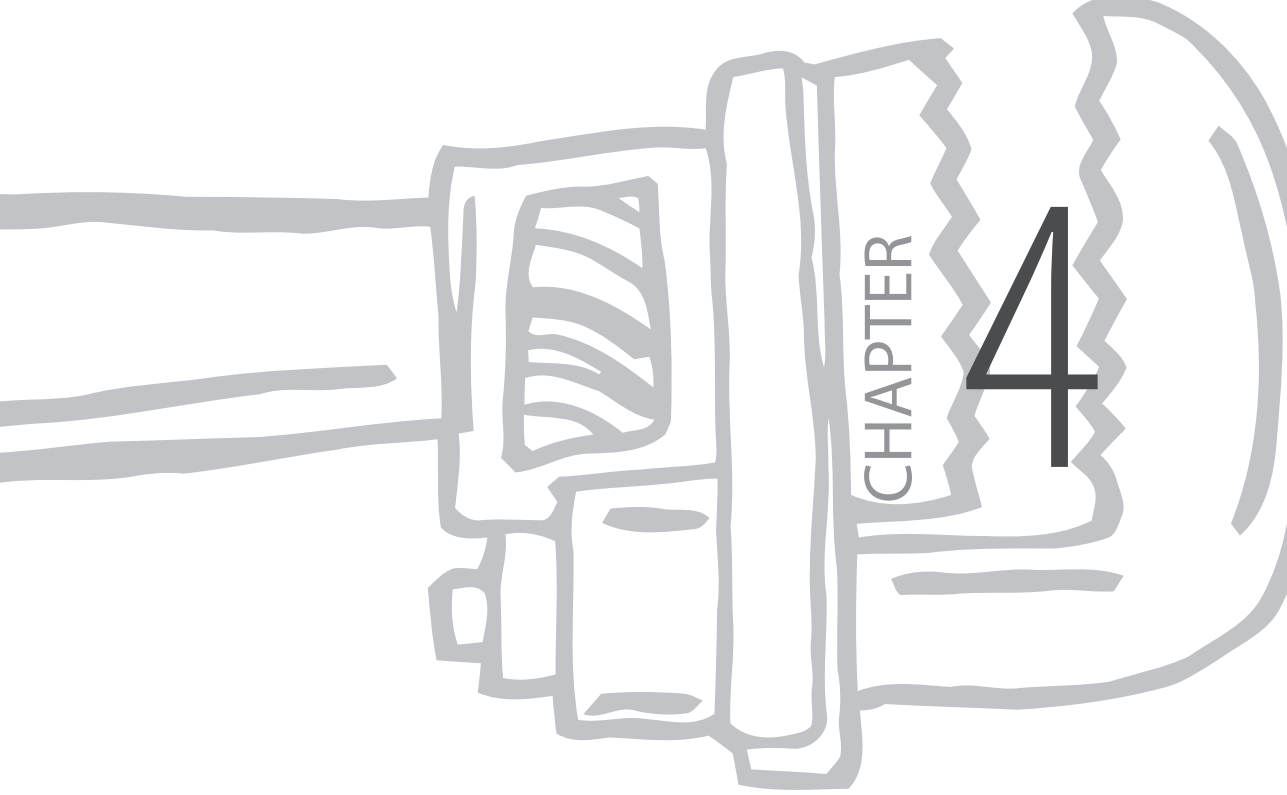

Heterogeneous MR arthrography findings in patients with Subacromial Impingement Syndrome - Diagnostic subgroups? -

Pieter Bas de Witte, MD, BSc [1]
Celeste L. Overbeek, BSc [1]
Ana Navas, MD [2]
Jochem Nagels, MD [1]
Monique Reijnierse, MD, PhD [2]
Rob G.H.H. Nelissen, MD, PhD [1]

1) Department of Orthopaedics, Leiden University Medical Center (LUMC), Leiden, the Netherlands
2) Department of Radiology, LUMC, Leiden, the Netherlands

Submitted to J. Electromyogr. Kinesiol., 2014

Abstract

Background: Subacromial impingement syndrome (SIS) is frequently diagnosed, but its underlying mechanisms are unclear and treatment results vary greatly. In the recent past, it has been increasingly reported that SIS symptoms might be the result of various underlying mechanisms that might need distinctive treatment strategies. Our goal was to evaluate a comprehensive set of specific Magnetic Resonance Imaging arthrography (MRA) characteristics that have been related with several potential underlying mechanisms for SIS in the literature, in patients clinically diagnosed with SIS. Our secondary aim was to define diagnostic subgroups with these MRA characteristics.

Methods: Patients with the clinical label SIS were included by experienced shoulder surgeons, based on symptoms, clinical tests and radiographs. MRAs of 47 patients were evaluated. MRA characteristics associated with SIS and subacromial narrowing in the literature were evaluated and categorized into three etiologic categories: 1) extrinsic: acromion shape, acromiohumeral distance, coracohumeral distance, caudal acromioclavicular osteophytes, internal impingement; 2) intrinsic: tendinosis, partial tendon tears, bursitis, supraspinatus tendon thickness; 3) dynamic (e.g. signs of glenohumeral micro-instability): glenohumeral index, biceps-supraspinatus tendon distance. All measurements were compared to control values from the literature. Cluster analysis was used to identify diagnostic subgroups.

Results: In 17 (36.2%) patients clinically diagnosed with SIS, signs of specific other conditions, including rotator cuff tendon tears and labrum lesions were found with MRA. In the remaining thirty patients, all had positive signs of one or more of the predefined etiologic mechanisms. With cluster analysis, patients could be categorized into two groups, with either predominantly findings corresponding with dynamic ((micro)instability) causes, or extrinsic (structural) causes.

Conclusions: MRA characteristics in patients with SIS symptoms are heterogeneous and many patients have specific other shoulder conditions causing symptoms. Patients without specific other conditions appear to have MRA characteristics associated with either an extrinsic (structural), or dynamic (e.g. micro-instability) based etiology.

Keywords: Shoulder Impingement Syndrome; Magnetic Resonance Imaging; Etiology; Rotator Cuff; Cluster Analysis

1. Introduction

Subacromial Impingement Syndrome (SIS) is diagnosed in 44-65% of the patients with shoulder complaints in primary health care.[1] SIS is generally defined as irritation of the soft tissues in the limited subacromial space, leading to pain with abduction, decreased active range of motion and loss of arm force.[2-4] Opinions concerning its etiology, diagnostic criteria, corresponding radiographic characteristics, and treatment strategies vary greatly.[1, 5-13] Nevertheless, there are many publications on "SIS" patients. Conflicting definitions of SIS are used across these studies, complicating interpretation of reported results.[14] More insight in underlying causes and identification of potential etiologic or diagnostic patient subgroups is needed in order to improve diagnostic criteria and treatment outcome of SIS symptoms. We investigated specific Magnetic Resonance Imaging (MRI) features related with SIS and subacromial narrowing in the literature, in patients clinically diagnosed with SIS, and we assessed whether diagnostic subgroups can be identified using a comprehensive combination of MRI arthrography features. Gathered information might serve as a foundation for future studies upon which clinical decision making and development of tailored treatment strategies can be based.

