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Associations Between In-Vivo Glenohumeral Joint Motion And Morphology

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Abstract

Joint morphology has a significant influence on joint motion and may contribute to the development of rotator cuff pathology, but the relationships between glenohumeral joint (GHJ) morphology and in-vivo GHJ motion are not well understood. The objectives of this study were to assess measures of joint morphology and their relationship with in-vivo joint motion in two populations: shoulders with intact rotator cuffs (n=48) and shoulders with rotator cuff pathology (n=36, including 5 symptomatic tears, 9 asymptomatic tears and 22 repaired tears). GHJ morphology was measured from CT-based three-dimensional models of the humerus and scapula. In-vivo GHJ motion was measured during shoulder abduction using biplane x-ray imaging. Associations between GHJ morphology and motion were assessed with univariate and best subsets regression. The only morphological difference identified between the populations was the critical shoulder angle (intact: 34.5±4.7°, pathologic: 36.9±5.0°, p=0.03), which is consistent with previous research. In intact shoulders, the superior/inferior (S/I) position of the humerus on the glenoid during shoulder abduction was significantly associated with the glenoid's S/I radius of curvature (p<0.01), conformity index (p<0.01), and stability angle (p<0.01). Furthermore, the S/I position of the humerus on the glenoid was negatively associated with the critical shoulder angle (p=0.04), which contradicts previous research. No significant associations between GHJ morphology and GHJ motion were detected in shoulders with rotator cuff tears. It is unknown if rotator cuff pathology compromises the relationships between GHJ morphology and motion, or if the absence of this relationship is a pre-existing condition that increases the likelihood of pathology.

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Keywords

rotator cuff; critical shoulder angle; glenoid inclination; glenoid morphology; glenohumeral joint motion

Introduction

Rotator cuff pathology is a common condition that is associated with pain, functional deficits, and a decreased quality of life (Yamamoto et al., 2010a). Although the specific etiology of this condition is not yet fully understood, subacromial impingement – i.e., superior migration of the humerus relative to the glenoid resulting in pathologic contact between the rotator cuff tendons and overlying acromial arch – has long been associated with rotator cuff tears (Neer, 1983; Yamaguchi et al., 2000). This association between rotator cuff pathology and altered joint motion has led a number of investigators to study the role of joint morphology, based on the premise that glenohumeral joint (GHJ) morphology may influence GHJ joint motion in a way that contributes to the development of rotator cuff pathology. For example, previous studies have reported that morphologic measures such as glenoid version (Tetreault et al., 2004; Tokgoz et al., 2007), glenoid inclination (Hughes et al., 2003), and acromial index (Nyffeler et al., 2006) are associated with rotator cuff pathology. However, the relationships between measures of GHJ morphology and GHJ motion – particularly under in-vivo conditions – are not especially well understood.

Recently, the critical shoulder angle (CSA), a measure of scapular morphology which accounts for both glenoid inclination and lateral extension of the acromion, has also been shown to be associated with rotator cuff tears (Moor et al., 2013; Moor et al., 2014). An increase in CSA is believed to lead to increased loads on the rotator cuff's supraspinatus tendon, resulting in superior migration of the humerus relative to the glenoid and subacromial impingement (Gerber et al., 2014). However, the association between CSA and joint motion has not, to our knowledge, been investigated under in-vivo conditions. Similarly, associations between other measures of GHJ morphology (e.g., stability angle, conformity index, glenoid and humeral radii of curvature, etc.) and in-vivo GHJ motion have also not been investigated. Therefore, the objectives of this study were to: 1) compare several measures of joint morphology between shoulders with intact rotator cuffs and shoulders with rotator cuff pathology, and 2) determine the association between these measures of joint morphology and in-vivo GHJ motion. Based on previous research, we hypothesized that the CSA (Moor et al., 2013; Moor et al., 2014) and glenoid inclination (Bishop et al., 2009; Hughes et al., 2003) would be significantly different between shoulders with intact rotator cuffs and shoulders with rotator cuff pathology. Additionally, we hypothesized that an increased CSA would be most significantly associated with the humerus positioned more superiorly on the glenoid during in-vivo shoulder abduction.

