Risk factors in idiopathic adhesive capsulitis: a case control study

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**Background:** The etiology of idiopathic adhesive capsulitis (IAC) of the shoulder is poorly understood. In this case control study, we examine potential risk factors for the development of IAC.

**Methods:** Consecutive patients who presented to the senior author with IAC between 2000 and 2009 were included retrospectively in this case control study. Complete data were available for 87 patients. An age-and sex-matched group of 176 patients who presented to the same practice during the same time period with non-shoulder related orthopedic complaints were recruited as the control group. Health records and patient-completed questionnaires were utilized to identify comorbidities and other risk factors.

**Results:** Bivariate analyses demonstrated that diabetes, hypothyroidism, a lower body weight, a lower body mass index (BMI), and a positive family history of IAC were all risk factors for IAC. Diabetes, BMI, and positive family history of IAC remained independent variables with multivariate logistic regression analyses. There was a trend towards increased incidence of Dupuytren’s disease in those with IAC, but this was not statistically significant. With regard to racial predilection, being born in the British Isles or having parents/grandparents born in the British Isles were risk factors for IAC.

**Conclusion:** We confirm diabetes as an independent predictor of IAC. In addition, we identify a possible racial predilection for the development of IAC. Future research is needed to confirm whether a specific genetic component or environmental factors is responsible.

**Level of evidence:** Level III, Case-Control Study.

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Risk factors in idiopathic adhesive capsulitis

It is unknown whether a genetic predisposition exists for IAC. To date, there are no reports linking the condition to a particular ethnicity. However, twin studies have shown a 2- to 3-fold increased risk of IAC in homozygotic twins than expected by chance,\(^1\) while reports on HLA-B27 prevalence in patients with IAC have been mixed.\(^6,26\) A few studies have suggested a link between IAC and Dupuytren’s disease, which share the similarities of nodular collagen deposition, band formation, and joint contracture.\(^7,27\) While strong evidence exists that Dupuytren’s disease has an inheritable component and a racial predisposition,\(^12,22\) this has not been shown in adhesive capsulitis.

Identifying the risk factors of a disease is important to gain understanding of its etiology. Previous studies are often limited in scope, do not control for many co-variables, and include low overall numbers of patients with adhesive capsulitis. The purpose of the present study is to examine presumed risk factors and to identify new risk factors associated with the development of IAC. In particular, we investigated whether ethnicity may be a risk factor in the development of this condition.

**Patients and methods**

All 512 patients who presented to the senior author (A.W.) during a 9 year period (2001-2009) with adhesive capsulitis were retrospectively reviewed (Figure). Of these patients, 384 had significant trauma preceding onset of symptoms or had radiological evidence of shoulder pathology, suggesting a secondary adhesive capsulitis. The remaining 128 patients with idiopathic adhesive capsulitis were invited to participate in the study. Strict selection criteria were observed for the diagnosis of idiopathic adhesive capsulitis.

The diagnostic criteria are as follows, and are in accordance with most definitions of adhesive capsulitis in literature\(^2,19,\):

- Insidious onset of pain and pain associated with passive glenohumeral motion;
- Restricted range of glenohumeral motion both actively and passively, with external rotation less than 50% of the normal side;
- A normal radiograph, and a shoulder ultrasound demonstrating no significant rotator cuff tear.

Patients were excluded if they:

- had a secondary causes of adhesive capsulitis such as a fracture, recent shoulder surgery, calcific tendonitis, or rotator cuff tears;
- declined to participate;
- were below the age of 18.

Based on date of presentation, an age- and sex-matched group of 231 patients who presented to the same practice during the same time period with non-shoulder/neck related orthopaedic complaints were recruited as the control group. The size of the groups was determined based on a power of 80% in detecting an estimated 20% difference in ethnicity between the groups (\(\alpha = 0.05, 2\text{-tailed}\)). Complete data were available for 87 patients with IAC and for 176 patients of the control group. All patients were examined by the same clinician (A.W.) and the examination results were recorded at time of consultation and collected retrospectively for the purpose of this study. Patient-completed questionnaires were mailed out and information from health records was retrospectively collected to identify comorbidities and other risk factors. The study protocol was reviewed and approved by the institutional ethics review committee.

