Cigarette smoking is associated with cubital tunnel syndrome

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Running title: Smoking and ulnar neuropathy
Abstract

Introduction: The aim of this study was to validate the potential association between cigarette smoking and cubital tunnel syndrome (CubTS).

Methods: One hundred patients with CubTS were compared with 100 controls with ulnar abutment syndrome matched for age, gender, and BMI. The smoking status was compared between patients and controls using the sign test and the Wilcoxon signed rank test. Conditional logistic regression was used to calculate the association between CubTS and pack-years smoked.

Results: A significant association was found between increased pack-years smoked and CubTS. A significant difference in the number of never smokers and ever smokers was observed between the patients with CubTS and controls. The difference in mean pack-years in the patients and controls was highly significant. A dose-dependent association with pack-years was found between patients and controls.

Discussion: High cumulative cigarette smoking is associated with CubTS.

Key words: cubital tunnel syndrome, ulnar neuropathy, smoking, risk factor, pathogenesis
Introduction

Various predictors such as gender, age, body mass index (BMI), or workers’ compensation status are thought to contribute to development of cubital tunnel syndrome (CubTS)\textsuperscript{1-7}. Recent studies have reported that cigarette smoking is also associated with its pathogenesis\textsuperscript{1,4,8,9}. However, other previous studies showed a negative association between smoking and development of CubTS\textsuperscript{5,7}. These studies have produced conflicting results, and the effect of smoking on the development of CubTS remains unknown. The aim of this study was to assess the relationship between cigarette smoking and CubTS.

Materials and methods

Patients

A total of 125 patients with CubTS who underwent surgical treatment in our hospital between 2002 and 2013 were enrolled retrospectively in the study. The diagnosis of CubTS required a Tinel sign at the cubital tunnel, paresthesia or numbness in the ulnar nerve distribution, and some degree of motor impairment, including weakness of pinch or grip, which was confirmed by physical examination. Electrodiagnostic testing was performed on all the patients according to a standard protocol\textsuperscript{10}. The criteria for electrodiagnosis of CubTS were a conduction velocity of \(<50\) m/s across the elbow and a decrease of conduction velocity of \(>15\%\) at the elbow compared to the forearm segment\textsuperscript{10}. The diagnosis of CubTS was established by each of 4 different examiners who performed surgery.

To examine pathogenesis of primary CuTS, we excluded patients with an ulnar neuropathy due to previous elbow trauma, rheumatoid arthritis (RA), cubitus varus or valgus deformity, ulnar nerve dislocation, or ganglion. These pathologies were diagnosed by interviews with the patients, clinical examinations, radiographs, laboratory data, or intraoperative findings. Only patients with primary osteoarthritis (OA) were included, while those with secondary OA with...
a history of trauma or inflammation of the elbow were excluded.

We selected subjects who underwent ulnar shortening osteotomy for ulnar abutment syndrome (UAS), because the pathogenesis of UAS has not shown to be associated with cigarette smoking. All the patients with UAS had ulnar-sided wrist pain, with radiographs showing positive ulnar variance (i.e., an increased ulnar length [> 1 mm] relative to the radius). A single examiner established the diagnosis of UAS using clinical symptoms and an anteroposterior radiograph of the wrist with the forearm in the neutral position. All the patients with UAS had ulnar-sided wrist pain, with radiographs showing positive ulnar variance. Ulnar shortening osteotomy was performed during the same study period. In this control group, symptoms and signs of ulnar neuropathy in the symptomatic arm were absent. Patients in the case and control groups never had undergone surgery of the ipsilateral upper extremity. The matched-pairs control group was selected on a 1:1 ratio based on gender, age (±3 years), and BMI (±2 kg/m²). An institutional review board approved the study and verbal informed consent was obtained in the outpatient clinic or by telephone.

**Smoking**

Smoking history and cigarette consumption were assessed by patient self-report. Patients and controls were classified as current smokers, past smokers, or never smokers. A current smoker was classified as a smoker of at least 1 cigarette daily for 3 months before the assessment, and a past smoker as a person who had smoked more than 100 cigarettes in the past. Cigarette consumption was quantified in pack-years, with 1 pack-year being equivalent to 20 cigarettes smoked daily for 1 year.

