

# Habitual Tea Drinking is Associated with Reduced Odds of Restrictive Spirometry Pattern in Non-smokers

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## Research

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# Abstract

## Background

Restrictive spirometry pattern (RSP) is found to be associated with an increased risk of all-cause and cardiovascular mortality. This study was aimed to examination of the association between tea consumption and RSP in smokers and non-smokers.

## Methods

A total of 14,997 eligible subjects were analyzed after excluding individuals with (1) age <20 years, (2) a history of asthma, lung cancer, tuberculosis, or any chest structural deformities, or (3) a history of connective tissue diseases. RSP was defined as FVC<80% of the predicted value and an FEV1/FVC ratio  $\geq 70\%$ . One traditional Chinese teapot containing 120ml was defined as one “cup.” Habitual tea consumption was defined as 120mL/d or more for at least 1 year. To evaluate the effects of cumulative dosage of tea over time, the variable “cup-year” was obtained by multiplying the number of daily cups of tea by the number of years one has consumed.

## Results

The amount of daily tea consumption and the prevalence of habitual tea drinking were significantly higher in the non-RSP group ( $65 \pm 191$  vs.  $110 \pm 242$  mL,  $p < 0.001$ ; 15.1% vs. 24.0%,  $p < 0.001$ ). In multiple logistic regression, habitual tea drinker (OR = 0.75, CI 0.63-0.89,  $p < 0.01$ ) and tea consumption no less than 3 cup-year (OR = 0.74, CI 0.61-0.89,  $p < 0.01$ ) were associated with a lower risk of RSP in non-smoking group while the association was insignificant in the smoking group.

## Conclusion

Habitual tea drinking and tea consumption of at least three cup-years were associated with a reduced risk of RSP in the non-smokers, but not in the smokers.

## Background

Pulmonary disorders, such as low forced vital capacity (FVC), forced expiratory volume in 1 second (FEV1), and FEV1/FVC are significant predictors of all-cause mortality [1]. Among these pulmonary impairments, obstructive lung diseases are the most well-recognized and contribute to most of the morbidity and mortality related to pulmonary impairments [2]. Restrictive spirometry pattern (RSP), which features with reduced FVC in the absence of airflow obstruction, has been shown to be as prevalent as chronic obstructive pulmonary disease (COPD) [3] as well as to be related to higher risks of all-cause and cardiovascular mortality [4, 5]. Multiple clinical factors have been associated with RSP, including age, female sex, white race, lower education, abdominal obesity [6], ex- and current smoking [7], low physical activity level [8] and comorbidities including diabetes [9, 10], metabolic syndrome [11, 12], hypertension

[10], stroke [13] and cardiovascular disease [14]. Careful management of these clinical conditions may be one way to prevent RSP.

Tea is a worldwide popular beverage, and tea consumption has been shown to lead to a reduced risk of cardiovascular disease, hypertension, diabetes, and lung cancer [15-18]. Twice daily tea consumption at a minimum has been found to be related to a lower risk of COPD [19]. As for subjects with COPD, smokers, especially those smoking over 20 pack-years, have been shown to have a higher prevalence of RSP compared with non-smokers [7]. However, little is known about the influence of tea consumption on RSP. Smoking has an impact on COPD and RSP, but the study of tea on lung function has been limited in non-smokers. This study was aimed toward an investigation of whether tea consumption is associated with RSP in adults based on smoking status.

## Methods

### Subjects

This study recruited 19,637 participants, aged 20 years or more, who underwent a health examination at National Cheng Kung University Hospital from October 2001 to August 2009. Subjects with 1) a history of asthma, lung cancer, tuberculosis, or any pulmonary structural deformities; 2) connective tissue diseases such as rheumatoid arthritis, systemic lupus erythematosus, ankylosing spondylitis; 3) associated clinical missing data were excluded. Finally, a total of 14,997 subjects (8,805 men and 6,192 women) with ages ranging from 20 to 97 years were included in the analysis. Consent from the participants were waived as all data was obtained anonymously and it did not include any personal identification information. The study protocol was approved by the Ethical Committee for Human Research at the National Cheng Kung University Hospital institutional review board, Taiwan (IRB number: B-ER-108-131).

