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Smoking and Risk of All-cause Deaths in Younger and Older Adults

A Population-based Prospective Cohort Study Among Beijing Adults in China

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Abstract: Cigarette smoking is the leading preventable cause of death worldwide. Few studies, however, have examined the modified effects of age on the association between smoking and all-cause mortality.

In the current study, the authors estimated the association between smoking and age-specific mortality in adults from Beijing, China. This is a large community-based prospective cohort study comprising of 6209 Beijing adults (aged ≥40 years) studied for approximately 8 years (1991–1999). Hazard ratios (HRs) and attributable fractions associated with smoking were estimated by Cox proportional hazard models, adjusting for age, sex, alcohol intake, body mass index, systolic blood pressure, hypertension, and heart rate.

The results showed, compared with nonsmokers, the multivariable-adjusted HRs for all-cause mortality were 2.7(95% confidence interval (CI):1.56–4.69) in young adult smokers (40–50 years) and 1.31 (95% CI: 1.13–1.52) in old smokers (>50 years); and the interaction term between smoking and age was significant ($P = 0.026$). Attributable fractions for all-cause mortality in young and old adults were 63% (95% CI: 41%–85%) and 24% (95% CI: 12%–36%), respectively. The authors estimated multivariate adjusted absolute risk (mortality) by Poisson regression and calculated risk differences and 95% CI by bootstrap estimation. Mortality differences (/10,000 person-years) were 15.99 (95% CI: 15.34–16.64) in the young and 74.61(68.57–80.65) in the old. Compared with current smokers, the HRs of all-cause deaths for former smokers in younger and older adults were 0.57 (95% CI: 0.23–1.42) and 0.96 (95% CI: 0.73–1.26), respectively.

The results indicate smoking significantly increases the risks of all-cause mortality in both young and old Beijing adults from the relative and absolute risk perspectives. Smoking cessation could also reduce the excess risk of mortality caused by continuing smoking in younger adults compared with older individuals.

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Abbreviations: AF = attributable fraction, CHD = coronary heart disease, CI = confidence interval, HR = Hazard ratio, RR = relative risk.

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INTRODUCTION

Cigarette smoking is the leading preventable cause of death worldwide.[1–6] There are a huge number of smokers in China. Two national surveys, conducted in 2002 and 2010, show the prevalence of current smoking in China was 57.4% and 52.9% in men and 2.6% and 2.4% in women, respectively.[7,8] Smoking cessation has been proved to be helpful in preventing various diseases, for example, cardiovascular disease, respiratory disease, cancer as well as premature death.[9–12] It, however, is difficult to carry it out in practice. Young adults, at low absolute risk for deaths, are more likely to consider smoking to be a less harmful risk factor that does not cause disease until later in life. In elderly people, a few studies suggested that the smoking-associated relative risk for some diseases, such as coronary heart disease (CHD), attenuated with aging.[13–15] These findings could erroneously suggest that smoking is only a weak risk factor for the elderly people and that smoking prevention should therefore be of low priority in the elderly, considering "quality-of-life issues outweigh the net gain in health."

One recent study, focusing on smoking and risk of CHD in different age groups, showed that the majority of CHD cases are attributable to smoking in all age groups.[16] The risk of death associated with smoking in different age group, however, are rarely investigated. Our study aims to investigate the risk of smoking for all-cause deaths in young and old smokers in a cohort study of Chinese male and female adults. This is of importance for advocating smoking cessation in different age groups.

MATERIALS AND METHODS

Study Participants

In the 1991 China National Hypertension Survey, a multistage random cluster sampling design was used to select a representative sample of the general Chinese population aged 15 years or older from all 30 provinces in mainland China.[17] In this investigation, the participants were selected from the National Hypertension Survey in Beijing City, China. Of these, 7601 subjects who were ≥40 years old were scheduled for follow-up 2 times in 1996 and 1999 by trained staff. In this study, we excluded

326 subjects who had a history of CHD (heart infarction, angina pectoris, or revascularization) or stroke in 1991. A total of 1066 individuals who failed to follow-up were also excluded. A total of 6209 individuals with a mean follow-up of 8.3 years were left for analysis.

