Subacromial Space Width: Does Overuse or Genetics Play a Greater Role in Determining It?

An MRI Study on Elderly Twins

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Background: Age and peripheral microcirculation disorders are the main causes of rotator cuff degeneration. Acromion variants may affect subacromial space width, causing a pathological narrowing of the space that may compromise the cuff integrity. However, it is not clear if the subacromial space width is genetically determined or if it changes according to loading conditions. To clarify this unresolved question, we performed an MRI (magnetic resonance imaging) study with the aim of evaluating the acromiohumeral distance in a group of elderly monozygotic and dizygotic twins, and we analyzed the obtained data using the twin design to separate the contributions of shared and unique environments.

Methods: We identified twenty-nine pairs of elderly twins. On MRI scans, we evaluated the acromiohumeral distance and health status of the rotator cuff tendons. Heritability, defined as the proportion of total variance of a specific characteristic in a particular population due to a genetic cause, was estimated as twice the difference between the intraclass correlation coefficients for monozygotic and dizygotic pairs. The influence of shared environment, due to environmental factors that contribute to twin and sibling similarity, was calculated as the difference between the monozygotic correlation coefficient and the heritability index. One-way ANOVA (analysis of variance) was used to estimate the differences among job categories, both in the total cohort and within zygosity groups.

Results: The intraclass correlation coefficient was substantially higher for monozygotic than for dizygotic twins, indicating a high degree of concordance of the acromiohumeral distance in pairs of individuals who shared 100% of their genes. The heritability index was 0.82, and shared and unique environmental contributions were both 0.09. There were no significant differences among subjects in different job categories, either in the total cohort (p = 0.685) or within the monozygotic (p = 0.719) and dizygotic groups (p = 0.957).

Conclusions: The acromiohumeral distance is mainly genetically determined and only marginally influenced by external factors.

Level of Evidence: Prognostic Level III. See Instructions for Authors for a complete description of levels of evidence.

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Articles regarding the shape of the subacromial space. The literature includes a huge number of studies on tendinopathy mostly involving anatomical variables (primarily in the anterior aspect of the acromion) that may pathologically influence tendon degeneration and tenocyte apoptosis. Changes disturb the turnover rate and proliferation of collagen, leading to tendon degeneration and tenocyte apoptosis.

**Materials and Methods**

In the absence of a rotator cuff tear, narrowing of the subacromial space may be the consequence of a tight posterior glenohumeral capsule; however, extrinsic mechanisms for rotator cuff tendinopathy mostly involve anatomical variables (primarily in the anterior aspect of the acromion) that may pathologically influence the subacromial space. The literature includes a huge number of articles regarding the shape and slope of the acromion, the acromial index, and the degree of acromial coverage; however, even today, it remains unclear whether the subacromial space width is primarily genetically determined (and only in part influenced by external factors) or changes over time according to the loads to which the shoulder is subjected (regardless of genetic predisposition).

To clarify this unresolved question, we compared the subacromial space width between elderly monozygotic (identical) and dizygotic (fraternal) twins, and we used the twin study design to separate the contributions of shared and unique environments.

**Materials and Methods**

Thanks to collaboration with the Genetic Epidemiology Unit of the National Institutes of Health, we recruited the study cohort from the Italian Twin Register (ITR). This is a population-based registry established in 2001 with the main purpose of using twin data to investigate hereditary and environmental factors that contribute to phenotypic expression of normal and/or pathological human characteristics. The ITR research activities have been approved by the Ethical Committee of the Istituto Superiore di Sanità.

From this database, we identified fifty pairs of twins in the same age range (fifty to seventy-five years) as most patients who are treated surgically for a rotator cuff tear.

Twin pairs in which at least one member had a history of glenohumeral or moderate to severe acromioclavicular arthropathy, shoulder fracture, rheumatoid disease or other autoimmune disease, glenohumeral or acromioclavicular instability, adhesive capsulitis, or rotator cuff tear were excluded. Twin pairs in which one or both members had been retired for more than five years were also excluded from the study, as were opposite-sex dizygotic twin pairs. The remaining twins who were willing to sign an informed consent form describing the aims and procedures of the study were included in the analysis. Zygosity was ascertained by comparing the genotypes of nine tetranucleotide multiallelic markers between the twins of each pair (accuracy, 99.98%).

