Association between Smoking and Erectile Dysfunction: A Population-based Study

Naomi M. Gades1, Ajay Nehra2, Debra J. Jacobson3, Michaela E. McGree3, Cynthia J. Girman1,4, Thomas Rhodes4, Rosebud O. Roberts1, Michael M. Lieber2, and Steven J. Jacobsen1

1 Department of Health Sciences Research, Division of Epidemiology, Mayo Clinic College of Medicine, Rochester, MN.
2 Department of Urology, Mayo Clinic College of Medicine, Rochester, MN.
3 Department of Health Sciences Research, Division of Biostatistics, Mayo Clinic College of Medicine, Rochester, MN.
4 Merck Research Laboratories, Blue Bell, PA.

Received for publication June 17, 2004; accepted for publication September 28, 2004.

The association between smoking and erectile dysfunction was evaluated in a cohort of 2,115 Caucasian men, aged 40–79 years, randomly selected from Olmsted County, Minnesota. Smoking status was assessed by questionnaire; during the fourth biennial examination, erectile dysfunction was assessed with the Brief Male Sexual Function Inventory. Of the 1,329 men with a regular sexual partner, 173 were current smokers, 836 had previously smoked, and 203 reported erectile dysfunction. Compared with former and never smokers, current smokers in their forties had the greatest relative odds of erectile dysfunction, 2.74 (95% confidence interval (CI): 0.44, 16.89), compared with 1.38 (95% CI: 0.51, 3.74), 1.70 (95% CI: 0.82, 3.51), and 0.77 (95% CI: 0.27, 2.21) for men in their fifties, sixties, and seventies, respectively. Compared with men who never smoked, men who smoked at some time had a greater likelihood of erectile dysfunction (age-adjusted odds ratio = 1.42, 95% CI: 1.00, 2.02), and there was a dose response. Although the causal pathway underlying this association is not clear, this study contributes to the growing literature describing an association between smoking and erectile dysfunction.

Abbreviation: ED, erectile dysfunction.

One of the US national health goals for 2010 is to decrease the prevalence of smoking in adults. In 2001, an estimated 46.2 million adults were current smokers, and the prevalence of cigarette smoking was higher among men than women (1). Smoking exacts enormous costs, with an estimated 440,000 premature deaths in the United States annually and approximately $157 billion in annual health-related economic losses (2). While much of the focus has been on cancer and cardiovascular diseases, these diseases tend to occur at older ages; therefore, younger adults and adolescents may discount the increased risk. Erectile dysfunction (ED) has been reported to be associated with smoking, and antismoking advertising campaigns have tried to use this information to their advantage (3).

Unfortunately, few population-based studies have evaluated the association between smoking and ED in the adult male population. The most commonly cited study in the United States is the Massachusetts Male Aging Study, which evaluated ED in men aged 40–70 years with a self-administered questionnaire. Results from this study indicated that cigarette smoking at baseline almost doubled the likelihood of moderate or complete ED at up to 10 years of follow-up. Former smokers, compared with never smokers, were not at increased risk of ED (4), but there was no information on dose response, that is, number of cigarettes smoked. Men were simply classified as former smokers, nonsmokers, or current smokers at baseline and follow-up (5). An earlier study of Vietnam-era veterans, aged 31–49 years, found that a higher percentage of smokers reported ED problems than did nonsmokers. However, neither number of years of smoking nor number of cigarettes smoked daily were significant predictors of ED in current smokers in this study (6).
Moreover, the young age of the men evaluated may have limited implications for men who smoke their entire lives.

Thus, despite the media attention, the association between smoking and ED is not well established, and a dose-response relation has not been reported to our knowledge. We sought to further our own understanding of this potential relation in our population-based cohort from The Olmsted County Study of Urinary Symptoms and Health Status among Men.

