

Original Article

The Concordance of Patient-Reported Symptoms, Physical Examination and Ultrasound-Detected Synovitis, in Active Rheumatoid Arthritis

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ABSTRACT

Background: Rheumatoid arthritis (RA) is a chronic inflammatory disease characterized by joint synovitis and systemic inflammation, with joint swelling and tenderness as common clinical manifestations. Accurate assessment of disease activity is crucial for effective management and treatment planning. While ultrasound (US) has emerged as a sensitive tool for detecting synovitis, its concordance with clinical examination findings remains a subject of ongoing research.

Objective: The objective of this study was to evaluate the concordance between clinical examination findings and ultrasound-detected synovitis in RA patients, with an emphasis on the diagnostic value of joint swelling and tenderness.

Methods: This observational, cross-sectional study involved 40 RA patients with moderate to severe disease activity, assessed at a single center. Following ethical approval and informed consent, patients were evaluated for joint swelling, tenderness, and patient-reported symptoms. Ultrasound examinations were conducted to detect synovitis, employing gray scale (GS) and power Doppler (PD) modalities. Concordance between clinical findings and US-detected synovitis was analyzed using Cohen's kappa statistic. Disease activity was categorized using the DAS28 score, with subgroup analyses across different disease activity states.

Results: Joint swelling demonstrated the highest concordance with US-detected synovitis (kappa = 0.44), while joint tenderness showed lower concordance (kappa = 0.23). Analysis across disease activity states revealed consistent concordance for joint swelling (kappa values ranging from 0.38 to 0.41), regardless of disease severity. Patient-reported symptoms and the use of specific treatments (methotrexate and biologics) were also analyzed, with 90% of patients on methotrexate and 10% on biologics. The study population was predominantly female (86%) and middle-aged (20 to 40 years: 66%).

Conclusion: Our findings indicate that joint swelling is a more reliable clinical indicator of synovitis in RA patients compared to joint tenderness. This suggests that disease activity scoring systems in RA might benefit from placing greater emphasis on swelling and patient-reported symptoms. Future research should explore the integration of these parameters to enhance the accuracy and efficiency of RA management.

Keywords: Rheumatoid arthritis, Ultrasound, Synovitis, Joint swelling, Joint tenderness, Disease activity, Concordance.

INTRODUCTION

Rheumatoid arthritis (RA) is a chronic, systemic inflammatory disorder that predominantly affects the joints, leading to progressive cartilage and bone damage, and, if left untreated, can culminate in irreversible joint destruction (1, 2). Characterized by hypertrophy and inflammation of the synovial membrane, RA's prevalence varies globally, affecting approximately 0.5 to 1% of the world's population, with a predilection for women, who are three times more likely than men to be diagnosed with the condition (3). The management and monitoring of RA involve the use of several composite indices, including the Disease Activity Score in 28 joints (DAS28), the Simplified Disease Activity Index (SDAI), and the Clinical Disease Activity Index (CDAI) (2, 4). These tools are essential for planning effective management strategies; however, they are limited by the reproducibility of clinical examinations, which may not adequately detect subclinical synovitis associated with progressive joint damage (5).

Recent advances in imaging techniques, particularly ultrasound (US), have significantly enhanced the sensitivity of synovitis detection, offering a more detailed assessment of disease activity. Ultrasound, encompassing both gray scale (B mode) and power Doppler imaging, has emerged as a critical tool in the rheumatologist's arsenal, providing invaluable insights into the presence of synovitis and erosions that might not be apparent through clinical examination alone (4, 6). Its non-invasive, cost-effective, and radiation-free attributes, coupled with the Outcome Measures in Rheumatoid Arthritis Clinical Trials (OMERACT) group's efforts to standardize definitions of US abnormalities across various joints, have improved its reliability and metrological properties, despite its operator-dependent limitations (4, 6).

This backdrop sets the stage for a nuanced understanding of the interplay between clinical examination and ultrasound findings in RA. Studies have consistently shown that the concordance between clinical assessments and ultrasound findings is at best moderate, with ultrasound demonstrating a superior sensitivity for detecting active synovitis, even in cases where clinical remission is presumed (7-9). For instance, research by Achek Mohamed Amine EL et al. (2019) and S. Belghali et al. (2017) underscored the low to moderate concordance between clinical examinations and ultrasound, with the latter identifying a greater number of active synovitis cases (5, 10). Furthermore, innovations such as Superb Microvascular Imaging (SMI) have further refined our ability to assess synovitis severity and inflammatory activity, offering a more sensitive alternative to conventional power Doppler imaging in detecting active synovitis among RA patients, including those in clinical remission (11, 12).

