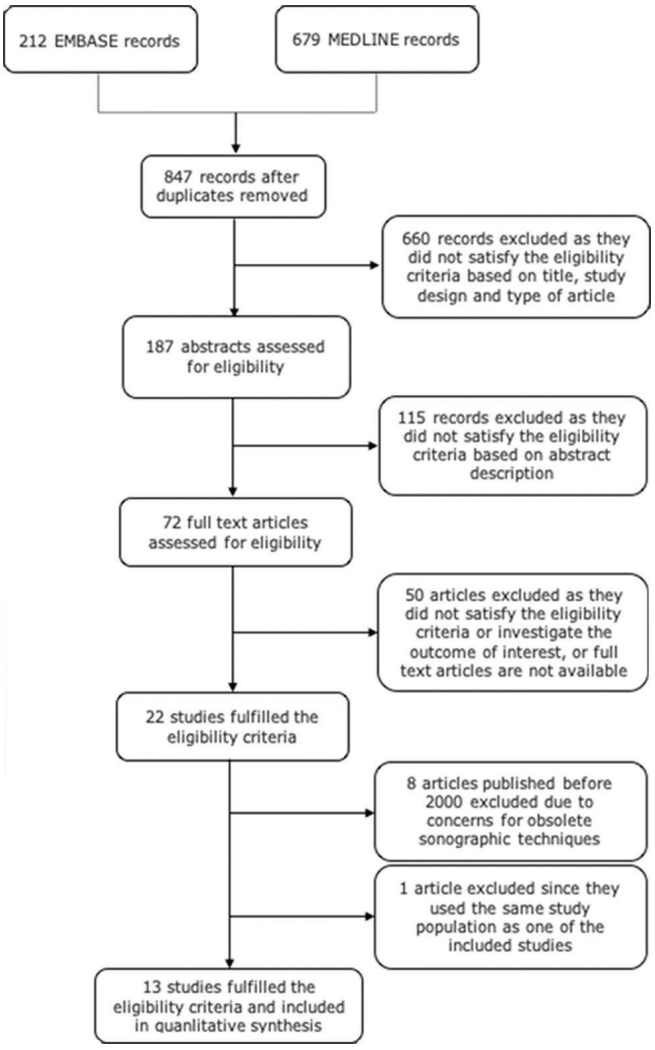

Figure 1: Search methodology and selection process

Critical Appraisal Checklist for Case Series. The assessment of methodological quality was performed by two independent reviewers (PW, PWE). The original checklist contains 10 questions that assess the potential risk of bias and could be answered with yes, no, or unclear. In our study, we used only 8 questions since the other two questions are not relevant to our outcomes of interest. The risk of bias was determined to be low if 70% of the answers scored yes, moderate if 50%–69% of the answers scored yes, and high if below 50% of the answers scored yes.[9] Disagreements among authors were settled by discussion with the senior investigator (EK).

Statistical methods

For studies that did not report values of test characteristics, we calculated sensitivity by dividing the number of persons or joints that have positive results on US by the number of persons or joints with confirmed condition.

Results

We identified a total of 212 articles retrieved from EMBASE and 679 articles from MEDLINE database, in which

44 duplicate articles were discarded, thus leaving 847 articles for title and abstract review. Of these, 660 articles were excluded as they did not satisfy the eligibility criteria based on study design and type of article and 115 articles were excluded based on abstract description. The remaining 72 articles were considered of interest and the full texts were retrieved for detailed evaluation. Subsequently, 50 articles were excluded as the outcome of interest was not reported and some of them were available only for abstracts with no full-text publications. Eight articles published before 2000 were excluded and one article was excluded since they used the same data set as one of the included studies, thus leaving only 13 articles included in the systematic review.[10-22] Figure 1 demonstrates the search methodology and selection process of this study.

Most of the included studies were considered to have low risk of bias. Two studies were classified as moderate risk[10,19] according to the JBI Critical Appraisal Checklist for case series [Table 1].

The included 13 articles consist of 8 retrospective, 4 prospective, and 1 retrospective and prospective studies globally. Most of the articles were published in English except Aloui-Kasbi *et al*.[10] which was written in French. Seven articles are studies in the pediatric population. Of the 13 articles included, there are 10 articles on OM, 3 articles on psoriatic arthritis (PsA), 1 article on rheumatoid arthritis (RA), and 1 article on gouty arthritis (GA). Four of the 13 studies had comparison group (s).[12,13,15,22] All of these used the recruited participants who ended up not having the diagnosis of interest as controls. Tables 2 and 3 show the characteristics of the studies included. Most studies computed sensitivity in their reports except five studies[10,11,14,17,21] that only reported number of positive findings and we calculated sensitivity from the data provided.

