·Clinical Research·

Cigarette smoking, body mass index associated with the risks of age-related cataract in male patients in northeast China

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Abstract

• AIM: To determine the association between cigarettes smoking, body mass index (BMI) and the risk of age-related cataract (ARC) in middle-aged and elderly men in Northeast China.

• METHODS: A hospital-based case control study was conducted. Cases (n =362) were men who had surgically treated ARC, 45-85 years old; controls frequency-matched (n= 362) were men who had been admitted to the same hospital as cases for other diseases not related with eye diseases. Cases and controls were matched with 1:1. The cases and controls were interviewed during their hospital stay, using a structured interviewer-administrated questionnaire that included information on sociodemographic characteristics, socioeconomic, lifestyle habits (tobacco smoking and alcohol consumption, *etc.*), anthropometric measures, personal medical history, and family history of ARC in first-degree relatives, and simultaneously BMI was calculated. The odds ratios (OR) and 95% confidence intervals (CI) of ARC were estimated using multiple logistic regression models.

• RESULTS: After adjusting for age and multiple potential confounders, higher BMI was associated with an increased risk of ARC. Cigarette smoking, years smoking or moderate cigarette smoking (1-29 cigarettes per day) had no relation with the risk of ARC (P>0.05), although patients smoking ≥ 30 cigarettes per day had an elevated risk of ARC as compared with the non-smokers (OR=1.55, 95% CI; 1.16-2.85, P=0.026). Higher BMI was associated with an increased risk of ARC. Both overweight and obesity was associated with an obviously increased risk for surgically ARC (OR=1.55, 95% CI:1.02-1.98, P=0.015 and OR=1.71, 95% CI:1.32-2.39, P=0.013 respectively) compared to normal BMI. Then participants were grouped into quartiles of BMI (Q1 to Q4), compared to controls in the lowest quartile, the OR for cases in the highest quartile of BMI was 1.54 (OR=1.54, 95% CI: 1.08-2.46, P=0.022). The results of univariate analysis showed cigarette smoking was not associated with ARC formation for men with lower or normal BMI (P>0.05). Compared to the non-smokers, for men of overweight or obesity, cigarette smoking was associated with a significantly increased risk for surgically ARC (OR=2.00, 95% CI: 1.49-6.65, P=0.003 and OR=1.66, 95% CI: 1.63-13.21, P= 0.002 respectively). Similarly, smokers in the highest quartile of BMI had approximately 1.5 times the risk of ARC as non-smokers in the lowest quartile (OR =1.46, 95% CI: 1.06-5.29, P<0.001). Followed multivariate models revealed that the association had never changed.

• CONCLUSION: Current cigarette smoking is positively related to ARC only among those who smoking 30 or more cigarettes per day. For men who are both overweight and obesity, cigarette smoking is associated with a significantly increased risk for ARC.

• KEYWORDS: age-related cataract; male; smoking; body mass index; risk
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INTRODUCTION

Age-related cataract (ARC) is a common eye disease in middle aged and elderly men, which is characterized by lens opacities and visual impairment due to the oxidation of lens proteins and degenerative changes to the lens caused by aging [1,2]. Visual impairment and blindness from cataract is an important public health problem throughout the world. Age-related cataract accounts for about half of the 32 million cases of blindness worldwide. Despite its high prevalence and cost, very little is known about its etiology and there are no established risk factors. The incidence of cataract extraction increases with age. Other recognized risk factors are ultraviolet radiation exposure, genetic factors, supplement use and selected drugs [3-5], whereas the epidemiological evidence is still controversial for smoking, alcohol consumption, obesity, body mass index (BMI) and other lifestyle habits [6-8]. However, these data have mainly been derived from white population in the United States [7], Europe [9], and Australia [10]. Few have been conducted in urban environments that are representative of the major population trends in Asia [11]. Furthermore, there are no studies among persons of general China, the largest racial/ethnic group in Asia. China has the most elderly population in the world, the number of ≥60 years old people accounting for 1/5 of the world and 50% of Asia. Up to date, a valid study has not yet been performed in Northeast China, Where smoking and alcohol consumption is very common among men, thus a case-control study was conducted to examine the relationship of cigarettes smoking and BMI with the risk of ARC in middle-aged men and elderly.

