European Radiology (2019) 29:566–577
https://doi.org/10.1007/s00330-018-5604-y

MUSCULOSKELETAL

Systematic review and meta-analysis of magnetic resonance imaging features for diagnosis of adhesive capsulitis of the shoulder

Chong Hyun Suh[1] · Seong Jong Yun[2] · Wook Jin[2] · Sun Hwa Lee[3] · So Young Park[2] · Ji Seon Park[4] · Kyung Nam Ryu[4]

Received: 14 March 2018 / Revised: 2 June 2018 / Accepted: 7 June 2018 / Published online: 5 July 2018

Abstract

Objectives To perform a systematic review and meta-analysis to identify magnetic resonance imaging (MRI) features that will aid in the diagnosis of adhesive capsulitis of the shoulder (ACS) and provide a summary of the diagnostic accuracy of the identified features

Methods The MEDLINE and EMBASE databases were searched for studies assessing the diagnostic accuracy of MRI features of ACS. Overlapping descriptors used to denote the same imaging finding in different studies were subsumed under a single feature. The pooled accuracy including the diagnostic odd ratios (DORs) with 95% confidence intervals (CIs) of the identified features was calculated using a bivariate random-effects model.

Results In total, 15 studies were included, and 74 overlapping descriptors were subsumed under six features. All six features were found to be informative for ACS diagnosis [coracohumeral ligament thickening: DOR, 13; 95% CI, 6-29; fat obliteration of the rotator interval (RI): DOR, 8; 95% CI, 3-24; RI enhancement: DOR, 44; 95% CI, 14-141; axillary joint capsule enhancement: DOR, 52; 95% CI, 27-98; inferior glenohumeral ligament (IGHL) hyperintensity: DOR, 31; 95% CI, 8-115; IGHL thickening: DOR, 28; 95% CI, 11-70]. The sensitivity and specificity of enhancement of the RI and axillary joint capsule and IGHL hyperintensity were > 80%.

Conclusions Six informative MRI features for ACS diagnosis were identified in this study with RI and axillary joint capsule enhancement and IGHL hyperintensity showing the highest diagnostic accuracy. Informative features observed on non-arthrogram MRI can be as helpful as features observed on direct magnetic resonance arthrography for ACS diagnosis.

Key points

- *Six informative MRI features for ACS diagnosis were identified (diagnostic odds ratio > 1).*
- *RI and axillary joint capsule enhancement and IGHL hyperintensity showed high sensitivities/specificities (> 80%).*
- *The use of non-arthrogram MRI is recommended for ACS diagnosis.*

Keywords Meta-analysis · Adhesive capsulitis of the shoulder · Frozen shoulder · Magnetic resonance imaging · Data accuracy

Abbreviations

ACS	Adhesive capsulitis of the shoulder
CE	Contrast enhanced
CHL	Coracohumeral ligament
CI	Confidence interval
DOR	Diagnostic odds ratios
IGHL	Inferior glenohumeral ligament
RI	Rotator interval

Electronic supplementary material The online version of this article (https://doi.org/10.1007/s00330-018-5604-y) contains supplementary material, which is available to authorized users.

✉ Seong Jong Yun
zoomknight@naver.com

[1] Department of Radiology and Research Institute of Radiology, Asan Medical Center, University of Ulsan College of Medicine, 88 Olympic-ro 43-gil, Songpa-gu, Seoul 05505, Republic of Korea

[2] Department of Radiology, Kyung Hee University Hospital at Gangdong, Kyung Hee University School of Medicine, 892 Dongnam-ro, Gangdong-gu, Seoul 05278, Republic of Korea

[3] Department of Emergency Medicine, Sanggye Paik Hospital, Inje University College of Medicine, 1342 Dongil-ro, Nowon-gu, Seoul 01757, Republic of Korea

[4] Department of Radiology, Kyung Hee University Hospital, 23, Kyungheedae-ro, Dongdaemun-gu, Seoul 02447, Republic of Korea

Introduction

Adhesive capsulitis of the shoulder (ACS), also known as frozen shoulder, is a condition with an uncertain etiology and is characterized by painful, gradual loss of both active and passive glenohumeral motion. Although the etiology is controversial, the underlying pathology is thought to be a combination of synovial inflammation and capsular fibrosis [1]. The prevalence of ACS in the general population is 2%-5%, with most patients over 40 years of age and slight female predominance. Contralateral shoulder involvement is uncommon [2].

ACS is usually diagnosed on the basis of clinical symptoms and imaging. The clinical diagnostic criteria for ACS include shoulder pain and a limited passive and active range of motion for > 3 months, without other causes that can explain the symptoms [3]. However, the clinical diagnosis of ACS is often challenging because several shoulder joint conditions manifest with overlapping clinical features. Thus, the role of imaging in the workup of patients with shoulder pain is critical from the perspective of treatment planning [4].

Magnetic resonance imaging (MRI) and magnetic resonance arthrography (MRA) are widely used for ACS assessment [5]. However, studies for ACS diagnosis have assessed the sensitivities and specificities of disparate MRI features. In addition, some features used for ACS diagnosis were often missing, nonspecific, or confusing because of inconsistent descriptions. As a result, despite the volume of reported data, there is no real consensus regarding the most reliable MRI features for ACS diagnosis. In this systematic review and meta-analysis, we aimed to identify the MRI features of patients with clinically or surgically confirmed ACS and summarize the diagnostic accuracy of these features.

Materials and methods

This meta-analysis followed the guidelines of the Preferred Reporting Items for a Systematic Review and Meta-analysis of Diagnostic Test Accuracy Studies (PRISMA-DTA) statement [6].

Literature search strategy

A computerized search of MEDLINE and relevant studies captured in only the EMBASE databases through 1 February 2018 was performed to identify relevant original literature concerning the diagnostic performance of MRI features of ACS. Search terms related to "adhesive capsulitis" or "frozen shoulder" were combined with "magnetic resonance imaging" or "magnetic resonance arthrography" as follows: [("adhesive capsulitis") OR ("frozen shoulder")] AND [(magnetic resonance imaging) OR (MR imaging) OR (MRI) OR (magnetic resonance arthrography) OR (MR arthrography)]. The bibliographies of identified articles were screened to determine additional relevant studies. The search was limited to studies in English. However, there were no restrictions for the publication date, species, or study setting. Two investigators (C.H.S. and S.J.Y.) screened the titles and abstracts for potential eligibility, and disagreements were resolved by discussion. Inclusion and exclusion criteria were described in the Supplemental materials.