"Impingement syndrome" was introduced in 1972 by dr. Neer as a combination of typical clinical findings with various underlying mechanisms and stages.[15] Over the years, this evolved to the "*subacromial* impingement syndrome", which (wrongfully) suggests high specificity and anatomic differentiation of this entity. Since 1972, many diagnostic tools have been developed, including ultrasound, MRI and MRI arthrography (MRA), that can more accurately differentiate between causes of shoulder symptoms.[16-18] Consequently, "SIS" has become increasingly controversial as a diagnostic label. Some consider SIS symptoms as a consequence of several possible underlying mechanisms and pathologies rather than a specific diagnosis.[19] Furthermore, several conditions can cause SIS symptoms and can be (mistakenly) diagnosed as SIS; in a recent study at our institution 17.5% of patients selected for a SIS trial by experienced shoulder surgeons had to be excluded after MRI evaluation because of specific other shoulder conditions.[20]

Various studies have reported on specific MRI or MRA findings in patients with impingement symptoms. Characteristics for *extrinsic* etiologic mechanisms (structural or anatomic causes) are a hooked acromion,[21] caudal acromioclavicular (AC) joint osteophytes,[22-25] or subcoracoid impingement (narrowed space between coracoid and humerus).[26-29] But also signs of *intrinsic* pathologies can be found, including tendinosis, partial RC tears and bursitis,[30-35] either as a cause of SIS symptoms, or consequent to other etiologic mechanisms. Lastly, SIS symptoms can be caused by *dynamic* compression of the subacromial tissues during arm-shoulder

motion, as a result of e.g. glenohumeral (micro)instability, with specific associated findings on MRI.[36-39]

The primary goal of the current study was to investigate a group of patients with the clinical diagnosis SIS with MRA and a broad set of specific measurements, in order to evaluate characteristics of the various reported etiologic mechanisms of SIS symptoms. Additionally, we aimed to identify actual diagnostic subgroups, using the comprehensive set of MRA characteristics.

2. Materials and Methods

2.1 Selection of participants

Patients with impingement symptoms were recruited by 3 experienced orthopaedic shoulder surgeons from Leiden University Medical Center (LUMC), the Hague Medical Center (MCH) and Rijnland Hospital, Leiderdorp in an ongoing prospective multicenter observational cohort study on SIS. Data collecting included kinematic, clinical and radiographic methods.[37] In the current study, MRA characteristics of all consecutive patients included from April 2010 until December 2012 are reported and compared with control values from the literature.

Patients were enrolled after clinical examination and shoulder radiographs (anteroposterior in external and internal rotation and axial views) at the outpatient clinic. Inclusion criteria were one or more of the following criteria in addition to a painful arc, a positive Neer impingement test with lidocaine, a positive Hawkins test, and diffuse lateral shoulder pain for >3 months: night pain or incapable of lying on the shoulder, scapulohumeral dysrhythmia, pain with retroflexion and/or internal rotation (e.g. putting on a jacket, overhead activities), positive Yocum test. Exclusion criteria were: age <35 or >60, clinical signs of adhesive capsulitis, history of fracture or dislocation of the shoulder, history of surgery around the shoulder, known co-morbidities on the affected shoulder (including benign or malignant tumours), Hill Sachs lesion, glenohumeral or symptomatic AC joint osteoarthritis (positive AC compression test and/or pain with palpation of the AC joint), rheumatic disorder, calcific tendonitis >3mm on radiographs or cervical radiculopathy or other neurological deficits.

The medical ethics committees of the participating hospitals agreed to all stages of the study. Eligible patients who were willing to participate in the entire SIS project and who signed informed consent underwent a study-specific MRA of the shoulder and kinematic evaluation in our laboratory for kinematics and neuromechanics (LK&N). Patients had standard treatment by their referring clinician outside of the scope of this study.

2.2 MR Arthrography

MRA extends the capabilities of conventional MRI because contrast solution distends the joint capsule, outlines intra-articular structures, and leaks into abnormalities like tendon tears.[40] We used fluoroscopic guidance for intra-articular contrast administration with a 20-22 Gauge needle. After correct needle positioning, checked with 1-2 cc of nonionic iodinated contrast (Ultravist 300, Bayer), a maximum of 15 cc of diluted Gadolinium DTPA (0.4 cc:100 cc 0.9% NaCl) was administered.

Standardised MR imaging was performed 30 minutes after contrast administration on a 1.5T unit (Avanto Siemens, Erlangen, Germany, or Philips Intera, Best, The Netherlands) with a dedicated shoulder coil and the arm in neutral position (with slight internal rotation). The following sequences were used: axial, coronal oblique, sagittal oblique, T1-weighted fast spin-echo with fat suppression and coronal oblique T2-weighted with fat suppression. The field of view was 16-18cm, slice thickness 3mm or 4mm with 1mm gaps.

2.3 MR Arthrography assessment

The MRA images were evaluated by an experienced musculoskeletal radiologist at the LUMC, unfamiliar with the underlying hypotheses of this study, using PACS IDS5 11.4 software (Sectra Medical Systems AB, Linköping, Sweden). With a standardized MRA check-list, specific other conditions that can cause SIS symptoms were evaluated in all patients, including SLAP (Superior Labrum Anterior-Posterior) lesion, os acromiale, pulley lesion, Hill Sachs lesion, biceps tear or (sub)luxation of the biceps tendon, glenohumeral ligament pathology, or full-thickness RC tendon tear.

Patients with SIS symptoms without signs of other specific shoulder conditions were assessed for the presence of MRA characteristics typically associated with etiologic mechanisms for SIS symptoms in the literature. All cut-off values to define pathologic observations were obtained from 95%-confidence intervals (95%-CI) of healthy control data from the literature. Where applicable, Taylor expansions were applied to calculate 95%-CI's of literature data.

MRA characteristics were categorized, using a theoretical framework for the etiology of SIS derived from our previous study in which we reported that SIS, i.e. "a misbalance between subacromial volume and the space needed for subacromial structures" can be caused by:[37]

1) *Encroachment of subacromial tissues by anatomic structures (extrinsic):*
   - Acromion shape (Bigliani classification, classic extrinsic theory)[41] on sagittal oblique MRA series. A higher classification, i.e. more hooked shape, has been related to SIS.[21, 23] Bigliani type 2 or 3 (sagittal plane) classifications were regarded indicative for "classic" extrinsic impingement.
   - Minimal acromiohumeral (AH) distance (classic extrinsic theory). A smaller distance implies risk for mechanic structural impingement.[42, 43] AH <8.2mm (coronal plane) was considered indicative for extrinsic impingement.[44]
   - Subcoracoid impingement (between coracoid and humerus): decreased coracohumeral (CH) distance.[28, 45] Based on the results of Richards et al. CH distance <9.6mm (transverse plane) was considered pathologic.[45] (Figure 1)
   - AC joint osteoarthritis: osteophytes can impinge on the underlying tissues.[22-24, 46] Caudal osteophytes >2mm (coronal plane) combined with a deformity in the contour of underlying RC tendons in patients with otherwise asymptomatic AC osteoarthritis (negative AC compression test and no pain with palpation of the AC joint) was considered contributing to SIS.[25] (Figure 2)
   - Internal (glenoid) impingement: structural narrowing between the greater tuberosity and the posterosuperior glenoid, entrapping RC tendons during abduction and external rotation. The combination of cystic changes within the posterolateral humeral head, posterior articular surface tear(s) of the infraspinatus (ISP) and/or Supraspinatus (SSP) and posterior labrum abnormalities was considered indicative of internal impingement.[29]

