



ORIGINAL ARTICLE

# Value of dynamic sonography in the management of shoulder pain in patients with rheumatoid arthritis



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## KEYWORDS

Dynamic sonography;  
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**Abstract** *Purpose:* The purpose of this study is to evaluate the role of dynamic high resolution ultrasonography in the detection of abnormalities of rheumatoid arthritis and to find out the value added to the management plan of the disease.

*Patients and methods:* 21 shoulders of rheumatoid arthritis patients complaining of shoulder pain were scanned with ultrasound (static and dynamic) and compared to clinical examination.

*Result:* The most predictive sign of rheumatoid arthritis was sub-acromial impingement which was screened and graded by ultrasound in (100%). Other US signs included sub-acromial bursitis in 14.2%, biceps teno-synovitis in 52.4%, supraspinatous tendinopathy in 57.1%, supraspinatous partial thickness bursal surface tear in 14.2% and joint effusion in 9.5% of our patients. The combination of more than one finding was of higher sensitivity than isolated sign alone.

*Conclusion:* Dynamic ultrasound examination for the diagnosis of shoulder impingement in Rheumatoid arthritis should be done in addition to the clinical and static ultrasound examination to improve the management plan.

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## 1. Introduction

Rheumatoid arthritis (RA) is a systemic chronic, autoimmune inflammatory disease that may affect many tissues and organs, but principally attacks flexible (synovial) joints. The process produces an inflammatory response of the capsule around

the joints (mainly synovial lining) secondary to swelling (hyperplasia) of synovial cells, excess synovial fluid, and the development of fibrous tissue (pannus) in the synovium (1). RA commonly involves the shoulders and is manifested by tenderness, nocturnal pain, and limited motion. Rotator cuff degeneration secondary to synovitis may limit abduction and rotation. Inflammation caused by rheumatoid arthritis may also cause rotator cuff tendinitis and bursitis (2).

Imaging techniques have played an important role in assessing disease progression and response to treatment in rheumatoid arthritis (RA) for many years (3).

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**Magnetic resonance imaging (MRI)** can directly visualize the bone and soft tissues in three dimensions, and has the potential to measure inflammatory activity and joint destruction (4). MRI is a reliable technique for the evaluation of the rotator cuff tendons, but it provides only a static evaluation of the shoulder joint and can only indirectly suggest the diagnosis of sub-acromial impingement (5).

**Ultrasound** is an effective and established technique in musculoskeletal imaging; its role in diagnostic imaging is continuing to expand with the development of further clinical applications and with the advancement of ultrasound technology (6). Sonography is well suited for examinations of the musculoskeletal system because structures are often superficial, examinations may be done in a position that is comfortable for the patient, and comparisons with the contra-lateral side are possible (7).

Real-time imaging capability of sonography is a particularly advantageous feature, permitting dynamic evaluation of a system on movement (7).

Dynamic sonography is a useful tool for the evaluation of a wide variety of musculoskeletal disorders that are best or only shown dynamically—that is, during motion, muscle contraction, probe compression, or position change of the patient. Many of these disorders cannot be diagnosed by any other imaging method (8).

## 2. Patients and methods

### 2.1. Patients

This study included 21 shoulder joints in 20 patients (12 females and 8 males) in the age range between 22 and 50 years with mean age 40.7 years with clinical diagnosis of rheumatoid arthritis and positive clinical impingement test (100%). Clinically, the duration of clinical pain ranged from 17 months. They underwent plain X-ray, ultrasound (static and dynamic) and Doppler examination as well as follow up (static dynamic sonography, Doppler examinations) were repeated for 16 shoulder joints after a course of medical treatment. All patients had no other underlying disease and none had undergone previous surgical treatment or intra-articular injection.

### 2.2. Clinical examination

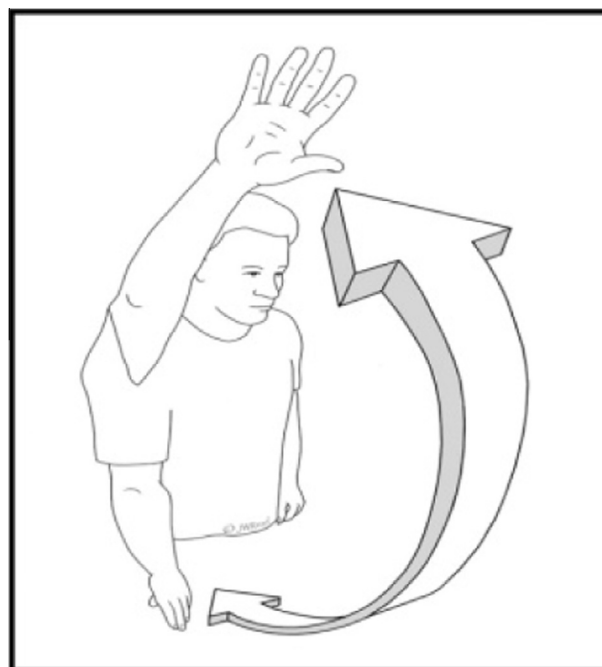
Elicitation of impingement pain was done by moving the supraspinatus insertion beneath the coraco-acromial arch. It was performed using: (a) The Neer test (fig. 1), which involves forward flexion of the arm with the thumb facing down and (b) The Hawkins test (fig. 2), which involves axial rotation of the already 90° abducted arm.