Materials and Methods

Following IRB approval, the effects of rotator cuff pathology on the relationship between joint motion and joint morphology was assessed in 84 shoulders from a convenience sample of subjects enrolled in on-going laboratory studies. The rotator cuff tear group (RCT) consisted of a total of 36 shoulders from 22 patients who had undergone unilateral surgical rotator cuff repair, 5 patients enrolled in physical therapy because of an ultrasound-documented symptomatic rotator cuff tear, and 9 patients with an ultrasound-documented asymptomatic rotator cuff tear. The average age of the subjects in the RCT group was 64.2 ± 10.0 (range: 43-77), with 21 dominant shoulders and 15 non-dominant shoulders. Patients with a symptomatic or repaired rotator cuff tear all were (or had been) suffering from a chronic tear with symptoms that had persisted for least 6 months. The group of shoulders with intact rotator cuffs (CTL) consisted of a total of 48 shoulders from subjects who had normal shoulder function and an ultrasound-documented intact rotator cuff. All ultrasound diagnoses were made by fellowship trained radiologists with extensive musculoskeletal experience. The average age of the subjects in the CTL group was 39.3 ± 16.7 (range: 20-76), with 40 dominant shoulders and 8 non-dominant shoulders. The RCT group consisted of 23 men and 13 women while the CTL group consisted of 27 men and 21 women. The gender distribution was not significantly different between groups (p=0.5). Of the 22 patients who had undergone rotator cuff repair, 9 patients had an asymptomatic rotator cuff tear in their contralateral shoulder and the remaining 13 patients had an intact rotator cuff in their contralateral shoulder. The 9 contralateral shoulders with an asymptomatic rotator cuff tear represent 9 of the 36 shoulders in the RCT group and the 13 contralateral shoulders with an intact rotator cuff represent 13 of the 48 shoulders in the CTL group.

GHJ Morphology

GHJ morphology was measured from computed tomography (CT) scans of the humerus and scapula. CT scans of the entire humerus and scapula were acquired (GE Medical Systems, LightSpeed 16, Piscataway, NJ, USA) in all shoulders. The scans had a slice thickness of 1.25mm and an in-plane resolution of approximately 0.5mm per pixel. The humerus and scapula were then manually segmented from other bones and soft tissue and reconstructed into 3D bone models (Mimics 10.1, Materialise, Leuven, Belgium).

Custom software was used to measure GHJ morphology from the 3D bone models, which has been described in detail previously (Peltz et al., 2015). Outcome measures included: the glenoid radius of curvature (ROC) in the anterior/posterior (A/P) and superior/inferior (S/I) directions, the humeral head radius of curvature, the glenohumeral conformity index (humeral head radius of curvature divided by the glenoid radius of curvature) in the A/P and S/I directions, and the glenohumeral stability angle (the angle of the humeral head enclosed by the glenoid) in the A/P and S/I directions.

In addition, glenoid inclination was assessed as described previously (Bishop et al., 2009) by calculating the angle between (1) a line connecting the intersection of the scapular spine with the scapula's medial border to the middle of the spinoglenoid notch and (2) a line connecting the superior and inferior margins of the glenoid (Figure 1). To assess CSA, we used the subject-specific CT-based bone models to determine the angle between (1) a line connecting the superior and inferior margins of the glenoid and (2) a line connecting the inferior margin of the glenoid to the lateral border of the acromion (Figure 1) (Moor et al., 2013).

GHJ Motion

Subjects were positioned with their shoulder centered within the three-dimensional (3D) imaging volume of a biplane x-ray system (Bey et al., 2011). The system consists of two 100 kW pulsed x-ray generators (EMD Technologies CPX 3100CV, Quebec, Canada) and two 40 cm image intensifiers (Shimadzu AI5765HVP, Kyoto, Japan) that are coupled to synchronized high-speed video cameras (Phantom v9.1, Vision Research, Wayne, NJ, USA). Images were acquired at 60 Hz as subjects performed coronal-plane abduction while seated from a position of adduction and neutral rotation to approximately 120° of humerothoracic abduction over two seconds. Abduction was chosen because it is a motion in which rotator cuff muscles are active (Kronberg et al., 1990) and has the highest isolation ratio for the supraspinatus (Brookham et al., 2010). Measures of GHJ motion were averaged over three trials for each subject over the range of glenohumeral joint motion that was common to all subjects (20-70°).

