Ultrasonographic findings of the shoulders in Egyptian patients with rheumatoid arthritis
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Introduction
Rheumatoid arthritis (RA) is a chronic systemic autoimmune inflammatory disease of unknown etiology that may affect many tissues and organs, but principally attacks the synovial joints. The pathology of the disease process often leads to the destruction of articular cartilage, bone erosions, and ankylosis of the joint [1]. Musculoskeletal ultrasonography (US) is an imaging modality now widely available in both scientific research and clinical rheumatology practice. Important advances have been made in the field of musculoskeletal US, allowing it to become a very powerful tool in rheumatological clinical practice. It is used for visualizing joints and soft tissues in patients with rheumatic diseases. US is not only able to image tendons, joints, nerves, muscles, skin, and blood vessels but also able to identify and quantify tendon pathology and synovial inflammation [2].

Objective
This study aimed to highlight the diagnostic value of musculoskeletal ultrasonography (US) in the evaluation of inflammatory changes in the shoulders of rheumatoid arthritis (RA) patients and to correlate those findings with the clinical, laboratory, and radiological parameters of the disease activity.

Patients and methods
This study included 40 RA patients diagnosed according to the 2010 American College of Rheumatology/European League Against Rheumatism classification criteria for RA. In addition, 20 age-matched and sex-matched healthy individuals were included. US assessment was performed bilaterally in RA patient’s shoulder and unilaterally in controls. All US examinations were carried out using LOGIQ P6 PRO machine equipped with 6–8 MHz broadband multifrequency linear transducer.

Result
US on shoulders detected that 21 (52.5%) RA patients studied had erosions, 18 (45%) RA patients had synovitis, 21 (52.5%) RA patients had tenosynovitis, seven (17.5%) RA patients had bursitis, and 18 (45%) RA patients had rotator cuff tendinopathy. There was a significant relation between US-detected erosion in RA patients and disease duration ($P = 0.037$) and rheumatoid factor (RF) level ($P = 0.02$), whereas there was no significant relation between US-detected erosion in RA patients and shoulder pain ($P = 0.185$), Disease activity score 28 (DAS28) ($P = 0.163$), erythrocyte sedimentation rate ($P = 0.519$), and C-reactive protein levels ($P = 0.561$). There was a significant relation between US-detected tenosynovitis in RA patients and shoulder pain ($P = 0.025$). There was no significant relation between US-detected bursitis in RA patients and disease duration ($P = 0.970$), shoulder pain ($P = 0.907$), DAS28 ($P = 0.471$), erythrocyte sedimentation rate ($P = 0.220$), and RF levels ($P = 0.755$), whereas there was a significant relation between US-detected bursitis in RA patients and C-reactive protein ($P = 0.036$).

Conclusion
US became a problem-solving approach and the tool of choice for cases with shoulder problem, and can provide an accurate answer to many clinical questions and give an accurate diagnosis of different pathological abnormalities encountered.

Keywords:
rheumatoid arthritis, shoulders, ultrasonographic
Musculoskeletal US should be viewed as an adjunct to the widespread use of conventional radiography in the evaluation of rheumatic disease. In the investigation of regional pain syndromes, US delivers valuable anatomical information that is not available on radiographs. In addition, US is able to demonstrate the presence of bone erosions in the early phase of RA when radiographs appear otherwise unremarkable [4].

Compared with MRI, US appears to be more accurate in the diagnosis of tendon changes. An additional benefit over MRI is the possibility to explore other relevant anatomical areas (i.e. the contralateral side) [5].

Musculoskeletal US should be performed when it is expected to add valuable information to history and physical examination of rheumatic patients. It is particularly useful in the context of a complex clinical and radiographic setting [6].

Moreover, it has potential in the monitoring of disease activity and progression. US as the initial diagnostic tool can replace other invasive and expensive tests, shorten examination times, and improve efficiency at rheumatology units [7].

**Patients and methods**

This study was conducted on 40 RA patients attending the Rheumatology, Physical Medicine, and Rehabilitation Department of Benha University Hospitals. These patients were diagnosed according to the 2010 American College of Rheumatology/European League Against Rheumatism (ACR/EULAR) classification criteria for RA [8]. Twenty apparently healthy age-matched and sex-matched volunteers recruited from the hospital personnel and patients’ relatives represented the control group. Prior written consent was taken from each patient and controls included in the study, and this study was approved by the Ethical Committee of Faculty of Medicine, Benha University.

