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CLINICAL RESEARCH

Accepted:	2014.09.18 2014.11.07 2015.02.18		Ultrasound Investigation Joint by Anterior Access Rheumatoid Arthritis an	in Patients with				
Stu Data Statistica Data Inte Manuscript P Literat	Contribution: Idy Design A Collection B al Analysis C rpretation D reparation E ure Search F Collection G	BC	Alexander P. Rozin Kohava Toledano Amir Dagan Alexandra Balbir-Gurman	Department of Rheumatology, Rambam Health Care Campus, Haifa, Israel				
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Background: Material/Methods:		-	The aim of this study was to measure glenohumeral joint (GHJ) parameters via the anterior access through ul- trasound and to compare to data from posterior and inferior accesses. Twenty healthy controls (M: F=15: 5, aged 45.1±11.2 years) and 16 patients (M: F=5: 11, aged 54.6±14.7 years) with active rheumatoid arthritis (RA) (DAS 28 4.6±1.2) were investigated (SonoSite-Titan). To make the GHJ visible on the anterior access, we used the original GHJ opening maneuver. The GHJ width was measured for every transducer position at 2 points. The positions were: posterior transversal, inferior longitudinal, anteri- or longitudinal along the articular line, anterior transversal upper, middle and lower. The joint width included thickness of cartilage plus synovial fluid/pannus. Rotator interval (RI) width and height (upper biceps channel) were measured.					
		Results: :lusions:	Our normal GHJ values by posterior and inferior accesses were within previously estimated values (<2 mm and <3 mm, respectively). We acquired the first values of GHJ width from the anterior access. The last were with- in a range of 0.7–1.7 mm for healthy controls. Patients with RA showed significantly enlarged joint cavities. RI was not inflamed. Posterior and inferior data of GHJ width were significantly correlated (p=0.01). The data did not correlate with anterior values (p=+0.44, p=–0.56). Synovitis was much more prominent in posterior, upper anterior transversal, and anterior longitudinal accesses. The GHJ may be visualized by anterior access using a special maneuver. Synovitis in the anterior region of the					
MeSH Keywords:			GHJ may develop at an independent rate. Anterior GHJ sonography may be complementary to the classic access. Shoulder Joint • Synovitis • Ultrasonography					
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MEDICAL SCIENCE MONITOR

Background

Ultrasound (US) scanning has been shown to be effective and useful for the investigation of shoulder diseases. It is easy to implement and return, is not expensive and not invasive, and is precise for assessment. The gleno-humeral joint is most inspected in the elderly population. Most shoulder syndromes are not related to joint diseases, but to adjacent tissue problems [1]. US is the preferred method for GHJ (glenohumeral joint) assessment by rheumatologists, but inflammatory changes in the GHJ have found limited attention in the medical imaging literature [2]. There is assessment of GHJ synovitis with disclosure of synovial fluid and pannus in subdeltoid (subacromial) bursa and biceps tendon, connected to the GHJ space [1,3] by axillary [4] and posterior [3] access. Subdeltoid bursitis and biceps tenosynovitis are commonly used for inflammatory assessment of the shoulder [5,6]. The anterior approach for GHJ assessment had not been used [1,5,7] before our last trial [8]. A problem in patients with synovitis in GHJ is the difficulty of raising the shoulder to the lateral side (abduction) for 90 degrees for the axillary approach.

We proposed the anterior access for GHJ synovitis assessment [8]. Certain positioning of the shoulder and measured data of healthy controls enabled the diagnosis of GHJ synovitis with minimal movement of the sore shoulder. In another report, we demonstrated US differences between the GHJ and subscapular tendon on the anterior approach [9]. These 2 publications showed anterior shoulder US in the sitting position with the arm externally rotated and supinated. We should have recognized the problems of these trials related to incorrect identification of the GHJ space. As we realized later, this incorrect detection was associated with missing of orienteer structures: hypoechoic GHJ cartilage located on round hyperechoic humeral head behind and fibrillar subscapular tendon situated forward of the GHJ space. From our present perspective, these elements are a cornerstone for GHJ visualization. Because of the lack of an obvious picture of these structures, the GHJ demonstration is unclear and subject to confusion with the subscapular tendon [8,9]. Moreover, our further experience with multiple anterior US studies showed that the presentation of the GHJ in position for supination and external rotation in the sitting position is associated with poor visualization of the GHJ cavity. The GHJ is hidden behind the humeral head, due to differences between the round humeral head and oval glenoid and the twisted GHJ structure forward-upper-laterally (Figure 1). Daily practice helped to resolve this problem. We found that the patient should be laid supine, elbow bent to 90 degrees, and the shoulder rotated maximally externally. This situation fixes the shoulder girdle, the glenoid moves anteriorly, the humeral head moves posteriorly, and greater complete external shoulder rotation is achieved, opening the GHJ for investigation (Figures 2 and 3). Shoulder CT shows that the glenoid surface is in a plane open to the upper, forward, and lateral sides (Figures 1A–1D and 2). This necessitates turning of the transducer according to the direction of the investigated joint placed along the glenoid surface. Thus, a longitudinal study of the GHJ requires a transducer position under certain angles along the joint line (Figure 2). Transversal study is implemented under an angle of 90 degrees to the joint line (Figure 3).