GHJ motion was assessed by tracking the 3D position of the humerus and scapula from images acquired from the biplane x-ray system. This model-based tracking technique has been shown to track 3D shoulder motion to an accuracy of within ±0.4 mm and ±0.5° (Bey et al., 2006). As previously described (Bey et al., 2006), GHJ contact patterns were estimated for each shoulder by combining joint motion measured from the biplane x-ray images with the subject-specific bone models reconstructed from the CT images. Specifically, the GHJ contact center was estimated by calculating the minimum distance between the glenoid and humerus at every point on the glenoid, and then determining the centroid of this distance map. The contact center was expressed relative to a glenoid-based coordinate system and the process was repeated for all frames of every trial. These calculations resulted in a contact path, i.e., a time-series of GHJ contact center data. Using these joint contact center data, the dynamic contact location was determined by calculating the average A/P contact center and the average S/I contact center over each trial. Dynamic joint excursion (i.e., the amount of glenohumeral joint translation that occurred during shoulder motion) was estimated by calculating the A/P and S/I contact center range over each trial. To account for differences in subject size, these joint contact center data were normalized relative to each shoulder's glenoid height (in the S/I direction) and width (in the A/P direction) as determined from the subject-specific bone models.

Statistical Analysis

Differences in morphological parameters were assessed between groups with unpaired two-tailed t-tests. Linear regressions and correlations were computed separately for each group (RCT or CTL) between each outcome (4 measures of GHJ motion) and predictor (9 bony morphology parameters), resulting in 72 separate linear regressions. In addition, a best subsets multiple regression analysis was performed for each outcome, and the model with the best adjusted R-squared was identified. Unlike R-squared, adjusted R-squared will only go up when an additional variable improves the prediction over and above what would be expected due to chance. Significance was set at $p \leq 0.05$.

Results

Reliability

As part of a previous study, the radius of curvature measurements were found to be accurate to within 4% (Peltz et al., 2015). These radius of curvature measurements were determined automatically from the CT-based bone models with custom software, so there was no trial-to-trial variability. To assess the reliability of measures of glenoid inclination and CSA, we performed 3 trials of each measurement on a subset of the subjects (n=5) in the current study. The coefficient of variation for each subject (standard deviation across the 3 trials divided by the mean of the 3 trials) ranged from 0.3-3.9% and the average COV across these 5 subjects was 2.2 ± 1.6%.

Morphological Parameters

CSA was significantly greater in shoulders with documented rotator cuff pathology (36.9 ± 5.0°) compared to subjects with intact rotator cuffs (34.5 ± 4.7°, p=0.03). However, no significant differences were detected between groups in humeral head ROC (RCT: 22.7±1.9mm, CTL: 22.0±2.1mm, p=0.16), glenoid S/I ROC (RCT: 35.3±6.1mm, CTL: 35.2±3.9mm, p=0.98), S/I conformity index (RCT: 0.66±0.1, CTL: 0.64±0.1, p=0.37), S/I stability angle (RCT: 58.1±10.9°, CTL: 57.7±11.6°, p=0.89), A/P ROC (RCT: 44.7±11.6mm, CTL: 48.7±15.4mm, p=0.20), A/P conformity index (RCT: 0.54±0.2, CTL: 0.50±0.2, p=0.28), A/P stability angle (RCT: 39.5±12.4°, CTL: 33.8±19.0°, p=0.12) or glenoid inclination (RCT: 92.9±3.7°, CTL: 91.8±4.6°, p=0.25) (Table 1).

Average S/I Contact Center

In shoulders with intact rotator cuffs, glenoid S/I ROC was found to positively correlate with average S/I joint contact center (r = 0.44, p=0.002, Table 2), indicating a flatter glenoid in the S/I direction was associated with a more superiorly located S/I joint contact center (Figure 2). Additionally, significant negative correlations were detected between average S/I joint contact center and S/I conformity index (r = -0.49, p=0.0004) and S/I stability angle (r = -0.54, p<0.0001, Table 2), indicating joints with increased conformity and stability had a more centrally located S/I joint contact center. Lastly, shoulders with intact rotator cuffs also exhibited a negative correlation with the critical shoulder angle (r = -0.30, p=0.04, Figure 3), indicating a larger critical shoulder angle (i.e., a more laterally extended acromion relative to the inclination of the glenoid) was associated with a more centrally located S/I contact center. The best subsets regression indicated a model with 3 parameters, all of which were highly significant (p<0.001): humeral head ROC, S/I ROC and S/I conformity index (Table 2).

In shoulders with rotator cuff pathology, no significant correlations were detected between any of the morphological parameters and the S/I joint contact center (Table 2). Similarly, the best subsets regression model included only the S/I conformity index and the critical shoulder angle, neither of which were significant (Table 2).