### 2.3. Imaging examinations

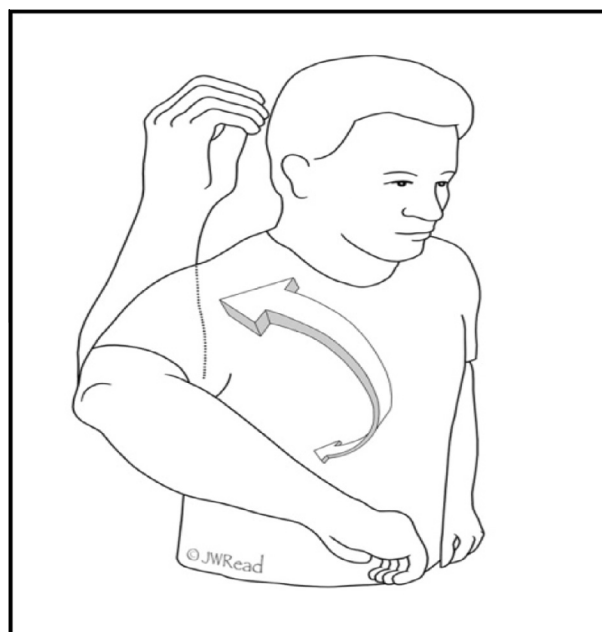
#### 2.3.1. Ultrasonography

2.3.1.1. *Devices.* The patients were examined using one of the following machines:

**S-7 GE (USA) ultrasound device** that is equipped by 5–12 MHz linear array transducer for musculoskeletal examination.



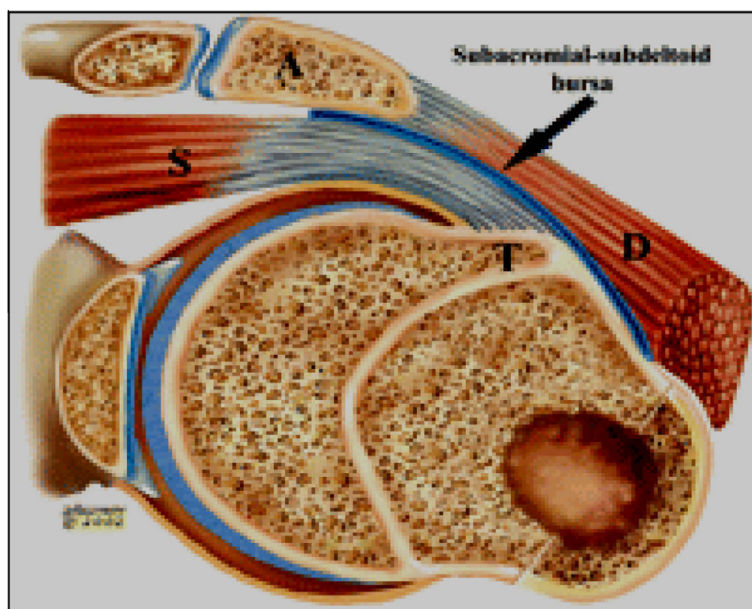
**Fig. 1** Neer impingement test. Pain is elicited during forward flexion of the shoulder while keeping the arm in full pronation (thumb down) (Awerbuch, 2008).



**Fig. 2** Hawkins impingement test. Pain is elicited after first forward flexing the arm to 90° and then applying internal rotation (Awerbuch, 2008).

**S-6 GE (USA) ultrasound device** that is equipped by 5–12 MHz linear array transducer for musculo-skeletal examination.

2.3.1.2. *Static ultrasonography.* Routine static sonography was done in transverse and longitudinal planes with the patient



**Fig. 3** Drawing (coronal plane, cut section) of left shoulder during active elevation of arm halfway between flexion and abduction with hand in pronation shows normal relationships between acromion (A), greater tuberosity (T) of humeral head, and intervening soft tissues—namely, supraspinatus tendon (S) and subacromial-subdeltoid bursa (arrow). D = deltoid muscle (10).

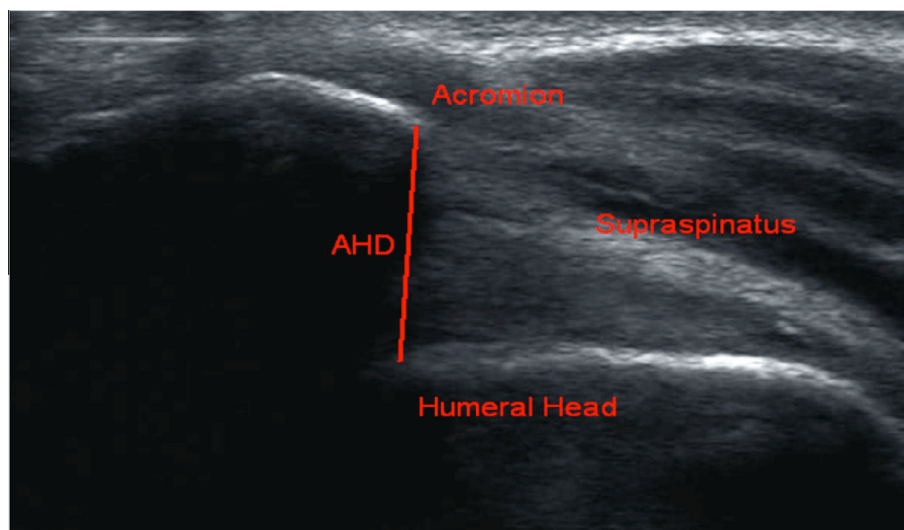
seated on a stool chair. Acromio-clavicular joint, rotator cuff muscles and tendons were examined.

The **subacromial space** consists of the humeral head, acromion, coracoacromial ligament, subacromial bursa, and the acromioclavicular joint (Neer, 1972) (10).

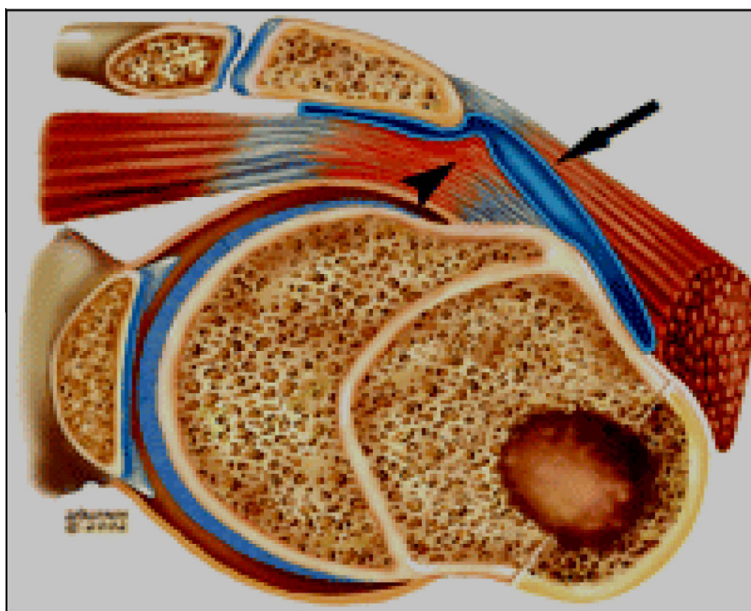
**Sub-acromial tunnel** (Acromiohumeral distance (AHD) means the space between the humeral head and the acromion was measured according to Mossad et al. (11). In neutral position, the vertical dimension of the subacromial tunnel was measured (fig. 3) as the minimum distance from the inferior aspect of the acromion to the point of entry of the tendon into the acoustic shadow of the humeral head. While in stress position, (when the arm is semiflexed, semiabducted and hand