2) *Intrinsic impingement*. For this category, we assessed:
   - Presence and location of RC tendinosis.[13, 31, 32] Patients were categorized in: tendinosis in 0, 1 or >1 tendons.
   - Presence of partial RC tendon tears and location (affected RC tendon(s), articular/bursal side, intratendinous).[34, 47] Patients were categorized in: partial tear in 0, 1, or >1 tendons.
   - Subacromial bursitis, defined as bursal fluid effusion with a width >3mm.[35]
   - Maximal SSP tendon thickness, measured in the coronal plane at 1.5cm from the footprint.[30, 33] (Figure 3) Based on the data of Milgrom et al, <5.9 and >6.3 were applied as cut-off values for pathologic tendon thickness.[33]
   - Maximum SSP tendon thickness was divided by the minimal AH-distance to obtain a relative measure of the amount of AH available for the SSP tendon.

3) *Dynamic impingement, e.g. due to (micro)instability:*

- Glenohumeral (GH) index: measure for the amount of bony support for the humeral head provided by the glenoid ((maximal glenoid diameter)/ (maximal humerus diameter), transverse plane).[48, 49] (Figure 4) GH-index <0.61 was considered indicative of (micro)instability.[48]
- Distance between the anterior edge of the tendon of the long head of the Biceps (LHB) and the anterior edge of the SSP tendon (4th slide after the base of the coracoid, sagittal plane). (Figure 5) Based on Provencher et al. a distance >4.0mm was considered indicative for micro-instability.[36]

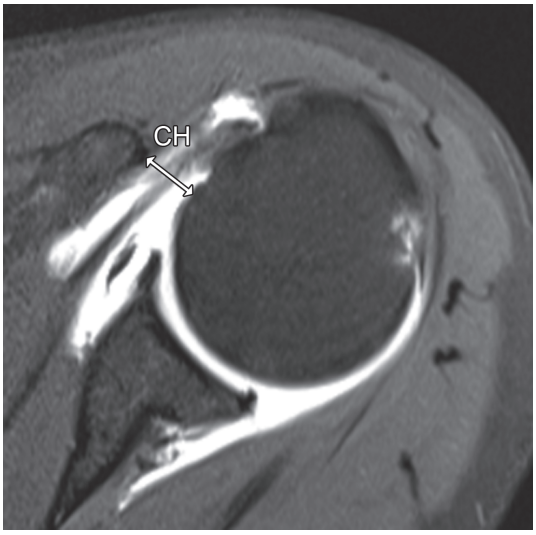

Figure 1. Coracohumeral (CH) distance.
Based on the results of Richards et al.[45] we considered CH distance <9.6mm as measured in the transverse plane as pathologic.

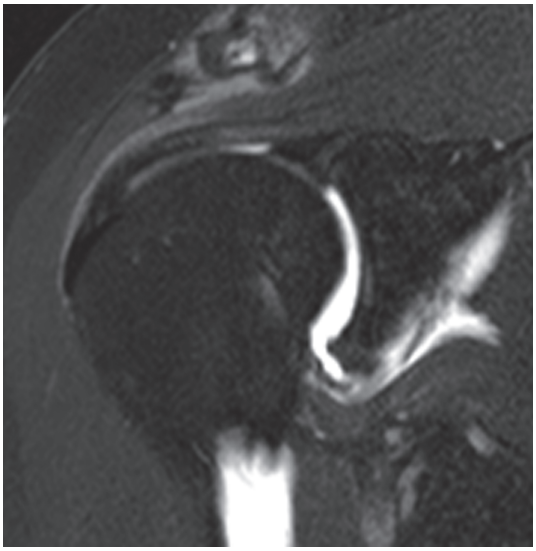

Figure 2. Example of caudal osteophytes >2mm in a patient with signs of acromionclavicular joint osteoarthritis on MRA, in combination with a deformity in the contour of the underlying subacromial tissues.

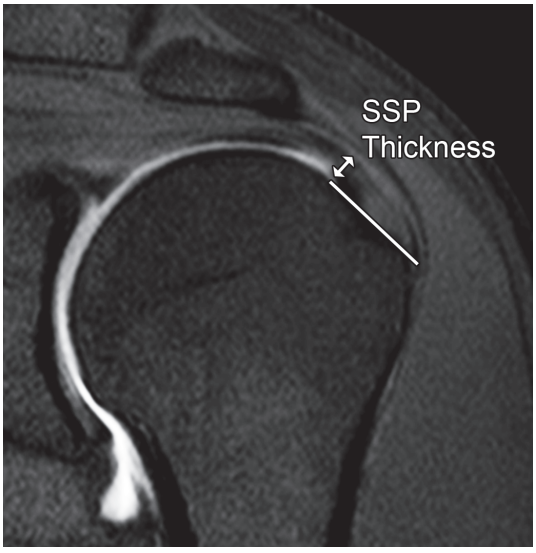

Figure 3. Maximal SSP tendon thickness, measured in the coronal plane at 1.5cm from the footprint.
Based on the data of Milgrom et al, <5.9 and >6.3 were applied as cut-off values for pathologic tendon thickness.[33]

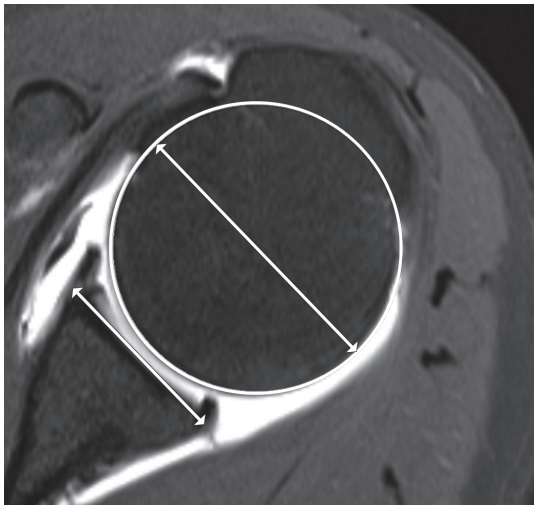

Figure 4. Glenohumeral (GH) index: measure for the amount of bony support for humeral head provided by the glenoid ((maximal glenoid diameter)/(maximal humerus diameter), transverse plane).
GH-index <0.61 was considered indicative of instability.[48]

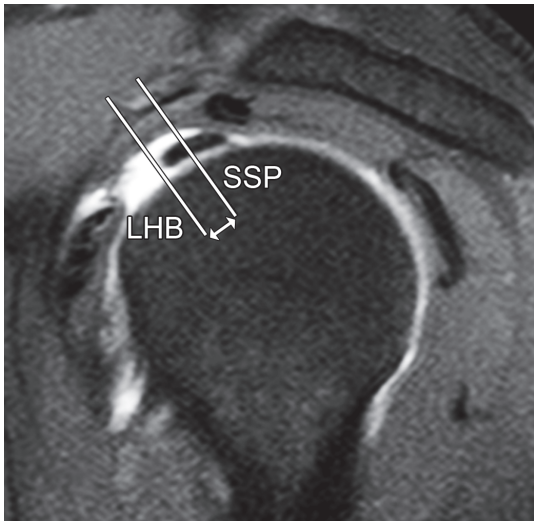

Figure 5. The distance between the anterior edge of the tendon of the long head of the Biceps (LHB) and the anterior edge of the Supraspinatus (SSP) tendon (4th slide after the base of the coracoid, sagittal plane).
A distance exceeding 4.0mm can be regarded indicative for micro-instability. According to Provencher et al. a more posterior LHB, more "tucked" under the SSP, should be expected in asymptomatic controls.[34]

2.4 Statistical analysis

Descriptive MRA data and patient demographics were collected. Means and standard deviations (SD), or medians and ranges where relevant, were calculated for each variable. The control cut-off values obtained from the 95%-confidence intervals of healthy control data reported in the literature (see above) were applied to assess whether patients had (pathologic) MRA characteristics associated with one or more of the hypothesized etiological mechanisms.