Patients were subjected to full history taking, clinical examination, modified health assessment score (HAQ) score assessment, plain radiography of both hands and shoulders, and laboratory investigations including erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), rheumatoid factor (RF), and anticitrullinated peptide antibodies. Disease severity was assessed using Larsen score. Disease activity was measured using DAS28 score.

US assessment was performed bilaterally in RA patient’s shoulder and unilaterally in controls. All US examinations were carried out using LOGIQ_P6 PRO machine equipped with 6–8 MHz broadband multifrequency linear transducer. The radiologist was blinded to clinical data, and patients and controls were asked not to talk to the radiologist about their clinical condition. A protocol-driven approach to shoulder US technique will ensure a comprehensive and efficient examination [9]. The transducer should be linear (with a flat rather than a curved surface) so that the sound beam propagates through the soft tissues in a similar linear manner, to ensure that the sound beam is directed perpendicular to the tendon fibers and minimize anisotropy. Results of this study were collected, tabulated, and statistically analyzed using SPSS (statistical package for social science) program version 22 (SPSS Inc., Chicago, Illinois, USA) on an IBM compatible computer.

**Results**

This study included 40 patients suffering from RA diagnosed according to the 2010 ACR/EULAR classification criteria for RA. All patients were recruited from the Rheumatology, Rehabilitation, and Physical Medicine Outpatients Clinic and Inpatients Department of Benha University Hospitals. There were 36 (90%) female and four (10%) male patients whose ages ranged between 31 and 65 years (mean: 48.45 ± 9.92 years). Twenty apparently healthy age-matched and sex-matched volunteers recruited from the hospital personnel and patients’ relatives represented the control group.

Clinical data are shown in Table 1. Disease duration ranged between 2 and 22 years, with a mean of 10.82 ± 5.58 years. Morning stiffness ranged between 1 and 5 h, with a mean of 2.20 ± 1.09 h.

Two (5%) patients were in remission, whereas six (15%) patients had low disease activity, 11 (27.5%) patients had moderate disease activity, and 21
(52.5%) patients had high disease activity (Fig. 1). Five (12.5%) RA patients had normal function, whereas 16 (40%) RA patients studied had mild functional loss, 11 (27.5%) RA patients had moderate functional loss, and eight (20%) RA patients had severe functional loss (Fig. 2).

Laboratory data are shown in Table 2. An overall 70% of our patients had positive RF level, whereas only 30% of the patients had negative RF level. There were statistically significant differences between the patient and control groups as regards hemoglobin%, ESR first hour, CRP, and RF levels.

US on shoulders detected that 21 (52.5%) RA patients studied had erosions, 18 (45%) RA patients had synovitis, 21 (52.5%) RA patients had long head of biceps (LHB) tenosynovitis, seven (17.5%) RA patients had bursitis, and 18 (45%) RA patients had supraspinatus tendinopathy (Table 3).

Conventional radiography detected erosions in 18 (45%) shoulders examined, whereas US-detected erosions in 21 (52.5%) (Table 4). There was a significant relation between US-detected erosion in RA patients and disease duration ($P = 0.037$) and RF level ($P = 0.02$), whereas there was no significant relation between US-detected erosion in RA patients and shoulder pain ($P = 0.185$), DAS28 ($P = 0.163$), ESR ($P = 0.519$), and CRP levels ($P = 0.561$) (Table 5). There was a significant relation between US-detected LHB tenosynovitis in RA patients and shoulder pain ($P = 0.025$), whereas there was no significant relation between US-detected LHB tenosynovitis in RA patients and disease duration ($P = 0.246$), DAS28 ($P = 0.710$), ESR ($P = 0.505$), CRP ($P = 0.360$), and RF ($P = 0.109$) levels (Table 6). There was no significant relation between US-detected bursitis in RA patients and disease duration ($P = 0.970$), shoulder pain ($P = 0.907$), DAS28 ($P = 0.471$), ESR ($P = 0.220$), and RF levels ($P = 0.755$), whereas there was a significant relation between US-detected bursitis in RA patients and CRP ($P = 0.036$) (Table 7). There was a significant relation between US-detected supraspinatus tendinopathy in RA patients and shoulder pain ($P = 0.038$), DAS28 ($P = 0.047$), and ESR levels ($P = 0.025$), whereas there was no significant relation between US-detected...
supraspinatus tendinopathy in RA patients and disease duration ($P = 0.496$), CRP ($P = 0.062$), and RF levels ($P = 0.315$) (Table 8). There was a significant relation between US-detected erosion, synovitis, tenosynovitis, bursitis, and supraspinatus tendinopathy in RA patients and HAQ score (Tables 9 and 10).