pronated), the later position brings the greater tuberosity of the humeral head underneath the acromion, in order to reveal if there is a considerable reduction in its dimensions that causes repeated shearing trauma of the rotator cuff tendon during shoulder movement. It was found that in cases of sub-acromial impingement, the vertical dimension of the subacromial tunnel measures less than 6 mm in neutral position and shows further reduction (about 25%) in stress position.

**2.3.1.3. Dynamic ultrasonography.** During the dynamic ultrasonography evaluation, the patient was instructed to elevate the arm halfway between flexion and abduction with the hand in pronation and the elbow extended while the ultrasound probe



**Fig. 4** Fig. 1. Normal subacromial space by ultrasound coronal plane showing Acromiohumeral Distance (AHD) measured from the most inferior aspect of the acromion to the humeral head.

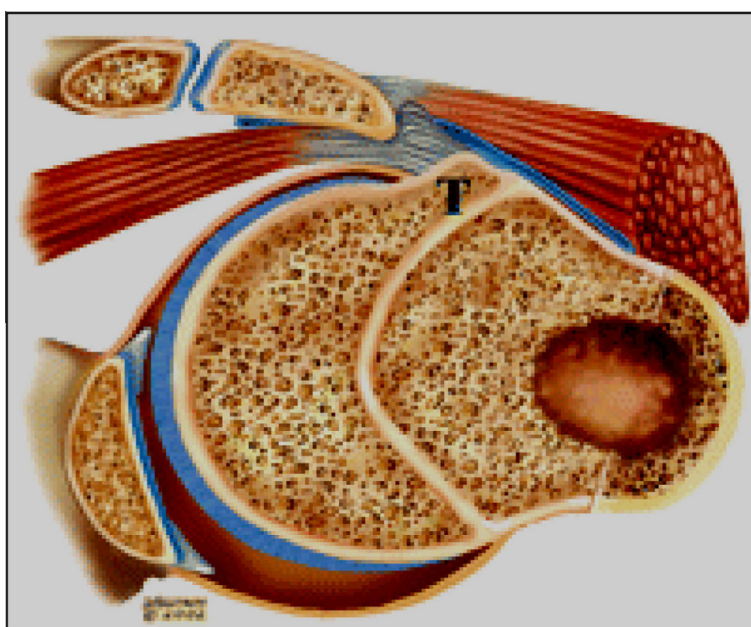


**Fig. 5** Drawing (coronal plane, cut section) of left shoulder during active elevation of arm halfway between flexion and abduction with hand in pronation explicitly depicts pooling of fluid in lateral aspect of subacromial-subdeltoid bursa (*arrow*) and alteration of normally convex surface of supraspinatus tendon (*arrowhead*) as arm is elevated. Supraspinatus tendon is not always involved in grade 2 subacromial impingement. There is also evidence of supraspinatus tendinosis and inflammatory changes in bursa (10).

**Table 1** Grading of dynamic sonographic findings (9)\* was as follows.

Grade	Clinical findings	Sonographic findings	Frequency
0	No pain elicited during shoulder motion	No evidence of anatomic impingement	2/21
1	Pain elicited during shoulder motion	No evidence of anatomic impingement	5/21
2	Pain elicited during shoulder motion	Evidence of soft-tissue/fluid impingement	14/21
3	Pain elicited during shoulder motion	Evidence of upward migration of the humeral head	0/21

\* Bureau et al. (8) Dynamic Sonography Evaluation of Shoulder Impingement Syndrome.



**Fig. 6** Drawing (coronal plane, cut section) of left shoulder during active elevation of arm halfway between flexion and abduction with hand in pronation shows upward migration of humeral head in relation to glenoid cavity, which prevents passage of greater tuberosity (T) and soft-tissue structures of supraspinatus outlet beneath acromion (10).



was positioned in the coronal plane along the long axis of the supraspinatus tendon, between the acromion and the greater tuberosity of the humerus.

The patient is asked to repeat the active movement a few times. The relationship between the acromion, the humeral head, and the intervening soft tissues -namely, the subacromial bursa and supraspinatus tendon- can be assessed during active shoulder motion (Figs. 3–5).

Grading of the dynamic sonographic findings was tabulated as follows (table 1).

Follow up was done for sixteen patients after one month duration.