MATERIALS AND METHODS

Materials Totally 362 males aged 45-85 years old (patient group), who were surgically treated between December 2009 and July 2011, were selected from the Department of ophthalmic ward Surgery of the First Affiliated Hospital and Third Affiliated Hospital of Liaoning Medical College, Jinzhou Central Hospital and Jinzhou Second People's Hospital. Inclusive criteria: (1) Males above 45 years old; (2)At least one eye was diagnosed with cortical, nuclear, and posterior sub capsular or mixed cataract based on slit-lamp photos; (3)vision of the eye with cataract loss to 0.3 or worse; (4)intraocular pressure(IOP): 10-21mmHg. Meanwhile, 362 male inpatients frequency-matched with diseases irrelative to the risk factors of age-related cataract or others eye diseases which lead to decreased vision were selected from the above hospitals as the control group. The controls were 45-85 years of age with an average of 69 years old. Controls were patients who had been admitted to the same hospital for diseases not related with cataract, with no lens opacities in either eye and with good visual acuity. Controls were excluded if they had medical conditions and treatments known to be related to cataract or affect vision (e.g. age-related macular degeneration, diabetic retinopathy, glaucoma, or acute or chronic uveitis). Participants were selected strictly based on the inclusive and exclusive criteria, and there was no bias in selecting subjects. Cases and controls were matched with 1:1; informed contents were obtained from all the enrolled subjects. All of the 724 participants were involved in the analysis of results. The odds ratios (OR) and 95% confidence intervals (CI) of ARC were estimated using multiple logistic regression models. The hospital-based case control study was conducted by the Department of Preventive Medicine in Liaoning Medical College and had approval from the Liaoning Medical College, First Affiliated Hospital and Third Affiliated Hospital of Liaoning Medical College. Consent for participation was obtained from the subjects and relatives to commencement of the survey, and informed, oral consent was obtained from all willing participants.

Methods

Data collection The cases and controls were interviewed during their hospital stay, using a standardized structured interviewer-administrated questionnaire that included information on sociodemographic characteristics, socio-economic, lifestyle habits (tobacco smoking and alcohol consumption, *etc.*), anthropometric measures, personal medical history, and family history of ARC in first-degree relatives. Height and weight were measured according to unified standards. Height and weight were measured with participants wearing lightweight clothing with no shoes, and simultaneously body mass index (BMI) was calculated. Participants were grouped into quartiles of BMI (Q1 to Q4). Factors included in the multivariate logistic regression models were those for which distributions varied both by disease status and by those that are risk factors for ARC in this population, *i.e.* age, years of education (<7, 7-11, and ≥12), occupation (worker, peasant, intellectual and others), place of residence, household income, hypertension and diabetes history and cigarette smoking status, years smoked, number of cigarettes smoked per day, smoking status in males with different BMI, BMI and quartiles of BMI.

Definitions Data on severity of cataracts using slit-lamp biomicroscope, as graded by lens opacity classification system (LOCSIII), were collected through ophthalmologists for the entire study population. Any cataract was defined as a nuclear, cortical or posterior subcapsular cataract in at least one eye. All participants were asked to report whether they had smoked 20 packs of cigarettes or more in their lifetimes and, if yes, they were smokers, on the contrary they were non-smokers [12]. Besides this, all participants were asked whether they currently smoke or had smoked in the past. Based on usual number of cigarettes reported in the questionnaire, men were categorized as never smoke, 1-19, 20-29 and >30 cigarettes per day. Based on duration of smoking, the participants were further classified as never smoke, 1-19, 20-29 and ≥ 30 years. Body mass index (BMI) was assessed from measured body mass and body height, and the standards of BMI in adults in China was 18.50-23.99 for normal, 24.00-27.99 for overweight and ≥28.0 for obesity, then the participants were further classified as BMI <18.50, 18.50-23.99, 24.00-27.99 and ≥28.0 subgroups respectively.