S/I Contact Center Range

In shoulders with intact rotator cuffs, no significant correlations were detected between S/I contact center range and any of the morphological parameters (p>0.06, Table 2). The best subsets regression model included 6 parameters, 4 of which were significant (Table 2). The significant parameters were S/I ROC (p=0.004), A/P ROC (p=0.02), S/I conformity index (p=0.03) and glenoid inclination (p=0.005) while S/I and A/P stability angle were included but not significant (p>0.07).

In shoulders with rotator cuff pathology, the only significant correlation detected with S/I contact center range was a positive relationship with the A/P stability angle (r = 0.37, p=0.03, Table 2), indicating an increased S/I contact center range was associated increased joint stability in the A/P direction. The best subsets regression model indicated S/I and A/P stability angle as significant contributors (p<0.02) while humeral head ROC and A/P ROC were included in the model but not significant (p>0.13, Table 2).

Discussion

The objectives of this study were to compare GHJ morphology between shoulders with intact rotator cuffs and shoulders with rotator cuff pathology, and to determine the extent to which GHJ motion was associated with GHJ morphology. We hypothesized that CSA and glenoid inclination would differ between shoulders with intact rotator cuffs and shoulders with rotator cuff pathology, and that the CSA would be an important predictor of GHJ motion during abduction. Shoulders with rotator cuff pathology had a significantly larger CSA than shoulders with intact rotator cuffs, and several morphological parameters other than CSA were strongly associated with GHJ motion in shoulders with intact rotator cuffs. CSA was significantly associated with GHJ motion in the shoulders with intact rotator cuffs, but the relationship was counter to what we expected. Lastly, no associations were detected between GHJ motion and morphology in shoulders with rotator cuff pathology.

Although the CSA was the only measure of joint morphology that was found to be significantly different between the shoulders with intact rotator cuffs and shoulders with rotator cuff pathology, these findings are consistent with previous research. For example, the finding that the CSA was significantly greater in shoulders with rotator cuff pathology than in shoulders with intact rotator cuffs agrees with previously published findings from Moor and colleagues (Moor et al., 2013). Specifically, Moor et al. reported an average CSA of 33.1° (range: 26.8-38.6°) in control subjects and 38.0° (range: 29.5-43.5°) in patients with rotator cuff tears. In the current study, the CSA of shoulders with intact rotator cuffs was 34.5° (range: 23.6-47.9°) and in shoulders with rotator cuff tears was 37.0° (range: 26.6-49.1°). Although the differences between shoulders with intact rotator cuffs and shoulders with rotator cuff pathology may be small, the study by Moor and colleagues indicated that small differences in the CSA are important clinically. They reported that within a 15° range of CSA, 3 very different distinct pathologies were represented. Specifically, CSA values of 25-30° were likely to be associated with glenohumeral arthritis, CSA values of 30-35° were associated with 'normal' patients and CSA values of 35-40° were likely to be associated with rotator cuff pathology.

In terms of glenoid inclination, we hypothesized that there would be significant differences between the shoulders with intact rotator cuffs and shoulders with rotator cuff tear pathology. However, failing to detect a significant difference in glenoid inclination is not unprecedented as previous research has reported that the glenoid inclination of individuals with a rotator cuff tear is greater than (Hughes et al., 2003), less than (Bishop et al., 2009), or no different than (Kandemir et al., 2006) the glenoid inclination of individuals with healthy shoulders. The study also failed to detect differences between the two subject populations in humeral head radius of curvature, glenoid radius of curvature, glenohumeral conformity index, or glenohumeral stability angle. However, these findings are not necessarily surprising since measures of joint morphology are not typically identified as primary etiology factors in the development of rotator cuff pathology.

In shoulders with intact rotator cuffs, the univariate regression analysis indicated that the humerus will be positioned more superiorly on the glenoid in shoulders with a flatter glenoid (i.e., higher S/I radius of curvature, Table 2). Similarly, the univariate regression analysis also indicated that the S/I joint contact center was significantly associated with the conformity index and stability angle. These three parameters (glenoid S/I radius of curvature, conformity index, and stability angle) were also identified as statistically significant in the best subsets regression model (Table 2). Taken together, these findings strongly suggest that joint morphology plays an important role in in-vivo joint motion, with agreement between the univariate and best subsets regression models suggesting that S/I glenoid radius of curvature and conformity index may be the best predictors of the S/I position of the humerus on the glenoid in shoulders with intact rotator cuffs. These findings are consistent with cadaveric experiments that have shown that artificially manipulating GHJ morphology – for example, by using bone grafts to increase the depth of the glenoid (Metcalf et al., 1999; Metcalf et al., 2001) – can significantly influence joint motion. Furthermore, these findings suggest that a superiorly positioned humerus, along with any associated pathology that may result from this, may be an inevitable consequence of GHJ morphology.