Baseline Examination

Trained staff interviewed participants in Beijing of China using a standard questionnaire to obtain information on demographic characteristics, medical history and life style risk factors.[17] The individuals were classified as smokers (current or former) and nonsmokers. "Current smokers" were defined as those who smoked at least 100 cigarettes in their lifetime and reported smoking every day or someday in the 3 months before the baseline visit. "Former smokers" were defined as those who reported having smoked at least 100 cigarettes during their lifetime but had given up smoking for more than three months at the time of investigation. "Ever smokers ", that is, smokers, included both current and former smokers. "Never smokers" were respondents with a lifetime smoking history of fewer than 100 cigarettes, and or a report of "never smoking." Alcohol consumption was defined as drinking alcohol at least 12 times during the last year before baseline investigation and the rest were classified as no drinking. Body weight and height were measured using standard methods. Body mass index was calculated as weight in kilograms divided by the square of height in meters (kg/m^2). After at least 10 minutes of rest in sitting position, blood pressure and heart rate were measured. Three blood pressure measurements were taken for each participant whereas participants were seated using a mercury sphygmomanometer according to a standard protocol. The mean of these 3 blood pressure measurements was used for data analysis. Resting heart rates were measured by palpating the radial pulse during a period of 15 seconds with a stop watch and multiplying by 4. If the pulse was irregular or difficult to count, the test was extended to 60 seconds and a stethoscope was used at the apex of the heart to count for a 60-second interval if necessary. Hypertension was defined as systolic blood pressure more than 140 mm Hg or diastolic blood pressure more than 90 mm Hg or taking antihypertensive drugs.

Follow-up and End Points

The follow-up examination, which was conducted in 1996 and 1999, respectively, included tracking study participants or their proxies to a current address, performing in-depth interviews to ascertain disease status and vital information, and obtaining hospital records and death certificates. The methods of outcome ascertainment were as follows: all participants and families of the deceased or other witness of the fatal events were invited to interview with the trained staff. If the invitees did not respond, the trained staff would visit the home or workplace of the participants to get information on morbidity and vital status, including cause of death. For those whose information could not be obtained by the aforementioned ways, messages were sent through telephone calls or by mail. For any deceased participants, the cause of death was ascertained by reviewing hospital charts or documents at a local Administrative Office, supplemented by interviews with local physicians, families or witness of the fatal event. An end point assessment committee reviewed and confirmed (or rejected) the hospital discharge diagnosis and cause of death based on the abstracted information, using pre-established criteria.

The primary outcome of interest for this study was death from all causes. Causes of death were coded according to the International Classification of Diseases, Ninth Revision. This study was approved by the Tulane University Health Sciences Center Institutional Review Board and the Cardiovascular Institute and Fu Wai Hospital Ethics Committee. Written informed consent was obtained from all study participants at their follow-up visit.

Statistical Analyses

Study participants were grouped into 2 age categories at the baseline examination (40–50 years old (n = 1838) and >50 years old (n = 4371)). In each group, the participants were also divided into smokers and nonsmokers. To address the benefit of smoking cessation, the participants were also divided into current smoking, former smoking, and nonsmoking groups. Given fewer subjects in younger subgroups based on this grouping, those who are younger than 60 years old (40–60) were classified as younger adults and the rest (>60 years) were termed older when former smoking group was considered. Continuous variables are shown as means (standard difference). Categorical variables are shown as counts and percentages. The cumulative risk of events in each group was estimated using Kaplan–Meier survival curves and compared by log-rank test. Cox proportional hazards models were used to compute the hazard ratio (HR) and adjust for important confounding factors. We examined whether age modified the smoking-deaths association using standard tests of interaction. The interaction P-value was based on the 2-category smoking and age variables as defined above. Multivariate adjusted absolute risk (mortality) was calculated by Poisson regression. We also calculated risk differences and derived 95% CIs by bootstrap estimation (1000 replications), with the 2.5 and 97.5 percentiles of the distribution as lower and upper limits.[16] The attributable fractions (AF) among current smokers was calculated based on the following formula: $AF = (HR - 1)/HR$, where HR is the hazard ratio for all-cause deaths among smokers relative to never smokers,[18] and 95% confidence intervals (CIs) were derived by bootstrap estimation(1000 replications) as used above. The data was analyzed separately for 2 age groups: 40 to 50 years, and >50 years. No interaction was found between smoking and sex on all-cause deaths; therefore, we did not analyze the data separately by sex strata.

The potential influence of preclinical disease was evaluated at baseline by excluding cases that occurred during first year of follow-up. All analyses were performed by using Stata 12.0 (StataCorp LP, College Station, Texas, USA), with 2-tailed t tests at the significance level of 0.05.

