

Joint Effect of Alcohol use and Tobacco Smoke on All-Cause Mortality and Premature Death in China: A Cohort Study

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Abstract

Background Tobacco smoke and alcohol use were associated with several diseases, study on joint effect of smoke and drink was rare.

Objective This study aims to investigate the joint effect of tobacco smoke and alcohol use on all-cause mortality and premature death in a contemporary cohort.

Methods China Health and Retirement Longitudinal Study (CHARLS) was an ongoing nationally representative survey for subjects aged over 45 years in China, which performed every 2 years for total of 3 waves from 2011 to 2015 in China. We used weighted logistic regression model to estimate the joint effect of tobacco smoke and alcohol use on total mortality and premature death.

Results After adjusting for the confounders, the odd ratios (ORs) value of all-cause mortality were 1.47 (95%CI: 1.03–2.08) and 1.51 (95%CI: 1.09–2.10) in smoker and non-drinker and smoker and drinker separately. Compared with non-smoker and non-drinker, smoker and drinker increased the odds of premature death by 3.14 (95%CI: 1.56–6.34). In the subgroup analysis, there was a 5-fold (OR = 4.95; 95%CI: 2.00-12.27) increase in the odds of premature death for female smoker and drinker.

Conclusion This study found a joint effect of tobacco smoke and alcohol use on all-cause mortality and premature death among a contemporary and nationally representative data in China. Our results suggested the joint effect was more pronounced in women, but further research was needed.

Introduction

Tobacco smoke is a well-established risk factors for many diseases including stroke, coronary heart disease (1). Additionally, several studies including the British Doctors Study (2), the American Cancer Society Cancer Prevention Study (3) and pooled analysis of Asia cohorts(4) have shown the increased risk of mortality from tobacco smoke. It has been reported that tobacco smoke is the second leading risk factor for death from any cause worldwide (5, 6) and was the leading cause of death among Chinese men(7).

Alcohol use is another leading risk factor for death and disability (8). Although some studies reported J-shaped association between alcohol use and all-cause mortality, which suggested that low alcohol use may confer some degree of protection(9, 10), this view was challenged by recent studies which use of mendelian randomization and meta-analyses (8, 11, 12). These protective associations between moderate alcohol and health may, however, be explained by the effect of biases (e.g., study design, confounders, selection of participants) (12, 13).

Although the effect of tobacco smoke and alcohol use on death has been well documented separately, studies on the joint effect of these two leading risk factors on deaths or early death were still rare.

Therefore, the aim of this study was to estimate the joint effect of tobacco smoke and alcohol use on all-cause mortality and premature death using a Chinese nationally representative cohort data.

Methods

Study population

Data for this study was drawn from the national baseline and follow up database of the China Health and Retirement Longitudinal Study (CHARLS). The first baseline survey of this study was conducted in 2011–2012, which involved 17 708 subjects. The details of study design for CHARLS has been reported previously (14, 15). In general, it is an ongoing nationally representative survey, which performed every 2 years for total of 3 waves from 2011 to 2015 in China. Adults aged 45 years or older living in China were enrolled in baseline survey, and been followed up in waves 2, 3 and 4. Subjects were chosen with a multi-stage stratified sampling design in 450 villages, 150 counties and 28 provinces to ensure the representativeness of the sample and can be weighted to obtain national estimates.