MATERIALS AND METHODS

Study population, subject recruitment, and data collection

In December 1989, The Olmsted County Study of Urinary Symptoms and Health Status among Men was initiated, and details have been published elsewhere (7–9). Briefly, a community-based, prospective cohort study design was used. Subjects were Caucasian men aged 40–79 years on January 1, 1990, randomly selected from the Olmsted County, Minnesota, population to describe the natural history of urinary symptoms and benign prostatic hyperplasia. The Rochester Epidemiology Project resources were used to enumerate the population; on the basis of 1990 census data from Olmsted County, approximately 96 percent of the county population was enumerated. Through the process, men were sampled within a 5-year age- and geographic-specific stratum (City of Rochester vs. the balance of Olmsted County). The community medical records of the selected men were reviewed for history of prostate cancer, prostatectomy, and other medical conditions that may impede normal voiding function apart from benign prostatic hyperplasia, including neurologic disease, lower back surgery, and urethral stricture. After exclusion for these preexisting conditions and/or treatments, 3,874 men were asked to join the study, and 2,115 agreed to participate (participation rate, 55 percent). Subsequently, individual participants were visited in their home and were asked to complete a questionnaire that documented demographic information and the severity of lower urinary tract symptoms using questions similar to those in the American Urological Association Symptom Index (10–12). All study procedures were approved by the Mayo Foundation Institutional Review Board. The cohort was actively followed biennially with a participation rate, 55 percent. Subsequently, individual participants were visited in their home and were asked to complete a questionnaire that documented demographic information and the severity of lower urinary tract symptoms using questions similar to those in the American Urological Association Symptom Index (10–12). All study procedures were approved by the Mayo Foundation Institutional Review Board. The cohort was actively followed biennially with a protocol that was similar to the initial examination.

Instrument measures

The baseline questionnaire included items on cigarette smoking and initially assessed whether men had smoked at least 100 cigarettes in their lifetime and, if yes, whether they currently smoked and how many cigarettes they smoked per day. Former smokers were asked how long ago they stopped smoking and for how many years they smoked. Based on the questionnaire responses, smoking status was categorized as current smoker with intensity of smoking (packs per day) and/or as ever smoker along with cumulative exposure (pack-years based on reported duration and intensity).

Erectile function was assessed by self-administered questionnaire during the fourth biennial examination. The questions on sexual function were taken from the Brief Male Sexual Function Inventory (13, 14). Erectile function was evaluated from the responses to questions about how often men had partial or full erections when sexually stimulated, how often their erections were firm enough for sexual intercourse, and how much difficulty they had in getting an erection, all in the past 30 days. Responses were scored as 0 = none at all, 1 = a few times, 2 = fairly often, 3 = usually, and 4 = always) and were summed (13, 14). Because previous work has shown that self-reported sexual function can be heavily influenced by the availability of a regular sexual partner (13), only those men with a regular sexual partner were included in the analysis. Information on comorbidities, including hypertension, diabetes, and coronary heart disease, was assessed through questionnaire response at baseline.

A total of 1,855 men who participated in 1990 also completed a questionnaire in 1996. Of those men, seven were missing information on smoking status, 238 on erectile function, and one on both. Of the remaining 1,609 men, 1,329 reported having a regular sexual partner.

Statistical analysis

Current smokers were categorized on the basis of number of packs of cigarettes smoked per day as light smokers (<1 pack/day) and moderate smokers (≥1 pack/day). For men who smoked at some time, cumulative exposure (pack-years) was categorized by tertile: 1–12.5 pack-years, 12.6–29.0 pack-years, and >29.0 pack-years. Additional analyses using alternative cutpoints did not change the results. ED was considered present if men scored ≤3 on the erectile function domain. Other cutpoints for the ED question showed similar results. The Mantel-Haenszel χ² test for trend was used to analyze the association between ED and smoking status. A Spearman rank correlation coefficient was used to quantify the relation between pack-years and ED, with and without adjustment for age. All statistical tests were two sided, and alpha <0.05 was considered significant. Odds ratios, both unadjusted and age adjusted, were estimated to quantify the association between current smoking and smoking at some time, compared with never smoking. To evaluate the potential confounding effects of age, hypertension, diabetes, or coronary heart disease, these factors were included in multiple logistic regression models comparing the association between smoking and ED. All statistical analyses were completed by using SAS statistical software (SAS Institute, Inc., Cary, North Carolina).

RESULTS

Of the 1,329 men with a regular sexual partner, the majority—836 (63.0 percent)—smoked at some time, and 491 (37.0 percent) never smoked. For two men, information on current smoking status was missing. Regardless of smoking status, approximately 15 percent of men reported having ED (table 1).