Another problem is that synovitis might develop at an early stage only within a limited region of the joint and in a region much more susceptible to inflammation and dilatation, such as the rotator interval, where the anterior upper region is covered only by the joint capsule, with lower resistance to distention. That region is referred to as the rotator interval, a distance between the supraspinatus (laterally) and subscapularis (medially) tendons attachment, when the shoulder is supinated and externally rotated. This region was recently used for synovial biopsy [10,11].

Study aims were:

1. To investigate the GHJ by the anterior approach in healthy controls.

A – Measurement of GHJ thickness at 3 points and average value calculation in the body supine position, with arm adducted, supinated, maximal externally rotated with elbow angle 90 degrees.

- By longitudinal access with transducer position laterally to coracoids along the GHJ line, located as diagonal from lower to forward and lateral direction with demonstration of the joint cartilage posteriorly and subscapular tendon anteriorly (Figure 2);
- By transversal access with 90 degrees to longitudinal and at 3 points: upper with coracoids visualization, middle and lower (Figure 3);
- B Measurement of rotator interval with assessment of width and height.
- 2. Comparison of data with results of classic values obtained by posterior and inferior (axillary) approaches.
- 3. Comparison of results between patients with RA and healthy controls.

Material and Methods

US [SonoSite-Titan S/N032P46 2.2 USA linear transducer (L38) MHz 5–10] was performed for 20 healthy controls and 16 patients with RA. The study was approved by the Ethics Committee (EC)/Institutional Research Board (RB) (N0260-10). Informed written patient consent was received from all patients in this study. US scan was obtained symmetrically on both sides. The diagnosis of RA relied on anamnesis data, physical examination, and laboratory findings. Synovial swelling, synovial tenderness,

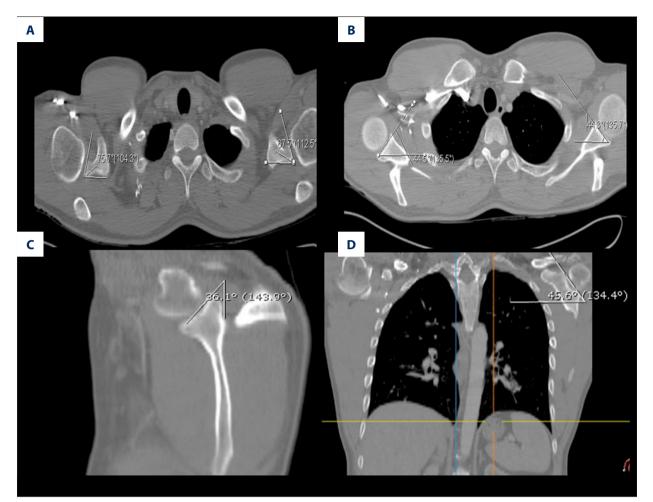


Figure 1. (**A–D**) The poor visualization of the anterior GHJ is because the GHJ is hidden behind the humeral head due to differences between the round humeral head and the oval glenoid and a twist of the GHJ structure forward-upper-laterally. This should be taken into consideration when localizing the transducer during US GHJ investigation.

local fever of joint region, active and passive limitation, accelerated erythrocyte sedimentation rate (ESR) upper 40 mm/hr (N<12), and C-reactive protein (CRP) upper 1.5 mg/dl (N<0.5) were clinical signs of active inflammation. These findings were summarized as ARA 1987 revised and 2010 ACR/EULAR inclusion criteria. Twenty healthy controls did not complain of shoulder pain and limitation and their physical examination was unremarkable.