A Ward's cluster analysis was used, in order to investigate potential diagnostic patient subgroups.[50] With cluster analysis, subjects are assigned to groups (clusters) based on individual characteristics. Each cluster contains subjects that are more similar to each other than to subjects in the other clusters. In this way, patients with similar characteristics can be classified into specific subgroups. Identified subgroups were compared with regards to MRA characteristics and demographics using one-way ANOVA or Chi-squared analyses where appropriate.

Analyses were processed using SPSS 16.0 software (SPSS Inc., Chicago, Illinois) and R 2.10.0 Statistics software (R Foundation, Vienna, Austria). P-values <0.05 were considered statistically significant.

3. Results

3.1 Patient characteristics

During the inclusion period, 75 patients were invited to participate in the larger SIS study project. 25 Patients could not be included: 14 declined, 5 had clinical signs of AC osteoarthritis, 4 had calcific tendonitis on radiographs, 1 had a history of shoulder surgery and 1 had frozen shoulder syndrome. The remaining 50 patients fulfilled the eligibility criteria after usual care clinical and radiographic evaluation and underwent the study-specific MRA.

In 3 patients, MRAs could not be assessed for study purposes, due to inadequate intra-articular distribution of contrast fluid. All remaining 47 patients showed pathologic signs with MRA evaluation. In 17 (36.2%) patients clinically diagnosed with SIS, signs of specific other shoulder conditions were found: full-thickness RC tear in 11 (64.7%), labrum abnormalities (not in combination with internal impingement) in 3 (17.6%), glenohumeral ligament lesions in 2 (11.8%) and calcific tendonitis >3mm in 1 (5.9%). The remaining 30 patients (63.8%) were considered as actual SIS patients (i.e. without specific other conditions causing symptoms), and were studied with regards to SIS-related characteristics on MRA. Demographics of both groups are displayed in table 1.

Variable	SIS (n=30)	Other shoulder conditions with MRI (n=17)
Age (years)	51.5 [6.4]	52.2 [6.1]
Male : Female	12 : 18	5 : 12
BMI	26.6 [4.2]	NA
Left arm dominant (No.)	5 (16.7)	NA
Dominant arm affected (No.)	16 (53.3)	NA

Table 1. Patient demographics, stratified for patients with the diagnostic label "subacromial impingement syndrome (SIS)" after clinical evaluation, radiographs and MR arthrography, and patients with specific other pathologies identified on MR arthrography causing SIS-like symptoms. (%), [SD]

3.2 MRI characteristics in SIS patients

In 5 patients, the obtained MRAs were not adequate to measure LHB-SSP distance (n=4) or CH distance (n=1). All other measurements of these patients were included in the analyses.

All 30 patients had positive signs for one or more of the predefined etiologic mechanisms. Firstly, for characteristics associated with *extrinsic* etiologic mechanism (i.e. encroachment of subacromial tissues by anatomic structures), 21 (70.0%) patients had a type 2 or 3 acromion. Mean AH distance was 8.0mm (SD=1.5), which was below the 8.2mm cut-off in 19 (59.4%) patients. In 16 (53.3%) both of these measurements for "classic" extrinsic impingement were positive. Furthermore, 12 patients (41.4%) had MRA signs of AC joint osteoarthritis (despite positive physical examination tests for AC osteoarthritis was an exclusion criterion) with caudal osteophytes >2mm impinging on the underlying tissues. Mean CH distance was 11.0mm (SD=3.1): below the 10.4mm cut-off in 12 patients (41.4%). There were no patients fulfilling all internal impingement criteria.

Secondly, *intrinsic* characteristics (either as a primary cause of SIS symptoms, or as a consequence of the other etiologic mechanisms) were found in 28 (93.3%) patients. 11 (36.7%) had tendinosis in one RC tendon (all SSP) and 5 (16.7%) had tendinosis in more than one tendon (all SSP and ISP). There were 5 (17.2%) patients with a partial SSP tendon tear (1 bursal side, 1 intratendinous, 3 articular side), 4 (13.8%) patients with a partial ISP tendon tear (all articular side) and 3 (10.3%) patients with an articular side tear in both the ISP and SSP tendon. Furthermore, 9 (30%) had bursitis and 25 (83.3%) had a pathologic SSP tendon thickness: <5.9mm in 5 (16.7%) and >6.3mm in 20 (66.7%). In 27 (96.4%), there were signs of intrinsic etiology, combined with positive findings of one or more of the other reported etiologic mechanisms.

Thirdly, for findings of *dynamic* mechanisms (i.e. motion-related causes of SIS symptoms, e.g. due to glenohumeral (micro)-instability), mean GH-index was 0.61 (SD=0.04) and mean LHB-SSP distance 4.5mm (SD=3.1). (Table 2) GH-index was below the 0.61 control cut-off in 14 (46.7%) patients, indicative for micro-instability.

The LHB-SSP distance was higher than the 4.0mm cut-off value in 11 (42.3%) patients. In 6 (23.1%) patients, both measurements were indicative for (micro)instability.

	SIS patients (n=30)	Indicative for SIS	
Variables	Mean	Cut-off	No. (%)
Structural etiology (extrinsic)			
Type of acromion		Type 2/3 [21, 23]	21 (70.0)
1 (No.)	9 (30.0)		NA
2 or 3 (No.)	21 (70.0)		NA
Min. acromiohumeral distance (mm)	8.0 [1.5]	<8.2 [44]	19 (59.4)
Coracohumeral distance (mm)	11.0 [3.1]	<9.6 [45]	10 (34.5)
Internal impingement (No.)	0 (0.0)	present [29]	0 (0.0)
AC-osteoarthritis & osteophyte >2 mm (No.)	12 (40.0)	present [25]	12 (40.0)
Intrinsic etiology			
Tendinosis		present [13, 31, 32]	16 (53.3)
No tendon (No.)	14 (46.7)		NA
1 tendon (No.)	11 (36.7)		NA
>1 tendon (No.)	5 (16.7)		NA
Partial rotator cuff tear		present [34, 47]	12 (40.0)
No tendon (No.)	18 (60.0)		NA
1 tendon (No.)	9 (30.0)		NA
>1 tendon (No.)	3 (10.0)		NA
Bursitis (No.)	9 (30.0)	present [35]	9 (30.0)
Max. thickness SSP tendon (mm)	5.2 [1.1]	<5.9 or >6.3 [33]	25 (83.3)
Max. Relative thickness SSP tendon	0.67 [0.19]		
Dynamic etiology			
Glenohumeral index	0.61 [0.04]	<0.61 [48]	14 (46.7)
Distance SSP-LHB (mm)	4.5 [3.1]	>4.0 [36]	11 (42.3)

Table 2. Positive MR arthrography characteristics for the various hypothesized etiologic mechanisms for SIS.
Findings presented for patients with SIS symptoms without any other shoulder pathologies with clinical investigation, radiographs and MR arthrography.
Applied cut-off values were obtained from the literature (references indicated).
((%), [SD], LHB: tendon of the long head of the biceps, SSP: Supraspinatus tendon)

3.3 Cluster analysis

Bigliani classification, caudal AC osteophytes, RC tendinosis, SSP tendon thickness, GH index and LHB-SSP distance were entered in the cluster analysis. Five patients could not be included in this analysis, because of missing values in one or more of the included variables.