The specific explanation for why relationships between joint morphology and joint motion were not identified in shoulders with rotator cuff tears is unknown, but there are several possible explanations. First, previous research has shown that normal in-vivo GHJ motion is not restored after rotator cuff repair (Bey et al., 2011), so the lack of associations between GHJ motion and morphology may be due to abnormal GHJ motion. Second, neuromuscular factors (e.g., muscle forces, muscle firing patterns) influence joint motion and have been shown to be altered in patients with rotator cuff pathology (e.g. (Davis et al., 2014; de Witte et al., 2014a; de Witte et al., 2014b; Hoellrich et al., 2005; Mendias et al., 2015; Shah et al., 2008; Steenbrink et al., 2006)), so it plausible that changes in neuromuscular function associated with rotator cuff pathology may mask the influence of joint morphology on joint motion. Similarly, it is possible that other aspects of the rotator cuff pathology (e.g., tear size, chronicity, etc.) or the surgical repair technique may have disrupted the relationship between joint morphology and joint motion, or that an aberrant relationship between joint morphology and joint motion contributed in some manner to the development of rotator cuff pathology.

The finding that an increase in the CSA was associated with a humerus located more *inferiorly* on the glenoid (Figure 3) contradicts previous studies which suggest that the humerus will be located more *superiorly* on the glenoid as CSA increases (Flieg et al., 2008; Gerber et al., 2014). Although there is insufficient evidence in the current study to clearly identify the mechanism of how an increased CSA is associated with a more inferiorly positioned humerus, the specific explanation may be related to contact between the rotator cuff tissues and the acromial arch. Previous research has shown that non-pathologic contact between the rotator cuff and overlying acromial arch regularly occurs during shoulder abduction (Wuelker et al., 1994; Yamamoto et al., 2010b). For example, the study by Poitras and colleagues demonstrated that subacromial contact pressure increases during shoulder abduction (Poitras et al., 2010). However, under in-vivo conditions it is unlikely that subacromial contact pressure would continue to increase with shoulder abduction, but rather that the humerus would translate inferiorly in response to increases in subacromial contact pressure. Therefore, in patients where a more laterally extended acromion contributes to a high(er) CSA, it is plausible that contact between the rotator cuff and acromial arch occurs at lower abduction angles, forcing the humerus to migrate inferiorly on the glenoid during abduction and explaining why increasing CSA was found to be associated with the humerus positioned more inferiorly on the glenoid. Alternatively, the discrepancy in findings between the current study and previous studies (which have relied on cadaveric experimental and computer simulations (Flieg et al., 2008; Gerber et al., 2014)) may be due to fundamental differences between in-vivo and in-vitro testing conditions.

As with any study, this investigation has several limitations. One notable limitation of this study is that the average age of subjects in the intact rotator cuff group (39.3 ± 16.7) was substantially lower than that of those in the rotator cuff pathology group (64.2 ± 10.0). However, the measures of glenoid and humeral ROC reported here are consistent with the data reported from elderly cadaver specimens (McPherson et al., 1997), which suggests that GHJ morphology may not change appreciably in skeletally mature adults in the absence of significant pathology. It is certainly possible that the relationship between joint morphology and joint motion may change with age, but we are unaware of any previous study that has evaluated the effect of age on the relationship between joint morphology and motion. Another limitation of this study is that the RCT group consisted of a convenience sample of subjects whose rotator cuff was asymptomatic (n=9), symptomatic (n=5), or had been surgically repaired (n=22). While it would have been ideal to determine relationships between joint morphology and joint motion in each of these subject groups, we did not have a sufficient sample size to conduct the analyses in the unrepaired symptomatic or asymptomatic tears. However, restricting the analyses to only the patients whose rotator cuff tear was surgically repaired did not change the findings appreciably (data not shown), and therefore pooling these subject populations is not viewed as a significant limitation of this study.

In conclusion, this study indicates that shoulders with rotator cuff tears have a larger CSA than shoulders with intact rotator cuffs, and that GHJ morphology is significantly associated with GHJ motion in shoulders with an intact rotator cuff. In particular, the study indicated that the humerus was positioned more superiorly on the glenoid during shoulder abduction in shoulders whose glenoid was flatter and less conforming. Surprisingly, the study also revealed a negative association between GHJ motion and CSA, with the humerus positioned more inferiorly on the glenoid during shoulder abduction in shoulders with a higher CSA. In shoulders with a rotator cuff tear, no relationships were detected between GHJ morphology and motion. It is unclear if a rotator cuff tear compromises the relationships between GHJ morphology and motion, or if the absence of this relationship is a pre-existing condition that increases the likelihood of a rotator cuff tear. Future efforts will continue to examine the complex relationship between bony morphology, rotator cuff pathology, and in-vivo GHJ motion.