Data extraction

The following data were extracted into standardized data forms: demographic and clinical characteristics of patients, including the mean age, sex, patient number, patient population, and clinical features; study characteristics, including authors, publication years, affiliations, patient recruitment durations, the study design, the reference standard, and blinding to the reference standard; MR characteristics, including the scanner type, technical parameters, and interpretations; and the diagnostic performance of MRI features of ACS, which was based on a 2 × 2 table including the number of true-positive, false-positive, false-negative, and true-negative results. If two or more reviewers independently assessed the diagnostic accuracy, the result with the highest accuracy was extracted. One reviewer (S.J.Y.) extracted data, while the second reviewer (C.H.S.) double-checked the accuracy of the extracted data.

Quality assessment

The methodological quality of the included studies was independently assessed by two reviewers (W.J. and S.Y.P.) using tailored questionnaires and criteria provided by Quality Assessment of Diagnostic Accuracy Studies-2 (QUADAS-2) [7]. Any disagreement was resolved by consensus.

Data synthesis and analyses

Patient demographic characteristics and extracted covariates were summarized using standard descriptive statistics. Continuous variables were expressed as means and 95% confidence intervals (CIs), while categorical variables were expressed as frequencies or percentages, unless stated otherwise.

We used a bivariate random-effects model for analyzing and pooling the diagnostic performance measures (sensitivity and specificity) for identified MRI features. To derive summary estimates of the diagnostic performance of each feature, we plotted estimates of the observed sensitivities and specificities in forest plots and hierarchical summary receiver-operating characteristic (HSROC) curves derived from individual study results [8]. These results were plotted using HSROC curves with 95% confidence intervals (CIs) and prediction regions. In addition, pooled sensitivities, specificities, diagnostic odds ratios (DORs), areas under the curve, and positive and negative likelihood ratios were calculated. Features showing a pooled

DOR with a 95% CI not including 1 were considered to be informative. If a feature was analyzed in < 4 studies or not clearly defined, a narrative description without data pooling was presented.

Heterogeneity among studies was determined using the I^2 inconsistency index (0%-40%, might not be important; 30%-60%, might represent moderate heterogeneity; 50%-90%, might represent substantial heterogeneity; 75%-100%, represents considerable heterogeneity) [9]. When heterogeneity was noted, heterogeneity by a "threshold effect" was analyzed by visual assessment of the coupled forest plots of the sensitivity and the specificity. A meta-analysis of diagnostic test accuracy studies simultaneously evaluates a pair of outcomes (i.e., sensitivity and specificity). Sensitivity and specificity are commonly inversely correlated and influenced by the threshold (cutoff value) [8]. In addition, the correlation between the sensitivity and false-positive rate was assessed using Spearman's correlation coefficient; a coefficient that was > 0.6 was considered to indicate a considerable threshold effect [10].

A meta-regression analysis was performed to further explore the reasons for heterogeneity by including covariates in the bivariate model. We considered the following covariates: study design, total number of patients, percentage of patients with ACS, percentage of female patients with ACS, non-ACS group characteristics, MR technique, contrast enhancement, magnet strength, slice thickness, and reader consensus.

We omitted Deeks' funnel plots [11] of individual studies to check for publication bias according to the PRISMA-DTA. We used the Midas and Metandi modules in Stata version 10.0 (StataCorp, College Station, TX) and R version 3.0.2 (R Foundation for Statistical Computing) with the Mada package to perform the statistical analyses.

Results

Literature search

Figure 1 shows a flow diagram summarizing the literature search. During the initial search, 269 studies were identified. After removing seven duplicates, we reviewed 262 titles and abstracts and excluded 235 studies for the following reasons: case reports/letters/editorials/conference abstracts (n = 87), review articles/guidelines/consensus statements (n = 62), not related to the field of interest (n = 85), and animal study (n = 1). After reviewing the full text of 27 eligible articles, we excluded 12 for the following reasons: insufficient data for 2 × 2 table reconstruction (n = 7) and no focus on the diagnostic performance of MRI features of ACS (n = 5). Eventually, 15 studies [12–26] evaluating the diagnostic performance of MRI features of ACS in 921 patients were included.

Study and patient characteristics

In total, 455 and 466 patients with and without ACS, respectively, were included. The proportion of ACS patients was 42.5%-76.2%, while that of female patients with and without ACS was 27.3%-88% and 0%-77.5%, respectively. One study [13] did not document the female patient number. The mean patient age in the ACS and non-ACS groups was 48-57.9 years and 41-62.3 years, respectively (Table 1).

The study design was prospective in five studies [13, 14, 23, 25, 26] and retrospective in ten [12, 15–22, 24]. All studies were single-center studies. Four studies [12–14, 24] involved consecutive patient enrollment, while 11 [15–23, 25, 26] involved nonconsecutive enrollment. Three studies [16, 17, 22]