Data Collection And Variable Definition

Each subject was administered a survey interview which include the information on date of birth, gender, educational level (illiterate, Primary, Secondary/High School, College/University or above), marital status (Married/ Divorced/ Widowed, Unmarried), residence status (Rural, Urban), tobacco smoking habits, alcohol consumption, height and weight, medicine usage and medical history. Blood was also taken for laboratory testing. We defined the history of cardiovascular (CVD) if subjects reported having history of stroke, heart failure or CHD. Overweight was defined as $24 \text{ kg/m}^2 \leq \text{BMI} < 28 \text{ kg/m}^2$ and Obesity were defined as $\text{BMI} \geq 28 \text{ kg/m}^2$. Blood pressure was measured by Omron model HEM-7200. The SBP and DBP were calculated by averaging available 3 blood pressure measurements (approximately 45 s apart) for each subject. We defined hypertension as a SBP of 140 mm Hg or more, or a DBP of 90 mm Hg or more, or self-reported use of antihypertensive treatment. Diabetes was defined as hemoglobin A_{1c} $\geq 6.5\%$, use of anti-diabetic medication, or self-reported history of diabetes. Dyslipidemia was defined as use of dyslipidemia medication or having one of the following conditions: total cholesterol $\geq 6.19 \text{ mmol/L}$, low density lipoprotein cholesterol $\geq 4.14 \text{ mmol/L}$, or triglyceride $\geq 2.27 \text{ mmol/L}$. Subjects are classified as tobacco smoker if he/she had ever smoker more 100 cigarettes in their life. An alcohol drinker was defined as a participant drinking alcoholic beverages at least once a month. participants were further divided into four groups: non-smoker/non-drinker, non-smoker/drinker, smoker/non-drinker, smoker/drinker.

Interviewees' status (dead or alive) were recorded in each wave however, death date were only recorded in wave 2 (2013 follow-up). We calculated the age of death from the interval between the date of birth and the death date. In our current analysis, we defined premature death according to the average life

expectancies in China in 2011, which was before age 72.7 years in men and 76.9 years in women (16). Detailed information about the data quality management has been estimated previously (17).

Statistical analysis

Summary statistics for the baseline characteristics and risk factors by gender were computed as the proportions or means, and compared across different smoke and drink status groups by using ANOVA or chi-square test. The joint effect of tobacco smoke and alcohol use on total mortality and premature death were estimated using weighted logistic regression model. Unadjusted and adjusted odds ratios (ORs) and their 95% CIs were obtained. The multivariable model was adjusted for gender, age, educational level, current residence status, marital status, hypertension, dyslipidemia, diabetes, history of CVD, overweight or obesity. All reported *P* values were 2-tailed, and values of $\alpha < 0.05$ were considered statistically significant. Analysis was performed with the Stata software version 15.0 (Stata Corporation).

Results

In this present study, we excluded 3.5% (628/17708) participants, because of the missing values in age/gender ($n = 495$), tobacco smoke ($n = 126$), alcohol use ($n = 7$). Therefore, the remaining 17080 participants are eligible for inclusion in the present analysis. We found that 26.8% (4583/17080) of participants were both cigarette smokers and alcohol drinkers with a substantially higher prevalence in male subjects (52.7% [4391/8332] in men and 2.19% [192/8748] in women). The mean age of participants among different smoke and drink groups were range from 50.3 to 60.9 years, most participants were from rural area and married. The prevalence of overweight or obesity was higher in non-smoker/non-drinker group. The prevalence of other cardiovascular related risk factors (hypertension, dyslipidemia, diabetes, history of CVD) was similar among four different smoke and drink groups (Table 1).

Table 1
Baseline characteristics among different smoke and drink groups, by sex

	Non-smoker/Non-drinker	Non-smoker/Drinker	Smoker/Non-Drinker	Smoker/Drinker	<i>P</i>
All participants					
Number of subjects	8029	2159	2309	4583	
Age(years)	50.30 (10.06)	59.26 (9.83)	60.89 (10.03)	59.57 (9.37)	< 0.001
Age group					< 0.001
<50	1798 (22.39)	483 (22.37)	395 (17.11)	868 (18.94)	
50–59	2885 (35.93)	754 (34.92)	795 (34.43)	1714 (37.40)	
60–69	2077 (25.87)	599 (27.74)	636 (27.54)	1321 (28.82)	
70–79	954 (11.88)	247 (11.44)	392 (16.98)	555 (12.11)	
≥ 80	315 (3.92)	76 (3.52)	91 (3.94)	125 (2.73)	
Middle school education (%)	2109 (26.32)	669 (31.00)	738 (31.99)	1752 (38.28)	
Rural (%)	6236 (77.75)	1656 (76.74)	1839 (79.71)	3603 (78.65)	0.064
Married (%)	6838 (85.17)	1896 (87.86)	1966 (85.15)	4152 (90.60)	< 0.001
Hypertension (%)	3159 (39.34)	834 (38.63)	810 (35.08)	1764 (38.49)	0.003
Dyslipidemia (%)	2630 (32.76)	659 (30.52)	770 (33.35)	1359 (29.65)	0.001
Diabetes (%)	653 (8.13)	178 (8.24)	167 (7.23)	288 (6.28)	0.001
Overweight or obesity (%)*	2886 (46.29)	712 (42.61)	588 (32.15)	1118 (31.98)	< 0.001
History of CVD (%)	1211 (15.08)	271 (12.55)	333 (14.42)	556 (12.13)	< 0.001
Male					
Number of subjects	1091	1083	1767	4391	
Age(years)	61.42 (10.47)	59.20 (9.96)	60.17 (9.75)	59.37 (9.26)	< 0.001
Age group					< 0.001