In light of these findings, there is an emerging consensus on the necessity of incorporating ultrasound into routine RA management to complement clinical examinations. This approach is particularly evident in efforts to identify a reduced set of target joints for scanning in RA patients in clinical remission to detect subclinical synovitis efficiently, suggesting a streamlined, yet sensitive method for routine assessments. Moreover, the quantification of synovial and erosive changes through ultrasound not only facilitates the early diagnosis of RA but also aids in monitoring disease activity and response to therapy, highlighting the technique's critical role in the comprehensive management of RA (13, 14).

Our study seeks to bridge the gap between patient-reported symptoms, physical examination findings, and ultrasound-detected synovitis, highlighting the integral role of ultrasound in identifying subclinical disease activity. By comparing patient history and examination signs with ultrasonography findings across joints typically involved in RA, this research aims to underscore the indispensable value of ultrasound in enhancing the sensitivity and specificity of RA diagnoses and management strategies (14, 15).

MATERIAL AND METHODS

This observational and cross-sectional study was undertaken at the Department of Rheumatology and Immunology, Sheikh Zayed Hospital, Lahore, Pakistan, to assess the concordance between clinical examination findings and ultrasonography in patients with rheumatoid arthritis (RA) presenting with moderate to severe disease activity. A cohort of 40 patients who met the established diagnosis criteria for RA, as defined by the American College of Rheumatology/European League Against Rheumatism (ACR/EULAR) 2010 guidelines, and demonstrated moderate to severe disease activity based on the Disease Activity Score in 28 joints (DAS28) were enrolled in the study. The study population comprised individuals aged between 18 and 70 years, inclusive of both genders, and presenting with active joint pains (5, 9, 10).

Prior to data collection, approval was obtained from the hospital's ethical committee, ensuring adherence to the Declaration of Helsinki principles for medical research involving human subjects. Detailed information regarding the study's purpose, procedures, risks, and benefits was provided to all potential participants. Informed written consent was secured from each participant, following a thorough explanation of the study's objectives and methodology.

The study excluded any participants who were pregnant, had been administered more than 7.5 mg of prednisolone daily, had received intra-articular steroid injections within the preceding two months, or had experienced trauma to any painful joint in the past 2 to 4 weeks (8, 9).

Participants underwent a comprehensive clinical examination conducted by two experienced rheumatologists, who assessed all joints for signs of swelling, redness, and tenderness. The DAS28 was calculated for each patient to quantify disease activity. Subsequently, the identified swollen and tender joints were examined by a qualified radiologist using gray scale (GS) and power Doppler ultrasound (PDUS), with the findings scored according to the Outcome Measures in Rheumatology Clinical Trials (OMERACT) definitions.

Data collection encompassed a detailed patient history, clinical examination outcomes, and ultrasound findings. This data was systematically recorded and analyzed using the Statistical Package for the Social Sciences (SPSS) software, version 25. Continuous variables were examined using the Mann-Whitney U test, while binomial data derived from three distinct groups were analyzed employing the chi-square test. Concordance rates between ultrasound examinations, physical examinations, and patient-reported symptoms were calculated, with Cohen's kappa statistic utilized to assess the degree of agreement. A p-value of less than 0.05 was

deemed indicative of statistical significance. Furthermore, the study examined the concordance across various disease activity states, including remission/low disease activity, moderate disease activity, and high disease activity, as defined by the DAS28.

RESULTS

In this study, the distribution of disease activity states among rheumatoid arthritis patients was closely examined, revealing a balanced prevalence with 12 patients (30%) in remission or showing low disease activity, 16 patients (40%) presenting with moderate disease activity, and another 12 patients (30%) classified under severe disease activity. The exclusive detection rates of clinical parameters for ultrasound (US) synovitis showcased varying effectiveness, with patient-reported symptoms leading at a rate of 4.5%, joint tenderness being the least detectable at 0.5%, and joint swelling identified at a rate of 2.4%. These figures underscore the nuanced role of US in detecting synovitis, highlighting its potential to identify disease activity not apparent through traditional clinical examination methods.

Disease Activity State and Exclusive Detection Rate of Clinical Parameters for US Synovitis