RESULTS

The mean follow-up period of this investigation was 8.3 years (51,835 person-years). There were 840 all-cause deaths. The overall death rate was 16.2 (95% CI: 15.1–17.3) per 1000 person-years. For smokers and never smokers, overall death rate was 20.3(95% CI: 18.3–22.4) and 13.9 (95% CI: 12.7–15.2) per 1000 person-years, respectively. A significant difference was observed between these 2 groups ($P < 0.001$). The death risks for smokers were significantly higher compared with never smokers in both the younger and older groups (Table 1).

Baseline characteristics of the study participants according to categories of age and smoking status are presented in Table 1. Compared with nonsmokers, smokers were more likely to be men with a higher alcohol consumption, lower body mass index, and higher heart rate.

TABLE 1. Baseline Characteristics of Study Participants According to Age and Smoking Status

	Age 40–50 Years			Age >50 Years		
Variables	**Smokers (N = 577)**	**Nonsmokers (N = 1261)**	***P* Value**	**Smokers (N = 1695)**	**Nonsmokers (N = 2676)**	***P* Value**
Age (SD), y	45.2 (3.2)	44.9 (3.2)	0.18	62.4 (7.8)	62.7 (8.5)	0.28
Male, %	88	23	<0.001	65.4	29.8	<0.001
SBP (SD),mm Hg	123.9 (18.5)	121.5(19.5)	0.01	137.2 (24.5)	137.8 (24.6)	0.37
DBP (SD),mm Hg	80.5 (11.8)	77.6 (11.5)	<0.001	79.6 (12.2)	79.6 (11.9)	0.88
Hypertension, %	31	30.7	0.89	51.4	54	0.10
Alcohol drinking,%	50.4	6.1	<0.001	39.4	7.5	<0.001
BMI(SD), kg/m^2	23.4 (3.1)	24.0 (3.5)	<0.001	23.3 (3.9)	24.3 (4.0)	<0.001
Heart rate(SD),beats/min	77.2 (8.9)	75.6 (9.9)	0.02	77.3 (10.8)	76.5 (12.4)	0.03
All-cause Deaths, per 1000 person-years (95% CI)	5.6 (3.9–8.1)	2.1 (1.4–3.1)	<0.001	25.7 (23.1–28.5)	19.9 (18.1–21.8)	<0.001

BMI = body mass index, CI = confidence interval, DBP = diastolic blood pressure, SBP = systolic blood pressure, SD = standard difference.

As shown by Kaplan–Meier curves (Figure 1), the associations of smoking with all-cause deaths in young individuals (Figure 1A) were stronger than that in the elderly group (Figure 1B), that is, the hazards ratios with smoking were higher in young individuals as compared with elderly.

We estimated multivariate-adjusted HRs, AFs and mortality differences of all-cause mortality in 2 age groups (40–50, and >50 years). After adjustment for age and other risk factors, the HRs for all-cause deaths remained higher in younger individuals (HR: 2.7, 95% CI 1.6–4.7) than that in the elderly (HR:1.3,95% CI 1.1–1.5). Significant interactions were detected between smoking and age on all-cause deaths ($p = 0.026$). The mortality-attributable factors among smokers were also higher in younger participants (63%; 95% CI: 41%, 85%) than that in elderly (24%; 95% CI: 12%, 36%). In contrast, the mortality differences (per 10,000 person-years) was higher in the older participants (74.6, 95% CI: 68.6–80.7) than younger (16.0, 95% CI: 15.3–16.6. Table 2).

After excluding study participants who died during the first year of follow-up, there is still a significant interaction between smoking and age on all-cause deaths ($P = 0.03$). The adjusted HRs, AFs, and mortality differences of all-cause mortality in 2 age groups are similar to the whole cohort of participants (Table 2).

Table 3 shows, compared with current smokers, the risk (HRs) of all-cause deaths for former smokers tended to decline in both younger and older adults, with a more remarkable decline found in younger individuals.

DISCUSSION

In this population-based prospective cohort study in Beijing City, the capital of China, we found that the HRs and AFs of all-cause mortality in smokers, relative to never smokers, were higher in younger participants than that in the elderly. A significant interaction was detected between smoking and age on all-cause mortality risk. In spite of this, we also found the mortality difference of all-cause mortality was higher in the elderly, compared with the young participants. This conclusion is reinforced by the analysis of outcomes in participants who survived more than 1 year. In addition, our investigation indicated that smoking cessation could reduce the greater risk mortality caused by continuing smoking in younger adults compared with older individuals.