**Statistical analysis**
Differences in the frequencies of smoking status between patients with CubTS and matched controls were investigated using the sign test for categorical data and the Wilcoxon signed rank test for continuous data. Conditional logistic regression analysis was used to compare the dose-dependent association of pack-years between patients and controls. Statistical significance was defined as a \( P \) value <0.05. The statistical analyses were performed using SPSS software v 19.0 (IBM Corp., Armonk, NY, USA).

Results

Of the 125 patients identified, 100 were included in the study, and 25 were excluded (6 with OA with previous elbow trauma, 5 with RA, 5 with cubitus varus or valgus deformity, 5 with ulnar nerve dislocation, 2 with ganglion, 1 with thoracic outlet syndrome, and 1 with a congenital bone disorder). Fifty-two patients were men, the mean age was 53 years, and the mean BMI was 22kg/m\(^2\). One hundred matched controls with UAS were included in the study, of whom 52 were men, with a mean age of 51 years and mean BMI of 21kg/m\(^2\).

Comparison of smoking status between patients with CubTS and UAS

As shown in Table 1, there was a significant difference in the proportion of subjects who had never smoked or were past smokers. The difference between mean pack-years of cigarettes smoked in the patients with CubTS and controls was highly significant. Table 1 also shows the dose-dependent association between pack-years smoked and the odds ratio for CubTS.

Discussion

Our data support previous studies that have reported cigarette smokers have an increased risk of CubTS\(^1\,^4\,^8\,^9\). Some studies did not match gender, age, and BMI between the patients and controls\(^4\,^9\), although these have been reported to be potential risk factors for the
pathogenesis of CubTS\textsuperscript{1-5,7}. It is therefore desirable to use control patients matched for these factors when investigating this disease, and a strong point of this study was that it was a case-control design.

The reason why cigarette smoking is associated with CubTS is unclear. Numerous studies have suggested that cigarette smoking is associated with peripheral nerve dysfunction\textsuperscript{11-14}. Nicotine has been shown to worsen the effects of ischemia in various tissues through its toxic effects\textsuperscript{11}, and it may impair recovery following peripheral nerve injury\textsuperscript{12}. The most probable explanation for the association between smoking and CubTS is that smoking reduces the blood supply of the ulnar nerve, which results in the nerve being vulnerable to compression or traction.

A limitation of this study is that patients with CubTS and UAS were enrolled retrospectively. We only enrolled patients and controls who had undergone surgical treatment, which may introduce its own bias. A prospective case-control study with or without surgical treatment avoid this selection bias. Second, small numbers of controls who were heavy smokers might affect the results. Despite such limitation, we believe that this study may help to resolve conflicting results of the association between smoking and risk for CubTS.
Abbreviations: body mass index (BMI), Cubital tunnel syndrome (CubTS), osteoarthritis (OA), rheumatoid arthritis (RA), ulnar abutment syndrome (UAS)
References


TABLE 1. Comparison of smoking status and dose-dependent association between patients with cubital tunnel syndrome and controls with ulnar abutment syndrome.

<table>
<thead>
<tr>
<th></th>
<th>Patients (n =100)</th>
<th>Controls (n =100)</th>
<th>OR (CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Smoking status</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never, n</td>
<td>55</td>
<td>79</td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Past, n</td>
<td>26</td>
<td>8</td>
<td></td>
<td>0.001</td>
</tr>
<tr>
<td>Current, n</td>
<td>19</td>
<td>13</td>
<td></td>
<td>0.33</td>
</tr>
<tr>
<td><strong>Pack-years</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 - 15</td>
<td>21</td>
<td>15</td>
<td>2.90 (1.14 to 7.40)</td>
<td>0.03</td>
</tr>
<tr>
<td>16 - 30</td>
<td>10</td>
<td>5</td>
<td>4.04 (1.12 to 14.59)</td>
<td>0.03</td>
</tr>
<tr>
<td>&gt;30</td>
<td>14</td>
<td>1</td>
<td>29.93 (3.19 to 280.91)</td>
<td>0.003</td>
</tr>
<tr>
<td><strong>Mean (range)</strong></td>
<td>25.8 (2-100)</td>
<td>11.8 (1-38)</td>
<td></td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

CI, confidence interval; OR, odds ratio