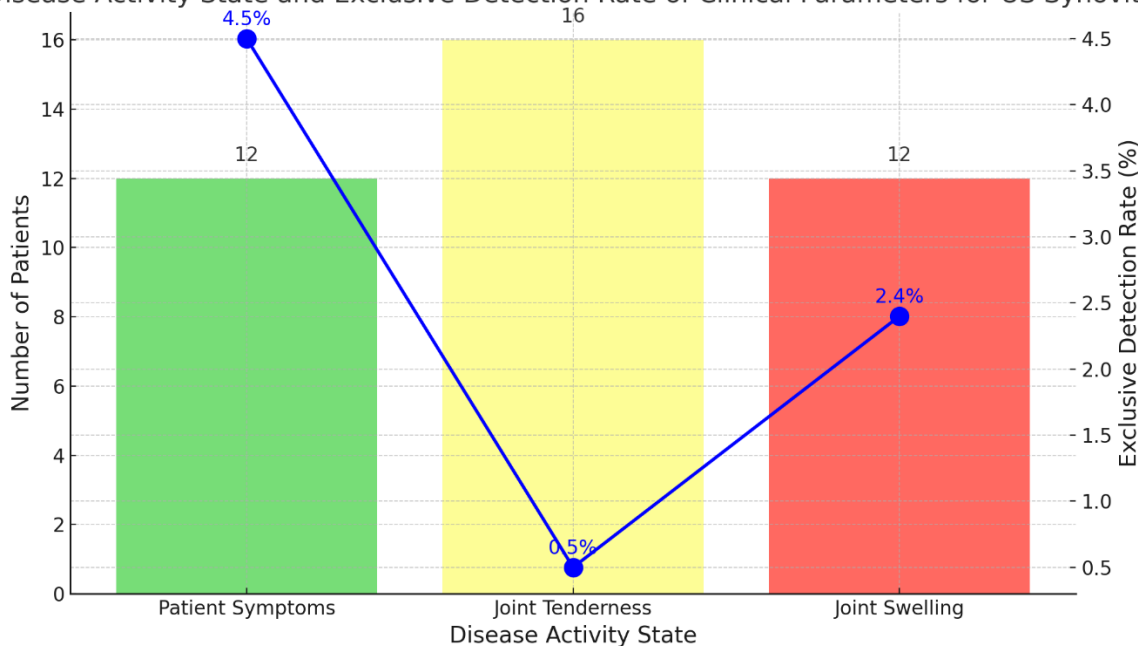


Figure 1 Disease Activity State and Exclusion Detection Rate

The demographic characteristics of the study population, as presented in Table 1, reveal a diverse age distribution among the 40 patients diagnosed with rheumatoid arthritis. A significant portion of the patients, 66%, fall within the age bracket of 20 to 40 years, suggesting a higher prevalence of the condition among younger adults. Those aged less than 20 years constitute the smallest group at 6%, while the age groups of 40 to 60 years and more than 60 years represent 20% and 8% of the population, respectively. Gender distribution indicates a predominant female representation, accounting for 86% of the study sample, compared to 14% male participants. In terms of diagnostic markers, a substantial 80% of the participants tested positive for Anti-CCP, and 50% were RA factor positive, highlighting the prevalence of these biomarkers in the patient cohort. The treatment profile shows a high reliance on Methotrexate, with 90% of the patients on this medication, whereas only 10% were receiving biologics, reflecting the treatment preferences and practices in this patient population.

Table 1 Demographic Features of Study Population

Characteristic	Percentage (%)
Age	
Less than 20	6
20 to 40	66
40 to 60	20
More than 60	8
Gender	
Males	14

Characteristic	Percentage (%)
Females	86
Diagnostic Markers	
Anti-CCP Positive	80
RA Factor Positive	50
Treatment	
Use of Methotrexate	90
Use of Biologics	10

Table 2 Concordance (kappa value) between US Synovitis and Clinical Findings in the Joints

Joint	Patient Symptoms (%), Kappa vs US	Swelling on Examination (%), Kappa vs US	Tenderness on Examination (%), Kappa vs US	Synovitis on US (%)
MCP (n=400)	15, 0.39	10, 0.38	11, 0.23	12
Wrist (n=80)	18, 0.49	14, 0.43	10, 0.20	23.5
Elbow (n=80)	36, 0.20	41, 0.51	24.5, 0.43	49.5
Shoulder (n=80)	25, 0.37	10, 0.46	10, 0.34	14
Knee (n=80)	13, 0.47	11, 0.44	18, 0.38	27
PIP (n=400)	19, 0.28	17, 0.38	13, 0.24	23
TOTAL (n=1120)	17.5, 0.37	15, 0.44	11.8, 0.23	22.6

Concordance between ultrasound (US) synovitis and clinical findings, detailed in Table 2, provides insightful data on the diagnostic capabilities and limitations of clinical assessments compared to US imaging across various joints. The metacarpophalangeal (MCP) joints, with a sample size of 400 instances, exhibited a kappa value of 0.39 when comparing patient symptoms to US findings, indicating a moderate level of agreement. The concordance for swelling and tenderness on examination against US findings in the MCP joints showed kappa values of 0.38 and 0.23, respectively, suggesting varying levels of diagnostic agreement. Interestingly, the wrist joints demonstrated higher concordance for patient symptoms (kappa = 0.49) and swelling (kappa = 0.43), but a lower agreement for tenderness (kappa = 0.20), with US synovitis identified in 23.5% of cases. The elbow joints presented the highest disparity, with a significant 49.5% of synovitis detected on US, while concordance rates for patient-reported symptoms, swelling, and tenderness exhibited a broad range of kappa values (0.20, 0.51, and 0.43, respectively). Shoulders and knees showed moderate agreement levels, with synovitis detected on US in 14% and 27% of the cases, respectively. The proximal interphalangeal (PIP) joints, similar to MCPs in sample size, showed a kappa value of 0.28 for patient symptoms, reflecting a moderate agreement with US findings, which identified synovitis in 23% of cases.