These results have important public health implications. First, given the higher HRs and AFs of all-cause mortality in smokers, relative to never smokers, in young participants and greater risk decline found in younger adults who quitting smoking, our investigation suggests smoking is more harmful in young adults relative to older adults and earlier smoking cessation could bring about greater benefits. This finding does not support the popular belief that smoking-related disease or

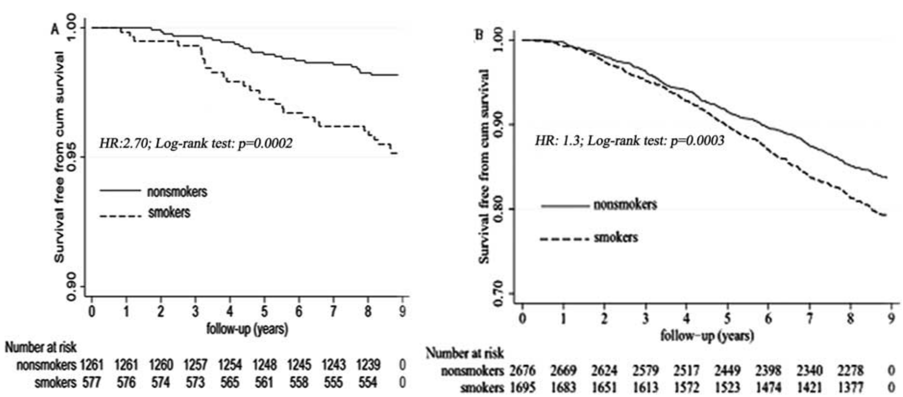

FIGURE 1. Survival plot indicating survival free from all-cause mortality among younger (A: 40–50 years) and older (>50 years) participants.

TABLE 2. Multivariate-Adjusted Hazard Ratios, Attributable Fractions and Mortality Differences of All-Cause Mortality in Smokers Relative to Nonsmokers According to 2 Age Groups (Total Cohort Participants or Excluding Participants Who Died During the First Year of Follow-up)

	Age 40–50 Years (N = 1838)	Age >50 Years (N = 4371)	P Interaction
Total cohort participants			
HR (95% CI)	2.7 (1.6–4.7)	1.3 (1.1–1.5)	0.026
AF (95% CI)	63.0% (40.6%–85.4%)	23.6% (11.5%–35.7%)	
Mortality difference/10,000 (95% CI)	16.0 (15.3–16.6)	74.6 (68.6–80.7)	
Excluding study participants who died during the first year of follow-up			
HR (95% CI)	2.5 (1.5–4.4)	1.3 (1.1–1.5)	0.03
AF (95% CI)	44.6% (4.8%–84.5%)	22.4% (9.7%–35.1%)	
Mortality difference/10,000 (95% CI)	14.7 (14.1–15.3)	68.6 (63.1–74.2)	

AF = attributable fraction, HR = hazard ratio, CI = confidence interval and P interaction are from a Cox proportional hazards model and a Poisson regression with bootstrap estimation, adjusted for age, sex, alcohol intake, body mass index, systolic blood pressure, hypertension, and heart rate.

deaths do not occur until old age. Though the HRs and AFs, however, are lower in the elderly, the mortality difference, that is, the absolute risk, is higher in these people. From the public health perspective, absolute risks have more important health implications. Taken together, these results suggest smoking prevention should be taken seriously in young adults as well as in the elderly.

Age has been proposed as an effect modifier of the association between smoking and CHD in several epidemiological studies.[13–16] The modified effect of age on the association between smoking and all-cause mortality, however, has rarely been investigated. Our results regarding the effect of smoking on all-cause mortality according to age are similar to the results of previous studies on the effect of smoking on CHD according to age,[14,16] that is, the relative risks and AFs of smoking in young adults is higher compared with the elderly; in contrast, the absolute risk of smoking in older is higher. Larsen et al[14] enrolled 6892 patients who underwent primary percutaneous coronary intervention (PCI) for ST-segment elevation myocardial infarction and compared the age-specific smoking rates for these patients with that of the general population. They found that the overall odds ratios for smoking in the ST-segment elevation myocardial infarction population compared with the general population increased as age declined. Tolstrup et al[16] reported that compared with never smokers, CHD risk was highest for youngest current smokers and lowest for the oldest smokers, and as for the absolute risk differences between current smokers and never smokers, the largest one was observed among the oldest participants.