The baseline data included medical history, medication, smoking status, alcohol use, exercise habit, and tea consumption. Cigarette smoking was calculated in pack-years by multiplying the number of packs of cigarettes smoked per day by the number of years the person has smoked. Subjects who smoked more than one pack of cigarettes per day for half a year were defined as currently smoking. Exercising for at least three times a week was defined as regular exercise. The questions for tea consumption included (1) Have you drunk tea habitually once a week for at least six months? (2) How much (in milliliters) tea do you drink each day? (3) How many times do you drink tea in one week? (4) How many years have you been drinking tea in this way? Different examples of tea containers were provided to assist participants to recall the amount of tea consumption. For example, there were traditional Chinese teapot (120 mL), mug (250 mL), aluminum foil packed tea (300 mL), canned tea (350 mL) and bottled tea (600ml). Tea consumption of 120mL per day or more for at least 1 year was defined as a habitual tea drinker [20]. To obtain the average of tea consumption per day, we multiplied the amount of tea consumed per day and the frequency per week according to the records in the questionnaire. The product was divided by seven to yield the final result.

Overweight was defined as body mass index (BMI) of 24 - 26.9 kg/ m<sup>2</sup> and obesity was defined as BMI  $\geq$  27 kg/m<sup>2</sup> based on the definition by the Department of Health in Taiwan [21]. Hypertension was defined as having a documented history of hypertension, records of currently using anti-hypertensive agents or blood pressure  $\geq$  140/90 mmHg measured with an automatic blood pressure monitor in a supine position after resting at least five minutes. Cerebrovascular disease was defined by a documented history of cerebrovascular disease or transient ischemic attack.

All subjects had blood tests after 12 hours of fasting for fasting plasma glucose, hemoglobin A1c, creatinine, total cholesterol (TC), high density lipoprotein-cholesterol (HDL-C), triglyceride (TG) and C reactive protein (CRP) level. Except for those who were pregnant or had established diagnosis of diabetes on medicine control, all participants were asked to take 75-g glucose and checked for 2-h post-load glucose level. Diabetes mellitus was defined by a documented history of diabetes, records of currently using anti-diabetic agents, fasting plasma glucose  $\geq$  126 mg/dl, 2-hour post-load glucose  $\geq$  200 mg/dl, or hemoglobin A1c  $\geq$  6.5%. The estimated glomerular filtration rate (eGFR) was calculated by MDRD formula:  $GFR = 186 \times [\text{serum creatinine}]^{-1.154} \times [\text{age}]^{-0.203} \times [0.742 \text{ if female}]$  [22]. The TC/HDL-C ratio was calculated and categorized as either  $<5.0$  or  $\geq 5.0$ . The CRP levels were stratified as either one in the highest quartiles or the lower three quartiles with a cutoff of 2.77 mg/dL.

### Pulmonary Function Test

The pulmonary function tests were performed by an experienced technician using an automated flow-sensing spirometer (Multi-Functional Spirometer HI-801; CHEST M.I., Inc) as recommended by the American Thoracic Society's. All participants taking the exam were in a sitting position with nose clip in place. At least two error-free reproducible maneuvers (FEV<sub>1</sub> and FVC within 5%) out of three acceptable maneuvers were performed. The participants would need to repeat the maneuvers up to six times if necessary. The parameters obtained in the study were FVC, FEV<sub>1</sub>, and FEV<sub>1</sub> to FVC ratio (FEV<sub>1</sub>/FVC). RSP was defined as of FVC  $< 80\%$  of predicted value and FEV<sub>1</sub>/FVC ratio  $\geq 70\%$  according to the definition of the American Thoracic Society [23].

### Statistical analyses

SPSS software (17th version, Chicago, Illinois, USA) was used to analyze statistical data. Continuous variables were presented as the mean  $\pm$  standard deviation. Categorical variables were presented as numbers (percentages). Independent sample t-test or Mann–Whitney U test was used to compare continuous clinical characteristics, and the Chi-square test was used for categorical parameter comparison between the group with and without RSP. Potential associated confounders for RSP included age, gender, BMI, hypertension, diabetes, cerebrovascular disease, TC/HDL-C ratio, CRP, and regular exercise and they were adjusted in the multiple regression model. The adjusted odds ratio (OR) and the 95% confidence interval (CI) of tea consumption were calculated for its associated risk of RSP. P value  $< 0.05$  was considered as statistically significant throughout the analyses.

## Results

A total of 1849 subjects (12.3%) had RSP. Table 1 shows the clinical characteristics of subjects with and without RSP. Subjects with RSP were more likely to be older, female, and had higher BMI. RSP group had a higher prevalence of hypertension, diabetes, cerebrovascular disease, eGFR <60, TC/HDL-C ratio  $\geq 5$ , highest quartile of CRP level, and current smoking status. However, subjects with RSP had a lower prevalence of regular exercise. In subjects with and without RSP, the amount of daily tea consumption was  $65 \pm 191$  and  $110 \pm 242$  mL ( $p < 0.001$ ) and the prevalence of habitual tea drinking was 15.1% and 24.0% ( $p < 0.001$ ), respectively.