The acromiohumeral distance and rotator cuff status (structural and qualitative condition) of the dominant shoulder were assessed by MRI (magnetic resonance imaging) (MAGNETOM Avanto Medical 76x32; Siemens). Oblique coronal, oblique sagittal, and axial T2-weighted spin-echo MRI scans (repetition time, 3200 ms; echo time, 85 ms) were obtained for the shoulders of all subjects. Coronal oblique shoulder images were in a plane parallel to the supraspinatus tendon. The patients were examined in the supine position with the arm at the side, the palm facing up, and the hand under the hip to keep the shoulder motionless.

The acromiohumeral distance was measured for each subject by three different physicians in a blinded fashion to assess inter-rater reliability. The assessors performed their evaluations one to twenty-four hours apart without knowledge of each other's assessments. The acromiohumeral distance was calculated in the coronal oblique projection as the distance between the most caudal point of the lower surface of the acromion and the most cranial point of the proximal aspect of the humerus.

One of the authors interviewed all participants about employment, recording specific information regarding both type and duration. Occupations

| TABLE I Baseline Characteristics of the Cohort |
|-----------------------------------------------|
| MZ Twins* (N = 30†) | DZ Twins* (N = 28‡) | P Value |
| Age (yr) | | | |
| Female | 62.40 ± 6.3 (53-72) | 63.78 ± 1.96 (60-66) | 0.264 |
| Male | 64.30 ± 2.86 (61-71) | 63.80 ± 1.83 (61-66) | 0.978 |
| Acromiohumeral distance (mm) | 10.13 ± 1.70 | 9.69 ± 1.74 | 0.197 |

*The values are given as the mean and standard deviation, with or without the range in parentheses. †10 female and 20 male. ‡18 female and 10 male.

| TABLE II Summary of Acromiohumeral Distance Heritability Analysis* |
|---------------------------------------------------------------|
| MZ Twins | DZ Twins |
| Mean Difference (mm) | P Value of Mean Squares | Among Pairs | ICC | Mean Difference (mm) | P Value of Mean Squares | Among Pairs | ICC | Heritability |
| -0.13 | <0.001 | 0.450 | 0.91 | 0.10 | <0.001 | 0.849 | 0.50 | 0.82 |

*MZ = monozygotic, DZ = dizygotic, and ICC = intraclass correlation coefficient.
were divided in three groups: "heavy manual workers" (cleaners, laborers, craft workers, transportation workers, and equipment operators), "administrative support workers" (administrative workers, technicians, and housewives), and "professional workers" (professionals and managers).

A flowchart of enrolled participants is shown in Figure 1.

Statistical Analysis

Power calculations were based on the correlation coefficient of the acromiohumeral distance. Assuming a Pearson correlation coefficient of 0.7, a two-tailed α value of 0.05 (sensitivity = 95%), and a β value of 0.20 (study power = 80%), we determined that at least fourteen twin pairs were required in the study (G*Power software, version 3; Universität Düsseldorf).

All data were analyzed by a single blinded researcher with use of SPSS software (version 18; SPSS, Chicago, Illinois). Calculated p values were two-sided, with p < 0.05 considered significant, and all results are reported with a 95% confidence interval (CI).

The intraclass correlation coefficient (ICC), with a 95% CI, was calculated to assess reliability. In particular, the ICC(3,2,1) was used to determine inter-rater reproducibility. The ICC, which is the most suitable statistical test for the assessment of reliability, can range from 0 to 1; 0.00 to 0.25 indicates little or no correlation, 0.26 to 0.49 indicates low correlation, 0.50 to 0.69 indicates moderate correlation, 0.70 to 0.89 indicates high correlation, 0.90 to 0.99 indicates very high correlation, and 1 indicates perfect correlation.31-43

Differences in means according to zygosity were evaluated with a pooled t test.

