Smoking Cessation and Risk of Age-Related Cataract in Men

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Context Although cigarette smoking has been shown to be a risk factor for age-related cataract, data are inconclusive on the risk of cataract in individuals who quit smoking.

Objective To examine the association between smoking cessation and incidence of age-related cataract.

Design Prospective cohort study conducted from 1982 through 1997, with an average follow-up of 13.6 years.

Setting and Participants A total of 20907 US male physicians participating in the Physicians’ Health Study I who did not have a diagnosis of age-related cataract at baseline and had reported their level of smoking at baseline.

Main Outcome Measures Incident age-related cataract defined as self-report confirmed by medical record review, diagnosed after study randomization and responsible for vision loss to 20/30 or worse, and surgical extraction of incident age-related cataract, in relation to smoking status and years since quitting smoking.

Results At baseline, 11% were current smokers, 39% were past smokers, and 50% were never smokers. Average reported cumulative dose of smoking at baseline was approximately 2-fold greater in current than in past smokers (35.8 vs 20.5 pack-years). Two thousand seventy-four incident cases of age-related cataract and 1193 cataract extractions were confirmed during follow-up. Compared with current smokers, multivariate relative risks (RRs) of cataract in past smokers who quit smoking fewer than 10 years, 10 to fewer than 20 years, and 20 or more years before the study were 0.79 (95% confidence interval [CI], 0.64-0.98), 0.73 (95% CI, 0.61-0.88), and 0.74 (95% CI, 0.63-0.87), respectively, after adjustment for other risk factors for cataract and age at smoking inception. The RR for never smokers was 0.64 (95% CI, 0.54-0.76). The reduced risk in past smokers was principally due to a lower total cumulative dose (RR of cataract for increase of 10 pack-years of smoking, 1.07; 95% CI, 1.04-1.10). A benefit of stopping smoking independent of cumulative dose was suggested in some analyses. Results for cataract extraction were similar.

Conclusion These prospective data indicate that while some smoking-related damage to the lens may be reversible, smoking cessation reduces the risk of cataract primarily by limiting total dose-related damage to the lens.

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also requested information on amount of cigarettes smoked for both current and past smokers. Subjects were asked, “When you smoke (or smoked), on average how many cigarettes per day do (did) you smoke (<1 pack per day, 1 pack per day, 1-2 packs per day, or ≥2 packs per day)?” Information on new occurrence of cataract and cataract extraction was ascertained on yearly follow-up questionnaires.

This investigation includes the 20907 participants who had no diagnosis of cataract and provided information about cigarette smoking at baseline. Following a report of a cataract diagnosis or extraction and receipt of written consent to obtain medical records pertaining to cataract, treating ophthalmologists or optometrists were contacted by mail to obtain information about presence of lens opacities, date of diagnosis, visual acuity loss, cataract extraction, other ocular abnormalities that could explain visual acuity loss, cataract type, and etiology.

End points were incident cataract and extraction of incident cataract. Cataract was defined as a self-report confirmed by medical record review initially diagnosed after randomization, age-related cataract in ever smokers. The significance of variables was tested using the likelihood ratio test. To calculate total cumulative dose, subjects were classified by pack-years of smoking. We used baseline data on amount smoked for current smokers and 60-month follow-up questionnaire data on amount smoked for past smokers (since information on amount smoked was collected only for current smokers at baseline) to calculate pack-years of smoking at baseline. We defined pack-years as the number of years of smoking times the number of packs of cigarettes smoked per day.

Cigarette smoking is associated with an increased risk of age-related macular degeneration (AMD) in this population, and subjects with cataract may have been identified because of presence of AMD. Therefore, we also conducted analyses in which we included diagnosis of AMD as a time-varying covariate. Relative risk (RR) estimates derived from these models, however, were not materially different from estimates derived from models that were unadjusted for diagnosis of AMD (data not shown).

RESULTS

At baseline, 11% of the study participants were current smokers, 39% were past smokers, and 50% were never smokers. Compared with current smokers, past smokers were older and, after adjusting for age, tended to report less alcohol use, diabetes, parental history of myocardial infarction, and multivitamin use, but more physical activity and past smokers were older and past smokers were intermediate between current and never smokers.