ED increased in men who ever smoked compared with never smokers based on cumulative exposure (pack-years) (p for trend < 0.0001). Compared with men who never smoked, men who smoked at some time were more likely to
have ED (table 2). A dose response was seen, with men smoking 12.6–29.0 pack-years and >29.0 pack-years having an increase in the likelihood of ED. The correlation coefficient between ED and smoking (pack-years) for smokers was –0.18 ($p < 0.0001$). However, after adjusting for age, the correlation coefficient was attenuated, –0.09 ($p < 0.02$), but remained significant.

When current smokers were compared with former and never smokers and were stratified by age, smokers in their forties had the greatest relative odds of having ED (odds ratio = 2.74, 95 percent confidence interval: 0.44, 16.89) compared with 1.38 (95 percent confidence interval: 0.51, 3.74), 1.70 (95 percent confidence interval: 0.82, 3.51), and 0.77 (95 percent confidence interval: 0.27, 2.21) for men in their fifties, sixties, and seventies, respectively. Compared with men who never smoked, men who currently smoked were more likely to have ED after we adjusted for age (table 3). However, the confidence intervals included 1.

Age was dichotomized because of an interaction between age and smoking status (table 3). When compared with the age-adjusted odds ratio, adjustments for hypertension, diabetes, or coronary heart disease did not change these results in men <70 years of age who currently smoked. However, these results did change for men ≥70 years of age who currently smoked (table 3).

**DISCUSSION**

In this study, smoking was associated with ED. This association was seen in current smokers, although the magnitude of this association decreased across increasingly older age groups. This finding suggests that smoking may have a more apparent impact on erectile function in young male smokers than it does in older male smokers. Importantly, there was also evidence of a dose response by intensity with cumulative exposure among persons who ever smoked.

This latter result, in particular, adds greater credence to previous reports (4–6) of an association between smoking and ED. Unlike previous studies (4), however, we found that former smokers, especially those who had smoked for more than 29.0 pack-years, were more likely to have ED than nonsmokers were. In addition, unlike the Centers for Disease

### TABLE 1. Distribution of smoking status and erectile dysfunction by age in The Olmsted County Study of Urinary Symptoms and Health Status among Men, Rochester, Minnesota, 1989–2003

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>All (n = 1,329)</th>
<th>40–49</th>
<th>50–59</th>
<th>60–69</th>
<th>≥70</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Never smoker</td>
<td>491</td>
<td>105</td>
<td>177</td>
<td>134</td>
</tr>
<tr>
<td></td>
<td>Former smoker†‡</td>
<td>661</td>
<td>83</td>
<td>263</td>
<td>185</td>
</tr>
<tr>
<td></td>
<td>Current smoker‡</td>
<td>173</td>
<td>47</td>
<td>68</td>
<td>42</td>
</tr>
<tr>
<td>Erectile dysfunction</td>
<td>203</td>
<td>5</td>
<td>29</td>
<td>73</td>
<td>96</td>
</tr>
</tbody>
</table>

* Age was calculated based on the date of the fourth-round questionnaire submission.
† For two men, information on lifetime smoking exposure was missing.
‡ For two men, information on current smoking status was missing.

### TABLE 2. Relative odds of erectile dysfunction in men who ever smoked vs. never smokers in The Olmsted County Study of Urinary Symptoms and Health Status among Men, Rochester, Minnesota, 1989–2003

<table>
<thead>
<tr>
<th>Erectile dysfunction</th>
<th>Yes</th>
<th>No</th>
<th>OR*</th>
<th>95% CI</th>
<th>Age† adjusted</th>
<th>Age† and comorbidity‡ adjusted</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.</td>
<td>%</td>
<td>No.</td>
<td>%</td>
<td>OR 95% CI</td>
<td>OR 95% CI</td>
</tr>
<tr>
<td>Never smoker</td>
<td>60</td>
<td>12.2</td>
<td>431</td>
<td>87.8</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>Ever smoker</td>
<td>141</td>
<td>16.9</td>
<td>695</td>
<td>83.1</td>
<td>1.46</td>
<td>1.05, 2.02</td>
</tr>
<tr>
<td>No. of pack-years§</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>60</td>
<td>12.2</td>
<td>431</td>
<td>87.8</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>1–12.5</td>
<td>31</td>
<td>11.4</td>
<td>242</td>
<td>88.6</td>
<td>0.92</td>
<td>0.58, 1.46</td>
</tr>
<tr>
<td>12.6–29.0</td>
<td>41</td>
<td>15.8</td>
<td>219</td>
<td>84.2</td>
<td>1.34</td>
<td>0.86, 2.07</td>
</tr>
<tr>
<td>&gt;29.0</td>
<td>62</td>
<td>22.5</td>
<td>214</td>
<td>77.5</td>
<td>2.08</td>
<td>1.41, 3.08</td>
</tr>
</tbody>
</table>