Twenty healthy controls (M: F=15: 5, aged 45.1 ± 11.2 years) and 16 patients (M: F=5: 11, aged 54.6 ± 14.7 years) with active rheumatoid arthritis (RA) (DAS 28 4.6 ± 1.2) were investigated (Table 1). In order to render the GHJ visible on the anterior access, we used the original GHJ opening maneuver: supine body position, elbow adducted to the body and flexed 90 degree on the bed, maximal external shoulder rotation (forearm on the bed). Three structural points are essential for anterior GHJ visualization: 1. GHJ hypoechoic cartilage; 2. A round hyperechoic humeral head behind it; 3. Subscapular fibrillar

tendon situated forward to the GHJ cartilage and space. The GHJ width was measured for every transducer position at 2 points. The positions were as follows: posterior transversal, inferior longitudinal, anterior longitudinal along to articular line, anterior transversal upper, middle and lower. The joint width included thickness of the cartilage plus synovial fluid/pannus. Rotator interval (RI) width {supraspinatus tendon (SST)- subscapular tendon (SSC)} and height (upper biceps channel) were measured. The GHJ width by posterior and inferior views was measured by standard methods (1, 2).

US scanning was performed as a cross-sectional study for 20 healthy controls from the Department of Preventive Medicine and for 16 patients with RA aged 20–60 years by classic approaches: posterior and inferior and new anterior access. The latter was accompanied by measurement of the GHJ space and the rotator interval in the upper limb position of supination and external rotation. Comparison was made between data of different positions and RA patients compared with controls.

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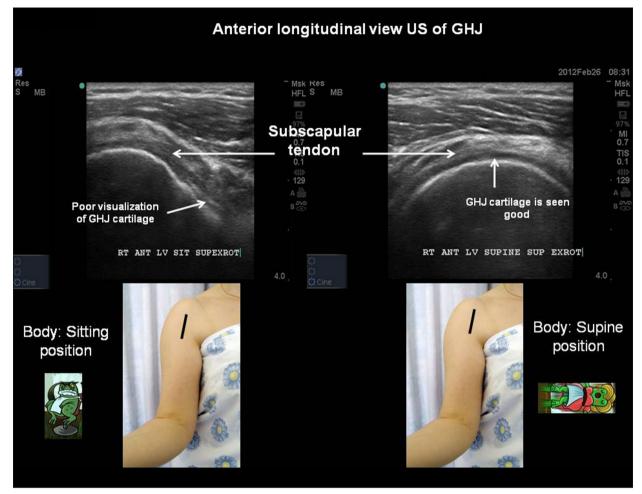


Figure 2. GHJ is poorly (sitting position, left) and well (supine position, right) (longitudinal anterior view) visualized. Arm is supinated and externally rotated with elbow adducted and flexed 90 degrees.

Anterior approach

Longitudinal view for GHJ space

 Measurement of GHJ at 2 points in supine position and supination and maximal external rotation of the arm with the elbow in adduction and flexion at 90 degrees.

The GHJ has a complex and hidden structure due to the round form of the humeral head and oval glenoid and deviation of the natural GHJ axis. According to the angles shown in Figure 1A–1D, it is necessary to use such angles to place the transducer for better visualization of the joint. In the first stage, when the arm is in supination and external rotation, the transducer should be located lateral to the coracoid and turned along to the glenoid plane up to 45 degrees (Figure 1A, 1B). Further deviation should be medial for the upper pole of the transducer and lateral for the lower pole along the line of GHJ (Figure 1C, 1D). Important orienteer points are the subscapular tendon forwardly and the GHJ cartilage at the bottom. Above the GHJ space, the joint capsule can be found, which may be positioned on the cartilage. In cases of lack of a visible capsule, the latter is right on cartilage and no intraarticular fluid presents. Our first publication lacked these orienteer points in visualization of the GHJ, which resulted in incorrect interpretation of the US data [8].

Transversal view for GHJ space

Measurement of the GHJ space at 2 points in supine, maximal external rotation of the shoulder with elbow flexion at 90 degrees.