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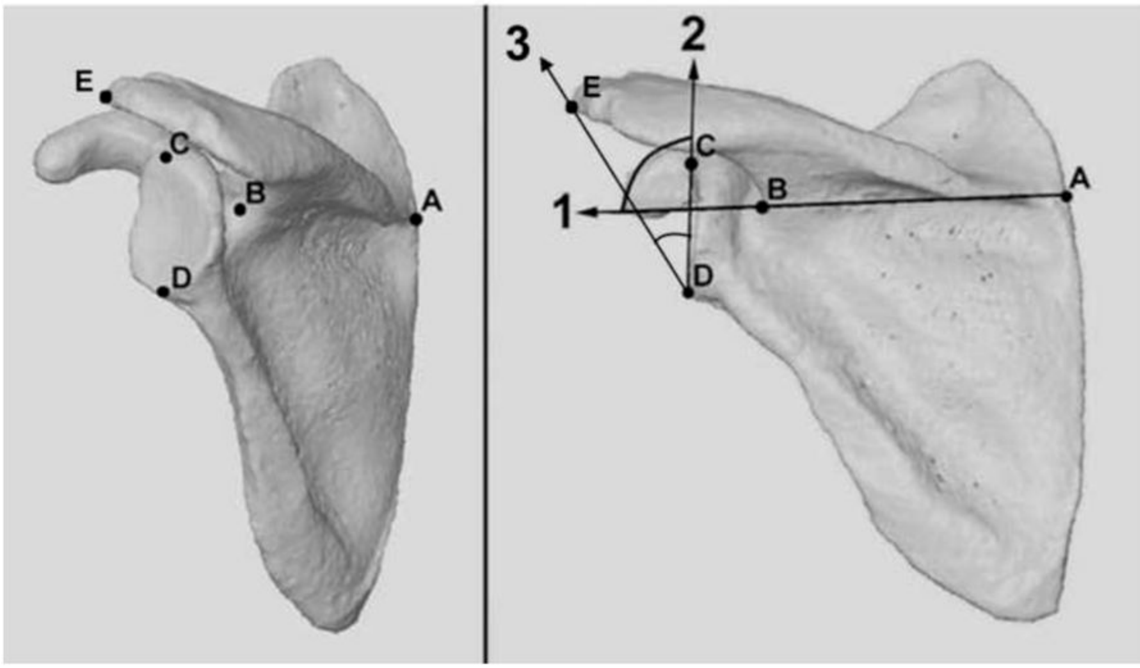

Figure 1.

Glenoid inclination was calculated as the angle formed between line 1 and line 2. Critical shoulder angle was calculated as the angle formed between line 2 and line 3. Line 1 was defined as connecting (A) the intersection of the scapular spine with the scapula's medial border and (B) the middle of the spinoglenoid notich. Line 2 was defined as connecting (C) the superior-most point on the glenoid rim and (D) the inferior-most point on the glenoid rim. Line 3 was defined as connecting (D) the inferior-most point on the glenoid rim and (E) the most lateral aspect of the acromion.