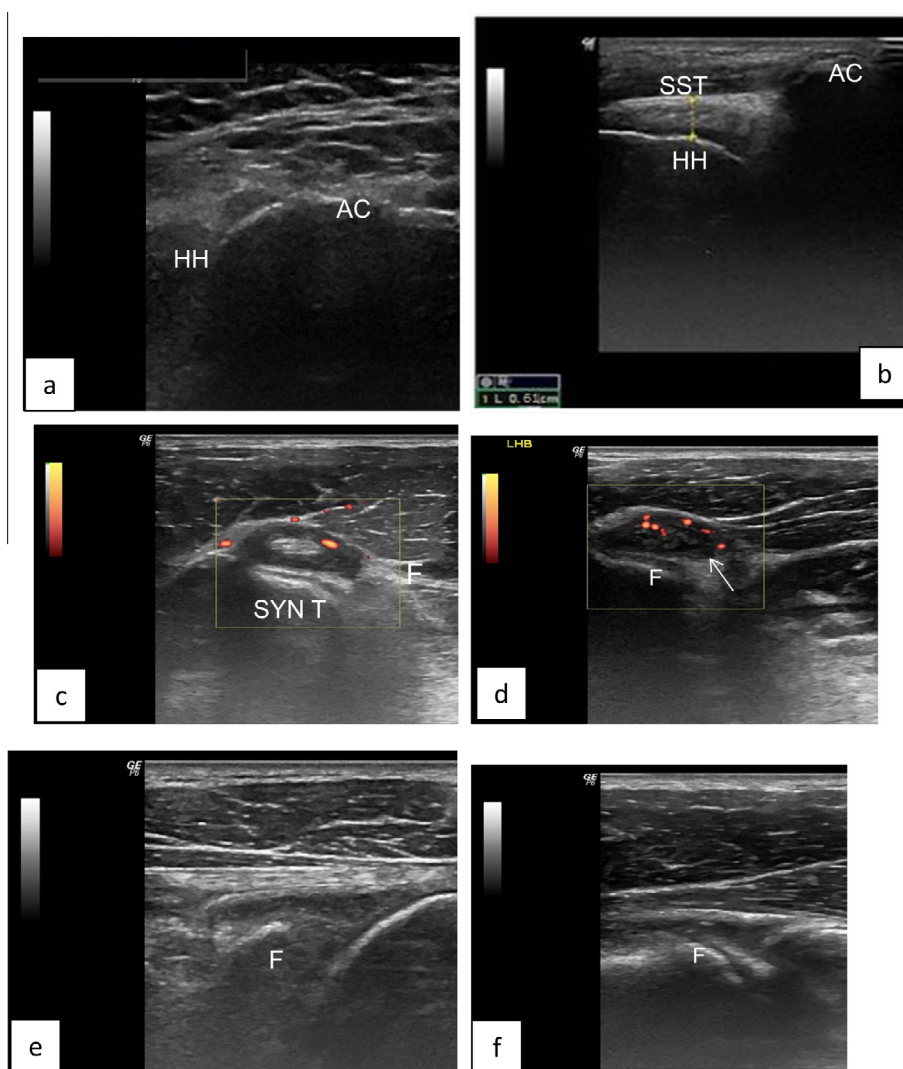
### 3. Result

Twenty-one shoulder joints for patients with rheumatoid arthritis were subjected to plain X-ray, static, dynamic

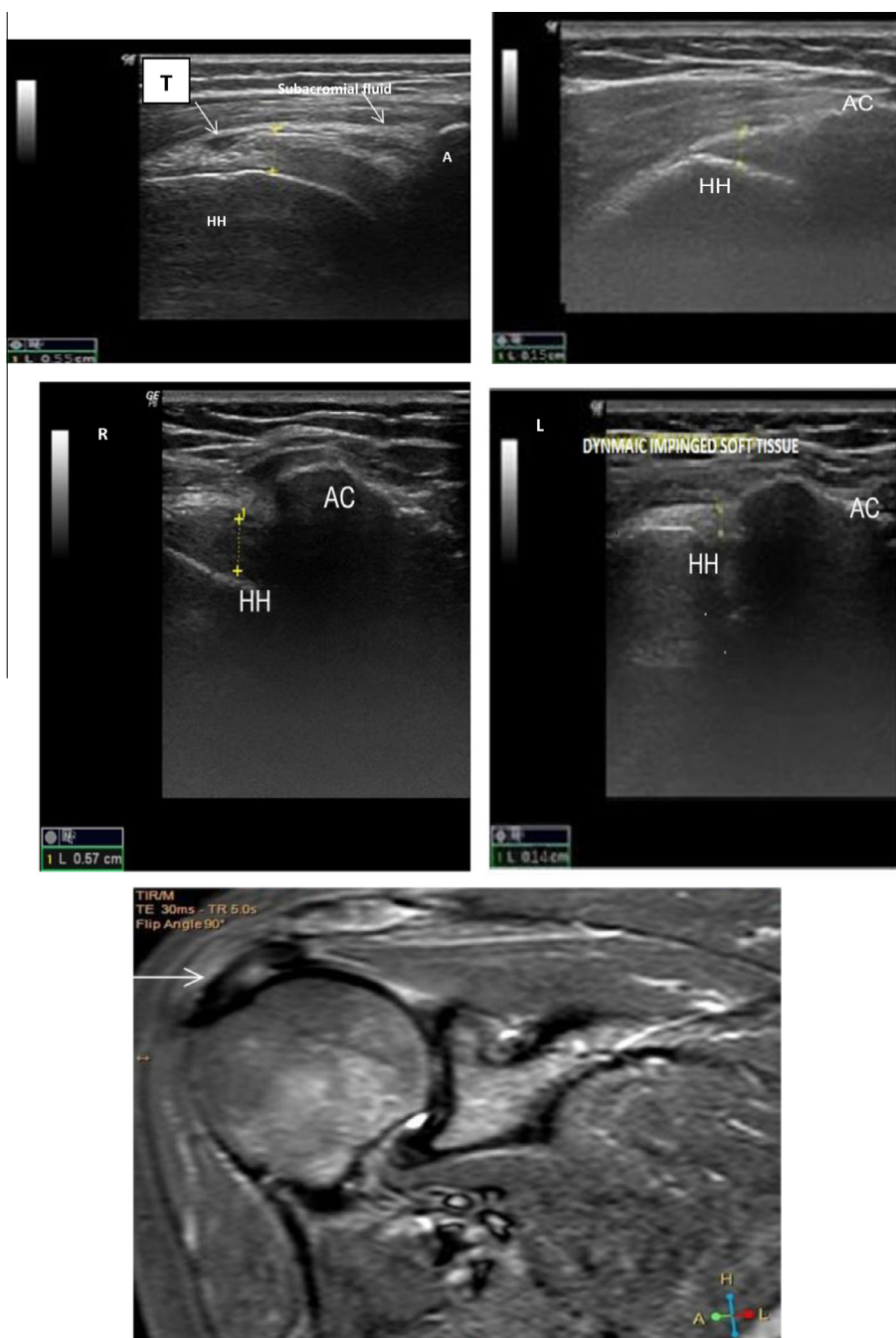
ultrasound and Doppler scans then follow up after treatment was requested for sixteen patients.