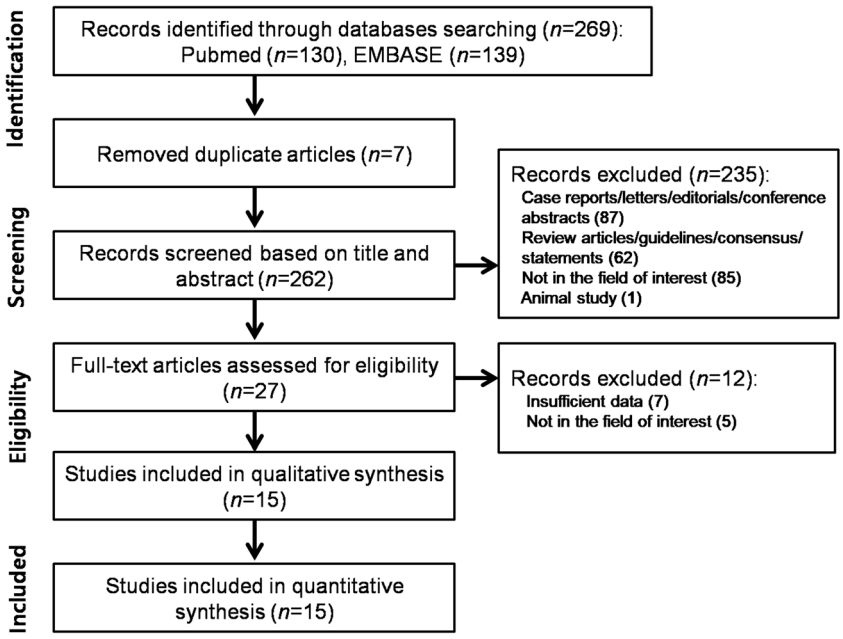

Fig. 1 Flow diagram showing the study selection process

Table 1 Characteristics of the subjects

Author	Total no. of patients	ACS:non-ACS, % of ACS	ACS			Non-ACS		
			Mean age, years (age range)	Male:female, % of female	Characteristics	Mean age, years (age range)	Male:female, % of female	Characteristics
Ahn KS et al [12]	103	50:53, 48.5%	53.5 (38-74)	20:30, 60%	Clinically diagnosed ACS	51.7 (22–78)	26:27, 50.9%	Shoulder pathologies without ACS
Carbone S et al [13]	113	48:65, 42.5%	57.9 (43–65)	NR	Clinically diagnosed ACS	62.3 (55-71)	NR	Negative for shoulder diseases
Chi AS et al [15]	30	15:15, 50%	55.8 (38–72)	5:10, 66.7%	Clinically diagnosed ACS	55.8 (38–72)	5:10, 66.7%	Negative for shoulder diseases
Connell D et al [16]	46	24:22, 52.2%	53.5 (38–71)	7:17, 70.8%	Surgically confirmed ACS	54.5, NR	12:10, 45.5%	RCT
Emig EW et al [17]	25	10:15, 40%	50 (23-66)	4:6, 60%	Radiologically diagnosed ACS	41 (28-56)	8:7, 46.7%	Normal volunteer
Gokalp G et al [18]	21	12:9, 57.1%	48 (42-55)	7:5, 41.7%	Clinically diagnosed ACS	48 (40–60)	2:7, 77.8%	Shoulder pathologies without ACS
Gondim Teixeira PA et al [19]	66	32:34, 48.5%	49.7 (NR)	14:18, 56.3%	Clinically diagnosed ACS	48, NR	16:18, 52.9%	Shoulder pathologies without ACS
Jung JY et al [20]	28	14:14, 50%	54 (46-63)	3:11, 78.6%	Clinically diagnosed ACS	46 (24–66)	11:3, 21.4%	Shoulder pathologies without ACS
Lee SY et al [21]	80	40:40, 50%	52.8 (34–68)	18:22, 55%	Clinically diagnosed ACS	52.8 (34–68)	18:22, 55%	NR
Mengiardi B et al [22]	44	22:22, 50%	54.7(31-77)	16:6, 27.3%	Surgically confirmed ACS	54.9 (28 –77)	16:6, 27.3%	Shoulder pathologies without ACS
Sasanuma H et al [23]	21	16:5, 76.2%	54.4 (39-79)	6:10, 62.5%	Clinically diagnosed ACS	47.6 (30-65)	5:0, 0%	Normal volunteer
Song KD et al [24]	80	35:45, 43.8%	50.1 (NR)	14:21, 60%	Clinically/radiologically diagnosed ACS	48.9, NR	22:23, 51.1%	Negative for shoulder diseases
Yoon JP et al [25]	104	52:52, 50%	55.1 (NR)	15:37, 71.2%	Clinically diagnosed ACS	53.1, NR	23:29, 55.8%	Shoulder pathologies without ACS
Zhao W et al [26]	120	60:60, 50%	50.2 (36–74)	24:36, 60%	Clinically diagnosed ACS	46.9, NR	24:36, 60%	Normal volunteer
Carrillon Y et al [14]	40	25:15, 62.5%	51 (40-69)	3:22, 88%	Clinically diagnosed ACS	61 (44-73)	8:7, 46.7%	RCT

ACS, adhesive capsulitis of the shoulder; RCT, rotator cuff tear; NR, not reported

used surgical findings as the reference standard, while 12 [12–15, 18–21, 23–26] used either clinical or radiologic findings (Table 2).

The MRI characteristics are summarized in Table 3. Twelve studies [12–19, 23–26] used non-contrast-enhanced (non-CE) or contrast-enhanced (CE) MRI and three [20–22] used direct MRA. Four studies used 3-T scanners, nine [13–18, 20–22] used 1.5-T scanners, one [26] used a 0.5-T scanner, and one [19] used a 1.5-T or a 3-T scanner. The slice thickness was 3 mm in ten studies [12, 15, 16, 18–22, 24, 25], 4 mm in three studies [14, 17, 26], and not reported in two studies [13, 23].

Categorization of MRI features

There were 73 overlapping descriptors in the 15 studies [12–26]. Of these, 22 were excluded from the meta-analysis because they referred to MRI features investigated in < 4 studies. In addition, nine descriptors were excluded because there was insufficient information for 2 × 2 table reconstruction. Finally, similar descriptors referring to the same imaging finding were merged and subsumed under a single MRI feature. Specifically, 42 descriptors were subsumed under six MRI features: coracohumeral ligament (CHL) thickening, fat obliteration of the rotator interval (RI), RI enhancement, axillary joint capsule enhancement, inferior glenohumeral ligament (IGHL) hyperintensity, and IGHL thickening. These were included in the meta-analysis. Supplemental Figure S1 presents a flow diagram showing the MRI feature categorization. Supplemental Table S1 presents a narrative summary of the descriptors excluded from the meta-analysis.

Study quality

Supplemental Figure S2 shows the risk of bias and applicability concerns for the included studies. Regarding patient selection, 11 studies [15–23, 25, 26] were considered to have a high bias risk because they were case-control studies with nonconsecutive enrollment. The index test in all studies [12–26] was evaluated after blinding from the reference standard. An unclear bias risk was considered for 12 studies [12–15, 18–21, 23–26] using clinical or radiological criteria for reference standard assessment and 14 studies [12–15, 17–26] that did not report the time interval between MRI and the reference standard.

Regarding patient selection, the applicability concern was high for three studies [17, 23, 26] including volunteers in the non-ACS group, while it was unclear for one study [21] that did not describe the non-ACS group characteristics. Regarding the index test, the applicability concern was high for 11 studies [12, 15, 17–25] that used different cutoff values of the IGHL or CHL thickness for ACS diagnosis. Moreover, 12 studies [12–15, 18–21, 23–26] were considered to have a high applicability concern regarding the reference standard,

Table 2 Characteristics of the studies

Author	Year	Locale	Study period	Study design	Reference standard	Blinding from reference standard
Ahn KS et al [12]	2015	South Korea	2011.1-2011.10	Retrospective, consecutive	Clinical symptoms and signs	Blinding
Carbone S et al [13]	2014	Italy	2010-2013	Prospective, consecutive	Clinical symptoms and signs	Blinding
Chi AS et al [15]	2017	USA	2010.1-2011.12	Retrospective , non-consecutive	Clinical symptoms and signs	Blinding
Connell D et al [16]	2002	Australia	1998.9-2001.7	Retrospective , non-consecutive	Surgical finding	Blinding
Emig EW et al [17]	1995	USA	NR	Retrospective , non-consecutive	Surgical finding	Blinding
Gokalp G et al [18]	2011	Turkey	NR	Retrospective , non-consecutive	Clinical symptoms and signs	Blinding
Gondim Teixeira PA et al [19]	2012	France	2008.1-2010.12	Retrospective , non-consecutive	Clinical symptoms and signs	Blinding
Jung JY et al [20]	2006	South Korea	NR	Retrospective , non-consecutive	Surgical/clinical symptoms and signs	Blinding
Lee SY et al [21]	2012	South Korea	2005.5-2010.5	Retrospective , non-consecutive	Surgical/clinical symptoms and signs	Blinding
Mengiardi B et al [22]	2004	Switzerland	1998.1-2003.4	Retrospective , non-consecutive	Surgical finding	Blinding
Sasanuma H et al [23]	2017	Japan	2015.1-2015.9	Prospective, non-consecutive	Clinical symptoms and signs	Blinding
Song KD et al [24]	2011	South Korea	2008.1-2009.12	Retrospective , consecutive	Clinical symptoms and signs/ radiographic finding	Blinding
Yoon JP et al [25]	2017	South Korea	2011-2014	Prospective, non-consecutive	Clinical symptoms and signs	Blinding
Zhao W et al [26]	2012	China	2006.7-2009.6	Prospective, non-consecutive	Clinical symptoms and signs	Blinding
Carrillon Y et al [14]	1999	France	NR	Prospective, consecutive	Clinical symptoms and signs	Blinding