Table 1. Age-Adjusted Prevalence of Baseline Characteristics That Are Possible Risk Factors for Cataract by Smoking Status at Baseline, Physicians’ Health Study I

<table>
<thead>
<tr>
<th></th>
<th>Never Smokers (n = 10 444)</th>
<th>Past Smokers (n = 8 190)</th>
<th>Current Smokers (n = 2 273)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age range, %, y</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>40-49</td>
<td>48.0</td>
<td>36.4</td>
<td>41.7</td>
</tr>
<tr>
<td>50-59</td>
<td>32.1</td>
<td>37.0</td>
<td>37.4</td>
</tr>
<tr>
<td>60-69</td>
<td>15.5</td>
<td>20.5</td>
<td>17.2</td>
</tr>
<tr>
<td>70-84</td>
<td>4.4</td>
<td>6.1</td>
<td>3.7</td>
</tr>
<tr>
<td>Diabetes, %</td>
<td>2.1</td>
<td>2.2</td>
<td>2.7</td>
</tr>
<tr>
<td>Hypertension, %†</td>
<td>12.7</td>
<td>14.1</td>
<td>13.9</td>
</tr>
<tr>
<td>BMI, mean, kg/m²</td>
<td>24.8</td>
<td>25.1</td>
<td>25.1</td>
</tr>
<tr>
<td>Alcohol use, %</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Daily</td>
<td>17.6</td>
<td>29.5</td>
<td>34.5</td>
</tr>
<tr>
<td>Weekly</td>
<td>49.3</td>
<td>51.8</td>
<td>43.8</td>
</tr>
<tr>
<td>Monthly</td>
<td>12.6</td>
<td>9.5</td>
<td>11.1</td>
</tr>
<tr>
<td>Physical activity, %‡</td>
<td>73.4</td>
<td>73.2</td>
<td>64.2</td>
</tr>
<tr>
<td>Parental history of MI, %§</td>
<td>13.3</td>
<td>13.1</td>
<td>14.3</td>
</tr>
<tr>
<td>Multivitamin use, %</td>
<td>18.5</td>
<td>20.3</td>
<td>21.3</td>
</tr>
<tr>
<td>Smoking history</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pack-years, mean (SD)</td>
<td>...</td>
<td>20.5 (17.4)</td>
<td>35.8 (21.0)</td>
</tr>
<tr>
<td>Age at starting smoking, mean (5th-95th percentile), y</td>
<td>...</td>
<td>19 (14-26)</td>
<td>19 (14-29)</td>
</tr>
<tr>
<td>Age at quitting smoking, mean (5th-95th percentile), y</td>
<td>...</td>
<td>38 (23-56)</td>
<td>...</td>
</tr>
</tbody>
</table>

*BMI indicates body mass index; MI, myocardial infarction; and ellipses, data not applicable.
†Reported systolic blood pressure of 160 mm Hg or higher, diastolic blood pressure of 95 mm Hg or higher, or history of treatment for hypertension.
‡Reported vigorous exercise once per week or more.
§Reported MI in either parent before age 60 years.
Compared with men who continued to smoke, past smokers had a statistically significant 23% reduced risk of cataract diagnosis (RR, 0.77; 95% confidence interval [CI], 0.66-0.88) and 28% reduced risk of cataract extraction (RR, 0.72; 95% CI, 0.60-0.86), after adjustment for other risk factors for cataract. The RR in never smokers compared with men who continued to smoke was 0.64 (95% CI, 0.54-0.76) for cataract diagnosis and 0.65 (95% CI, 0.53-0.79) for cataract extraction.