Among the studies with OM, there are seven studies on unspecified OM, for which we assume they were acute OM, 2 studies on chronic OM with reactivation, and one study on mastoiditis. We did not include mastoiditis as part of other OMs as it has a different pathophysiology, and the definitions of acute and chronic mastoiditis are different from other OMs. PR or PT/PE are the most described measurement on US reported in 6 studies (1 in chronic OM), followed by subperiosteal fluid/subperiosteal collection (SF/SC) in 5 studies, cortical changes in 4 studies (2 in chronic OM) and increased vascularity on Doppler US in 3 studies. Sensitivity of PR/PT/PE on US in confirmed OM ranges from 33% to 100% but was reported in only 8% of chronic OM. SF/SC, which encompasses the terms of subperiosteal abscess and juxtacortical fluid in some studies, was detected in 32%–76% of cases. Cortical changes were seen in only 33% of OM, 33%–83% of chronic OM, and 100% of mastoiditis cases. Increased vascularity was noted from 55% to 86% in cases of OM. Fistulous formation was seen in 14% of OM and 79% of chronic OM. Small hyperechoic spots were noted in 14% of OM[16] [Table 4].

Periosteal changes in PsA are described as PR and increased Doppler signal. PR was appreciated near 16%–59% of active PsA joints. Doppler signal was increased in 7% [Table 5].

Periosteal changes are rarely detected in RA joints. Small hyperechoic spots suggestive of tophi eroding into bone were seen in 87.5% in GA [Table 5],[16] which is substantially greater than described in other studies.[23] Inter-rater reliability was reported in only 1 study.[16] None of the studies reported PPV, NPV, or intra-rater reliability.

Discussion

Our results showed that PT/PE is commonly detectable in OM, although the sensitivity varies between studies. We believe

Table 1: Assessment of methodological quality of included studies according to the Joanna Briggs Institute critical appraisal checklist for case series

First author	Year	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Total (yes)	% yes	Risk
Aloui-Kasbi	2004	N	U	Y	Y	U	Y	Y	U	4	50	Moderate
Azam	2005	Y	Y	Y	Y	Y	N	Y	Y	7	87.5	Low
Balanika	2009	Y	Y	Y	Y	Y	Y	Y	Y	8	100	Low
Ezzat	2011	Y	Y	Y	Y	Y	Y	Y	Y	8	100	Low
Fournié	2006	Y	Y	Y	N	Y	N	Y	Y	6	75	Low
Inusa	2013	Y	Y	Y	Y	Y	N	Y	Y	7	87.5	Low
Lu	2019	Y	Y	Y	Y	Y	Y	Y	Y	8	100	Low
Mantsopoulos	2015	Y	Y	Y	Y	Y	Y	Y	Y	8	100	Low
Naranje	2015	Y	Y	Y	Y	Y	Y	Y	Y	8	100	Low
Paliwal	2021	U	Y	N	Y	U	Y	Y	N	4	50	Moderate
Sankowski	2013	N	Y	Y	N	Y	Y	Y	Y	6	75	Low
Venkatesh	2003	Y	Y	Y	Y	Y	Y	Y	N	7	87.5	Low
William	2000	Y	U	Y	Y	Y	Y	Y	Y	7	87.5	Low

Q1: Were there clear criteria for inclusion in the case series?; Q2: Was the condition measured in a standard, reliable way for all participants included in the case series?; Q3: Were valid methods used for identification of the condition for all participants included in the case series?; Q4: Did the case series have consecutive inclusion of participants?; Q5: Did the case series have complete inclusion of participants?; Q6: Was there clear reporting of the presenting site (s)/clinic (s) demographic information?; Q7: Was there clear reporting of the demographics of the participants in the study?; Q8: Was there clear reporting of clinical information of the participants?; Y: Yes; N: No; U: Unclear; NA: Not applicable