NR, not reported

Table 3 Magnetic Resonance [Magnetic Resonance Imaging (MRI) or Magnetic Resonance Arthrography (MRA)] Characteristics

Author	Scanner			Technical parameters			Interpretation	
	Vendor	Model	Magnet strength	MR technique	Conventional sequence	Minimum ST (mm)	No. of readers	Reader experience
Ahn KS et al [12]	Siemens/ Philips	TrioTim/Achieva	3.0T	Non-CE MRI, CE MRI	T1WI, T2FS, PDFS, FS-T1CE	3	2, Independent	11/5
Carbone S et al [13]	Siemens	Avanto	1.5T	Non-CE MRI	NR except T2FS	NR	2, Independent	NR
Chi AS et al [15]	Siemens	Magnetom	1.5T	Non-CE MRI	T1WI, T2WI, T2FS, PDFS	3	2, Independent	13/5
Connell D et al [16]	GE	Signa Horizon	1.5T	Non-CE MRI, CE MRI	T2WI, T2FS, FS-T1CE	3	2, Consensus	NR
Emig EW et al [17]	GE	Signa	1.5T	Non-CE MRI	T2WI, T2FS	4	2, Consensus	NR
Gokalp G et al [18]	Siemens	Magnetom Vision	1.5T	Non-CE MRI , CE MRI	T1FS, T2FS, PDFS, FS-T1CE	3	2, Consensus	NR
Gondim Teixeira PA et al [19]	GE	Signa HDx/Signa HDxt	1.5T/3.0T	Non-CE MRI, CE MRI	T1WI, T2FS, FS-T1CE	3	2, Independent	3
Jung JY et al [20]	GE	Twin Speed	1.5T	Direct MRA	T1FS, T2WI, intermediate-WI	3	2, Consensus	NR
Lee SY et al [21]	Siemens/GE	Magnetom Vision Plus/Signa Excite	1.5T	Direct MRA	T1FS, T2WI	3	2, Consensus	15/2
Mengiardi B et al [22]	Siemens	Expert/Symphony	1.0T/1.5T	Direct MRA	T1WI, T1FS, T2WI, intermediate-WI	3	2, Consensus	10/5
Sasanuma H et al [23]	Siemens	Skyra	3.0T	CE MRI	in-phase/opposed phase image, water-only/fat-only image	NR	2, Independent	>15
Song KD et al [24]	Philips	Gyroscan Intera Achieva	3.0T	CE MRI	T1FS, T2WI	3	2, Independent	5/trainee
Yoon JP et al [25]	GE	Signa HDxt/Discovery MR750w	3.0T	Non-CE MRI, CE MRI	T1FS, T1WI, T2WI, FS-T1CE	3	2, Independent	8/9
Zhao W et al [26]	GE	Signa Contour	0.5T	Non-CE MRI	T1FS, T1WI, T2FS, STIR	4	2, Consensus	>5
Carrillon Y et al [14]	Philips	Gyroscan ACS	1.5T	CE MRI	T1FS, T2WI, FS-T1CE	4	2, Independent	NR

No., number; CE, contrast enhanced; WI, weighted image; FS, fat suppression; PD, proton density; T1CE, T1 contrast enhancement; STIR, short tau inversion recovery; NR, not reported

because the clinical or radiological criteria used in these studies were unclear.

Overall diagnostic accuracy

The pooled sensitivities and specificities for the six MRI features are presented in Table 4, along with pooled areas under the curve, pooled DORs, pooled positive likelihood ratios, and pooled negative likelihood ratios. According to pooled DORs with 95% CIs, all six MRI features were informative for ACS diagnosis. All features except CHL thickening showed a pooled sensitivity of > 80%. In fact, two of these five features showed a pooled specificity of > 90%. All features except fat obliteration of RI showed a pooled specificity of > 75%, with four of these five features showing a pooled specificity of ≥ 80%. Forest plots and HSROC curves for the six features are shown in Fig. 2 and Supplemental Figure S3, respectively. A forest plot could not be generated for CHL thickening because of unstable or asymmetrical data; the threshold effect was shown (correlation coefficient, 0.712; 95% CI, −0.457-0.979).

Substantial heterogeneity was considered present for four features, namely fat obliteration of RI, RI enhancement, IGHL hyperintensity, and IGHL thickening. However, the threshold effect was not shown (Table 4). Considerable heterogeneity was not observed for axillary joint capsule enhancement. Results of meta-regression analysis were described in Supplemental materials.

Discussion

In this systematic review and meta-analysis, six informative MRI features for ACS diagnosis were identified, of which RI and axillary joint capsule enhancement showed the highest sensitivity and CHL thickening showed the highest specificity. Features with the highest pooled DOR included RI and axillary joint capsule enhancement and IGHL hyperintensity. There was a general tendency for the features to show relatively high specificity and low sensitivity. CHL thickening was the only feature with moderate sensitivity and high specificity.

IGHL hyperintensity and RI and axillary joint capsule enhancement showed sensitivities and specificities of > 80%. Moreover, IGHL thickening showed a sensitivity of > 80% and a specificity of 79%. According to the meta-regression analyses, sensitivity of IGHL thickening was increased to 94% in studies using 3.0-T devices. However, their specificity decreased to 68%, respectively.