Treatment policy was conducted according to the clinical examination data and sonographic findings as follows:

- Seven patients were of grade 0 and I shoulder impingement fig. 6a,b,c and fig. 7a–e. Physiotherapy was prescribed with no need of invasive treatment.
  - Fourteen patients were of grade II shoulder impingement; management was done according the presence or absence of rotator cuff tears fig. 8 (a–c)
- I. Three patients with supra-spinatous partial bursal type tear were subjected to physiotherapy.
- One patient did not improve and was referred to orthopedic consultation and surgery.
  - Two patients improved and were maintained on this treatment policy.



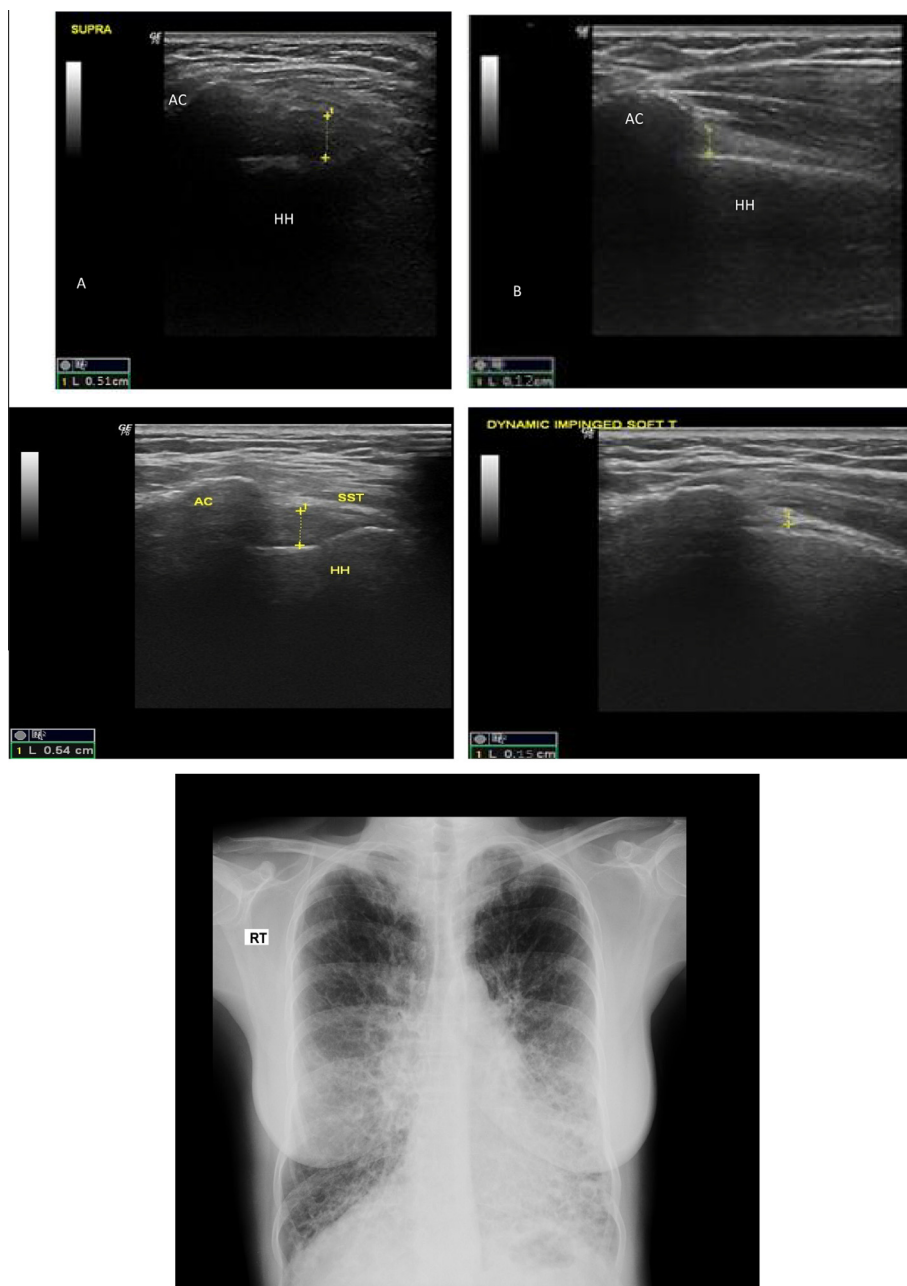
**Fig. 7** (a) to (f) showing a male patient 22 years old, complaining of right shoulder pain since 3 months, known RA patient since 1 year with no history of trauma – **Impingement test: positive. Pain during active shoulder motion. (grade 1 impingement)**, (b) **Static and dynamic US coronal view showed:** that there was no evidence of anatomic impingement as the humeral head (*HH*) passed easily and freely underneath the acromion (*AC*) during shoulder motion, (c) **Power Doppler US TS view showed:** evidence of long head of biceps (*LHB*) tenosynovitis with relative synovial thickening (*SYN T*) (3 mm), synovial effusion (*F*) and increased vascularity, (d) **Follow up after corticosteroids injection Power Doppler US TS view showed:** decreased amount of biceps synovial fluid (*F*) with improvement.



**Fig. 8** (a–d) showing a female patient 49 years old, known RA patient since 13 years old complaining of right shoulder pain for about 3 months, with no history of trauma. (a) Static US coronal image showing subacromial fluid (white right arrow) as rim of hypoechoic fluid seen deep to the acromion (A). Partial thickness tear of the supraspinatus tendon seen as a focal hypoechoic defect interrupting its fibers. Subacromial tunnel measures 0.55 cm. T tear, A acromion, HH humeral head, (b) dynamic US coronal image the subacromial tunnel that became accentuated in stress position with soft tissue impingement AC acromion, HH humeral head, (c) static (right R image) and dynamic (left L image) US coronal images show no improvement after physiotherapy. AC acromion, HH humeral head, (d) coronal MRI STIR image showing partial tear of the supraspinatus tendon appears as focal hyperintense area.