The resulting cluster diagram contained 2 main clusters: cluster I with 8 patients (32.0%) and cluster II with the remaining 17 (68.0%) patients. Cluster I included patients with a more *extrinsic* related etiology, with significantly higher Bigliani classifications (all had type 2 or 3 classifications), a significantly lower LHB-SSP distance and a higher GH-index (both pleading against glenohumeral (micro) instability), more females and more bursitis compared to cluster II, which contained patients with more positive signs for *dynamic* related etiology, e.g. related with glenohumeral (micro)instability. (Table 3)

	Cluster I Extrinsic (n=8)	Cluster II Dynamic (n=17)	Difference	
Variables	Mean	Mean	Mean	p-value
Demographics				
Age (years)	47.8 [7.0]	51.4 [6.2]	3.7	0.20
Male : Female	1 : 7	10 : 7	NA	**0.03**
Structural etiology (extrinsic)				
Type of acromion				**0.03**
1 (No.)	0 (0.0)	7 (41.2)	NA	
2 or 3 (No.)	8 (100.0)	10(58.8)	NA	
Min. acromiohumeral distance (mm)	8.6 [1.5]	7.7 [1.3]	0.9	0.13
Coracohumeral distance (mm)	10.8 [3.6]	11.4 [3.3]	0.62	0.69
Internal impingement (No.)	0 (0.0)	0 (0.0)	NA	NA
AC-osteoarthritis & osteophyte >2 mm (No.)	1 (12.5)	7 (41.2)	NA	0.15
Intrinsic etiology				
Tendinosis				0.26
No tendon (No.)	4 (50.0)	10 (58.8)	NA	
1 tendon (No.)	4 (50.0)	4 (23.5)	NA	
>1 tendon (No.)	0 (0.0)	3 (17.6)	NA	
Partial rotator cuff tear				0.52
No tendon (No.)	6 (75.0)	9 (52.9)	NA	
1 tendon (No.)	2 (25.0)	7 (41.2)	NA	
>1 tendon (No.)	0 (0.0)	1 (5.9)	NA	
Bursitis (No.)	4 (50.0)	2 (11.8)	NA	**0.04**
Max. thickness SSP tendon (mm)	5.6 [1.3]	5.0 [0.8]	0.6	0.23
Max. Relative thickness SSP tendon	0.66 [1.17]	0.67 [0.19]	0.01	0.86
Dynamic etiology				
Glenohumeral index	0.63 [0.03]	0.60 [0.05]	0.03	0.09
Distance SSP-LHBT (mm)	1.3 [1.7]	6.0 [2.5]	4.7	**<0.01**

Table 3. Comparison of the two identified etiologic subgroups after cluster analysis.
Cluster 1 included patients with a more extrinsic related etiology, more females, with a higher GH-index, a significantly lower LHB-SSP distance, more bursitis and significantly higher Bigliani classifications compared to cluster II, which contained patients with more positive signs for a (micro)instability related etiology.
((%), [SD], LHB: tendon of the long head of the biceps, SSP: Supraspinatus tendon)

4. Discussion

Our results show that in patients clinically diagnosed with SIS by experienced shoulder surgeons, MRA characteristics of various underlying causes can be found. And in many patients, SIS symptoms actually appear to be associated with specific other shoulder conditions, mistakenly diagnosed as SIS. All remaining patients had pathologic MRA characteristics, that were either associated with *extrinsic* impingement etiologic mechanisms (e.g. bony structures impinging on underlying tissues), or with *dynamic* motion-related impingement etiologic mechanisms (e.g. glenohumeral (micro)instability). Almost all patients showed signs of intrinsic pathology, either as a primary cause of SIS symptoms, or secondary to the other etiologic mechanisms.

It is important to note that the current study doesn't specifically advocate the use of MRA as an early step in the diagnostic process of SIS. And with the current results, it's not possible to design e.g. specific diagnostic criteria or diagnostic flow charts for SIS symptoms. The main goal was to thoroughly investigate a group of patients clinically diagnosed with SIS, for signs of various potential underlying mechanisms and other pathologies that can cause SIS symptoms. Our results show that SIS is indeed not a clear-cut and specific diagnostic label, despite its terminology, suggesting specificity and anatomic differentiation.

4.1 Heterogeneous findings in SIS patients

There is no consensus on a specific definition or a set of clinical or radiological characteristics that encompass SIS. Despite this, acromionplasty, which is based on the classic extrinsic etiologic theory (1972),[15] is a frequently performed surgery for SIS symptoms and one of the most performed orthopaedic surgeries in general.[51] However, its success rates are highly variable[52-55] and good clinical outcome has been reported for patients in whom the acromial shape is not altered.[20, 56-60] These contradicting results stress the need for a better understanding and better diagnostic strategies to identify the probable different phenotypes of shoulder pain that are often diagnosed as SIS, in order to target treatment to the principal underlying etiologic mechanism.

We found that 17 of 47 patients (36.2%) clinically diagnosed with SIS had specific other shoulder conditions with MRA. In the remaining 30 patients, all patients had positive signs of the predefined potential etiologic mechanisms. 28 (93.3%) Had signs of intrinsic etiology (either primary, or secondary to other underlying mechanisms). With cluster analyses, 2 main subgroups of patients with distinct MRA characteristics could be identified, with statistically significant differences between both groups. One cluster had primarily characteristics suggestive for structural extrinsic etiology and the other had primarily characteristics of dynamic (motion-related) causes, including glenohumeral (micro)instability. This supports the categorization in the predefined etiologic mechanisms. It is plausible that more tailored diagnostics and treatment strategies need to be developed for these and potential other underlying subgroups in patients with SIS symptoms.

4.2 Extrinsic etiologic mechanisms

According to the *classic* extrinsic mechanism, SIS symptoms can be the result of impingement of the acromion on the RC tendons. Several authors have reported a relation between a hooked acromion and SIS.[21, 59, 61-63] Accordingly, in our study, 24 (80.0%) patients had a type 2 or 3 acromion, which is much higher than the prevalence in the literature for asymptomatic individuals.[64] However, 22 of these patients also

had signs of other potential etiologic mechanisms, including AC osteoarthritis with subacromial osteophytes, or even glenohumeral (micro)instability (not extrinsic). Additionally, many authors have reported on the difficulties in assessing acromion shape and others contradict the often suggested relation between acromion and SIS.[12, 61, 65] This underlines that SIS symptoms are not necessarily always caused by a hooked acromion, and that the indications of acromionplasty might be more questionable than often suggested.