Our results may have important clinical implications because the identified MRI features can be used not only to confirm the clinical diagnosis but also to decide the treatment plan. Because many shoulder joint conditions manifest with a limited range of motion, ACS diagnosis using only clinical

Table 4 Pooled sensitivity, specificity, diagnostic odd ratio (DOR), area under the curve, likelihood ratio (LR), threshold effect of individual MR features

MR features	No. of studies	Sensitivity, %	Specificity, %	DOR	Pooled area under the curve	Pooled positive LR	Pooled negative LR	Threshold effect
Coracohumeral ligament thickening	5	64 (39, 86)	88 (75, 94)	13 (6, 29)	NA	5.2 (2.9, 9.4)	41 (22, 75)	0.712 (-0.457 0.979)
Fat obliteration of the rotator interval	11	86 (73, 93)	57 (40, 73)	8 (3, 24)	0.80 (0.77, 0.84)	2.0 (1.3, 3.0)	24 (11, 51)	0.062 (−0.559, 0.638)
Rotator interval enhancement	6	91 (73, 98)	81 (60, 92)	44 (14, 141)	0.93 (0.90, 0.95)	4.8 (2.2, 10.4)	11 (4, 34)	0.490 (−0.534, 0.931)
Axillary joint capsule enhancement	6	90 (84, 94)	85 (79, 90)	52 (27, 98)	0.92 (0.89, 0.94)	6.1 (4.3, 8.5)	12 (7, 20)	-0.062 (-0.832 0.789)
Inferior glenohumeral ligament hyperintensity	4	88 (63, 97)	81 (65, 91)	31 (8, 115)	0.89 (0.86, 0.92)	4.6 (2.5, 8.6)	15 (4, 50)	0.298 (−0.929, 0.979)
Inferior glenohumeral ligament thickening	9	88 (69, 96)	79 (67, 88)	28 (11, 70)	0.88 (0.85, 0.91)	4.2 (2.7, 6.6)	15 (6, 40)	0.303 (−0.452, 0.805)

Data in parentheses are 95% CIs. MR, magnetic resonance; CI, confidence interval; NA, not available because of computation failure

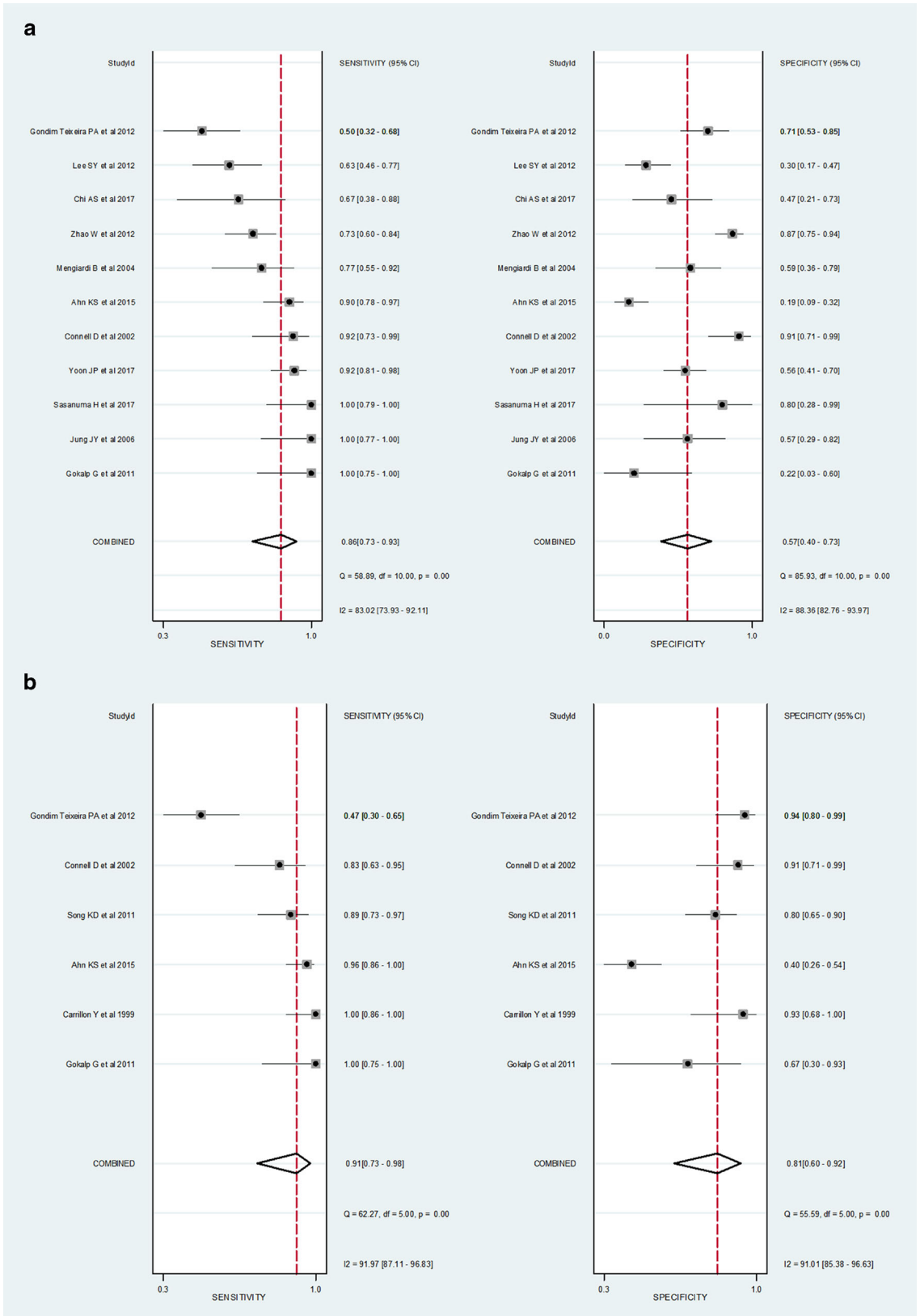

Fig. 2 Coupled forest plots of pooled sensitivity and specificity show MR features with informative pooled sensitivities and specificities with 95% confidence intervals. Coupled forest plots of pooled sensitivity and specificity could not be generated for coracohumeral ligament (CHL) thickening because of unstable or asymmetrical data. **a** Fat obliteration of the rotator interval (RI). **b** RI enhancement. **c** Axillary joint capsule enhancement. **d** Inferior glenohumeral ligament (IGHL) hyperintensity. **e** IGHL thickening