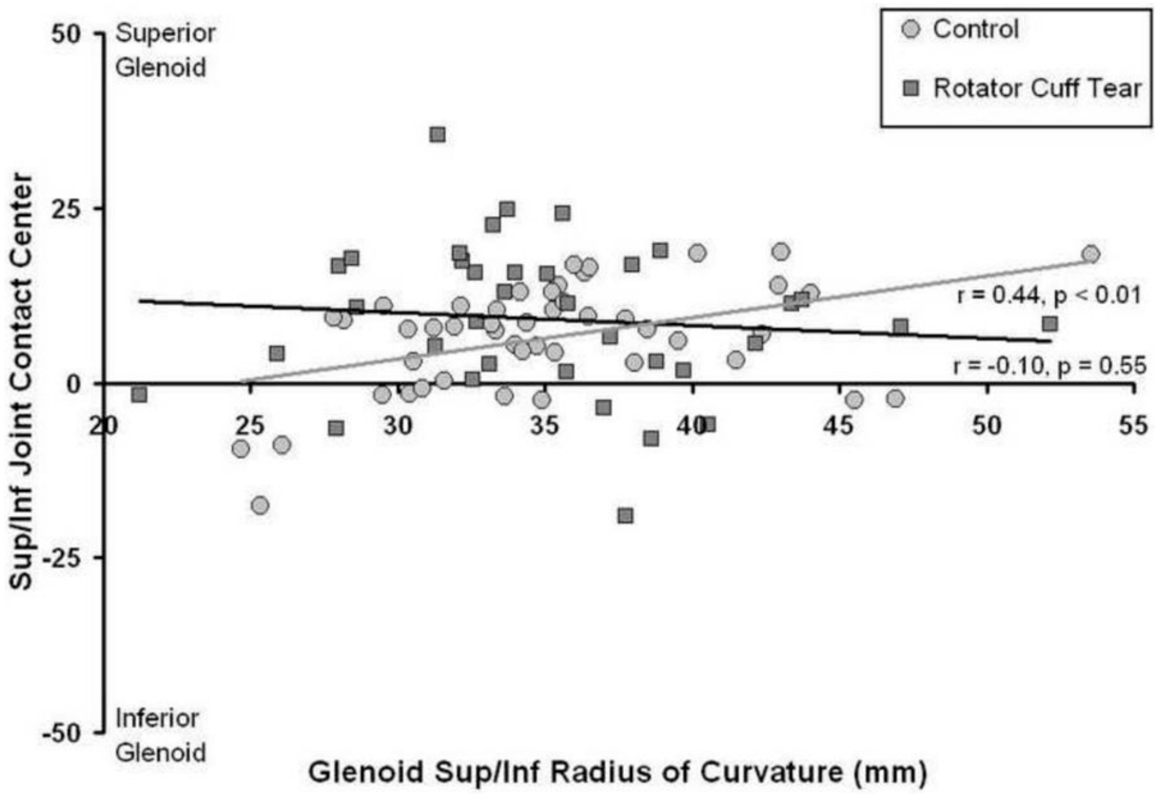

Figure 2.

The superior/inferior joint contact center – i.e., the average location of the center of contact of the humerus on the glenoid – was significantly associated with the glenoid's superior/inferior radius of curvature in shoulders with intact rotator cuffs ($p < 0.01$), but not in the shoulders with rotator cuff pathology ($p = 0.55$).