An assessment of the GHJ by the transversal view relies on identification of the coracoid, situated at the level of the upper part of the GHJ. A region between the coracoid and the head of the humerus belongs to the GHJ space. At a level of the middle GHJ, the coracoid is not seen and a plane of the glenoid is under a larger angle to the sagittal axis up to 45 degrees compared with the upper region (Figure 1A, 1B). At the

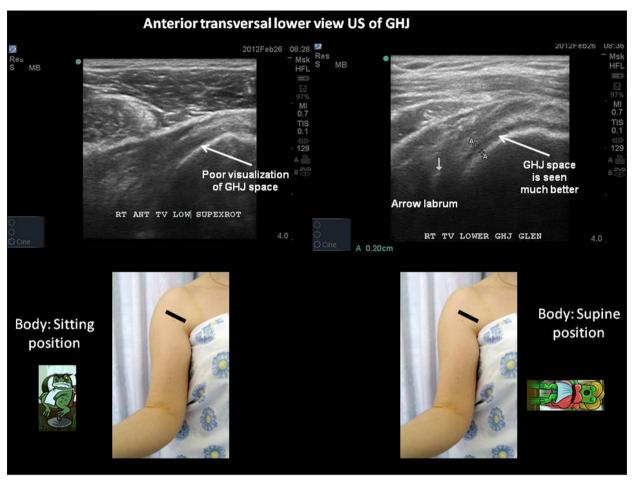


Figure 3. Transversal anterior GHJ study is implemented under an angle of 90 degrees to the joint line. Body supine, elbow flexed at 90 degrees, arm supinated, maximally externally rotated.

Diagnosis	No. of patients	Age	Gender: M/F	Disease duration (years)	Disease activity DAS 28	IS/CS/Biological therapy (N of patients)
Rheumatoid arthritis	16	54.6±14.7	5: 11	5.0±2.6	4.6±1.2	12/6/4
Healthy controls	20	45.1±11.2	15: 5	NA	NA	NA
Total	36	49.3±12.8	20: 16	5.0±2.6	4.6±1.2	12/6/4

 Table 1. Demographic and clinical data of patients with glenohumeral synovitis and controls.

IS – immunosuppressor; CS – corticosteroid; NA – not applicable.

level of the lower GHJ, one can visualize the anterior recessus of the synovial cavity.

Measurement of rotator interval

The rotator interval (RI) investigation is performed in a sitting position with supination and external rotation of the arm at 30 degrees. The RI is a triangular region between the upper edge of the subscapularis, the forward edge of the supraspinatus and the coracoid. The RI may be measured as the distance between the SST and the SSC in the upper transversal position of the transducer placed above the biceps groove. The RI also has the height of the biceps groove. The RI reflects the condition of the GHJ and is distended due to intra-articular effusion or synovitis.

Classic posterior access

The investigation is implemented in the sitting position with the arm in the neutral position. The transducer is placed above

Transducer position	Controls Rt (mm)	Controls Lt (mm)	RA Rt (mm)	RA Lt (mm)	p (Rt; Lt)
Posterior	1.4±0.5	1.3±0.4	4.5±3.8	4.3±2.9	<0.001; <0.001
Inferior	1.7±0.5	2.1±0.7	3.6±2.9	3.9±2.8	0.001; 0.002
RI width	10.4±2.3	9.7±3.0	10.7±2.5	10.0±3.3	0.66; 0.79
RI height	7.6±1.3	7.4±1.2	6.9± 2.2	7.2±1.7	0.27; 0.69
Anterior LV	1.1±0.4	1.1±0.3	2.0±1.3	2.4±1.1	<0.001; <0.001
Anterior TV upper	1.3±0.4	1.3±0.4	2.5±1.5	2.6±1.2	<0.001; <0.001
Anterior TV middle	1.2±0.4	1.2±0.3	1.6±0.9	1.9±0.8	0.002; <0.001
Anterior TV lower	1.1±0.4	1.2±0.3	2.5±1.9	1.9±1.2	<0.001; 0.005

Table 2. Data of US GHJ measurements: posterior, inferior and anterior positions, rotator interval in patients with RA and controls.

RI - rotator interval; LV - longitudinal view; TV - transversal view; Lt - left; Rt - right.

 Table 3. Spearman correlations between posterior and inferior, posterior and anterior, and inferior and anterior GHJ parameters of patients with rheumatoid arthritis.

	Values	Posterior right	Inferior right	Anterior LV right	Anterior TV right	Posterior left	Inferior left	Anterior LV left
Posterior right	Correlation coefficient	1.000	0.318	-0.009	.279	0.380	0.120	-0.14
	р		0.087	0.963	.136	0.038	0.528	0.459
Inferior right	Correlation coefficient	0.318	1.000	057	.155	057	0.158	0.082
	р	0.087		.764	.413	.764	0.405	.666
Anterior LV right	Correlation coefficient	009	057	1.000	.436*	237	162	.359
	р	.963	.764		.016	.207	.393	.051
Anterior TV right	Correlation coefficient	.279	.155	.436	1.000	*–.147	141	.283
	р	.136	.413	.016		.438	.456	.129
Posterior	Correlation coefficient	.380*	057*	237	147	1.000	.460	.146
left	Р	.038	.764.	.207	.438		.011	.442
Inferior left	Correlation coefficient	.120	.158	162	141	.460*	1.000	.108
	Р	.528	.405	.393	.456	.011		.563
Anterior LV	Correlation coefficient	140	082	.359	.283	.146	.108	1.000
left	Р	.459	.666	.051	.129	.442	.569	

the head of the humerus transverse to the shoulder axis; the distance between the humeral head and the infraspinatus should be 2 mm or less in healthy controls and increased in joint effusion or synovitis [3].