Statistical Analysis All the data were summed up, checked and input to establish database by the second author, then processed using SPSS Version 13.0 software. Univariate and multivariate logistic regression models were constructed to investigate odds ratios (OR) and corresponding 95% confidence intervals (CI) for ARC and association with smoking consumption and BMI. Factors included in the multivariate logistic regression models were those for which distributions varied both by disease status and by those that

Table 1 Distribution of the general states of the subjects in both groups (*n*, %)

Characteristics	Cases	Controls	χ^2	*P*
Age (a)			2.486	0.993
≥60	273(75.41)	269(74.31)		
<60	89(24.59)	93(25.69)		
Occupation			3.125	0.473
Workers	141(38.95)	145(40.06)		
Peasants	67(18.51)	69(19.06)		
Intellectuals	108(29.83)	99(27.35)		
Others	46(12.71)	49(13.53)		
Education (a)			2.361	0.329
<7	153(42.27)	132(36.46)		
7-11	155(42.82)	169(46.69)		
≥11	54(14.91)	61(16.85)		
Place of residence			2.872	0.315
City	251(69.34)	255(70.43)		
Rural	55(15.19)	43(11.89)		
Others	56(15.47)	64(17.68)		
Diabetes	130(36.54)	92(27.31)	6.797	0.022
Hypertension	104(28.08)	55(15.00)	14.125	<0.001
Household income per month (RMB)			1.352	0.177
<1000	11(3.04)	10(2.76)		
1000-	204(56.35)	205(56.63)		
2000-	78(21.55)	75(20.72)		
≥3000	69(19.06)	72(19.89)		

are risk factors for ARC in this population, *i.e.* age, years of education (<7, 7-11, and ≥12), occupation (worker, peasant, intellectual and others), place of residence, household income, hypertension and diabetes history and cigarette smoking status. These independent variables had a prior evidence or biological plausibility as a predictor of ARC. Each variable was specified prior to analysis as nominal, categorical or continuous according to the form most commonly used in other studies or according to the form that would allow the most robust statistical analysis. Univariate models accounted for age, following which a multivariate models was constructed using significant univariate predictors ($P<0.05$). A final multivariate analysis was also done including all variables. The relationship between the investigated factors and ARC were analyzed with the Mantel-Haenszel chi-square method; the significance of differences in smoking and BMI among groups was examined using a two-sample *t* test. To determine whether the association between smoking consumption and ARC risk varied by level of obesity, we entered a series of indicator terms for cross-categories of BMI [quartiles of weight (in kg) divided by height squared (in m)] and smoking consumption in the multivariate logistic regression models. *OR*, 95% CI and *P* value*s* were reported. All *P* values were two-side and were considered statistically significant when the values were <0.05.

RESULTS

Form the sampling process, there were 724 eligible participants, respectively, a total of 362 cases aged 45-85 (mean age: 69.43±11.77) years old in the patient group and 362 cases aged 45-85 (mean age: 69.44±11.65) years old in the control group were involved in the analysis of results.

Demographic information on participants (including the distributions of age, education, occupation, place of residence and household income and personal diseases history) was shown in Table 1. There were no noticeable differences in age, years of education, occupation, place of residence and household income between the two groups ($P>0.05$). The results showed that there were more hypertension (28.08%) and diabetes patients (36.54%) in the patient group than in the control group (15.00% and 27.31%), after adjusted by age, the risk of ARC was higher in hypertension males than in the control group ($\chi^2=14.125$, $P<0.01$).