	Non-smoker/Non-drinker	Non-smoker/Drinker	Smoker/Non-Drinker	Smoker/Drinker	<i>P</i>
<50	198 (18.15)	253 (23.36)	319 (18.05)	855 (19.47)	
50–59	332 (30.43)	367 (33.89)	638 (36.11)	1655 (37.69)	
60–69	308 (28.23)	299 (27.61)	490 (27.73)	1254 (28.56)	
70–79	202 (18.52)	124 (11.45)	264 (14.94)	517 (11.77)	
≥ 80	51 (4.67)	40 (3.69)	56 (3.17)	110 (2.51)	
Middle school education (%)	428 (39.34)	460 (42.51)	668 (37.83)	1724 (39.32)	< 0.001
Rural (%)	777 (71.22)	772 (71.35)	1390 (78.75)	3441 (78.38)	< 0.001
Married (%)	978 (89.64)	1003(92.70)	1563(88.46)	4008(91.28)	< 0.001
Hypertension (%)	402 (36.85)	425 (39.24)	570 (32.26)	1671 (38.06)	< 0.001
Dyslipidemia (%)	356 (32.63)	333 (30.75)	573 (32.43)	1300 (29.61)	0.077
Diabetes (%)	76 (6.97)	95 (8.77)	116 (6.56)	275 (6.26)	0.031
Overweight or obesity (%)*	300 (38.56)	342 (42.59)	408 (29.76)	1058 (31.63)	< 0.001
History of CVD (%)	139 (12.74)	143 (13.20)	197 (11.15)	511 (11.64)	0.292
Female					
Number of subjects	6938	1076	542	192	
Age(years)	58.97 (9.96)	59.32 (9.70)	63.22 (10.56)	64.30 (10.49)	< 0.001
Age group					< 0.001
<50	1600 (23.06)	230 (21.38)	76 (14.02)	13 (6.77)	
50–59	2553 (36.80)	387 (35.97)	157 (28.97)	59 (30.73)	
60–69	1769 (25.50)	300 (27.88)	146 (26.94)	67 (34.90)	
70–79	752 (10.84)	123 (11.43)	128 (23.62)	38 (19.79)	
≥ 80	264 (3.81)	36 (3.35)	35 (6.46)	15 (7.81)	

	Non-smoker/Non-drinker	Non-smoker/Drinker	Smoker/Non-Drinker	Smoker/Drinker	P
Middle school education (%)	1681 (24.27)	209 (19.42)	70 (12.94)	28 (14.58)	< 0.001
Rural (%)	5459 (78.77)	884 (82.16)	449 (82.84)	162 (84.82)	0.003
Married (%)	5860 (84.46)	893 (82.99)	403 (74.35)	144 (75.00)	< 0.001
Hypertension (%)	2757 (39.74)	409 (38.01)	240 (44.28)	93 (48.44)	0.008
Dyslipidemia (%)	2274 (32.78)	326 (30.30)	197 (36.35)	59 (30.73)	0.092
Diabetes (%)	577 (8.32)	83 (7.71)	51 (9.41)	13 (6.77)	0.582
Overweight or obesity (%)*	2586 (47.39)	370 (42.63)	180 (39.30)	60 (39.74)	< 0.001
History of CVD (%)	1072 (15.45)	128 (11.90)	136 (25.09)	45 (23.44)	< 0.001
*missing N = 2035 for male and N = 1814 for female					