Compared with men who continued to smoke, 10 years before study entry had an approximately 20% reduced risk of cataract diagnosis after adjustment for other cataract risk factors and average number of cigarettes smoked per day or age at starting smoking (Table 2). There was little additional reduction in risk in men who had quit less than 10 years before study entry. For cataract extraction, there was an approximately 25% reduced risk in men who had quit less than 10 years before study entry vs those who continued to smoke. Similarly, there appeared to be little additional reduction in risk in men who quit smoking 10 or more years before study entry. For both end points, risk of cataract in long-term quitters appeared to remain slightly (but not significantly) elevated compared with risk in never smokers.

When we examined the independent contributions of total cumulative dose and smoking status to risk of cataract among ever smokers, the best-fitting multivariate model included only a term for total cumulative dose (RR, 1.07; 95% CI, 1.04-1.10). Thus, there was a 7% increased risk of cataract associated with a 10-pack-year increase in smoking exposure. Addition of a 2-level categorical term for smoking status (past vs current, RR, 0.85; 95% CI, 0.73-1.00) was suggestive of an independent benefit associated with being a past smoker, but did not significantly improve the fit of the model based on the likelihood ratio test ($P = .08$). For cataract extraction, the best-fitting model did include a term for smoking status (past vs current, RR, 0.80; 95% CI, 0.65-0.97) in addition to a continuous term for total pack-years of smoking (for a 10-pack-year increase, RR, 1.05; 95% CI, 1.01-1.09), suggesting a benefit for past smokers that was independent of total cumulative dose. There were no significant interactions between smoking status and cumulative dose for either end point.

**COMMENT**

In this cohort of US male physicians, the risk of cataract in past smokers appeared to be intermediate between the risks in continuing smokers and never smokers. Compared with those who continued to smoke, a lower risk of cataract in past smokers was apparent in men who had quit smoking less than 10 years before study entry, with little additional reduction in risk associated with longer time since quitting smoking. The lower risk in past smokers was due primarily to their lower total cumulative dose of smoking, although there was evidence of a benefit of quitting smoking that was independent of cumulative dose, suggesting that some smoking-related damage in the lens may be reversible on smoking cessation.

Several previous studies have examined the risk of cataract in former smokers. A population-based, cross-sectional survey of 838 Maryland watermen indicated that the risk of pure nuclear opacities decreased during the first 10 years following smoking cessation and continued to decrease with longer time since quitting. In the Lens Opacities Case-Control Study, there was an increased risk of nuclear sclerosis among current smokers (RR, 1.7; 95% CI, 1.0-2.8), but none was reported for past smokers. The results of 2 other studies suggest that the risk of cataract....

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**Table 2. Relative Risks of Cataract Diagnosis and Extraction by Years Since Quitting Smoking**

<table>
<thead>
<tr>
<th>Past Smokers, Years Since Quitting Smoking</th>
<th>Current Smokers (n = 2272)</th>
<th>Never Smokers (n = 10450)</th>
<th>&lt;10 (n = 1640)</th>
<th>10 to &lt;20 (n = 2795)</th>
<th>≥20 (n = 2541)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cataract Diagnosis</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of cases†</td>
<td>250</td>
<td>868</td>
<td>149</td>
<td>261</td>
<td>450</td>
</tr>
<tr>
<td>Age- and treatment-adjusted RR (95% CI)</td>
<td>1.00</td>
<td>0.66 (0.57-0.76)</td>
<td>0.83 (0.68-1.02)</td>
<td>0.77 (0.65-0.92)</td>
<td>0.79 (0.67-0.92)</td>
</tr>
<tr>
<td>Multivariate RR (95% CI)‡</td>
<td>1.00</td>
<td>0.67 (0.58-0.77)</td>
<td>0.81 (0.66-1.00)</td>
<td>0.75 (0.63-0.90)</td>
<td>0.79 (0.67-0.92)</td>
</tr>
<tr>
<td>Multivariate RR (95% CI)§</td>
<td>1.00</td>
<td>0.64 (0.54-0.76)</td>
<td>0.79 (0.64-0.98)</td>
<td>0.73 (0.61-0.88)</td>
<td>0.74 (0.63-0.87)</td>
</tr>
<tr>
<td><strong>Cataract Extraction</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of cases†</td>
<td>155</td>
<td>507</td>
<td>85</td>
<td>152</td>
<td>243</td>
</tr>
<tr>
<td>Age- and treatment-adjusted RR (95% CI)</td>
<td>1.00</td>
<td>0.64 (0.54-0.77)</td>
<td>0.78 (0.60-1.02)</td>
<td>0.74 (0.59-0.93)</td>
<td>0.73 (0.59-0.89)</td>
</tr>
<tr>
<td>Multivariate RR (95% CI)‡</td>
<td>1.00</td>
<td>0.66 (0.54-0.79)</td>
<td>0.76 (0.58-0.99)</td>
<td>0.72 (0.57-0.91)</td>
<td>0.73 (0.59-0.90)</td>
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<td>Multivariate RR (95% CI)§</td>
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<td>0.75 (0.57-0.98)</td>
<td>0.70 (0.56-0.88)</td>
<td>0.69 (0.56-0.85)</td>
</tr>
</tbody>
</table>