For the other (non-classic) extrinsic mechanisms, subcoracoid narrowing was found in 10 (33.3%) patients. But subcoracoid impingement is a clinical diagnosis and CH-narrowing on MRI should be related to clinical findings.[28] None of our patients had subscapularis tendon pathology with clinical and MRI evaluation.

With regards to AC-osteoarthritis, 12 (41.4%) patients had osteophytes impinging on subacromial tissues, of whom none had clinical symptoms pointing to AC-osteoarthritis (positive AC compression test, or pain with palpation of the AC joint). In support of this, a previous MRI study reported a prevalence of AC-osteoarthritis signs in 93% asymptomatic middle-aged individuals.[66] Although direct symptoms of AC-osteoarthritis itself can be absent, the condition can indirectly cause SIS symptoms due to actual impingement on the RC by caudal osteophytes.[23-25, 46]

Hébert et al. reported that a decreased acromiohumeral (AH) distance on MRI is associated with SIS.[44] Although often linked to a hooked acromion, AH narrowing can also be caused by e.g. glenohumeral (micro)-instability and/or pathologic kinematics. Hence, both diagnostic subgroups identified with our cluster analysis can, at least in theory, come with "structural" (extrinsic) or "dynamic" ((micro)-instability) AH narrowing. We found 19 (59.4%) patients with AH narrowing (<8.2mm). There was no difference in AH distance between both subgroups of the cluster analysis. In our view, the AH distance on MRI is a poor indicator for "classic" extrinsic SIS. This is supported by Mayerhoefer et al., who found no significant correlation between acromion morphology and AH distance.[43]

4.3 Intrinsic etiologic mechanisms

We found 28 (93.3%) patients with signs of intrinsic etiologic mechanisms. Various authors suggest intrinsic mechanisms can be a cause of SIS.[1, 67-69] But signs of intrinsic etiologies might also be secondary to other etiologic mechanisms. For example, it has been suggested that bursal side tendon tears suggest extrinsic etiology (i.e. impingement by bony structures), whereas articular side tears suggest intrinsic etiology.[67, 69] This could not be confirmed in our study where the majority of the observed partial tears were on the articular side, and not on the bursal side, where they would be expected if caused by encroachment by e.g. the acromion.[70] And overall, 27 of 28 patients with signs of intrinsic etiologic mechanisms also had characteristics of the other hypothesized etiologic mechanisms.

4.4 Dynamic impingement

Several authors have reported pathologic motion patterns and glenohumeral (micro)instability can lead to SIS, due to relative cranialisation of the humerus with respect to the scapula/acromion during arm motion.[36-39] We identified 19 (70.0%) patients with a GH-index (<0.61) and/or LHB-SSP distance (>4.0mm) suggestive for GH (micro)instability. In the final cluster analysis, a dynamic impingement subgroup of 17 patients could be identified, with an average GH-index of 0.60 and an average LHB-SSP distance of 6.0mm, both outside the confidence intervals of values reported for healthy asymptomatic subjects. Additionally, Bigliani acromion classifications were significantly lower in this subgroup, compared to the other identified ("extrinsic") subgroup. Although not investigated in this study, acromionplasty theoretically makes less sense as a treatment for patients with generally signs of (micro)instability instead of extrinsic causes.

4.5 Limitations

Our study is subject to some limitations. Firstly, the diagnosis of SIS, even by experienced shoulder surgeons, may be subjected to variability. Secondly, we did not investigate a control group, due to ethical considerations regarding exposure to contrast injections and MRA. We did, however, compare our results to 95% confidence intervals of control values available from the literature, obtained from healthy subjects. Thirdly, we applied control values of AH distance obtained from a study of Hebert et al.[44] They used an open MRI, where subjects were in erected position with the arm alongside the body (gravitational forces present). This could have led to a relatively larger AH compared to standard MRIs, as applied in our study. We were unable to find another publication reporting on MRI-based AH control values with SD's or confidence intervals. Overall, this could have implicated that the number of patients we classified as having a pathologic AH is overestimated. However, AH cut-off values were not used in the cluster analysis, which we used to identify potential etiologic patient subgroups. Fourthly, we were unable to find publications on GH-index values based on MRI. Therefore, we used the studies of McPherson (cadavers and radiographs) and Van Den Bogaert (cadavers and Computed Tomography).[48, 49] Lastly, the final group of SIS patients was relatively small, partially due to the high number of patients who appeared to have other specific pathologies with MRA evaluation, which is actually also an important outcome of our study. Despite the small number, we were able to identify MRA characteristics for various etiologic mechanisms and to classify patients into significantly different diagnostic subgroups.

5. Conclusions

Various pathologic MRA findings can be demonstrated in patients clinically diagnosed with SIS. These findings can be related with several underlying mechanisms that can cause SIS symptoms. Even more, in many patients specific other diagnoses (e.g. full-thickness RC tear, labrum abnormalities, glenohumeral ligament lesions and calcific tendonitis) can be found, possibly causing the SIS symptoms. With regards to etiologic mechanisms in patients without specific other shoulder conditions on MRA, some patients have predominantly signs associated with dynamic or motion related etiology (e.g. decreased GH index or increased distance between LHB and SSP tendons, which are signs of glenohumeral (micro)instability), whereas in others, there are predominantly signs associated with extrinsic etiology (e.g. hooked acromion). Practically all patients show signs of intrinsic problems (e.g. tendinosis), that can be either primary, or secondary to dynamic or extrinsic causes.

Hence, in patients clinically diagnosed with SIS, signs of various underlying mechanisms or even various underlying diseases can be found. This underlines SIS is a pain syndrome and not a specific diagnosis. The (wrongful) use of SIS as a specific diagnostic label is one of the explanations for the great variations in treatment outcomes of the many reported treatment strategies for SIS symptoms. We advise the use of additional imaging with e.g. ultrasound, MRI and/or MRA to further investigate underlying causes of symptoms when studying patients with "SIS" in a research setting, or when considering invasive treatment in case of persisting SIS symptoms in clinical practice.[71] Possibly, patients with predominantly signs of dynamic mechanisms need different treatment pathways than patients with signs of extrinsic mechanisms.

Acknowledgements

The authors would like to acknowledge E.R.A. van Arkel, MD, PhD (Dept. of Orthopaedics, Medical Center Haaglanden (MCH), the Hague, the Netherlands) C.P.J. Visser, MD, PhD (Dept. of Orthopaedics, Rijnland Hospital, Leiderdorp, the Netherlands) for their support in the design of the study and for referring patients, Eric van Zwet, MS, PhD (Department of Medical Statistics and BioInformatics, LUMC) for his help with the statistics of this paper, and the Radiology departments of LUMC and MCH for acquiring the MR arthrograms.

This study is part of a larger project funded by ZonMw, the Netherlands Organization for health research and development (NOW) (grant number 40-00703-98-8564), and the Dutch Arthritis Association (grant number 09-1-303).