The distributions of smoking states, number of cigarettes smoked per day, or years smoked and BMI between the two groups, and the relationship between these factors and the development of ARC were shown in Table 2. Within this population, 67.14% in cases group and 66.30% in controls group were smokers. After adjusting for age, the results did not show any significant association between smoking states, number of cigarettes smoked per day, years smoked and ARC formation. With the increased number of cigarettes smoked per day, those currently smoked ≥30 cigarettes per day had an elevated risk of ARC as compared with the non-smokers (*OR*=1.55, 95% CI 1.16-2.85, $P=0.026$).Then

Table 2 The association between smoking status, BMI and age-related cataract in two groups

Variable	Cases	Controls	Age-adjusted		Multiple confounders-adjusted	
	n (%)	*n* (%)	*OR* (95% CI)	*P*	*OR* (95% CI)	*P*
Smoking history						
No	119(32.87)	122(33.70)	1.00		1.00	
Yes	243(67.13)	240(66.30)	1.04(0.84-1.92)	0.560	0.94(0.69-1.37)	0.716
Ever smokers	95(26.24)	103(28.45)	0.95(0.61-1.38)	0.801	1.12(0.93-2.31)	0.614
Current smokers	148(40.88)	137(37.85)	1.11(0.89-2.36)	0.709	1.04(0.78-1.89)	0.538
Number of cigarettes smoked per day						
0	99(27.35)	102(28.33)	1.00		1.00	
1-	75(20.72)	90(24.86)	0.86(0.69-1.37)	0.557	0.90(0.53-1.76)	0.715
20-	80(22.10)	98(27.07)	0.84(0.54-1.28)	0.224	0.84(0.50-1.39)	0.652
⩾30	108(29.83)	72(19.89)	1.55(1.16-2.85)	0.026	2.05(1.72-4.82)	0.001
Years smoked(a)						
0	99(27.35)	102(28.18)	1.00		1.00	
1-	71(19.61)	77(21.27)	0.95(0.57-1.46)	0.788	0.83(0.49-1.14)	0.641
20-	83(22.93)	89(24.59)	0.96(0.71-1.61)	0.855	0.98(0.77-1.63)	0.914
⩾30	109(30.11)	94(25.96)	1.19(0.96-2.14)	0.147	1.03(0.82-1.81)	0.290
BMI(kg/m^2)						
<18.5	54(14.92)	58(16.02)	1.34(1.03-1.64)	0.019	1.93(1.25-1.62)	0.031
18.5-	50(13.81)	73(20.17)	1.00		1.00	
24.0-	120(33.15)	113(31.22)	1.55(1.02-1.98)	0.015	1.52(1.29-2.23)	0.024
⩾28	138(38.12)	118(32.59)	1.71(1.32-2.39)	0.013	1.89(1.47-2.88)	0.015
Quartile of BMI						
Q1 (16.96-21.16)	65(17.96)	84(23.21)	1.00		1.00	
Q2 (21.17-22.86)	89(24.58)	100(27.62)	1.15(0.74-1.69)	0.719	1.13(0.74-1.72)	0.566
Q3 (22.87-25.10)	103(28.45)	90(24.86)	1.48(0.98-2.33)	0.264	0.96(0.58-1.67)	0.813
Q4 (25.11-32.18)	105(29.01)	88(24.31)	1.54(1.08-2.46)	0.022	2.21(1.12-3.77)	0.001

adjusting for multiple potential confounders, the results revealed there was also significant association between severely smoking (smoked ≥ 30 cigarettes per day) and the risk of ARC (*OR*=2.05, 95% CI: 1.72-4.82, *P*=0.001).

In the results of analysis which after only adjusted for age, higher BMI was associated with an increased risk of ARC. Lower BMI, overweight and obesity were all associated with a obviously increased risk for surgically ARC (*OR*=1.34, 95% CI: 1.03-1.64, *P*=0.019, *OR*=1.55, 95% CI: 1.02-1.98, *P*=0.015 and *OR*=1.71, 95% CI: 1.32-2.39, *P*=0.013 respectively) compared to normal BMI. Multivariate analysis suggested that the results had no changed (*OR*=1.93, 95% CI: 1.25-1.62, *P*=0.031, *OR*=1.52, 95% CI: 1.29-2.23, *P*=0.024 and *OR*=1.89,95% CI: 1.47-2.88,*P*=0.015 respectively).