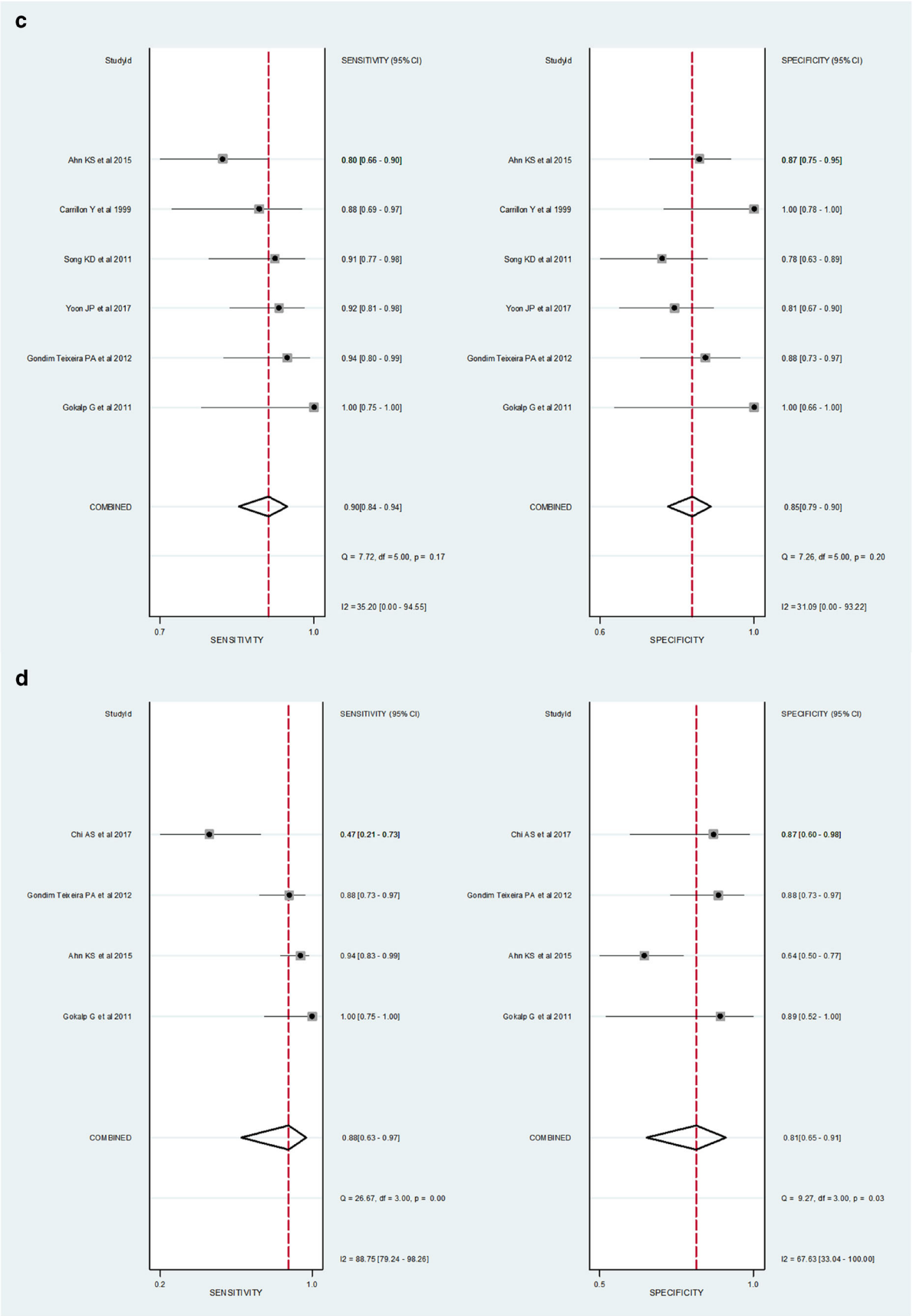

Fig. 2 (continued)

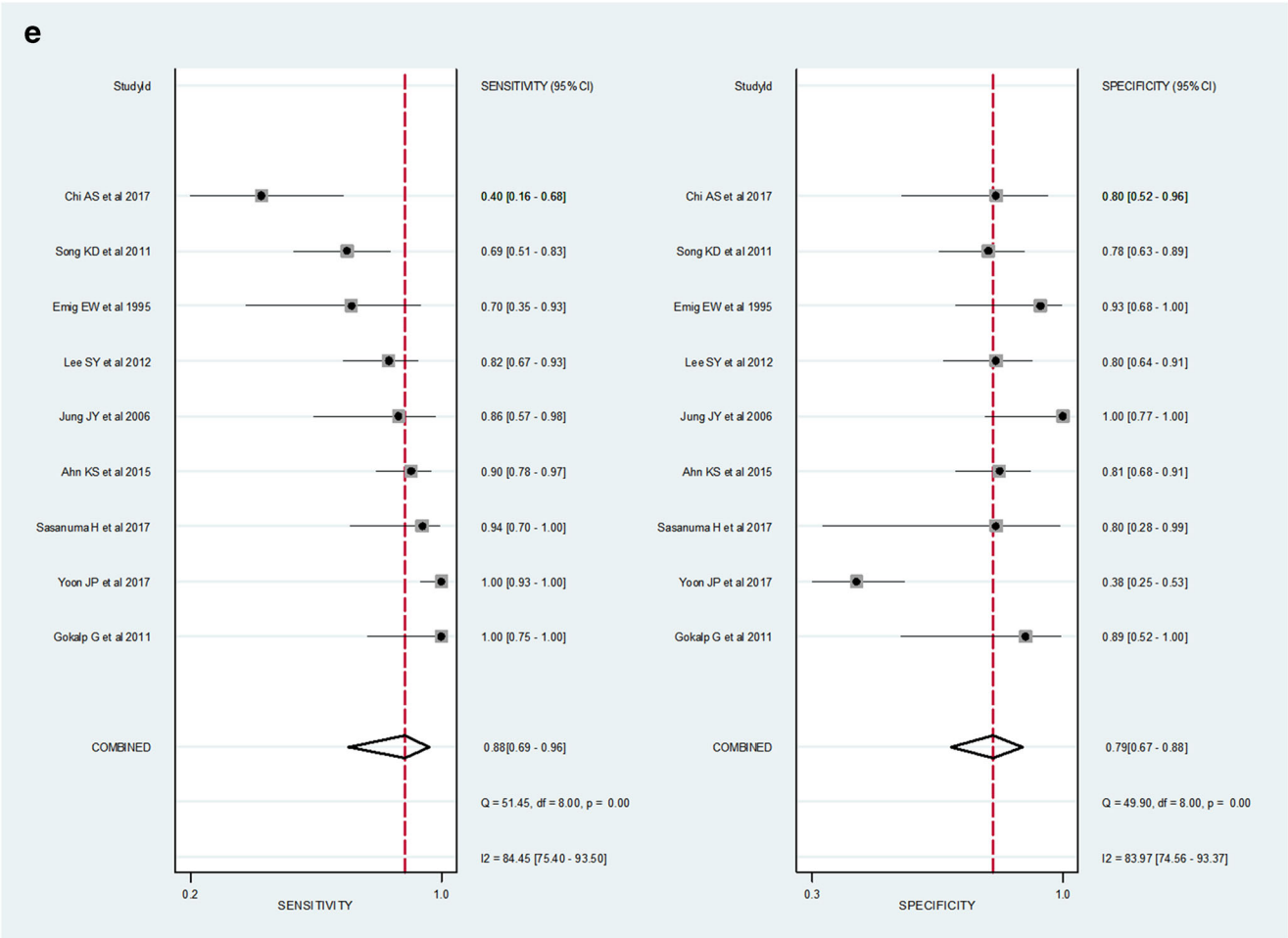

Fig. 2 (continued)

criteria can result in overlooking other shoulder diseases such as rotator cuff tears [4]. In addition, if ACS is diagnosed early using informative MRI features, immediate treatment such as physiotherapy or intra-articular steroid injection can help in shortening the duration of joint stiffness, thereby reducing the morbidity rate.