II. Eleven patients had no supra-spinatus tears; treatment was chosen according to the patients' preference where six patients chose local corticosteroid injections and five patients preferred physiotherapy; then follow up ultrasound scanning was performed

- Five out of eleven patients improved (pain less and better range of movement), when maintained on same treatment.
- Six out of the eleven patients did not improve;
- Two of them after physiotherapy were subjected to corticosteroids.



**Fig. 9** (a–e) Female patient 30 years old, a known RA patient since 2 years complaining of left shoulder pain for about 2 months with no history of trauma. – Impingement test: positive. Grade 2 impingement, (a) Static and (b) dynamic US coronal view showed: relative narrowing (0.51 cm) of the sub-acromial tunnel that became accentuated in stress position with soft tissue impingement, (c) Static and (d) dynamic US coronal view follow up after corticosteroid intra-articular injection showed no improvement. SST supraspinatous tendon, (e) Plain X-ray chest PA view showing diffuse interstitial pulmonary thickenings mounting to basal bronchiectatic changes associated with extension to both hila as well as shillouting cardiac.

- Four did not improve on corticosteroids and were subjected to searching for source of systemic infection. Three of them show chest infection on clinical and X-ray examination (fig. 9) while one patient showed urinary tract infection by urine analysis.

Lastly the sonographic findings were assessed and tabulated as follows (table 2).

The results were gathered and tabulated according the frequency and percentage Tables 3–8.

Sonographic findings of shoulder impingement at the patients of rheumatoid arthritis were as follows:

- Narrowed acromio-clavicular joint space (5/21) 23%
- Narrowed sub-acromial tunnel (10/21) 47%
- Supraspinatous tendinopathy (12/21) 57.1%
- Subacromial bursitis (3/21) 14.2%

**Table 2** Sonographic findings were assessed as follows.

Shoulder abnormality	Diagnostic criteria
Impingement syndrome	Narrowing of subacromial tunnel and/or pooling of fluid in the lateral aspect of subacromialsubdeltoid bursa
Biceps tenosynovitis	Synovial effusion, thickness and vascularity
Supraspinatous partial thickness bursal surface tear	Partial fiber discountiuty
Joint effusion	Presence of fluid from posterior labrum to posterior infraspinatous tendon

**Table 3** Frequency and percentage according to the clinical impingement test.

Complaint	Frequency	Percentage
Shoulder pain	17	85
Pain and limitation of movement	3	15
Total	20	100

- Partial thickness bursal surface tear supraspinatous tendon (3/21) 14.2%
- Biceps tenosynovitis (11/21) with 8/11 shows hyper-vascularity on Doppler while 3/11 show no increased vascularity.

#### 4. Discussion

Painful shoulder is one of the most common conditions in patients with rheumatoid arthritis.

Subacromial impingement syndrome in rheumatoid arthritis patients is a clinical entity that was proposed by Neer in 1972 (9) and Kim et al. (10). This syndrome is the result of chronic irritation of the supraspinatus tendon against the undersurface of the anterior one third of the acromion, the coracoacromial ligament, and the acromioclavicular joint. It is often difficult to diagnose clinically because the presentation may be confusing and clinical tests lack specificity (9,10).

There is a need for further trials investigating whether the static and/or dynamic US examination of the shoulder in RA patients offers a possibility of improving treatment. Musculoskeletal Ultrasound has proved to be an effective, noninvasive, sensitive, reproducible, low-cost and readily available diagnostic tool. Some authors consider this tool as one of the most useful tools in the exploration of the shoulder and

**Table 5** Frequency and percentage according to the dynamic ultrasound findings for shoulder impingement at the rheumatoid patients.

	Frequency	Percentage
G0	2	9.5
G1	5	23.8
G2	14	66.7
G3	0	0
Total	21	100.0

recommend US together with plain films as the first step examination. Some limitations of this method are subjectivity, long-term intensive training and different technical characteristics of the ultrasound device (12).

Dynamic sonography evaluation of sub-acromial impingement must be regarded as a sub-acromial impingement imaging test that can provide valuable information to the clinician and that can be easily integrated into a routine sonography shoulder examination protocol. Sonography can show which structure is being impinged and can show upward migration of the humeral head, thus providing significant information about the potential intrinsic and extrinsic causes of this syndrome (10).

MRI is a reliable technique for the evaluation of the rotator cuff tendon abnormality, but it provides only a static evaluation of the shoulder joint. The major limiting factors of dynamic MR are the restricted availability of open magnets and the fact that the MR technology only allows sequential imaging of single-plane shoulder motion that do not entirely reproduce physiologic shoulder motion (10).

*In the present study*, the static ultrasound examination has a role in detecting common associated findings in cases of shoulder impingement in rheumatoid arthritis patients; the findings with frequency included are as follows: **Acromio-clavicular**

**Table 4** Static ultrasound and Doppler findings are tabulated as follows.

Sonographic findings	Positive	Negative	Frequency (%)
Acromio-clavicular joint narrowing	5/21	16/21	23
Subacromial bursitis	3/21	18/21	14.2
Subacromial tunnel narrowing	10/21	11/21	47
Supraspinatous tendonopathy	12/21	9/21	57
Supraspinatous tendon partial tear	3/21	19/21	14.2
Joint effusion	2/21	19/21	9.5
Biceps teno-synovitis	11/21	10/21	
Increased doppler vascularity (synovitis)	8/11	3/11	72.7

N.B. No cases had full thickness rotator cuff tear.



**Table 6** Frequency and percentage according to reduction in sub-acromial tunnel in neutral position (less than 6 mm).

	Frequency	Percentage
No narrowing of subacromial tunnel (more than 6 mm)	5	23.8
Narrowing in subacromial tunnel (less than 6 mm)	16	76.2
Total	21	100

**Table 7** Frequency and percentage according to the distance of sub-acromial tunnel (6 mm) after stress test (dynamic movement).