*RR indicates relative risk; CI, confidence interval.
†Ninety-six cases of cataract diagnosis and 51 cases of cataract extraction were excluded because of missing information on age at starting smoking, age at quitting smoking, or number of cigarettes smoked.
‡Cox regression models adjusted for age, aspirin and β-carotene treatment assignment, diabetes, hypertension, body mass index, alcohol use, physical activity, parental history of myocardial infarction, current multivitamin use, and number of cigarettes smoked (<20/d, 20/d, >20/d to 40/d, or >40/d).
§Cox regression models adjusted for covariates in the above footnote, with age at starting smoking in place of number of cigarettes smoked.
cigarettes Case-Control Study: risk factors for cataract. 

Several possible limitations of the study should be considered. The prospective study design reduces the possibility of bias in reports of cigarette smoking or other potential risk factors according to disease outcome. Random misclassification of cigarette exposure is a possibility, but would tend to underestimate any true association between cigarette smoking and cataract. Random misclassification of cataract would also underestimate any true effect of smoking, but was minimized by the use of medical records to confirm the self-reports. Nonrandom misclassification of cataract is unlikely since medical records were reviewed without knowledge of participants’ exposure status. Morbidity follow-up was more than 99% complete (through December 1997) and medical records were obtained for 92% to 94% of current, past, and never smokers who reported cataract. Thus, bias due to incomplete follow-up is not likely to distort these results.

Mechanisms linking cigarette smoking and cataract have been described, including a direct effect on the lens, as well as indirect effects on antioxidant levels and levels of endogenous proteolytic enzymes, thought to be important for removal of damaged protein from the lens. Stopping smoking may alleviate further direct damage to lens proteins and, perhaps, allow reversal of some of the early deleterious effects of smoking.

Cataract is a leading cause of visual impairment in the United States and represents a major drain on health care resources. Approximately 1.35 million cataract operations are performed yearly in the United States at an estimated cost of $3.5 billion. Given these considerations, recognition that smoking is an important, avoidable cause of age-related cataract can be expected to have major public health implications. The data presented extend previous findings by demonstrating that smoking cessation reduces the risk of cataract primarily by limiting total smoking-related damage to the lens. The data also indicate that some damage in the lens may not be reversed with smoking cessation, underscoring the importance of early cessation of smoking and, preferably, the avoidance of smoking altogether.

**Funding/Support:** This study was supported by research grants HL 26490, HL 34959, CA 34944, CA 40360, and EY 06633 from the National Institutes of Health.

**REFERENCES**


21. Taylor A, Davies KJA. Protein oxidation and loss of protein from the lens.21 Stopping smoking may alleviate further direct damage to lens proteins and, perhaps, allow reversal of some of the early deleterious effects of smoking.

Our findings in the Physicians’ Health Study I are in broad agreement with previous studies that indicate a reduced risk of cataract in past smokers compared with current smokers, due primarily to lower total cumulative dose in past smokers. We found no evidence to indicate that even the most heavily exposed men in our population did not benefit from smoking cessation.

However, our data show that compared with men who have never smoked, past smokers appear to have a slightly elevated risk of cataract that may persist for years following smoking cessation.

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