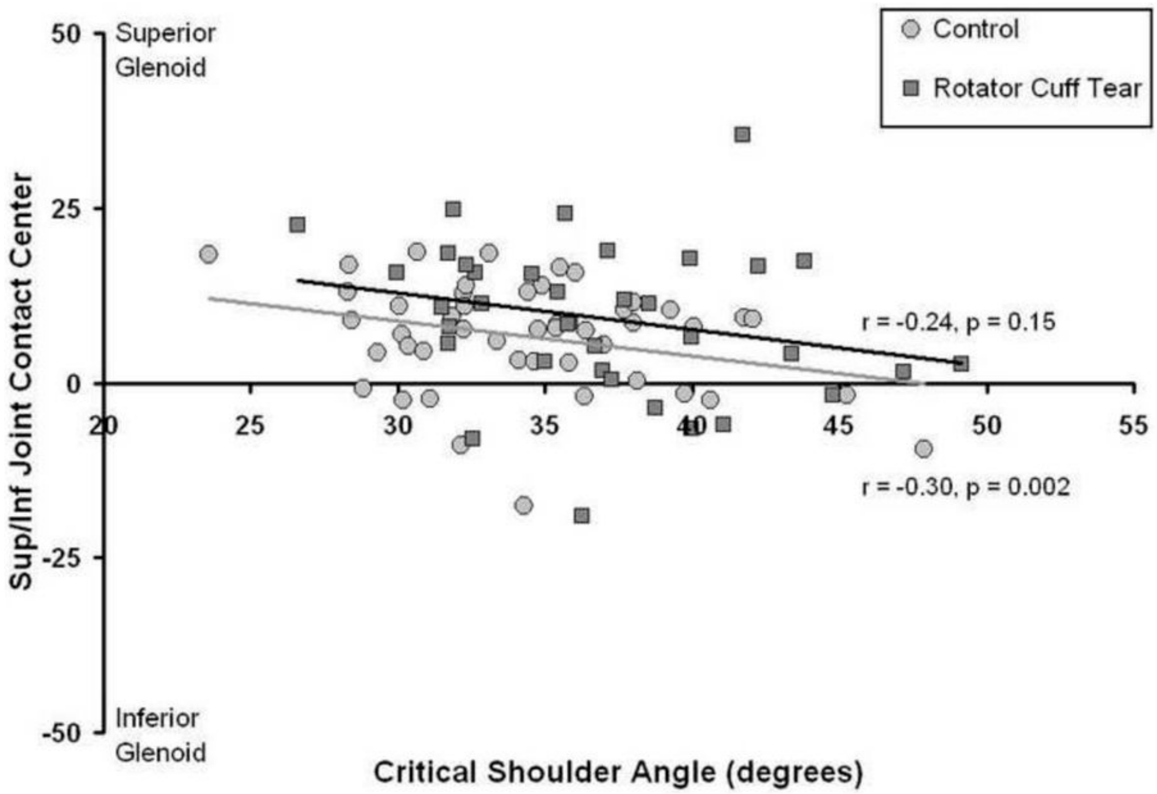

Figure 3.

The superior/inferior joint contact center – i.e., the average location of the center of contact of the humerus on the glenoid – was significantly associated the critical shoulder angle in shoulders with intact rotator cuffs (p = 0.002), but not in the shoulders with rotator cuff pathology (p = 0.15).

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Table 1

Morphological parameters assessed in shoulders with intact rotator cuffs (CTL) and rotator cuff tears (RCT). ROC = radius of curvature, CI = conformity index, SA = stability angle, GI = glenoid inclination.

	HH ROC	Superior/Inferior			Anterior/Posterior			GI	CSA
		ROC	CI	SA	ROC	CI	SA		
CTL	22.0±2.1	35.2±3.9	0.64±0.1	57.7±11.6	48.7±15.4	0.50±0.2	33.8±19.0	91.8±4.6	34.5±4.7
RCT	22.7±1.9	35.3±6.1	0.66±0.1	58.1±10.9	44.7±11.6	0.54±0.2	39.5±12.4	92.9±3.7	37.0±5.0
p-value	0.16	0.98	0.37	0.89	0.20	0.28	0.12	0.25	0.03*

Table 2

Univariate correlations and best subsets regression model coefficients for correlations of all parameters with superior/inferior average contact center (S/I CC) and range (S/I Range) for shoulders with intact rotator cuffs (CTL) and shoulders with rotator cuff tears (RCT). HH = humeral head, ROC = radius of curvature, CI = conformity index, SA = stability angle, GI = glenoid inclination.

		Univariate Correlations (p-value)									Best Subsets Regression Model Coefficients (p-values)										
		HH ROC	Superior/Inferior			Anterior/Posterior			GI	CSA	Const.	HH ROC	Superior/Inferior			Anterior/Posterior			GI	CSA	Adj R^2
			ROC	CI	SA	ROC	CI	SA					ROC	CI	SA	ROC	CI	SA			
S/I CC	CTL	0.14 (0.33)	0.44 (<0.01)	-0.50 (<0.01)	-0.54 (<0.01)	0.14 (0.35)	-0.17 (0.24)	-0.18 (0.23)	-0.21 (0.16)	-0.30 (0.04)	152.9 (<0.01)	7.0 (<0.01)	-4.0 (<0.01)	-250.0 (<0.01)	--	--	--	--	--	--	0.47
	RCT	0.13 (0.44)	-0.10 (0.55)	0.17 (0.32)	0.07 (0.69)	0.02 (0.93)	0.02 (0.90)	0.01 (0.97)	-0.11 (0.53)	-0.24 (0.15)	13.8 (0.43)	--	--	27.3 (0.19)	--	--	--	--	--	-0.6 (0.10)	0.05
S/I Range	CTL	0.16 (0.28)	-0.01 (0.96)	0.12 (0.43)	0.04 (0.78)	-0.11 (0.48)	0.07 (0.65)	0.04 (0.78)	0.27 (0.06)	0.08 (0.61)	-119.4 (<0.01)	--	1.2 (<0.01)	116.7 (0.03)	-0.6 (0.12)	-0.3 (0.02)	--	-0.2 (0.07)	0.8 (<0.01)	--	0.20
	RCT	0.10 (0.56)	0.07 (0.67)	-0.08 (0.62)	-0.19 (0.26)	-0.22 (0.20)	0.26 (0.13)	0.37 (0.03)	-0.12 (0.49)	-0.12 (0.48)	17.7 (0.32)	-1.2 (0.13)	--	--	-0.3 (0.02)	0.3 (0.14)		0.6 (<0.01)	--	--	0.23