Percentage of reduction in subacromial tunnel	Frequency	Percentage
25%	8	50
25.5%	3	18.8
26%	3	18.8
0%	2	12.4
Total	16	100

**Table 8** Frequency and percentage of sonographic findings and improvement according to the patient's follow up after treatment.

Criteria of follow up	Frequency	Percentage
Improvement of impingement	3	14.3
Improvement of impingement and tenosynovitis	1	4.8
Improvement of tenosynovitis	5	23.8
Improvement of effusion and tenosynovitis	1	4.8
Decrease in biceps tendon vascularity	4	19
No improvement	7	33.3
No follow up (not indicated)	4	19.0

**joint narrowing (5/21), Subacromial bursitis (3/21), Supraspinatous tendonopathy (12/21), Supraspinatous tendon tear (3/21), Joint effusion (2/21), Biceps teno-synovitis (11/21) and Doppler vascularity added to the value of the examination showing active synovitis in 8 of the 11 cases.**

This is in agreement with multiple studies (10,13–17); which reported ultrasound sensitivity varying between 70% and 100% for detecting similar associated findings in rheumatoid arthritis patients with shoulder impingement.

*In our study*, the vertical dimension of the sub-acromial tunnel was measured in both neutral and stress positions, revealed that 76.2% (16/21) showed narrowing less than 6 mm in the neutral position. On stress test, 50% of these cases showed 25% reduction, 18.8% showed 25.5% reduction, 18.8% showed 26% reduction while 12.4% showed no changes.

This is in agreement with the study (10) that had detected - by dynamic ultrasonography- the significant reduction of the sub-acromial tunnel during active shoulder movement to stress position in rheumatoid arthritis patients.

*In our study*, we found that patients with grade 1 clinical shoulder impingement show no evidence of anatomic impingement during the dynamic sonography evaluation. We referred this pain to be due to degeneration or contact with coracoacromial ligament.

This is in agreement with the study (18) where patients with grade 1 shoulder impingement showed no evidence of anatomic impingement during the dynamic evaluation. They hypothesized that in patients with grade 1 subacromial impingement, pain can result from impingement occurring on a hypertrophic degenerative acromioclavicular joint or from contact with the coracoacromial ligament.

Consequently, there is an agreement between both studies that sonography does not permit direct visualization of the relationships between the supraspinatus tendon and the acromioclavicular joint because of the osseous structures blocking the ultrasound beam.

*In this study*, we found that in rheumatoid arthritis patients with grade 2 sub-acromial impingement (66%), there was relative narrowing of the sub-acromial tunnel that became accentuated in stress position and /or pooling of fluid occurred in the lateral aspect of the subacromial-subdeltoid bursa.

This is in agreement with the study (18) which showed that grade 2 sub-acromial impingement is associated with impingement of the soft tissues between the acromion and greater tuberosity.

*This present study* showed that by dynamic ultrasonography we can characterize the subacromial impingement in RA patients into 3 grades where we have found that the majority of cases (66.7%) were classified as grade 2, (23.8%) as grade 1 and only two shoulders (9.5%) as grade 0 with no cases classified as grade 3. Correlation between the clinical and ultrasound findings in grade 0 or grade I means that these two cases are not false negative.

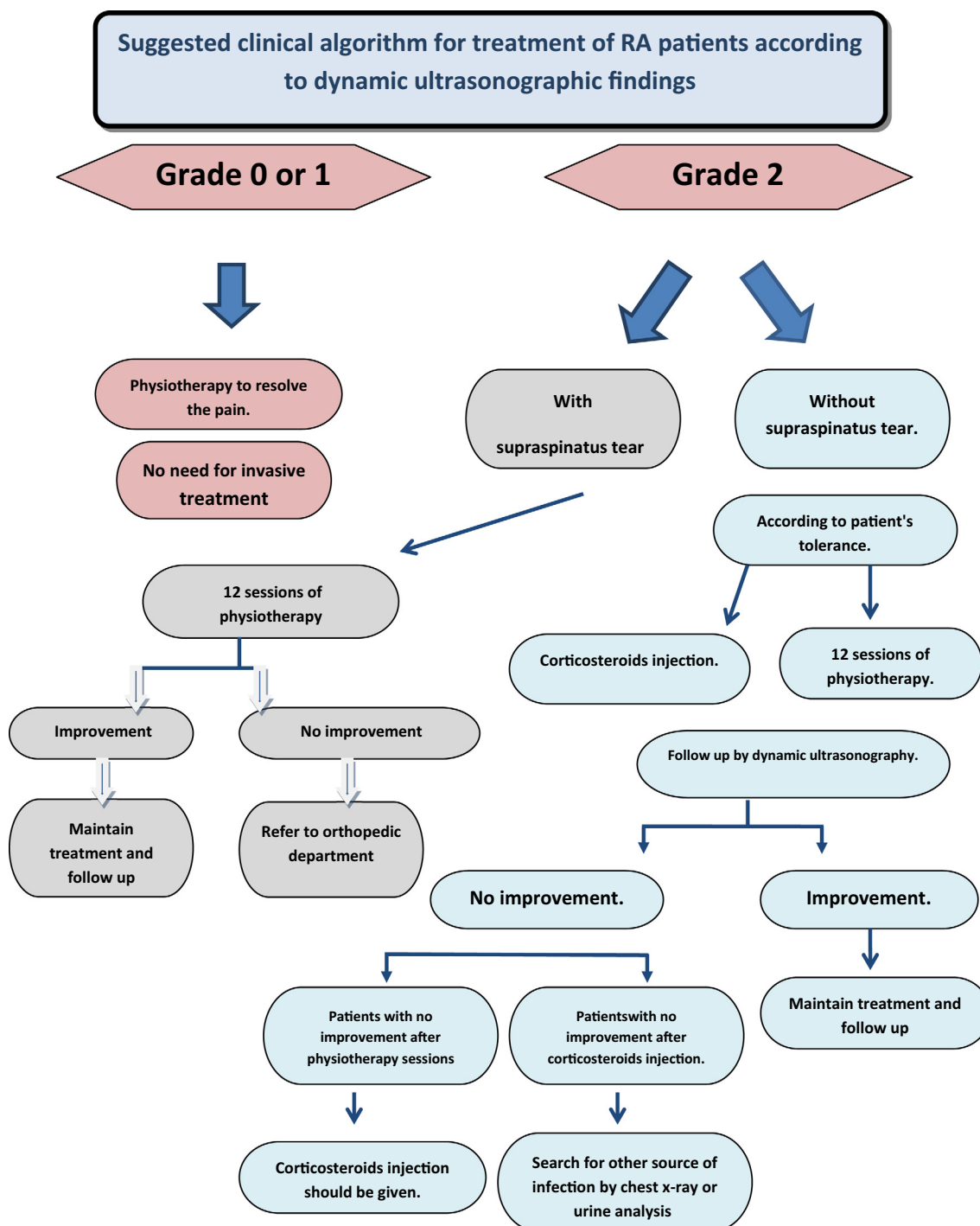
This is in agreement with the study (10) that had detected the majority of the cases (86%) were classified as grade 1, 2, or 3, but two shoulders (14%) were classified as grade 0. This should not be interpreted as two false-negative cases. These two cases merely reflect a disparity between the diagnosis of subacromial impingement made at clinical examination and the findings on dynamic sonography evaluation and emphasize the fact that this diagnosis is difficult to establish.