Then participants were grouped into quartiles of BMI (Q1 to Q4), after adjusted by age and multiple potential confounders, the results consistently showed that the highest quartile of BMI was significantly associated with ARC formation compared to controls in the lowest quartile(Q4 *vs* Q1 *OR* 1.54, 95% CI: 1.08-2.46, *P*=0.022 and *OR* 2.21, 95% CI: 1.12-3.77, *P*=0.001).

Univariate analysis suggested that the relationship between smoking status and ARC was different among males with different BMI. Smoking had no noticeable correlation with ARC in males who had a low BMI (<18.50) and normal BMI (18.50-23.99). However, as BMI (24.0-27.9 and ⩾28.0) increased, smoking was associated with a significantly increased risk for surgically treated ARC (*OR*=2.00, 95% CI: 1.49-6.65, *P*=0.003 and *OR*=1.66, 95% CI: 1.63-13.21, *P*=0.002 respectively). Similarly, smokers in the highest quartile of BMI (25.11-32.18) had approximately 1.5 times the risk of ARC as non-smokers (*OR*=1.46, 95% CI: 1.06-5.29, *P* <0.001). Final multivariate analysis also supported the results of univariate analysis (*OR*=2.89, 95% CI: 1.35-3.16, *P*=0.002) (Table 3).

DISCUSSION

The case-control study comprised of 362 patients with ARC and 362 controls was conducted to explore the relationship of smoking and BMI with the risk of ARC. Because the patients and controls were matched with 1:1, there were no noticeable differences in demographic characteristics between the two groups, such as age, years of education, occupation, place of residence and household income. The factor of personal diseases history was not matched, so our results showed that the hypertension and diabetes male patients had a negative correlation with risk of ARC, which

Table 3 Relationship between smoking states and ARC in males with different body mass index (BMI)

BMI(kg/m^2)	Smoking	Cases *n* (%)	Controls *n* (%)	Age-adjusted		Multiple confounders-adjusted	
				OR(95%CI)	*P*	*OR*(95%CI)	*P*
<18.5	No	23(6.35)	21(5.80)	1.00		1.00	
	Yes	13(3.59)	13(3.59)	0.91(0.24-3.29)	0.874	0.64(0.46-1.75)	0.745
18.5-	No	144(39.78)	156(43.09)	1.00		1.00	
	Yes	40(11.05)	32(8.84)	1.35(0.95-2.42)	0.672	1.07(0.76-1.98)	0.156
24.0-	No	54(14.92)	72(19.89)	1.00		1.00	
	Yes	51(14.09)	34(9.39)	2.00(1.49-6.65)	0.003	1.91(1.26-2.91)	0.002
≥28.0	No	16(4.42)	19(5.25)	1.00		1.00	
	Yes	21(5.80)	15(4.15)	1.66(1.63-13.21)	0.002	2.74(1.70-4.23)	0.001
Quartile of BMI							
Q1 (16.96-21.16)	No	11(3.04)	10(2.76)	1.00		1.00	
	Yes	14(3.87)	14(3.87)	0.91(0.52-1.31)	0.794	0.93(0.55-1.62)	0.801
Q2(21.17-22.86)	No	63(17.40)	62(17.13)	1.00		1.00	
	Yes	163(45.03)	171(47.24)	0.94(0.66-1.85)	0.801	1.02(0.58-2.29)	0.709
Q3(22.87-25.10)	No	37(10.22)	43(11.88)	1.00		1.00	
	Yes	48(13.26)	35(9.67)	1.59(0.94-3.61)	0.433	1.24(0.57-2.63)	0.290
Q4 (25.11-32.18)	No	12(3.31)	15(4.14)	1.00		1.00	
	Yes	14(3.87)	12(3.31)	1.46(1.06-5.29)	<0.001	2.89(1.35-3.16)	0.002

demonstrated that keeping normal blood pressure and fasting plasma glucose concentration was good to our health, our findings were agreed with previous studies[13,14].