Heritability (h²), defined as the proportion of total variance of a specific characteristic in a particular population due to a genetic cause, was estimated as twice the difference between the ICC (r) for monozygotic (MZ) pairs and that for dizygotic (DZ) pairs (h² = 2[rMZ₂ - rDZ₂]).44 The shared environmental influence (c²), due to environmental factors that contribute to twin and sibling similarity, was estimated as the difference between the monozygotic ICC and the heritability index (c² = rMZ₂ - h²). The unique environmental influence (e²), due to environmental factors that contribute to differences between twins and between siblings, was estimated as the difference between 1 and the monozygotic ICC (e² = 1 - rMZ₂).

One-way ANOVA (analysis of variance) was used to estimate the differences among the three job types, both in the total cohort and within the monozygotic and dizygotic twin groups.

Source of Funding

No external funding was received for this study.

Results

Twenty-nine of the fifty twin pairs met the inclusion criteria and were analyzed. Their mean age (and standard deviation) was 63.72 ± 3.37 years (range, fifty-three to seventy-two years). Fifteen were monozygotic pairs (mean age, 63.66 ± 4.32 years; range, fifty-three to seventy-two years), and fourteen were dizygotic pairs (mean age, 63.78 ± 1.96 years; range, sixty to sixty-six years). The baseline characteristics of the subjects are reported in Table I.

The inter-rater reproducibility was high, with an ICC(3,2,1) value of 0.784 (95% CI, 0.692 to 0.856). The mean of the three acromiohumeral distance measurements was 10.13 ± 1.70 mm in

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Fig. 1

Flow of participants through the trial. GH = glenohumeral, AC = acromioclavicular, MZ = monozygotic, and DZ = dizygotic.
the monozygotic twin pairs and 9.69 ± 1.74 mm in the dizygotic twin pairs (p = 0.197).

ICCs of the acromiohumeral distance for the monozygotic and the dizygotic twins are reported in Table II. The ICC was consistently high for the monozygotic twins, indicating a high degree of concordance for the acromiohumeral distance in individuals who shared 100% of their genes. The dizygotic twins showed a lower correlation, which indicated a lower concordance in this group of twins who shared, on average, 50% of their genes. The difference in correlation between monozygotic and dizygotic twins suggested strong genetic influences on the acromiohumeral distance. In accordance with that result, the calculated heritability index was 0.82, while the contributions of shared and unique environment were both 0.09.

The acromiohumeral distance value was 9.91 ± 1.88 mm in the twenty-seven subjects in the heavy manual worker group, 9.70 ± 1.66 mm in the nineteen subjects in the administrative support worker group, and 10.25 ± 1.50 mm in the twelve subjects in the professional worker group; the differences among the groups were not significant (p = 0.685). In the monozygotic twins, the acromiohumeral distance was 10.25 ± 1.88 mm in the heavy manual worker group, 9.88 ± 2.30 mm in the administrative support worker group, and 10.60 ± 1.31 mm in the professional worker group (p = 0.719). In the dizygotic twins, the acromiohumeral distance was 9.55 ± 1.89 mm in the heavy manual worker group, 9.60 ± 0.80 mm in the administrative support worker group, and 9.80 ± 1.79 mm in the professional worker group (p = 0.957) (Table III).

**Discussion**

Our understanding of the role of extrinsic factors in the genesis of rotator cuff impingement syndrome and tears is changing, strengthening the hypothesis that tendon degeneration, principally caused by age and peripheral microcirculation disorders, is the primary cause of the rotator cuff tear.

Anatomical variants of the scapular apophysis may affect the width of the subacromial space, in extreme cases resulting in a pathological narrowing of the space that may jeopardize the health status of the rotator cuff tendons.

More than forty years ago, Neer hypothesized that the presence of a spur at the anteroinferior aspect of the acromion might be the main cause of mechanical abrasion between the rotator cuff and the coracoacromial arch. Subsequently, Bigliani et al. classified the acromion shape into three patterns that were more or less prone to rotator cuff tendinopathy. A higher prevalence of rotator cuff tears was also attributed to a flatter slope of the acromion and to a decreased lateral acromial angle. Oh et al. classified acromial spurs into distinct morphologies and suggested that the most common heel-type spur might be a risk factor for full-thickness rotator cuff tears.