*In our study*, the patients who were classified into grade 2 impingement (14 cases) and those with positive findings of rotator cuff tear, effusion and biceps tenosynovitis (16 cases) underwent follow up by dynamic ultrasonography after medical treatment, physiotherapy or injection of corticosteroids to detect whether the patients improved or not after treatment.

Dynamic ultrasonography allowed detection of positive findings in RA patients so rheumatologist can adjust the appropriate treatment for the patients.

This is in agreement with the study (19) that showed that conservative treatments of shoulder problems in RA include medical treatment and physiotherapy, and treatment with local injections of corticosteroids was guided by the results of the dynamic ultrasound.

The high prevalence of rotator cuff tears in RA shoulders shown in these series warrants precaution against empirical treatments; it would be more desirable to obtain an exact anatomical diagnosis in order to optimize treatment. Few studies have compared the outcome of treatment for peri-articular shoulder lesions with or without an accurate imaging tech-



**Fig. 10** Suggested clinical algorithm for treatment of RA patients according to dynamic ultrasonographic findings.

nique. A recent surgical series revealed that RA patients with both partial and full-thickness rotator cuff tears had significant improvements in overall pain and satisfaction after the repair.

This is also in agreement with the study (20) that reported that clinicians need diagnostic certainty to optimize management. A reported ultrasound abnormality enables the clinician to fulfill the doctor's half of the bargain in the doctor-patient relationship, by delivering a diagnosis with the promise of treatment.

*The study* has proved that dynamic ultrasonography is useful in the management of RA by classifying sub-acromial

impingement into grades in which the rheumatologist can decide the algorithm of treatment.

*In our study*, patients with grade 0 and grade 1 did not receive invasive injection and only physiotherapy sessions were needed to resolve the pain.

This is in agreement with the study (21) that stated that physical therapy encompasses a large range of treatments. It was designed to relieve pain by improving overall shoulder function.

*In our study*, we found that the rheumatologist can decide the mode of treatment according to the results given by

dynamic ultrasonography in follow up. In case of patients with grade 2 who received physiotherapy sessions and showed no improvement, another mode of treatment can be given as corticosteroids injection.

This is in agreement with the study (22) that stated that the goal of physical therapy is to optimize the function of the shoulder joint complex through improvements of strength, range of motion, and proprioception. If a patient has made little progress after several weeks, or if the patient has significantly limited function secondary to pain initially, corticosteroid injection may provide significant pain control that allows an improved range of motion and progression into physical therapy.

*In our study*, patients with grade 2 impingement who received corticosteroids injection and showed no improvement in follow up by dynamic ultrasonography were referred to search for other source of infection.

*In this study*, four patients did not improve after corticosteroid injection, to search for other source of infection urine analysis was done for one patient and revealed pus cells and chest X-ray was done for the other three patients proved to have chest infection.

This is in agreement with the study (23) that stated that persistent pain unresponsive to therapy - including injection therapy - should prompt the physician to consider other causes.

*In our study*, patients with evidences of partial thickness tear of rotator cuff muscle detected by ultrasonography that received physiotherapy sessions and showed no improvement were referred to orthopedic department to consider surgery.

This is in agreement with the study (24) which stated that, if a patient with a rotator cuff tear does not respond to physical therapy, he or she should be referred to a specialist to discuss rotator cuff repair or debridement.

Limitations of our study included absence of a gold standard for assessing the shoulder lesion, such as MRI. The small number of patients did not allow further statistical analysis and the general limitation of the study was the dependence on the technical characteristics of the US device.

## 5. Conclusion

In this study, we found that dynamic ultrasonography is useful in direct visualization of the relationship between the acromion, subacromial bursa, supraspinatus tendon and greater tuberosity of the humeral head during active shoulder movement.

With the advantages of being an easily available, widely spread, quick, non-costly, non-invasive, non-painful and having no contra-indications, dynamic ultrasonography - in competent hands - become a problem solving and the examination of choice for cases of subacromial impingement, that 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.

Dynamic ultrasonography evaluation of subacromial impingement in rheumatoid arthritis patients must be regarded as a sub-acromial impingement imaging test that can provide useful information to the clinician and that can be easily be integrated into a routine ultrasonography shoulder examination protocol. It can show which structure is being impinged upon and can show upward migration of the humeral head by the dynamic process, thus providing valuable information

about the syndrome and its grade and can be more accurate than sole clinical examination or static US evaluation without dynamic evaluation. This has proved useful addition to the treatment policy protocol and thus provides the clinician the best modality for treatment which will definitely affect the management of the disease.

The study had proved that dynamic ultrasonography is useful in the management of RA by classifying subacromial impingement into grades that can help the rheumatologist to decide the clinical algorithm of treatment as follows (fig. 10).

## Conflict of interest

There is no conflict of interest.

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