The informative MRI features identified in this study are also useful for correlating clinical impairment and the disease stage. Several studies [21, 27–31] investigated the relationship between MRI features and clinical features. Although the results are controversial, it is believed that IGHL and CHL thickening is an important anatomical and pathophysiological abnormality in ACS, because the thickness and ratio of IGHL and CHL show the strongest correlation with limited passive range of motion in ACS patients [21, 27–30]. In contrast, Ahn et al [27] and Lee et al [21] reported no association between fat obliteration of RI and clinical impairment.

Regarding clinical stages, ACS is considered to have four stages: preadhesive (stage 1), freezing (stage 2), frozen (stage 3), and thawing (stage 4) [32]. MRI findings reflect both synovial inflammatory and capsular fibrotic conditions, depending on the clinical stage [29, 31]. Previous studies [29, 31] demonstrated that joint capsule edema and fat obliteration of RI were more common in patients with early-stage (stage 1 or 2) ACS than in patients with late-stage (stage 3 or 4) ACS; fat-suppressed T2-weighted MRI may help in capsular edema detection, even in early stages. Also, Park et al [28] found that CHL was significantly thicker in stage 3 disease than in stage 2 disease. These results support several previous histological studies [33, 34] that have speculated that reactive capsular fibrosis follows synovial inflammation.

Invasive direct MRA was considered a standard investigation for ACS in the past [35]. Recently, however, it has not been used as a first-line diagnostic tool because of its invasiveness and the availability of alternative reliable MR techniques. RI and axillary joint capsule enhancement can be detected on CE MRI, while IGHL hyperintensity and thickening can be detected on both CE MRI and non-CE MRI. In addition, our meta-regression analysis for the MR technique showed that the sensitivity and specificity of IGHL thickening on MRI were not significantly different from those on direct MRA (sensitivity, $p = 0.43$; specificity, $p = 0.19$). Thus, we recommend the use of non-arthrogram MRI rather than direct MRA for ACS diagnosis.

Regarding the cutoff values for IGHL and CHL thickening, the proposed IGHL thickness that was considered abnormal showed a wide variation (2-8 mm). A value of > 3 mm was the most commonly used (three of nine studies) [21, 23, 25]. In contrast, the proposed CHL thickness that was considered abnormal showed a narrow variation (2-4 mm) and a value of > 4 mm was the most commonly used (three of five studies) [19, 22, 23]. Because we did not have raw data from studies assessing the IGHL and CHL thickness, a single cutoff value for both parameters cannot be calculated on the basis of this meta-analysis.

The present meta-regression analysis also showed that the study design and total patient number caused heterogeneity. For IGHL thickening, studies with a prospective design and ≥ 100 patients showed higher sensitivity and lower specificity than studies with a retrospective design and < 100 patients. Further prospective studies with larger sample sizes are necessary to determine the cutoff values, sensitivity, specificity, and positive and negative predictive values for all and individual informative MRI features.

This study had some limitations. First was the relatively small number of included studies. Several studies were excluded because they did not assess the diagnostic test accuracy or calculate sensitivities and specificities. However, those studies demonstrated that MRI features were useful for ACS diagnosis, in agreement with our findings. Second, as suggested earlier, methodological differences were observed in the included studies, which were heterogeneous in design, total patient number, and decision criteria. Although the statistical analysis of heterogeneity in effect sizes indicated homogeneity among studies, the methodological diversity has contributed to misinterpretation of the pooled estimates. Inevitably, relevant data for each analytical level could not be retrieved from all studies. Third, we could not assess the diagnostic accuracy of various combinations of features. In clinical practice, ACS diagnosis relies on multiple MRI features combined with clinical findings. In fact, there have been attempts to build diagnostic criteria for ACS that combine MRI features [15]. This study [15] may contribute to future studies on diagnostic algorithms for ACS by providing more comprehensive MRI features as potential predictors. Fourth, most of the included studies lacked detailed definitions and descriptions for the MRI features, thereby limiting the threshold analysis. Judgment of whether an MRI feature is present may vary depending on the threshold used, and unlike numerical or quantitative thresholds of other diagnostic tests, the threshold for imaging diagnosis often must be given qualitatively or descriptively. Even with a pre-specified threshold, image interpretation may be subjective and prone to interobserver variability. The effect of different diagnostic thresholds on heterogeneity could not be adequately analyzed because of the lack of detailed definition of MRI features assessed in each study. Finally, the enrolled studies showed a relatively low QUADAS-2 score (≥ 4, three studies [36]; < 4, 12 studies [12, 13, 15, 17–21, 23–26]). This was inevitable because of the disease characteristics and urgency (initial clinical diagnosis and conservative treatment) [5]. Therefore, the low study quality caused by the disease characteristics did not undermine the reliability of our results.

In conclusion, six informative MRI features for ACS diagnosis were identified in this study with RI and axillary joint capsule enhancement and IGHL hyperintensity showing the highest diagnostic accuracy. Informative features observed on noninvasive MRI can be as helpful as features observed on direct MRA for ACS diagnosis. The informative MRI features summarized in this study will aid the diagnosis and management of ACS in clinical practice.

Funding The authors state that this work has not received any funding.

Compliance with ethical standards

Guarantor The scientific guarantor of this publication is Seong Jong Yun, MD, PhD.

Conflict of interest The authors of this manuscript declare no relationships with any companies, whose products or services may be related to the subject matter of the article.

Statistics and biometry One of the authors (Chong Hyun Suh, MD) has significant statistical expertise.

Informed consent Written informed consent was not required for this study because the nature of our study was a systemic review and meta-analysis.

Ethical approval Institutional Review Board approval was not required because the nature of our study was a systematic review and meta-analysis.