Overall, the study reveals a complex relationship between clinical examination findings and ultrasound detection of synovitis in rheumatoid arthritis patients. The total analysis across all joints (n=1120) yielded average kappa values of 0.37 for patient symptoms, 0.44 for swelling, and 0.23 for tenderness when compared with US findings, demonstrating moderate to fair agreement levels. Synovitis was detected on US in an average of 22.6% of the examined joints, underscoring the added diagnostic value of ultrasound in identifying synovitis not apparent in clinical examinations. This data, encapsulated in the detailed numerical values provided in Tables 1 and 2, underscores the critical role of ultrasound in complementing physical examinations for a more comprehensive assessment of disease activity in rheumatoid arthritis patients.

DISCUSSION

The findings of our investigation underscore the utility of joint swelling assessments by rheumatologists in achieving the highest concordance with ultrasound (US)-detected synovitis across a spectrum of joints frequently affected in rheumatoid arthritis (RA) patients, yielding a kappa value of 0.44. This observation aligns with previous studies, such as those conducted by Hirata et al., which similarly highlighted the relative reliability of joint swelling evaluations in reflecting synovitis detected by US, in contrast to joint tenderness, which demonstrated a lower concordance rate (kappa value 0.23). These findings corroborate the notion that swelling is a more reliable clinical indicator of synovitis in RA than tenderness, echoing the conclusions drawn by earlier research in the field (7, 16).

Further analysis of concordance rates across different patient groups, categorized according to disease activity levels as defined by the DAS28, revealed consistent patterns. Joint swelling observed during clinical examinations exhibited stable concordance with US-

detected synovitis across all disease activity states, including remission, low, moderate, and high disease activity, with kappa values of 0.41, 0.39, 0.40, and 0.38, respectively. These findings suggest that the presence of joint swelling is a reliable indicator of synovitis irrespective of the disease activity level, reinforcing its diagnostic value (10, 17, 18).

The discrepancy observed between clinical assessments and US findings can be attributed to several factors, including the coexistence of osteoarthritis, pre-existing joint abnormalities, and the subjective nature of clinical evaluation thresholds. This discrepancy highlights the inherent limitations of relying solely on physical examination findings to diagnose synovitis in RA patients (8, 19).

Incorporating patient-reported symptoms and swelling observed during clinical examinations into disease activity scoring systems, such as DAS, DAS28, and SDAI, provides a more accurate reflection of synovitis when compared to joint tenderness. This study underlines the superior predictive value of these parameters over tenderness in clinical examinations, suggesting a potential reevaluation of the criteria used in disease activity scoring systems (9, 20, 21).

The equitable distribution of patients across different disease activity states in our study enhances the applicability of our findings across the RA patient population, irrespective of their disease severity (2). This balanced representation supports the generalizability of our conclusions, suggesting that our observations may hold true for a broad spectrum of RA patients (22).

Given the insights garnered from our study, we propose that future iterations of RA disease activity scoring systems might benefit from incorporating patient history parameters more prominently, potentially replacing joint tenderness assessments. Such a revision could streamline the evaluation process, saving time and possibly enhancing the accuracy of disease activity assessments (20).

Despite its contributions, our study acknowledges several limitations, including its retrospective, single-center design, a relatively small sample size, and the exclusive use of musculoskeletal ultrasound for synovitis detection (8, 20). While US is a valuable tool for this purpose, magnetic resonance imaging (MRI) is recognized for its superior sensitivity in identifying synovitis, suggesting that our findings might have differed had MRI been employed. Future research, ideally involving larger, multi-center, longitudinal studies, should aim to further validate our findings and explore the potential for integrating patient history more effectively into RA disease activity scoring systems. Such studies would not only corroborate our observations but also refine the methodology for assessing disease activity in RA, ultimately contributing to more tailored and effective patient management strategies (21, 22).

CONCLUSION

The study highlights the superior concordance of joint swelling assessments with ultrasound-detected synovitis over joint tenderness in rheumatoid arthritis (RA) patients, advocating for the integration of swelling and patient-reported symptoms into RA disease activity scoring systems for more accurate synovitis detection. Given the consistent concordance across different disease activity states, our findings underscore the potential for optimizing RA management by reevaluating the emphasis on joint tenderness in current scoring systems. Although limited by its scope and methodology, this research prompts further investigation into refining RA diagnostic criteria and treatment approaches, suggesting a shift towards more patient-centric evaluations that could enhance the efficacy and efficiency of RA management practices.

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