**Discussion**

RA is a chronic, systemic inflammatory disorder that primarily affects the synovial joints, resulting in deformed and painful joints. The disease may also have signs and symptoms in organs other than the joints [1].
RA is an autoimmune disease of unknown origin, characterized by chronic joint inflammation leading to destruction of the bone and cartilage, reduction in functional capacity, and increased mortality [3].

Painful shoulder is one of the most common conditions in rheumatology and represents an important source of referral for rheumatologic consultation. Shoulder pain may be caused by different intra-articular, periarticular, and/or extra-articular mechanisms, which in turn can be present in a broad range of inflammatory and noninflammatory diseases, such as polymyalgia rheumatica, RA, or degenerative disorders [5].

RA commonly involves the shoulders and is manifested by tenderness, nocturnal pain, and limitation of movement or motion. Inflammation caused by RA may also cause rotator cuff tendinitis and bursitis and may result in frozen shoulder [1].

The location of shoulder pain is a poor indicator of its origin, and the value of clinical examination alone is often limited with regard to making a decision for further management with certainty. The results of shoulder imaging affect the decision to proceed with surgery or to continue conservative management depending on the extent of the lesion [10].

US has become an effective, noninvasive, reproducible [11], low-cost, and readily available tool to assess joints and surrounding areas in patients with different rheumatic conditions. It allows visualization of soft tissue and detects fluid collection and can discriminate between intra-articular and periarticular involvement in different anatomical areas [12].

High-resolution US is being increasingly applied for the analysis of RA. Grey scale US is used for visualization of the joint structures, enabling a distinction between synovial hypertrophy and other causes of apparent joint swelling, such as subcutaneous edema or tenosynovitis. Power Doppler (PD) allows an assessment of synovial vascularity and hence a distinction between inflamed and nonvascular synovial swelling [13].

This study aimed to assess the diagnostic value of musculoskeletal US in the evaluation of inflammatory changes in the shoulders of RA patients and to correlate those findings with the clinical and laboratory parameters of the disease activity and also compare the role of US with conventional radiology in detecting shoulder affection in RA patients. Moreover, we aimed to study the relation between the shoulder ultrasonic abnormalities and functional capacity of the patients.

Our study demonstrated erosion in the shoulder using US in 21 (52.5%) cases and using conventional radiography in 18 (45%) cases; thus, US is more diagnostic for erosion in RA. Moreover, the previous findings are in accordance with those of Wakefield et al. [14], who documented that US is a reliable technique that detects more erosions compared with conventional radiography, especially in early RA.

Moreover, Hermann et al. [15] found that erosions of the humeroscapular joint were detected using conventional radiography in 26 patients, using...
US in 30 patients, and using MRI in 39 patients; the differences were statistically significant for the comparisons of conventional radiography with MRI and for US versus MRI \( (P<0.0001) \).

We found that the most common image abnormalities in shoulder US in RA patients were erosion and LHB tenosynovitis in 52.5% of our cases, supraspinatus tendinopathy in 45%, and bursitis in 17% of cases. This is in agreement with the findings of Hyun et al. [16], who found that the most frequent US findings of the shoulder in their RA patients was long-head tenosynovitis.

We found insignificant correlations \( (P = 0.185) \) between US-detected erosion and shoulder pain; this is similar to that reported by Gill et al. [17], who detected that MRI shoulder pathology is apparent in both symptomatic and asymptomatic shoulders and clinical symptoms may not match radiological findings. In this work, there was a significant correlation between US-detected erosion and positivity of RF \( (P = 0.04) \); this is nearly similar to that reported by Tammakota et al. [18], who observed joint erosions to be more common in RA patients with positive RF on studying 83 clinically diagnosed RA patients.