Even though many years have passed since these milestone publications, we still debate whether the subacromial space width (primarily the result of the acromion shape) is influenced by possible overloading or is genetically determined. Wang and Shapiro were proponents of the first hypothesis, observing that the shape of the acromion progressed from flat to curved or hooked as age increased. Analogously, in 2001, Shah et al. conducted a macroscopic, radiographic, and histologic study on eighteen cadaveric shoulders (twelve pairs from six cadavers and six unpaired) and observed a common pattern of degeneration of collagen, fibrocartilage, and bone in all of the curved and hooked acromions. Therefore, they concluded that the shape of the acromion is acquired in response to traction forces applied via the coracoacromial ligament and is not congenital in origin. However, the results of both publications lacked supporting statistical analysis and did not provide information on the impact of the various acromion shapes on the subacromial space. In addition, the authors did not provide information on the limb dominance or occupation of the subjects. Mahakkanukrauh and Surin supported the same theory. They performed an anatomical study on 346 skeletons and observed that occurrence of acromial osteophytes and increasing age were significantly correlated; furthermore, no sex differences were noted in the frequency of osteophytes.

The main purpose of our study was to assess the influence of genetic factors on the acromiohumeral distance; therefore, we conducted an MRI study on elderly monozygotic and dizygotic twins. Studies on twins provide a useful tool to evaluate the contribution of genes and environment on the disease or trait of interest.

As the reliability of acromiohumeral distance measurements made using radiographs has not been supported by the studies that we reviewed, an MRI assessment was preferred. Furthermore, a recent study found that the acromiohumeral distance better reflected the clinical status of patients with subacromial impingement than the acromial shape did.
We evaluated dizygotic twins as the control rather than a more general control group, because this is required to estimate the heritability according to the twin methodology\(^9\) and also because non-twin siblings would have posed an additional issue of age differences, which could influence the results.

In the case of quantitative traits, the phenotypic similarity between twins is estimated by the ICC. For the acromiohumeral distance, we determined this by the correlation of the values within each pair of twins. The resulting heritability index showed genetic factors to be the main cause of the variability of the acromiohumeral distance, with shared and unique environmental factors contributing only slightly to the variability.

The role of genetic factors is also supported by the results of the acromiohumeral distance comparisons of the three groups of workers. No significant differences were found among groups who performed or had performed different types of labor. This was confirmed both in the whole study cohort and within the monozygotic and dizygotic subjects. These data appear to be partially in contrast with those of Frost and Andersen\(^2\), who observed that shoulder-intensive work was a risk factor for impingement syndrome. Analogously, van Rijn et al.\(^7\) noted that highly repetitive work was associated with the occurrence of subacromial impingement, and Roquelaure et al.\(^8\) observed that skilled blue-collar workers were more likely to develop subacromial impingement, especially if forced to abduct the arm repeatedly. Finally, in a longitudinal study, Svendsen et al.\(^1\) showed that forceful work, work with elevated arms, and repetitive work each doubled the risk of surgery for subacromial impingement.

Our study suggests that the anatomical features that influence the width of the subacromial space are mainly genetically determined. However, if the subacromial space is already constitutionally narrow, external factors would strongly contribute to further reduction of the space, making it too tight. This might occur as a consequence of the ossification of the acromial insertion of the coracoacromial ligament\(^6\); of contracture of the posterior capsule of the glenohumeral joint, which would lead to upward migration of the humeral head\(^12,38\); or of scapular muscle performance deficits\(^7\).

The low number of twin pairs in our study did not allow us to apply quantitative genetic models\(^9\) to estimate the heritability by taking into account individual differences in age and sex as well as relevant environmental exposures such as work activities. It would be interesting to evaluate the results of our study considering males and females separately, but the sample size would be too small. The heterogeneous nature of the study cohort is not considered a potential source of error, as the aim of the study was to evaluate the differences between monozygotic and dizygotic twins.

In conclusion, the acromiohumeral distance is primarily genetically determined and is less influenced by external factors.

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