**Statistical methods**

Continuous variables are expressed as mean ± SD and categorical values as percentages. Bivariate statistical analyses were performed using the Student t test for parametric continuous variables, Mann-Whitney U test for non-parametric continuous variables, the \(\chi^2\) test for categorical variables, and Fischer exact test used for categorical variables of low numbers. Multivariate logistic regression analyses were performed post hoc to identify independent risk factors. Odds ratio with 95% confidence interval is reported for point estimation. All reported \(P\) values are 2-sided and \(P\) value < .05 was considered significant. Data were analyzed using the SPSS software package (version 15; SPSS, Chicago, Illinois, USA).

**Results**

Patient groups and participation rates are demonstrated in the Figure. Eighty-seven patients and 176 patients were included for the IAC and control groups, respectively (response rate: 68% and 76%, respectively). Patients with IAC had symptoms for an average of 204 days prior to presentation to us. Seventy-five (86%) patients with IAC were right arm dominant, and the IAC occurred in the dominant arm in 39 (45%). Average passive abduction was 88°. Average passive external rotation was 29°. Of the patients in the control group, the majority (57%) presented with knee-related complaints. Presentations of the rest included elbow, wrist, and hand problems. Tables I and II demonstrate risk factors analyzed between IAC and control groups.

**Demographics and comorbidities**

Bivariate analysis was performed and comorbidities that were found to be associated with IAC were diabetes \((P = .005, \text{OR: } 3.05, \text{CI: } 1.40-6.61)\) and hypothyroidism \((P = .049, \text{OR: } 5.33, \text{CI: } 1.01-27.9)\); however, of these 2, only diabetes was found to be an independent predictor of IAC on multivariate regression analysis. There was also a trend of increasing incidence of Dupuytren’s disease in the IAC group but this was not statistically significant \((P = .068)\) (Table I).
Unexpectedly, lower absolute body weight and lower body mass index (BMI) were associated with increased risk of IAC ($P = .011$ and $P = .020$, respectively). For each 1 kg lower weight, there was a 3% increased risk of adhesive capsulitis.

Those patients with IAC were more likely than their controls to have a first degree relative (parent, sibling, or child) with a past history of adhesive capsulitis ($P < .001$, OR: 6.03, CI: 2.43-10.50). This factor was an independent predictor of IAC.

Handedness, activity level, employment status and smoking status were not significantly different across the 2 groups.

**Ethnicity**

The majority of respondents were born in Australia (83%), and had parents and grandparents also born in Australia. The second largest group were those born in the British Isles (England, Scotland, Wales, and Ireland). With bivariate analyses, being born in the British Isles or having parents and grandparents born in the British Isles was associated with IAC. When analyzing the risk factor “Born in the British Isles” with other variables in Table I, this factor remained an independent predictor of IAC ($P = .015$, OR:2.25, CI: 1.17-4.32). There was no association identified with other countries or regions of origin (Table II).

**Discussion**

Despite being a relatively common condition, our understanding of adhesive capsulitis is limited. In particular, the etiology of the idiopathic variety of adhesive capsulitis, a condition that can seemingly affect patients spontaneously, has proven elusive. So far, diabetes is the only consistent risk factor to have been identified. Other comorbidities are more weakly associated, and include Dupuytren’s disease, hypothyroidism, ischaemic heart disease, and Parkinson’s disease.

Our results confirm that diabetes is an independent predictor of IAC, with an OR of 3.05 (CI: 1.40, 6.61). However, we were surprised to find that a lower body weight is associated with increased risk of IAC. For every kilogram of lower body weight, there was a 3% increase in risk of IAC. The effect does not seem to be related to height.

Figure Flow chart demonstrating patient cohort numbers and response rates.
our study may be confounding between hypothyroidism and diabetes. It has been shown that thyroid disease is more common in patients with diabetes, and there is increased risk of thyroid autoimmunity in adult type 2 diabetic patients with GAD65 autoantibodies. Whether diabetic and thyroid autoantibodies are more prevalent in patients with IAC would form an interesting topic for future research.