Table 2 shows the joint effect of smoke and drink on all-cause mortality. Generally, the odds of all-cause mortality was higher in smoker/non-drinker group (Unadjusted analysis: OR = 1.28; 95%CI: 1.06–1.54). Similar result was found in subgroup analysis, there was a 2.4-fold (Unadjusted analysis: OR = 2.34; 95%CI: 1.60–3.43) increase in the odds of all-cause mortality for smoker/non-drinker in female. The odds of all-cause mortality was higher in smoker/drinker, smoker/drinker increased the odds of all-cause mortality with an OR value equal to 1.75 (95%CI: 1.39–2.19, unadjusted analysis). The subgroup analysis in female, the OR value was 3.14 (95%CI: 1.82–5.14, unadjusted analysis). In multivariable regression, after controlling for the confounders, the associations remained significant. The ORs value of all-cause mortality were 1.47 (95%CI: 1.03–2.08) and 1.51 (95%CI: 1.09–2.10) in smoker/non-drinker and smoker/drinker separately. In the subgroup analysis, the smoker/non-drinker (OR = 1.56; 95%CI: 0.99–2.44) and smoker/drinker (OR = 2.02; 95%CI: 0.95–4.30) in female increased odds of all-cause mortality compared with non-smoker/non-drinker in female. Although the associations were not significant after controlling for confounders, the lower limits of 95%CI were pretty close to 1.

Table 2
Odds ratio of all-cause mortality among different smoke and drink group, by sex

	Non-smoker/Non-drinker	Non-smoker/Drinker	Smoker/Non-Drinker	Smoker/Drinker
All participants				
Unadjusted	1.00	0.99 (0.62, 1.56)	1.28 (1.06, 1.54)	1.75 (1.39, 2.19)
Adjusted*	1.00	1.06 (0.61, 1.86)	1.47 (1.03, 2.08)	1.51 (1.09, 2.10)
Male				
Unadjusted	1.00	0.78 (0.37, 1.65)	0.83 (0.60, 1.15)	1.11 (0.77, 1.61)
Adjusted*	1.00	1.18 (0.50, 2.80)	1.42 (0.96, 2.10)	1.46 (0.94, 2.26)
Female				
Unadjusted	1.00	0.89 (0.57, 1.37)	2.34 (1.60, 3.43)	3.14 (1.82, 5.41)
Adjusted*	1.00	0.87 (0.50, 1.50)	1.56 (0.99, 2.44)	2.02 (0.95, 4.30)
*Adjusted variables includes gender, age, middle school education, residence status, marital status, hypertension, dyslipidemia, diabetes, history of CVD, overweight or obesity.				

Compared with non-smoker and non-drinker, smoker/drinker increased the odds of premature death in unadjusted analysis (OR = 2.12; 95%CI: 1.46–3.08). After controlling for confounders, the OR value was 3.14 (95%CI: 1.56–6.34). The odds of premature death was 2.2-fold (Adjusted analysis: OR = 2.17; 95%CI: 1.11–4.22) higher in smoker/non-drinker. In unadjusted analysis, the OR of premature death in smoker/non-drinker was 1.49 (95%CI: 0.90–2.45). In the subgroup analysis, there was a 5-fold (Unadjusted analysis: OR = 5.36; 95%CI: 2.32–12.36; Adjusted analysis: OR = 4.95; 95%CI: 2.00–12.27) increase in the odds of premature death for female smoker/drinker. The odds of all-mortality and premature death were similar and not significant between non-smoker/non-drinker group and non-smoker/drinker group. (Table 2, Table 3)

Table 3
Odds ratio of premature death among different smoke and drink groups, by sex¹