Table 2: Characteristics of included studies: Osteomyelitis

Year	First author	Country of the study	Study design	Study population	Medical diagnosis	No. of patients with the diagnosis of interest	No. of joints/fingers investigated	Diagnosis of comparison group	No. of patients in comparison group
2000	William	Oman	Retrospective	Patients (age 3-24 years) who had sickle cell disease patients and clinical suspicion of OM over a 18-month period	OM	16	19	ON	19 sites from 15 patients
2003	Venkatesh	Canada	Retrospective	Patients (age 28-89 years) who were diagnosed with reactivated chronic OM recruited between April 1993 and December 1997	Reactivated chronic OM	12	12		
2004	Aloui-Kasbi	Tunisia	Prospective and retrospective	Patients (age 4 months - 14 years) with pseudotumoral OM recruited between December 1989 and June 2003	OM	9	9		
2005	Azam	India	Prospective	Patients (age 7 months to 15 years) diagnosed to have OM based on the positivity of two of the four criteria: classic symptoms, positive bone or blood culture, pus aspirated from bone and typical radiographic changes between June 2002 to December 2003	OM	55	55		
2009	Balanika	Greece	Retrospective	Patients (age 35-70 years) with history of post-traumatic/postoperative Chronic OM and had undergone previous surgeries or had orthopedic devices, who presented with signs and symptoms of infection reactivation between September 2004 and May 2007	Reactivated chronic OM	24	24	Non OM	16
2011	Ezzat	Egypt	Retrospective	Patients (age 0-18 years) diagnosed with clinical suspicion of OM who were referred to radiology department between July 2006 to May 2007	OM	25	25	Hematoma	2
2013	Inusa	UK	Retrospective case control	Patients (age 0-18 years) who were admitted to pediatrics department from October 2003 to December 2010	OM	41	41	VOC	58
2015	Mantsopoulos	Germany	Retrospective	Patients (age 18 months - 13 years) with clinical suspicion of mastoiditis between 2004 to 2012	Mastoiditis	9	9		
2019	Lu	Taiwan	Retrospective	Patients (age over 20 years) selected from the rheumatology department between January 2010 to June 2015	OM	7	7		
2021	Paliwal	India	Prospective	Patients (age 6-12 years) who were referred to the radiology department from July 2019 to July 2020 by clinical and laboratory criteria considered to be indicative of acute OM	OM	5	5		

OM: Osteomyelitis; VOC: vasoclusive crisis; ON: Osteonecrosis

the variability is largely due to the timing of US examination after presentation, and due to cutoff values used to establish positivity. Azam *et al*.[11] demonstrated that PR was detected from day 4 to 15 and no PR was detected on the first 3 days. This is in agreement with Paliwal *et al*.[19] who reported PR in up to 80% of OM cases scanned on day 3–7. Inusa *et al*.[15] studied PR in the first 6 days and detected only 39% when used 4 mm as a cutoff value. However, they would have detected up to 69% if PE cut-off with <4 mm in depth had been used. Earlier in OM, SF/SC might be more sensitive. William *et al*.[22] reported SF can be seen very early in the course of the disease: In up to 74% of cases within 72 h after presentation. While Inusa *et al*.[15] also reported SF in the first 4 days of disease, they found a sensitivity of only 14%. Moreover, it was not increased between day 0–4 and day 4–7 (14% and 13%, respectively). Using a cutoff value of 1 mm for SF depth instead of 4 mm, increased sensitivity 53% (10/19) to 64% (14/19).[22] Increased vascularity on Doppler US appeared to be well-appreciated on day 3–7,[11,19] although none of the studies specifically described Doppler signal findings on the

Table 3: Characteristics of included studies: Arthritis

Year	First author	Country of the study	Study design	Study population	Medical diagnosis	No. of patients with the diagnosis of interest	No. of joints/ fingers investigated
2006	Fournié	France	Prospective	Patients (mean age of 42.8 years) who met Fournié criteria for PA contributing to 25 fingers or 75 joints	PsA	20	25 fingers 75 joints
2013	Sankowski	Poland	Retrospective	Patients (age 20-70 years) who were diagnosed with PA by dermatologists and rheumatologists	PsA	66	66
2015	Naranje	India	Prospective	Patients (age 18-62 years) who were diagnosed to have PA at the rheumatology outpatient clinic	PsA	30	30
2019	Lu	Taiwan	Retrospective	Patients (age over 20 years) selected from the rheumatology department between January 2010 to June 2015	RA Gouty arthritis	18 8	18 8

PsA: Psoriatic arthritis; RA: Rheumatoid arthritis

Table 4: Periosteal findings of osteomyelitis on ultrasound

Ultrasonographic measurements	Sensitivity	Medical diagnosis	First authur
Periosteal reaction	33	OM	Aloui-Kasbi
Periosteal reaction	64	OM	Azam
Periosteal elevation	62	OM	Inusa
Periosteal thickening or elevation	80	OM	Paliwal
Periosteal reaction	8	Reactivated chronic OM	Venkatesh
Periosteal elevation	100	Mastoiditis	Mantsopoulos
Subperiosteal collection	76	OM	Azam
Subperiosteal abscess	32	OM	Ezzat
Fluid collection	44	OM	Inusa
Juxtacortical fluid	29	OM	Lu
Subperiosteal fluid	74	OM	William
Increased periosteal vascularity	55	OM	Azam
Increased periosteal vascularity	86	OM	Lu
Increased periosteal vascularity	80	OM	Paliwal
Cortical irregularity	33	OM	Aloui-Kasbi
Cortical irregularity	83	Reactivated chronic OM	Venkatesh
Cortical discontinuity	58	Reactivated chronic OM	Venkatesh
Cortical discontinuity	33	Reactivated chronic OM	Balanika
Delineated defect of cortex	100	Mastoiditis	Mantsopoulos
Fistulous tract formation	14	OM	Lu
Fistulous tract extension to cortex	79	Reactivated chronic OM	Balanika
Small hyperechoic spots	14	OM	Lu

OM: Osteomyelitis

first 3 days. In general, increased vascularity is a nonspecific sign on US, which can be seen in conditions other than OM since it reflects local inflammation by detecting blood moving in the investigated area.[24] A combination of PR, SC/SF, and Doppler signal should be studied over the time course of the disease to conclude the utility of these findings for OM diagnosis.