Table I
Analyses of comorbidities, demographic, and employment factors and IAC

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>IAC group (total n = 87)</th>
<th>Control group (total n = 176)</th>
<th>P value</th>
<th>Odds ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (male %)</td>
<td>31 (36%)</td>
<td>74 (42%)</td>
<td>.318</td>
<td></td>
</tr>
<tr>
<td>Age (mean, SD)</td>
<td>56.0 (9.4)</td>
<td>55.3 (10.4)</td>
<td>.568</td>
<td></td>
</tr>
<tr>
<td>Smoker (%)</td>
<td>7 (8%)</td>
<td>16 (9%)</td>
<td>.778</td>
<td></td>
</tr>
<tr>
<td>Weight kg (mean, SD)</td>
<td>73.6 (13.6)</td>
<td>79.2 (17.8)</td>
<td>.011*</td>
<td></td>
</tr>
<tr>
<td>Height cm (mean, SD)</td>
<td>167.5 (9.7)</td>
<td>168.4 (10.0)</td>
<td>.493</td>
<td></td>
</tr>
<tr>
<td>BMI (mean, SD)</td>
<td>26.2 (4.0)</td>
<td>27.8 (5.7)</td>
<td>.020*</td>
<td></td>
</tr>
<tr>
<td>Work Type (%)</td>
<td>Manual</td>
<td>32 (37%)</td>
<td>57 (32%)</td>
<td>.813</td>
</tr>
<tr>
<td>Deskwork</td>
<td>28 (32%)</td>
<td>55 (31%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mixed</td>
<td>17 (20%)</td>
<td>37 (21%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Retired</td>
<td>10 (11%)</td>
<td>26 (15%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Work Capacity (%)</td>
<td>Full time</td>
<td>24 (28%)</td>
<td>71 (40%)</td>
<td>.100</td>
</tr>
<tr>
<td>Part time</td>
<td>28 (32%)</td>
<td>41 (23%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No work</td>
<td>35 (40%)</td>
<td>66 (36%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lift &gt;10kg per day (%)</td>
<td>0 times</td>
<td>22 (25%)</td>
<td>25 (14%)</td>
<td>.110</td>
</tr>
<tr>
<td>&lt;3 times</td>
<td>33 (38%)</td>
<td>65 (37%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3-10 times</td>
<td>19 (22%)</td>
<td>49 (28%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10+ times</td>
<td>12 (14%)</td>
<td>35 (22%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes (%)</td>
<td>17 (20%)</td>
<td>13 (7%)</td>
<td>.005*</td>
<td>3.05 (1.40-6.61)</td>
</tr>
<tr>
<td>Ischaemic heart disease</td>
<td>7 (8%)</td>
<td>9 (5%)</td>
<td>.438</td>
<td></td>
</tr>
<tr>
<td>Dupuytren (%)</td>
<td>7 (8%)</td>
<td>5 (3%)</td>
<td>.068</td>
<td></td>
</tr>
<tr>
<td>Epilepsy</td>
<td>1 (1%)</td>
<td>1 (1%)</td>
<td>.553</td>
<td></td>
</tr>
<tr>
<td>Hyperthyroidism (%)</td>
<td>2 (2%)</td>
<td>6 (3%)</td>
<td>.798</td>
<td></td>
</tr>
<tr>
<td>Hypothyroidism (%)</td>
<td>5 (6%)</td>
<td>2 (1%)</td>
<td>.049*</td>
<td>5.33 (1.01-27.9)</td>
</tr>
<tr>
<td>Carpal Tunnel (%)</td>
<td>6 (7%)</td>
<td>21 (12%)</td>
<td>.211</td>
<td></td>
</tr>
<tr>
<td>Irritable bowel synd (%)</td>
<td>14 (16%)</td>
<td>21 (12%)</td>
<td>.352</td>
<td></td>
</tr>
<tr>
<td>Trigger finger (%)</td>
<td>2 (2%)</td>
<td>15 (9%)</td>
<td>.072</td>
<td></td>
</tr>
<tr>
<td>Depression (%)</td>
<td>16 (18%)</td>
<td>33 (19%)</td>
<td>.944</td>
<td></td>
</tr>
<tr>
<td>Anxiety (%)</td>
<td>16 (18%)</td>
<td>32 (18%)</td>
<td>.967</td>
<td></td>
</tr>
<tr>
<td>Chronic Fat, g (%)</td>
<td>3 (3%)</td>
<td>3 (2%)</td>
<td>.383</td>
<td></td>
</tr>
<tr>
<td>1st degree relative with adhesive capsulitis</td>
<td>25 (29%)</td>
<td>13 (7%)</td>
<td>&lt;.001*</td>
<td>6.03 (2.88-12.63)</td>
</tr>
</tbody>
</table>

IAC, idiopathic adhesive capsulitis; CI, confidence interval; BMI, body mass index.