References

1. **Michener LA, McClure PW, Karduna AR** Anatomical and biomechanical mechanisms of subacromial impingement syndrome. *Clin Biomech (Bristol , Avon)* 2003;18:369-79.
2. **Bigliani LU, Levine WN** Subacromial impingement syndrome. *J Bone Joint Surg Am* 1997;79:1854-68.
3. **Codman EA** The shoulder, rupture of the supraspinatus tendon and other lesions in or about the the subacrominal bursa, 1934.
4. **Koester MC, George MS, Kuhn JE** Shoulder impingement syndrome. *Am J Med* 2005;118:452-5.
5. **Johansson K, Oberg B, Adolfsson L, Foldevi M** A combination of systematic review and clinicians' beliefs in interventions for subacromial pain. *Br J Gen Pract* 2002;52:145-52.
6. **Dorrestijn O, Stevens M, Diercks RL, van der MK, Winters JC** A new interdisciplinary treatment strategy versus usual medical care for the treatment of subacromial impingement syndrome: a randomized controlled trial. *BMC Musculoskelet Disord* 2007;8:15.
7. **Dorrestijn O, Stevens M, Winters JC, van der MK, Diercks RL** Conservative or surgical treatment for subacromial impingement syndrome? A systematic review. *J Shoulder Elbow Surg* 2009;18:652-60.
8. **Kelly SM, Wrightson PA, Meads CA** Clinical outcomes of exercise in the management of subacromial impingement syndrome: a systematic review. *Clin Rehabil* 2010;24:99-109.
9. **Smidt N, Green S** Is the diagnosis important for the treatment of patients with shoulder complaints? *Lancet* 2003;362:1867-8.
10. **van der Windt DAWM, Bouter LM, Koes BW, de Jong BA** Diagnostics of shoulder complaints: interobserver agreement between general practitioners and physiotherapists mediocre. *Ned Tijdschr Geneeskd* 1998;142:1262-5.
11. **Bamji AN, Erhardt CC, Price TR, Williams PL** The painful shoulder: can consultants agree? *Br J Rheumatol* 1996;35:1172-4.
12. **Bright AS, Torpey B, Magid D, Codd T, McFarland EG** Reliability of radiographic evaluation for acromial morphology. *Skeletal Radiol* 1997;26:718-21.
13. **Lewis JS** Rotator cuff tendinopathy/subacromial impingement syndrome: is it time for a new method of assessment? *Br J Sports Med* 2009;43:259-64.
14. **Green S, Buchbinder R, Glazier R, Forbes A** Systematic review of randomised controlled trials of interventions for painful shoulder: selection criteria, outcome assessment, and efficacy. *BMJ* 1998;316:354-60.
15. **Neer CS** Anterior acromioplasty for the chronic impingement syndrome in the shoulder: a preliminary report. *J Bone Joint Surg Am* 1972;54:41-50.
16. **Papadonikolakis A, McKenna M, Warme W, Martin BI, Matsen FA** Published evidence relevant to the diagnosis of impingement syndrome of the shoulder. *J Bone Joint Surg Am* 2011;93:1827-32.
17. **Bureau NJ, Beauchamp M, Cardinal E, Brassard P** Dynamic sonography evaluation of shoulder impingement syndrome. *AJR Am J Roentgenol* 2006;187:216-20.
18. **Read JW, Perko M** Shoulder ultrasound: diagnostic accuracy for impingement syndrome, rotator cuff tear, and biceps tendon pathology. *J Shoulder Elbow Surg* 1998;7:264-71.
19. **McFarland EG, Selhi HS, Keyurapan E** Clinical evaluation of impingement: what to do and what works. *J Bone Joint Surg Am* 2006;88:432-41.
20. **Henkus HE, de Witte PB, Nelissen RG, Brand R, van Arkel ER** Bursectomy compared with acromioplasty in the management of subacromial impingement syndrome: a prospective randomised study. *J Bone Joint Surg Br* 2009;91:504-10.
21. **Epstein RE, Schweitzer ME, Frieman BG, Fenlin JM, Jr., Mitchell DG** Hooked acromion: prevalence on MR images of painful shoulders. *Radiology* 1993;187:479-81.
22. **Strobel K, Pfirrmann CW, Zanetti M, Nagy L, Hodler J** MRI features of the acromioclavicular joint that predict pain relief from intraarticular injection. *AJR Am J Roentgenol* 2003;181:755-60.
23. **Roidis NT, Motamed S, Vaishnav S, Ebramzadeh E, Karachalios TS, Itamura JM** The influence of the acromioclavicular joint degeneration on supraspinatus outlet impingement and the acromion shape. *J Orthop Surg (Hong Kong)* 2009;17:331-4.

24. **Oh JH, Kim JY, Lee HK, Choi JA** Classification and clinical significance of acromial spur in rotator cuff tear: heel-type spur and rotator cuff tear. *Clin Orthop Relat Res* 2010;468:1542-50.
25. **de Abreu MR, Chung CB, Wesselly M, Jin-Kim H, Resnick D** Acromioclavicular joint osteoarthritis: comparison of findings derived from MR imaging and conventional radiography. *Clin Imaging* 2005;29:273-7.
26. **Lo IK, Burkhart SS** The etiology and assessment of subscapularis tendon tears: a case for subcoracoid impingement, the roller-wringer effect, and TUFF lesions of the subscapularis. *Arthroscopy* 2003;19:1142-50.
27. **Bonnet CS, Walsh DA** Osteoarthritis, angiogenesis and inflammation. *Rheumatology (Oxford)* 2005;44:7-16.
28. **Giaroli EL, Major NM, Lemley DE, Lee J** Coracohumeral interval imaging in subcoracoid impingement syndrome on MRI. *AJR Am J Roentgenol* 2006;186:242-6.
29. **Mulyadi E, Harish S, O'Neill J, Rebello R** MRI of impingement syndromes of the shoulder. *Clin Radiol* 2009;64:307-18.
30. **Cholewinski JJ, Kusz DJ, Wojciechowski P, Cielinski LS, Zoladz MP** Ultrasound measurement of rotator cuff thickness and acromio-humeral distance in the diagnosis of subacromial impingement syndrome of the shoulder. *Knee Surg Sports Traumatol Arthrosc* 2008;16:408-14.
31. **Giaroli EL, Major NM, Higgins LD** MRI of internal impingement of the shoulder. *AJR Am J Roentgenol* 2005;185:925-9.
32. **Seeger LL, Gold RH, Bassett LW, Ellman H** Shoulder impingement syndrome: MR findings in 53 shoulders. *AJR Am J Roentgenol* 1988;150:343-7.
33. **Milgrom C, Moran DS, Safran O, Finsestone AS** Do the rotator cuff tendons of young athletic subjects hypertrophy in response to increased loading demands? *J Shoulder Elbow Surg* 2012.
34. **Schaeffeler C, Mueller D, Kirchhoff C, Wolf P, Rummeny EJ, Woertler K** Tears at the rotator cuff footprint: prevalence and imaging characteristics in 305 MR arthrograms of the shoulder. *Eur Radiol* 2011;21:1477-84.
35. **White EA, Schweitzer ME, Haims AH** Range of normal and abnormal subacromial/subdeltoid bursa fluid. *J Comput Assist Tomogr* 2006;30:316-20.
36. **Provencher MT, Dewing CB, Bell SJ, McCormick F, Solomon DJ, Rooney TB, Stanley M** An analysis of the rotator interval in patients with anterior, posterior, and multidirectional shoulder instability. *Arthroscopy* 2008;24:921-9.
37. **de Witte PB, Nagels J, van Arkel ER, Visser CP, Nelissen RG, de Groot JH** Study protocol subacromial impingement syndrome: the identification of pathophysiologic mechanisms (SISTIM). *BMC Musculoskelet Disord* 2011;12:282.
38. **Jobe FW, Kvitne RS, Giangarra CE** Shoulder pain in the overhand or throwing athlete. The relationship of anterior instability and rotator cuff impingement. *Orthop Rev* 1989;18:963-75.
39. **Belling Sorensen AK, Jorgensen U** Secondary impingement in the shoulder. An improved terminology in impingement. *Scand J Med Sci Sports* 2000;10:266-78.
40. **Steinbach LS, Palmer WE, Schweitzer ME** Special focus session. MR arthrography. *Radiographics* 2002;22:1223-46.
41. **Bigliani LU, Morrison DU, April EW** The morphology of the acromion and its relationship to rotator cuff tears. *Orthop Trans* 1986;10:228.
42. **Saupe N, Pfirrmann CW, Schmid MR, Jost B, Werner CM, Zanetti M** Association between rotator cuff abnormalities and reduced acromiohumeral distance. *AJR Am J Roentgenol* 2006;187:376-82.
43. **Mayerhoefer ME, Breitenseher MJ, Wurnig C, Roposch A** Shoulder impingement: relationship of clinical symptoms and imaging criteria. *Clin J Sport Med* 2009;19:83-9.
44. **Hebert LJ, Moffet H, Dufour M, Moisan C** Acromiohumeral distance in a seated position in persons with impingement syndrome. *J Magn Reson Imaging* 2003;18:72-9.
45. **Richards DP, Burkhart SS, Campbell SE** Relation between narrowed coracohumeral distance and subscapularis tears. *Arthroscopy* 2005;21:1223-8.
46. **Liotard JP, Cochard P, Walch G** Critical analysis of the supraspinatus outlet view: rationale for a standard scapular Y-view. *J Shoulder Elbow Surg* 1998;7:134-9.