	Non-smoker/Non-drinker	Non-smoker/Drinker	Smoker/Non-Drinker	Smoker/Drinker
All participants				
Unadjusted	1.00	0.84 (0.48, 1.46)	1.49 (0.90, 2.45)	2.12 (1.46, 3.08)
Adjusted ²	1.00	1.11 (0.57, 2.15)	2.17 (1.11, 4.22)	3.14 (1.56, 6.34)
Male				
Unadjusted	1.00	0.29 (0.11, 0.83)	0.69 (0.28, 1.68)	1.01 (0.46, 2.22)
Adjusted ²	1.00	0.50 (0.17, 1.47)	1.17 (0.46, 2.93)	1.57 (0.71, 3.47)
Female				
Unadjusted	1.00	1.31 (0.66, 2.61)	2.20 (0.99, 4.89)	5.36 (2.32, 12.36)
Adjusted ²	1.00	1.25 (0.59, 2.66)	2.01 (0.83, 4.83)	4.95 (2.00, 12.27)
¹ Premature death defined as mortality before age 72.7 years in men and 76.9 years in women, which were the average life expectancies in China in 2011. however, Age of death can only be estimated among CHALS 2013 follow up.				
² Adjusted variables include gender, age, middle school education, residence status, marital status, hypertension, dyslipidemia, diabetes, history of CVD, overweight or obesity.				

Discussion

In our present analysis, we found that alcohol consumption could strengthen the harmful effect from cigarette smoking. Our estimate indicate that compared with the nonsmoker and non-smoker, those who both smoke and drink could have 75% higher risk of death or 112% more likely to die early. We have also indicated that women are likely to have higher risk of all-cause mortality or premature death from the combine effect of tobacco smoke and drink use than men.

Alcohol use has been reported to increase risk of all-cause mortality; however this is generally found to be varied by the amount consumed with a U or J shape being reported. This usually indicated as a lower overall mortality among subject with light to moderate drinking while a higher rate of death among those heavy drinkers(9, 10). However, A study from a large cohort showed that the beneficial effect from the light and moderate alcohol use was offset by cigarette smoke and the risk of total mortality increase with

the smoking intensity from 0.8 (95% CI: 0.6, 1.0) for non-smoker to 1.0 (0.9, 1.2) for moderate smokers and 1.4 (95% CI: 1.2, 1.7) for heavy smokers(18). The negative combined effect from smoking and drinking was also reported in other studies(19, 20). Our study was consistent with these findings in general and found that the highest risk was observed among those who both smoke and drink alcohol.

Premature death of a middle-aged person is often devastating to a household and is often associated with decreased income, and mortality in the affected families. Identification of the associated risk is crucial to health planning and policy development(21). In our study, we also tried to explore the adverse association of this synergy effect of cigarette smoking and alcohol consumption with premature death. Consistent with the results for all-cause mortality, we found that, compared with non-smoker and non-drinker, smoker and drinker was significantly associated with early death, despite of the non-significance among subgroup by gender due to the small sample size.

It is noteworthy that the gender difference was found in both all-cause mortality and premature death. It has been noted that women smokers and/or drinker are more likely to have greater mortality risk. This phenomena has been reported in previous publications(1, 4, 9, 19, 22, 23) assessing smoking or drink risk, even among those with existing diseases, such as diabetes (24). The mechanisms underlying the sex difference in mortality may be attribute to their biological or related to differences in smoking behaviour between men and women. It seems that men are likely to be exposed more risks than women, which may confer the risk from smoke or drink use. This can be told from our data. In our study, we found that 52.7% of men were both cigarette smokers and alcohol drinkers, whereas, only 2.19% was found in women.

Several limitations of the study should be mentioned. First, due to the limited information from this public database, further analysis by drink amount or the cause of death, such as CVD mortality or cancer mortality are not available. Several studies have shown that the effect of alcohol consumption on mortality is generally found to depend on the amount consumed and presented differently by cause-specific mortality. However, this was argued by other studies suggesting that the nonlinear relationship is explained by the study design or selected bias across age-sex strata(11, 12). Second, this study is an ongoing study and the follow-up period is relative short. Thus, the statistical power is limited for subgroup analysis by gender. Third, as date of death was only released for data of 2013 follow-up survey, information on age of death and premature death can only be obtained for this survey.

In summary, our present analysis indicated that alcohol consumption could further increase the risk of total death or premature death from smoking. Further studies are needed to confirm the higher risk of death from joint effect of smoking and drink among female population.

Declarations

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Contributors: HZ and XB did the analysis and drafted the initial manuscript. NZ and CL critically reviewed and revised the manuscript. KY critically reviewed the results of analyses, and reviewed and revised the manuscript. All authors were responsible for the study concept and design and approved the final draft of the manuscript. KY is the guarantor. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

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