Inferior (axillary) approach

Classic axillary access is performed in the sitting position with the transducer placed on the axillary region longitudinal to the shoulder axis, with the shoulder abducted to 90 degrees,

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Figure 4. Cartilage of normal GHJ (A – AA, BB) and the cartilage with synovitis (B – AA) are shown. Protrusion of synovial tissue to the subscapular tendon is seen (arrows). Anterior longitudinal view, body supine, elbow flexed at 90 degrees, arm supinated, maximally externally rotated.

usually laid on the physician's shoulder. Joint space distention to 3.5 mm and more is defined as synovitis or effusion.

In using the anterior approach, we would like to emphasize the need to perform identification and measurement of the GHJ complying with:

- patient in the supine position;
- researcher discloses main criteria to identify the GHJ: subscapular tendon presence above and GHJ cartilage occurrence below the GHJ space and above the humeral head, with elbow flexed at 90 degrees and maximally externally rotated;
- GHJ may be found only within the joint cartilage, ending at the line of joint capsule attachment – the anatomical neck of GHJ. Contrary to the hip joint, where the capsule is distended further than the cartilage edge.

Inclusion criteria

- 1. Healthy controls aged 20–60 years, according to the conclusion of the Department of Preventive Medicine
- Patients with RA according to ARA 1987 revised criteria and disease activity DAS 28 >3.0
- 3. Patients with RA according to 2010 ACR/EULAR classification criteria for RA (Table 1)

Exclusion criteria

- 1. Past shoulder trauma.
- 2. Shoulder osteoarthritis.
- 3. Rotator cuff disorders.
- 4. Shoulder injections.
- 5. Cervical spondylosis with nerve root compression.
- 6. Cervical symptomatic disc syndromes.

Statistical analysis

Data were analyzed using SPSS 12.0 software. Comparison between continuous variables of the joint width was done with the Mann-Whitney U non-parametric test. For group comparison, a two-tailed Student's t-test was used. Spearmen's nonparametric correlation was performed to examine relationships between the data of posterior, inferior, and anterior access. Such correlation may reflect the similar intensity of inflammation in different compartments of the GHJ. P value of 0.05 or less was considered as statistically significant.

Results

Results are presented in Tables 2 and 3. GHJ values by posterior and inferior access were within the previously estimated range (posterior GHJ width <2 mm, inferior <3.0) for healthy patients [1-4]. Posterior measurement showed 1.4-1.3 mm of GHJ width form right and left arm with standard deviation (SD) 0.5–0.4 mm. Inferior position presented data of GHJ width of 1.7-2.1 mm and SD of 0.5-0.7 mm. We acquired the first values of the GHJ width from the anterior access in healthy patients. There were of 1.1-1.1 mm and SD 0.4-0.3 mm for longitudinal view (LV), 1.3-1.3 mm and SD 0.4-0.3 for upper transversal view, 1.2-1.2 mm with SD 0.4-0.3 mm for middle transversal view and 1.1-1.2 mm with SD 0.4-0.3 mm for lower transversal view. The last three approaches were within GHJ width range of 0.7-1.7 mm for healthy controls. Patients with RA showed significantly enlarged joint cavities in the posterior, inferior and anterior (transversal upper) access: 4.5-4.3 mm, SD 3.8-2.9 mm; 3.6-3.9 mm, SD 2.9-2.8; 2.5-2.6, SD 1.5-1.2 respectively. Anterior middle and lower transversal position also showed increased GHJ width values: 1.6-1.9 mm, SD 0.9-0.8 mm. All RA patients showed enlarged GHJ compared with healthy controls (p<0.005). The rotator interval (RI) showed width of 10.4-9.7 mm, SD 1.3-1.2 mm, height of 7.6–7.4 mm, SD 1.3–1.2 mm for healthy population. RI was not inflamed and showed undistinguished data from RA group: width of 10.7-10.0 mm, SD 2.5-3.3 mm, height 6.9-7.2 mm, SD 2.2-1.7 mm (p=0.66, p=0.27). Posterior and inferior data of the GHJ width correlated significantly (p=0.011) (Table 3, column before last, line 10). The data did not correlate with the anterior values (p=0.44, p=0.56) (Table 3, last column, lines 10, 12). Synovitis was much more prominent in the posterior, upper anterior transversal and anterior longitudinal transducer positions. Normal GHJ space in comparison to GHJ synovitis with enhanced synovial tissue protruded to the subscapular tendon is shown on Figure 4. Necessary prerequisite of such imaging is certain position of the body (supine) and the arm flexed in elbow, adducted and externally rotated.