47. **Tuite MJ** Magnetic resonance imaging of rotator cuff disease and external impingement. *Magn Reson Imaging Clin N Am* 2012;20:187-200, ix.
48. **McPherson EJ, Friedman RJ, An YH, Chokesi R, Dooley RL** Anthropometric study of normal glenohumeral relationships. *J Shoulder Elbow Surg* 1997;6:105-12.
49. **Van Den Bogaert M, Van DM, Heylen S, Foubert K, Van GF** Validation of a CT-based determination of the glenohumeral index. *Acta Orthop Belg* 2011;77:167-70.
50. **Ward JH** Hierarchical Grouping to Optimize An Objective Function. *Journal of the American Statistical Association* 1963;58:236-&.
51. **Yu E, Cil A, Harmsen WS, Schleck C, Sperling JW, Cofield RH** Arthroscopy and the dramatic increase in frequency of anterior acromioplasty from 1980 to 2005: an epidemiologic study. *Arthroscopy* 2010;26:S142-S147.
52. **Altchek DW, Warren RF, Wickiewicz TL, Skyhar MJ, Ortiz G, Schwartz E** Arthroscopic acromioplasty. Technique and results. *J Bone Joint Surg Am* 1990;72:1198-207.
53. **Ellman H, Kay SP** Arthroscopic subacromial decompression for chronic impingement. Two- to five-year results. *J Bone Joint Surg Br* 1991;73:395-8.
54. **Sachs RA, Stone ML, Devine S** Open vs. arthroscopic acromioplasty: a prospective, randomized study. *Arthroscopy* 1994;10:248-54.
55. **Van Holsbeeck E, DeRycke J, Declercq G, Martens M, Verstreken J, Fabry G** Subacromial impingement: open versus arthroscopic decompression. *Arthroscopy* 1992;8:173-8.
56. **Brox JI, Staff PH, Ljunggren AE, Brevik JI** Arthroscopic surgery compared with supervised exercises in patients with rotator cuff disease (stage II impingement syndrome). *BMJ* 1993;307:899-903.
57. **Budoff JE, Rodin D, Ochiai D, Nirschl RP** Arthroscopic rotator cuff debridement without decompression for the treatment of tendinosis. *Arthroscopy* 2005;21:1081-9.
58. **Goldberg BA, Lippitt SB, Matsen FA, III** Improvement in comfort and function after cuff repair without acromioplasty. *Clin Orthop Relat Res* 2001;Sep:142-50.
59. **Morrison DS, Frogameni AD, Woodworth P** Non-operative treatment of subacromial impingement syndrome. *J Bone Joint Surg Am* 1997;79:732-7.
60. **Wirth MA, Basamania C, Rockwood CA, Jr.** Nonoperative management of full-thickness tears of the rotator cuff. *Orthop Clin North Am* 1997;28:59-67.
61. **Hirano M, Ide J, Takagi K** Acromial shapes and extension of rotator cuff tears: magnetic resonance imaging evaluation. *J Shoulder Elbow Surg* 2002;11:576-8.
62. **Jacobson SR, Speer KP, Moor JT, Janda DH, Saddemi SR, MacDonald PB, Mallon WJ** Reliability of radiographic assessment of acromial morphology. *J Shoulder Elbow Surg* 1995;4:449-53.
63. **Nordt WE, III, Garretson RB, III, Plotkin E** The measurement of subacromial contact pressure in patients with impingement syndrome. *Arthroscopy* 1999;15:121-5.
64. **Schippinger G, Bailey D, McNally EG, Kiss J, Carr AJ** Anatomy of the normal acromion investigated using MRI. *Langenbecks Arch Chir* 1997;382:141-4.
65. **Zuckerman JD, Kummer FJ, Cuomo F, Greller M** Interobserver reliability of acromial morphology classification: an anatomic study. *J Shoulder Elbow Surg* 1997;6:286-7.
66. **Stein BE, Wiater JM, Pfaff HC, Bigliani LU, Levine WN** Detection of acromioclavicular joint pathology in asymptomatic shoulders with magnetic resonance imaging. *J Shoulder Elbow Surg* 2001;10:204-8.
67. **Ko JY, Huang CC, Chen WJ, Chen CE, Chen SH, Wang CJ** Pathogenesis of partial tear of the rotator cuff: a clinical and pathologic study. *J Shoulder Elbow Surg* 2006;15:271-8.
68. **Uhthoff HK, Sano H** Pathology of failure of the rotator cuff tendon. *Orthop Clin North Am* 1997;28:31-41.
69. **Ozaki J, Fujimoto S, Nakagawa Y, Masuhara K, Tamai S** Tears of the rotator cuff of the shoulder associated with pathological changes in the acromion. A study in cadavera. *J Bone Joint Surg Am* 1988;70:1224-30.
70. **Burkhead W.Z., Burkhart S.S., Gerber C.** Symposium: The rotator cuff: Debridement versus repair - Part I. *Contemp Orthop* 1995;31:262-71.
71. Dutch Orthopaedic Association Guideline: Subacromial Pain Syndrome, 2013.