Our findings show that, compared with current smokers, the risk of all-cause deaths for former smokers tended toward greater decline in younger adults than elderly. These results are also in accord with previous evidence.[19,20] One prospective study,[19] which enrolled 34,439 British male doctors and studied for 50 years, suggests smoking cessation at age 50 halved the hazard of mortality, and cessation at age 30 avoided almost all of it. Another prospective investigation[20] of 1.2 million UK women indicated that stopping smoking before age 40 years could help to avoid more than 90% of the excess mortality caused by continuing smoking; stopping before age 30 years avoid more than 97% of it. The fact that the decline in risk did not reach statistical significance in our investigation may be attributed to insufficient sample size of subgroups and mixing different smoking cessation duration in our study.

Our findings were strengthened by the large sample size of the general Beijing adult population, the longer prospective design and larger numbers of hard primary outcomes of interest, which provided information on the sequence of events and convincing results.

LIMITATIONS

There were a few limitations in our investigation worth mentioning. First, although we excluded cardiovascular disease

TABLE 3. Multivariate-Adjusted Hazard Ratios of All-Cause Mortality in Former Smokers and Never Smokers, Relative to Current Smokers, According to 2 Age Groups

		Age 40–60 Years					Age >60 Years				
	N	N	HR (95% CI)*	P*	HR (95% CI)†	P†	N	HR (95% CI)*	P*	HR (95% CI)†	P†
Current smokers§	1953	1249	–	–	–	–	704	–	–	–	–
Former smokers	319	113	0.57 (0.23–1.42)	0.23	0.57 (0.23–1.42)	0.23	206	0.89 (0.68–1.17	0.42	0.96 (0.73–1.26)	0.77
Never smokers	3937	2543	0.71 (0.51–1.0)	0.05	0.66 (0.48–0.89)	0.007	1394	0.67 (0.56–0.80)	<0.001	0.73 (0.61–0.87)	<0.001

HR = hazard ratio), 95% CI = confidence interval, and P value are from a Cox proportional hazards model.
* Adjusted for age and sex.
† Adjusted for age, sex, alcohol intake, body mass index, systolic blood pressure, hypertension, and he art rate.
§ Reference group.

at baseline, we did not remove other potential diseases, which may confound the association between smoking and all-cause deaths. To eliminate the potential influence of preclinical disease, we excluded those who died during first follow-up year and found that the results were similar to those derived from the whole population. Second, there was a small number of women, especially young women, who smoked in our investigation. This may be the reason that we did not find the interaction between smoking and sex on deaths and precluded us to further analyze the population based on sex strata. Third, the follow-up rate of our study (85.3%) was relatively low. The main reason for failure to follow-up in our study, however, was participants moving away from Beijing City, especially going abroad. The baseline characteristics between those who lost and who did not were comparable except that the former were younger. These may not modify the association between smoking and all-cause deaths. Fourth, we only assessed smoking status at baseline. Nevertheless, the participants could have changed their smoking behavior during follow-up, which would likely result in an inexact assessment of the relation between smoking and mortality outcomes. Another limitation is the absence of data regarding the differences of disease characteristics and life style in the 1990s and nowadays, which to some extent may limit the possibility to extrapolate the results to current practice. The smoking pattern in China, however, has changed little in the last 3 decades. The 4 national smoking surveys in China showed that the current smoking prevalence decreased mildly from 33.88% in 1984 to 28.1% in 2010 for adults aged 15 years or older.[21] In a population-based survey performed in Beijing in 2006, which enrolled 3214 subjects with an age of 40+ years, 1042 participants (32.4%) were current smokers or former smokers.[22] In contrast, in our survey conducted in Beijing for similar aged groups in 1991, the prevalence of current or former smoking is 36.6%. This shows, like the national smoking pattern, the prevalence of smoking in Beijing has also changed little in recent decades. Therefore, the etiological linkage such as HRs from Beijing survey data collected during 1990s can be used to get some implications for tobacco control of the current Beijing population. In addition, we focused on the association between smoking and all-cause deaths in this study. The difference between smoking patterns or disease characteristics may have less effect on their associations. Finally, unmeasured confounds such as passive smoking maybe existed in current study, which could result in overestimation of the association between smoking and mortality outcomes.

In conclusion, our study indicates that smoking significantly increases the risk of all-cause mortality in both young and old Chinese adults from the relative and absolute risk perspectives. Smoking cessation could reduce the greater risk of the excess mortality caused by continuing smoking in younger adults compared with older individuals. This important public health finding adds to the voluminous data on the hazardous effects of smoking.

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