* OR, odds ratio; CI, confidence interval.
† Age was calculated based on the date of the fourth-round questionnaire submission.
‡ Comorbidities include the occurrence of hypertension, diabetes, or coronary heart disease.
§ For two men, information on lifetime smoking exposure was missing.
TABLE 3. Relative odds of erectile dysfunction in men who currently smoke vs. never smokers in The Olmsted County Study of Urinary Symptoms and Health Status among Men, Rochester, Minnesota, 1989–2003

<table>
<thead>
<tr>
<th>Erectile dysfunction</th>
<th>OR*</th>
<th>95% CI*</th>
<th>Age† adjusted</th>
<th>Comorbidity‡ adjusted</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Age &lt; 70 years</td>
<td>Age ≥ 70 years</td>
</tr>
<tr>
<td>No.</td>
<td>%</td>
<td>No.</td>
<td>%</td>
<td>OR</td>
</tr>
<tr>
<td>Never smoker</td>
<td>60</td>
<td>12.2</td>
<td>431</td>
<td>87.8</td>
</tr>
<tr>
<td>Current smoker</td>
<td>25</td>
<td>14.5</td>
<td>148</td>
<td>85.5</td>
</tr>
</tbody>
</table>

*OR, odds ratio; CI, confidence interval.
†Age was calculated based on the date of the fourth-round questionnaire submission.
‡Comorbidities include the occurrence of hypertension, diabetes, or coronary heart disease.
§Age was dichotomized because of an interaction between age and smoking status (p < 0.09).
¶For two men, information on current smoking exposure was missing.
Control and Prevention study (6), we found that number of pack-years of smoking was significantly associated with ED in former and current smokers. This finding is partially supported by results from a study conducted in community-based populations in Brazil, Italy, Japan, and Malaysia (15). In that study, no association was found between ED and current smoking status, however. Our results also differed from those in a population-based study conducted in Belgium (16), which found odds ratios for ED of 0.76, 1.90, and 1.01 for current male smokers in their forties, fifties, and sixties, respectively, compared with nonsmokers. However, the intensity of cigarette exposure was not quantified in that study, precluding the authors’ ability to examine a dose-response relation. In concurrence with our study, a community-based Dutch study (17) in a similar age group, 50–78 years, found that smokers had a higher occurrence of ED, although smoking intensity again was not quantified. The Health Professionals Follow-up Study (18) also found that smoking was associated with risk of ED. While this study quantified cigarette exposure in current smokers using number of cigarettes per day, this information was not included in the assessment of the relative risk for ED.

Interestingly, we saw the relative odds of ED in current smokers decrease with increasing age, when stratified by age. This finding concurs with those from a report by Mirone et al. (19), in which cigarette smoking was associated with ED in men without a history of cardiovascular disease, cardiopathy, hypertension, diabetes, or neuropathy. Therefore, in the absence of these comorbid conditions, as is more likely in younger men, the effect of smoking as an independent risk factor for ED may be more apparent, as seen in our results. Alternatively, another explanation for this outcome may be survivorship bias, because smokers have higher mortality rates and therefore would be less represented in the sample. Furthermore, men who had undergone prostate surgery or had prostate cancer were excluded at baseline, which may have biased the baseline sample because these conditions are also associated with increasing age.

Although the evidence for an association between smoking and ED is growing, the mechanism behind this association is not completely understood. Andersson (20) recently reviewed physiologic and pathophysiologic pathways involved in ED and concluded that ED has overlapping pathophysiologic origins but may have final common pathways that mediate ED. Comorbidities, such as hypertension, hypercholesterolemia, and diabetes, are associated with decreased function of nerves and endothelium, resulting in circulatory and structural changes in penile tissues, arterial insufficiency, and defective smooth muscle relaxation. However, when we adjusted for these factors in our multivariable models, an association between smoking and ED persisted among younger men, suggesting that other mechanisms may prevail.