Independently associated risk factors demonstrated by multivariate regression analysis are in boldface.

* Bivariate analyses demonstrating statistically significant factors (P < .05).

Table II
Analysis of ethnicity and IAC

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Adhesive capsulitis (n = 87)</th>
<th>Control group (n = 176)</th>
<th>P value</th>
<th>Odds ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Born in British Isles</td>
<td>22 (25%)</td>
<td>23 (13%)</td>
<td>.015</td>
<td>2.25 (1.17-4.32)</td>
</tr>
<tr>
<td>Both parents born in British Isles</td>
<td>23 (26%)</td>
<td>22 (13%)</td>
<td>.006</td>
<td>2.52 (1.31-4.83)</td>
</tr>
<tr>
<td>All grandparents born in British Isles</td>
<td>26 (30%)</td>
<td>23 (13%)</td>
<td>.001</td>
<td>2.83 (1.50-5.35)</td>
</tr>
</tbody>
</table>

IAC, idiopathic adhesive capsulitis; CI, confidence interval.

When analyzed with other variables in Table I, “born in British Isles” remained as an independent risk factor for IAC on multivariate logistic regression.
Anecdotally, it was our experience that a large number of people with IAC were of Celtic or Northern European descent. Dupuytren’s disease is a condition shown to have originated in the Celtic regions, with a significant risk of developing the disease in persons of Celtic background. One of the aims of the present study was to determine whether a similar racial predilection was also true for IAC. The location of our practice (Mornington Peninsula, Melbourne, VIC, Australia) was well suited to answer this question, as the locality had a good mix of European and Asian migrants as well as patients who were locally born. While it is very difficult to define race and racial origin in a study utilizing questionnaires, we have used countries of birth as surrogates. Such technique has commonly been used in the past. We believe also that the inclusion of parental and grandparental countries of birth increases the reliability of such a surrogate marker in reflecting a patient’s racial origins. Our findings confirm that patients with IAC were over 2 times more likely to have been born in the British Isles, or are descendants of those born there, than the control group (Table II). Multivariate regression analyses show that this is an independent risk factor and that no other countries or regions were associated in this manner. To our knowledge, this is the first time that IAC has been associated with a particular race or region of the world. The mechanism of association remains open to speculation. Processes of cellular degradation, such as the expression of matrix metalloproteinase and mitogen activated protein kinases, have previously been implicated in the onset of IAC. Whether genetic mutations that are more prevalent in particular regions of the world are partially responsible for the increased incidence seen will form the next step of investigation.

We were unable to establish a statistically significant association between Dupuytren’s disease and IAC. While a type II error cannot be ruled out here, another explanation is that Dupuytren’s disease tends to occur at a later age than adhesive capsulitis. Therefore, by examining the incidence of Dupuytren’s disease in a cohort of patients with adhesive capsulitis, our study would be less likely to find an association than a study that examine the incidence of adhesive capsulitis in a cohort of patients with Dupuytren’s disease.

One of the problems traditionally associated with the investigation of IAC has been the loose definition of the term utilized in some studies. The term “adhesive capsulitis” has been misapplied to patients with other causes of stiff and painful shoulders, such as calcific tendonitis, rotator cuff tears, or biceps tendinitis. In our study, we carefully controlled the selection of patients to ensure that those with other diagnoses or secondary adhesive capsulitis were excluded. All patients were required to have a radiograph, ultrasound, and complete clinical assessment by the same orthopaedic shoulder surgeon to ensure consistency and accuracy of diagnosis and selection. Other areas of strength for the present study is our large numbers of patients with IAC, and our use of multivariate analyses to eliminate possible confounding factors.

One weakness of the study design is the use of a questionnaire to gather data on some of the risk factors. This is naturally open to the usual criticism of ascertainment bias, validity of self-reporting, and case definition. However, the prevalence of comorbidities from our data appears to be comparable to other reports on disease prevalence. In addition, the use of a well-matched control group from a similar background reduces the effect of bias and we believe allows for a meaningful comparison.

**Conclusion**

Our findings show that diabetes and lower BMI are independent risk factors for IAC. From an ethnicity point of view, being born in the British Isles or being the children/grandchildren of people born in the British Isles are also risk factors. This sheds new light on the etiology of IAC and suggests a genetic component may exist for this condition. Future research is required to identify whether specific genetic predilections or if environmental factors are the cause.

**Disclaimer**

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**References**