Methodology
- meta-analysis
- performed at one institution

References

1. Hsu JE, Anakwenze OA, Warrender WJ, Abboud JA (2011) Current review of adhesive capsulitis. J Shoulder Elbow Surg 20: 502–514
2. Harris G, Bou-Haidar P, Harris C (2013) Adhesive capsulitis: review of imaging and treatment. J Med Imaging Radiat Oncol 57: 633–643
3. Brue S, Valentin A, Forssblad M, Werner S, Mikkelsen C, Cerulli G (2007) Idiopathic adhesive capsulitis of the shoulder: a review. Knee Surg Sports Traumatol Arthrosc 15:1048–1054
4. Boenisch U, Lembcke O, Naumann T (2000) Classification, clinical findings and operative treatment of degenerative and posttraumatic shoulder disease: what do we really need to know from an imaging report to establish a treatment strategy? Eur J Radiol 35: 103–118

5. Zappia M, Di Pietto F, Aliprandi A et al (2016) Multi-modal imaging of adhesive capsulitis of the shoulder. Insights Imaging 7:365–371
6. McInnes MDF, Moher D, Thombs BD et al (2018) Preferred reporting items for a systematic review and meta-analysis of diagnostic test accuracy studies: The PRISMA-DTA Statement. JAMA 319:388–396
7. Whiting PF, Rutjes AW, Westwood ME et al (2011) QUADAS-2: a revised tool for the quality assessment of diagnostic accuracy studies. Ann Intern Med 155:529–536
8. Lee J, Kim KW, Choi SH, Huh J, Park SH (2015) Systematic review and meta-analysis of studies evaluating diagnostic test accuracy: a practical review for clinical researchers-part II. Statistical methods of meta-analysis. Korean J Radiol 16:1188–1196
9. Higgins J, Green S Cochrane handbook for systematic reviews of interventions. Version 5.1.0. The Cochrane Collaboration. http://handbook.cochrane.org/chapter_9/9_5_2_identifying_and_measuring_heterogeneity.htm.
10. Deville WL, Buntinx F, Bouter LM et al (2002) Conducting systematic reviews of diagnostic studies: didactic guidelines. BMC Med Res Methodol 2:9
11. Deeks JJ, Macaskill P, Irwig L (2005) The performance of tests of publication bias and other sample size effects in systematic reviews of diagnostic test accuracy was assessed. J Clin Epidemiol 58:882–893
12. Ahn KS, Kang CH, Kim Y, Jeong WK (2015) Diagnosis of adhesive capsulitis: comparison of contrast-enhanced MRI with noncontrast-enhanced MRI. Clin Imaging 39:1061–1067
13. Carbone S, Napoli A, Gumina S (2014) MRI of adhesive capsulitis of the shoulder: distension of the bursa in the superior subscapularis recess is a suggestive sign of the pathology. Eur J Radiol 83:345–348
14. Carrillon Y, Noel E, Fantino O, Perrin-Fayolle O, Tran-Minh VA (1999) Magnetic resonance imaging findings in idiopathic adhesive capsulitis of the shoulder. Rev Rhum Engl Ed 66:201–206
15. Chi AS, Kim J, Long SS, Morrison WB, Zoga AC (2017) Non-contrast MRI diagnosis of adhesive capsulitis of the shoulder. Clin Imaging 44:46–50
16. Connell D, Padmanabhan R, Buchbinder R (2002) Adhesive capsulitis: role of MR imaging in differential diagnosis. Eur Radiol 12:2100–2106
17. Emig EW, Schweitzer ME, Karasick D, Lubowitz J (1995) Adhesive capsulitis of the shoulder: MR diagnosis. AJR Am J Roentgenol 164:1457–1459
18. Gokalp G, Algin O, Yildirim N, Yazici Z (2011) Adhesive capsulitis: contrast-enhanced shoulder MRI findings. J Med Imaging Radiat Oncol 55:119–125
19. Gondim Teixeira PA, Balaj C, Chanson A, Lecocq S, Louis M, Blum A (2012) Adhesive capsulitis of the shoulder: value of inferior glenohumeral ligament signal changes on T2-weighted fat-saturated images. AJR Am J Roentgenol 198:W589–W596
20. Jung JY, Jee WH, Chun HJ, Kim YS, Chung YG, Kim JM (2006) Adhesive capsulitis of the shoulder: evaluation with MR arthrography. Eur Radiol 16:791–796
21. Lee SY, Park J, Song SW (2012) Correlation of MR arthrographic findings and range of shoulder motions in patients with frozen shoulder. AJR Am J Roentgenol 198:173–179
22. Mengiardi B, Pfirrmann CW, Gerber C, Hodler J, Zanetti M (2004) Frozen shoulder: MR arthrographic findings. Radiology 233:486–492
23. Sasanuma H, Sugimoto H, Fujita A et al (2017) Characteristics of dynamic magnetic resonance imaging of idiopathic severe frozen shoulder. J Shoulder Elbow Surg 26:e52–e57
24. Song KD, Kwon JW, Yoon YC, Choi SH (2011) Indirect MR arthrographic findings of adhesive capsulitis. AJR Am J Roentgenol 197:W1105–W1109
25. Yoon JP, Chung SW, Lee BJ et al (2017) Correlations of magnetic resonance imaging findings with clinical symptom severity and prognosis of frozen shoulder. Knee Surg Sports Traumatol Arthrosc 25:3242–3250
26. Zhao W, Zheng X, Liu Y et al (2012) An MRI study of symptomatic adhesive capsulitis. PLoS One 7:e47277
27. Ahn KS, Kang CH, Oh YW, Jeong WK (2012) Correlation between magnetic resonance imaging and clinical impairment in patients with adhesive capsulitis. Skeletal Radiol 41:1301–1308
28. Park GY, Park JH, Kwon DR, Kwon DG, Park J (2017) Do the findings of magnetic resonance imaging, arthrography, and ultrasonography reflect clinical impairment in patients with idiopathic adhesive capsulitis of the shoulder? Arch Phys Med Rehabil 98:1995–2001
29. Park S, Lee DH, Yoon SH, Lee HY, Kwack KS (2016) Evaluation of adhesive capsulitis of the shoulder with fat-suppressed T2-weighted MRI: association between clinical features and mri findings. AJR Am J Roentgenol 207:135–141
30. Park YH, Park YS, Chang HJ, Kim Y (2016) Correlations between MRI findings and outcome of capsular distension in adhesive capsulitis of the shoulder. J Phys Ther Sci 28:2798–2802
31. Sofka CM, Ciavarra GA, Hannafin JA, Cordasco FA, Potter HG (2008) Magnetic resonance imaging of adhesive capsulitis: correlation with clinical staging. HSS J 4:164–169
32. Hannafin JA, Chiaia TA (2000) Adhesive capsulitis. A treatment approach. Clin Orthop Relat Res:95–109
33. Bulgen DY, Binder A, Hazleman BL, Park JR (1982) Immunological studies in frozen shoulder. J Rheumatol 9:893–898
34. Bunker TD, Reilly J, Baird KS, Hamblen DL (2000) Expression of growth factors, cytokines and matrix metalloproteinases in frozen shoulder. J Bone Joint Surg Br 82:768–773
35. Lee JC, Sykes C, Saifuddin A, Connell D (2005) Adhesive capsulitis: sonographic changes in the rotator cuff interval with arthroscopic correlation. Skeletal Radiol 34:522–527