One area of interest that may have potential is the impact of smoking on hormones related to sexual function. In a study conducted by Krause and Muller (21), testosterone levels increased with the number of cigarettes smoked. This finding was supported by a recent study by Svartberg et al. (22), who found that after adjustment for age and body mass index, smokers had significantly higher levels of total testosterone, free testosterone, and sex hormone-binding globulin. Similarly, in a study of cigarette smoking conducted by Field et al. (23), smokers had increased serum levels of dehydroepiandrosterone (18 percent higher, \( p = 0.0002 \)), dehydroepiandrosterone sulfate (13 percent higher, \( p = 0.0007 \)), cortisol (5 percent higher, \( p = 0.01 \)), androstenedione (33 percent higher, \( p = 0.0001 \)), testosterone (9 percent higher, \( p = 0.009 \)), dihydrotestosterone (14 percent higher, \( p = 0.004 \)), and sex hormone-binding globulin (8 percent higher, \( p = 0.004 \)) after accounting for differences in body mass index and age. These data suggest that serum sex hormone concentrations and possibly adrenal steroids may be influenced by cigarette smoking in middle-aged men. These findings are not consistent across studies, however. For example, Shaaarawy and Mahmoud (24) found that total testosterone was lower in smokers compared with nonsmokers. Similarly, Hautanen et al. (25) found that dehydroepiandrosterone sulfate was the only sex hormone positively associated with smoking (\( p < 0.001 \)). These studies demon-
strate that the relation between smoking and sex hormone levels is still obscure and needs further investigation.

Beyond the dose-response relation noted in our study, the greater magnitude of association between smoking and ED in the younger age group is interesting. In 2001, the Morbidity and Mortality Weekly Report found that current smoking prevalence was highest among persons aged 18–24 years (26.9 percent) and 25–44 years (25.8 percent) and was lowest among those aged >65 years (10.1 percent) (1). As our data suggest, there is a potentially stronger association between smoking and ED in men in these younger age groups. The public health campaigns focusing on the association between smoking and ED in younger men make the potential risks of smoking more immediate for this age group.

In addition to the previously mentioned potential limitations, other factors also need to be considered. These cross-sectional data describe an association and do not prove cause and effect. However, a dose-response relation was found. Moreover, although our study had complete data for more than 1,000 men, increased stratification resulted in small sample sizes and concomitant limited power and precision. Note that all participants in The Olmsted County Study of Urinary Symptoms and Health Status among Men are Caucasian and were 40–79 years of age at study entry. Therefore, the generalizability of these findings to other ethnic populations and age groups may be limited. The 55 percent response rate may also limit generalizability. However, with the approval of the Mayo Clinic’s Institutional Review Board, a comparison of responder and nonresponder groups through the community medical record resources of the Rochester Epidemiology Project demonstrated few differences between responders and nonresponders (26, 27).

More importantly, the use of questionnaires to assess smoking status and sexual function may have associated social desirability and respondent biases, respectively. However, it is likely that these biases would have diminished the association between smoking and ED. Moreover, the questions regarding smoking status were consistent with other tobacco-use surveillance tools used by the National Health Interview Survey (28, 29), and the Brief Male Sexual Function Inventory consists of questions that are established tools for assessing sexual function (13, 14, 30).

In summary, data from this random sample of community men demonstrate an association between smoking and ED. Although these cross-sectional data do not prove cause and effect, a dose-response relation is present. Moreover, the association may be of greater magnitude in the younger age group, in whom other traditional causes of ED are not as prevalent compared with the older age group. These data add to the growing body of literature supporting this association. However, the underlying mechanism for this association is not immediately apparent. Thus, attempts by the media to link smoking and ED in their public health campaigns are done with the expectation that men who will not quit smoking for other health reasons may quit to preserve their sex lives, and such attempts may be well founded.

ACKNOWLEDGMENTS

This project was supported by research grants from the Public Health Service, National Institutes of Health (DK58859, AR30582, and RR000585) and by Merck Research Laboratories.

The authors thank the Olmsted County Study personnel for their help with the study and Sondra Buehler for her assistance in preparing the manuscript.

REFERENCES