The present study revealed high statistically significant correlations \( (P = 0.005) \) between US–detected shoulder synovitis and DAS28 \( (P = 0.005) \), ESR \( (P = 0.046) \), and CRP \( (P = 0.045) \); this is in agreement with the findings of Hameed et al. [19], who conducted study on 50 patients with RA. In contrast with our results, using US, Weidekamm et al. [20] reported a significant correlation between wrist PD scoring and clinical findings, but not ESR or CRP.

We found an insignificant correlation between shoulder synovitis and RF \( (P = 0.316) \); this is similar to the findings of Geng et al. [21], who revealed that total PD score for synovitis was in correlation with swollen joint counts, tender joint counts, ESR, and CRP, but not the titer of RF and anticyclic citrullinated peptide.

This study showed a statistically significant correlation between US–detected erosion in shoulder joint and disease duration \( (P = 0.03) \); this is consistent with the findings of Amaya-Amaya et al. [22], who studied factors associated with nonerosive arthritis using US and documented a significant positive correlation between nonerosive RA and short disease duration.

We found a significant correlation between US-detected shoulder synovitis and disease duration \( (P = 0.03) \), DAS28 \( (P = 0.005) \), ESR \( (P = 0.04) \), and CRP \( (P = 0.04) \). In accordance with our findings, Naredo et al. [23] emphasized a closer relation between US measures and ESR, CRP, and DAS28 in 60 joints of 94 patients with RA.

Similar finding was reported by Strikhum et al. [24], who confirmed a significant correlation between MRI-detected erosion measure on the wrists and disease duration in 16 patients with RA.

Possible explanation for insignificant correlation between US-detected erosion in shoulder joint and DAS28 is the striking heterogeneity in clinical pattern of RA disease, wherein joint erosive disease may never have a high acute phase response, whereas others remain nonerosive despite persistently high joint counts. Joint erosions may represent the effect of previously active disease, especially if not associated with high-PD signal of active synovitis. Furthermore, this reflects the inclusion of patients with long-standing disease in our study, wherein joint swelling is not always a reliable finding.

We discovered that there was an insignificant correlation between US-detected erosion and functional capacity \( (P = 0.02) \); this is in contrast to the findings of Živković et al. [25], who showed that there was an inverse significant correlation between functional capacity and radiological progression measured using Larsen score in 98 RA patients. Meanwhile, we found a significant correlation between functional capacity and synovitis \( (P = 0.039) \); this is similar to that reported by de Oliveira et al. [26], who revealed a significant correlation between shoulder synovitis and HAQ in 40 RA patients. This could be explained by the fact that synovitis detected by means of Doppler reflects ongoing disease activity, which would probably affect the HAQ score.

Moreover, Welsing et al. [27] studied the effect of disease activity and joint destruction on functional capacity changes over the course of the disease and concluded that, in early RA, functional capacity is mostly associated with disease activity, and, in late disease, associated with joint damage.

Furthermore, we detected a significant correlation between US-detected tenosynovitis and functional capacity \( (P = 0.02) \), and this was supported by data excluded by Shidara et al. [28], who demonstrated that impairment of the shoulder, wrist, knee, and ankle significantly affects functional capacity in patients with RA. Care of these joints was suggested to be especially important for better functional outcomes.

We emphasized a significant correlation between shoulder bursitis and functional capacity, and this is in agreement with the findings of Francine et al. [29], who showed that the patients with shoulder complaints may have limitation to perform daily activities and pain even with negative image finding.
Conclusion
Our results suggested that US imaging is an important additional technique that supplements conventional radiography of the shoulder joints in RA. Although conventional radiography may be sufficient in the follow-up of well-known joint processes in RA, the initial diagnostic examination should include US in cases of negative radiographic findings and contrast-enhanced MR should be used as a problem-solving approach. US becomes a problem-solving approach and the tool of choice for cases with shoulder problem, which can provide an accurate answer to many clinical questions and give an accurate diagnosis of different pathological abnormalities encountered, which are complex and multifactorial in most of the cases. The diagnostic role of US should be reflected in the management plan for determining the best therapeutic modality for treating the pathology of shoulder affection either by means of rest, exercise, local injection or physical modalities in conjunction with treatment of disease activity if the disease is active as indicated by laboratory investigations and activity scores.

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Conflicts of interest
There are no conflicts of interest.

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