In reactivated chronic OM, PR was seen only in 8% but the fistulous tract extension was seen in 79%[12] and cortical irregularity was seen in 83%.[21] Although the sensitivity of cortical discontinuity was only 33%–58%, the specificity was 93%.[12] These findings are promising as potential parameters to be used as a noninvasive tool for the diagnosis of reactivation in chronic OM.

Information on periosteal changes in PsA is very limited. The US definition of PR was not reported in any of the three manuscripts detailing these abnormalities. However, Sankowski *et al*. demonstrated that US was more sensitive for PR than plane film radiography and MRI for PsA.[20]

The diagnostic value of US for GA has gained more attention since arthrocentesis, which is the gold standard for the diagnosis, is not always possible and sensitivity can vary.[25] Hyperechoic aggregates are monosodium urate crystal depositions in the early stage of gouty joints before they become discernible on radiography or morphologically deformed.

A major limitation of our study is the high methodological heterogeneity between studies. US investigations were

Table 5: Periosteal findings of psoriatric arthritis, rheumatoid arthritis and gouty arthritis on ultrasound

First author	Medical diagnosis	No. of joints	Ultrasonographic measurements	Test characteristics
				Sensitivity
Fournié	Psoriatric arthritis	75	Periosteal reaction	16
			Increased doppler signal	7
Sankowski		66	Periosteal reaction on wrist joints	59.1
			Periosteal reaction on MCP joints	16.7
Naranje		30	Periosteal reaction	33
Lu	Rheumatoid arthritis	18	Periosteal vascularity	16.7
			Juxtacortical fluid	11.1
			Fistulous tract formation	5.6
			Small hyperechoic spots	0
	Gouty arthritis	8	Periosteal vascularity	25
			Small hyperechoic spots	87.5

MCP: Metacarpophalangeal

performed at different timescales, without standardized cut-off values for positivity criteria, and without a uniform definition for PR on US imaging. For these reasons, it was difficult to statistically interpret the results. Sensitivities computed from the included studies may not be generalizable. Moreover, most of the studies lack internal validity. None of the studies reported intra-rater reliability and only two studies reported inter-rater reliability. There should be specific criteria to uniformly diagnose PR on US.

Conclusions

SF may be seen on US in the 1st few days of bone infection, with PT/PE following over the 1st week in most cases of OM. In PsA, PR is less sensitive but might be specific, relative to RA. There is, however, a scarcity of studies evaluating US for periosteal evaluation. Consensus definitions of periosteal abnormalities on US need to be defined, and reliability for these abnormalities will need to be established.

Data availability

The data supporting this systematic review are from previously reported studies and datasets, which have been cited.

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PW and EK were involved in planning the work. PW and PWE collected the data and performed the analysis. PW drafted the manuscript and designed the figures. EK aided in interpreting the results and worked on the manuscript. All the authors discussed the results and commented on the manuscript.

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Conflicts of interest

There are no conflicts of interest.

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Supplementary Material

Supplementary Material 1: Searching strategy

MEDLINE Database:
(periosteum OR periostitis OR periosteal) AND (ultrasound OR sonography OR ultrasonography, Doppler) AND (psoriatic OR arthritis OR spondylitis OR spondylarthritis OR osteomyelitis OR osteoarthropathy).

EMBASE Database:
1. “periosteum”/exp OR periosteum
2. “periosteal”/exp OR periosteal
3. “periostitis”/exp OR periostitis
4. ”periosteal reaction”/exp OR periosteal reaction
5. “echography”/exp OR echography
6. “ultrasound”/exp OR ultrasound
7. “sonography”/exp OR sonography
8. “doppler flowmetry”/exp OR doppler flowmetry
9. “doppler ultrasonography’/exp OR doppler ultrasonography
10. “psoriatic arthritis”/exp OR psoriatic arthritis
11. “arthritis”/exp OR arthritis
12. “spondylitis”/exp OR spondylitis
13. “spondylarthritis”/exp OR spondylarthritis
14. “spondyloarthropathy”/exp OR spondyloarthropathy
15. “osteomyelitis”/exp OR osteomyelitis
16. #1 OR #2 OR #3 OR #4
17. #5 OR #6 OR #7 OR #8 OR #9
18. #10 OR #11 OR #12 OR #12 OR #13 OR #14 OR #15
19. #16 AND #17 AND #18.