The association between smoking states and ARC in both groups was discussed in our study. Our finding showed that, smoking, number of cigarettes smoked per day, or years smoked had no relation with the risk of ARC. With the increased number of cigarettes smoked per day, those currently smoked ≥30 cigarettes per day had an elevated risk of ARC as compared with the non-smokers. These results showed that severe smoking elevated the risk of ARC largely, which might be important in the development of ARC, suggests that smoking is one of the relatively few known modifiable factors associated with cataract. Suggested mechanisms by which smoking might damage the lens include an increase in oxidative stress caused by a lowering of circulating nutrients with antioxidant capabilities[15, 16] or lens damage from by-products of smoke, such as cadmium or isocyanate.

The relationships between BMI and ARC have been consistent in epidemiologic studies. Our results indicated that higher BMI was associated with an increased risk of ARC. BMI is strongly correlated with fat mass, making it a useful measure of overall obesity. In our data, after adjustment for potentially confounding variables, obese men had an elevated risk of cataract. Dates from previous prospective investigations are consistent with this observation [17]. Our results also indicated that after adjusted by age and multiple potential confounders, the relationship between smoking status and ARC was different among males with different BMI. Smoking had no noticeable correlation with ARC in males who had a low BMI (<18.50) and normal BMI (18.50-23.99). However, as BMI (24.0-27.99 and ≥28.0) increased, smoking was associated with a significantly increased risk for surgically treated ARC.

There are plausible biological pathways through which obesity might cause earlier development of cataract. Obesity is a risk factor for increased serum uric acid concentrations and gout, factors related to increased risk of cataract [18]. Overweight individuals also have higher amounts of systemic inflammation, which may also be a risk factor for cataract [19]. Last, abdominal adiposity is a strong risk factor for glucose intolerance and insulin resistance, conditions closely related to development of type 2 diabetes and high blood pressure. Diabetes causes earlier cataract formation, possibly through several pathways [20], and at least some laboratory [21, 22] and epidemiologic studies[14, 23, 24] suggested a relation of blood pressure with cataract.

In our study, patients and controls were selected strictly based on the inclusive and exclusive criteria, and there was no bias in selecting subjects. Hospital controls may differ from the general population, but they also had a greater response rate and were less prone to recall bias compared with population-based controls.

Furthermore, the questionnaire was submitted to both patients and controls from the same recruitment areas by the same interviewers and under similar conditions, thus limiting the potential sources of information bias. In addition, the hospital has complete medical equipments, and the questionnaires were proved to be authentic and highly reproducible. All these provide reassurance against information bias. In order to avoid confounding bias, the patients and controls were matched with 1:1. That is, when selecting subjects, each patient was matched with a control under the same condition of age, race or ethnicity and occupation et al. which could be relevant to the risk factors of ARC. In the analysis to outcomes, we applied strata of age, so as to compare the relationship of smoking states, BMI and risks of ARC between the two groups. In this way, the confounding bias could also be avoided.

Potential limitations of our study must also be considered. Although detailed information on a multitude of potential confounders may explain the observed association. Being retrospective, there are inherent limitations in the study. Our case-control study is based on the inherent assumption that patients who are not undergoing cataract surgery do not have cataract. It is possible that some patients had cataract, which had no clinical effect or which did not undergo operation as a result of other different reasons. This may be a potential confounder. However, as the study population is relatively homogeny demographically, we believe that the results were not influenced significantly.

In conclusion, our results showed that heavy smoker, higher BMI might be risk factors of the development of ARC. For men who were both overweight and obesity, cigarette smoking was the significantly reasons for ARC. Quitting smoking consumption or reducing the number of cigarettes smoked per day as much as possible, keeping healthy well-balanced diet and moderate activity, then maintaining normal body mass and blood pressure, through reducing BMI to cut down the risk of ARC. Because it was not possible to determine whether the studied factors we found caused ARC. It will be particularly important to study the relationship between these factors and ARC in a prospective manner, which could not only identify our results but also provide a rationale for effective medical or preventive interventions targeted toward high risk groups of ARC.

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