Discussion

US is a useful instrument for rheumatologists who wish to investigate the joint's outside and inside structures. Early recognition of shoulder involvement can be an essential step in preventing further damage. For treatment success, it is important to have an accurate analysis of the causes of shoulder pain and the extent of the rheumatoid processes [2]. US is very suitable for the evaluation for changes in joint tissues and is a rapid, safe and inexpensive method, usually convenient for patients. However, axillary and some posterior techniques for GHJ investigation might face serious difficulties because of the local nature of inflammation involving more anterior areas of the GHJ, sparing the posterior and inferior compartments [2,4].

We offer the anterior access for GHJ investigation performed during supination and external rotation of the shoulder in the

supine patient position as an addition to the classic access. Firstly, such access might to be much less painful for patients with synovitis. Our process of understanding of this method was not free of errors [8] and recognition of the main orienteer triad of the anterior GHJ cavity – round humeral head, round GHJ cartilage and subscapular tendon forward – helped us to visualize the anterior joint access [9].

The second advantage of such an approach is improved visualization of the GHJ. The accurate injection technique is possible with US, which is important to avoid local destruction of tendons. The technique is easily performed in the anterior access.

Do the design and the results of this study allow drawing a definite conclusion over this topic? We tried to measure GHJ width at three positions: two classic and one new using certain maneuver opening the anterior GHJ. We received data which is similar in healthy controls and statistically increased in patients with active RA synovitis. No doubt, this is only first step but that showed possibility to assess GHJ from anterior view. This is main result of the study.

In our trial US findings are not compared to relevant measures of disease activity such as acute phase reactants and composite measures of disease activity. We are planning to do it in further trials. Assessment of US disease activity in comparison with acute phase markers is a value instrument to evaluate concurrent validity [14].

This is one of the initial steps, and larger groups are needed for further clarification of the validity of the anterior access in assessment of GHJ synovitis.

We have several surprises as results of the study.

- 1. Rotator interval, which is usually considered as a sensitive place of inflammation, stayed within normal range in patients with active rheumatoid arthritis and inflamed GHJ. This region (RI) might present less resistance to increased intra-articular pressure and should extend easy. Why should upper part of the joint stay intact? This may be seen only in local nature of inflammation within GHJ. And this is leading message of the trial. Lack of correlation between anterior and inferior, anterior and posterior compartments results from skip character of inflammation. One should investigate all regions of the GHJ in order to diagnose of inflammation, which may be local and not diffuse.
- 2. Intensity of inflammation in the checked groups was not high. We did not observe severe effusions or synovial cyst ruptures. Our group was with moderate localized inflammation of GHJ. That may be due to concomitant therapy of a part of patients.

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We recognize several flaws of the study:

- 1. Unequal proportion of males and females in the investigation group and controls: M: F 15/5 vs. 5/11. However, within the 2 groups (ill and healthy) there was no difference in cartilage thickness between men and women, which is why the impact of this factor on cartilage values seems to be minimal.
- 2. Limited experience of cartilage measurement. We planned to measure the cartilage thickness at 3 points according to 3 cartilage parts. However, because of the group of healthy controls with preserved cartilage and concentric loss of the cartilage in patients with RA, we decided to measure at 2 points on a border of middle and marginal portions. Further work-up and elaboration of the issue are needed.
- 3. Measurement of correlation between data of the cartilage width in posterior, inferior, and anterior access. We think

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that this correlation may be associated with a similar intensity of inflammation. However, lack of correlation may be indicative of independence of the inflammatory process within various compartments of the GHJ. Also, such a statement may be suggestive and not precise.

Conclusions

The GHJ may be visualized by the anterior access using a special maneuver. Synovitis in the anterior region of the GHJ may develop at an independent rate. Anterior GHJ sonography may be complementary to the classic access.

Conflict of interest

The authors declare that they have no conflicts of interest.

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