Table 2 shows the relationship between the clinical variables and RSP in smokers and non-smokers based on multiple logistic regression model. In non-smoking group, after adjusting confounders, habitual tea drinkers had a lower associated risk of RSP (model 1, OR = 0.75, CI 0.63-0.89,  $p < 0.01$ ). Tea consumption  $\geq 3$  cup-year was inversely related to RSP (model 2, OR = 0.74, CI 0.61-0.89,  $p < 0.01$ ), while tea consumption <3 cup-year was not. In the smoking group, there was no significant association between tea consumption, presented as habitual drinking and tea consumption  $\geq 3$  cup-year, and RSP.

## Discussion

This study showed that habitual tea drinking and tea consumption of at least 3 cup-years had a lower associated risk of RSP in non-smokers but not in smokers. The association was independent of age, gender, BMI, CRP levels, regular exercise and co-morbidities such as hypertension, diabetes and cerebrovascular disease. One cross sectional study conducted in Korea demonstrated that green tea intake  $\geq 2$  times per day was associated with an increase in pulmonary function and a reduced associated risk of COPD [19], but RSP was not studied in the study. Two studies investigated the association of catechin and flavonoid, the polyphenols abundant in tea, with pulmonary function [24, 25]. One population-based study of young Chilean found that comparing those with the highest quintile of intake of catechin versus the lowest quintile, the former group had a significantly higher FVC by 70 mL [24]. The Chilean study also applied Food Frequency Questionnaire (FFQ) from which the flavonoid content was estimated, but the main dietary sources of these antioxidants in Chilean are fruits and vegetables. The other study was a multi-centric population-based study in European adults and suggested that intake of total flavonoid might be related to a lower risk of spirometric restriction [25]. It applied FFQ and US Department of Agriculture (USDA) Database for the Flavonoid Content of Selected Foods to investigate the intake of flavonoid that was habitually consumed in the general population. Though the consumables investigated in these two studies were not tea, considering the effects of the same key components in the tea, the results of the present study lined with those of these studies. In another study examining the relationship between lung function and dietary antioxidants in 680 middle-aged European adults over a 10-year period, intake of apples, bananas, tomatoes, herbal tea, and vitamin C was found to be associated with a slower decline in FVC [26]. Unlike the herbal teas commonly consumed in Europe, green, oolong and black teas are the main types of teas consumed in the East. In addition, we further used the term "cup-year" to assess the cumulative effect of tea consumption over

time, as in the case of "pack-year" for smoking. We found that tea consumption of  $\geq 3$  cup-year was associated with a 26% lower risk of RSP disease in the non-smoking group, but not in the  $< 3$  cup-year group. So far as we know, this is the first study examining the effects of tea consumption on RSP among subjects with different smoking status.

Little is known about the exact mechanisms underlying the association of tea consumption with RSP. Previous studies showed associations of RSP with heart failure [27], arterial stiffness [28], metabolic syndrome [11, 12] and chronic kidney disease [29, 30]. The common entity within these diseases or lifestyles are the raised oxidative stress, systemic inflammation and risks of cardiovascular diseases. The antioxidant phenolic compounds, the flavonoids, in tea may play a major role in the mechanism. Flavonoids exist in most plant foods, but the concentration is particularly high in tea. The three major classes of flavonoids are flavonols, flavones and catechins. Studies either in vitro or ex vivo have shown that tea extracts, such as flavonoids and its secondary metabolites, may participate in manipulating the smooth muscle relaxation, nitric oxide synthase activity in endothelial cells, vascular inflammation reduction, and renin activity inhibition through its anti-inflammatory and anti-oxidative effects [17, 31]. In addition, studies also showed that flavonoids and tea catechins can significantly improve endothelial function [32, 33]. Through reducing multiple aspects of cardiovascular risks by improving endothelial system, increasing nitric oxide production, and vascular relaxation, long-term tea consumption may have protective effects on RSP and thereby further reducing lung tissue damages in non-smokers.

In this study, tea consumption was not associated with reduced risks of RSP in the smoking group no matter what cumulative dosage of tea the participant was consuming. (data not shown). One previous study found that regular green tea drinking might protect smokers from DNA damages by eliminating free radicals associated with smoking [34]. Chan, K.H., et al also found green tea might ameliorate the derangement between local oxidative stress and protease/anti-protease in the airways after exposure to cigarette smoking [35]. One potential explanation for the associations was that the injury in the lungs from smoking could be too overwhelming to be compensated by the anti-oxidative effects of tea. This study provided a direction for further studies on the association between tea consumption and RSP in the future.

In this study, aging, female gender, obesity, diabetes, hypertension, highest quartile group of CRP, and less regular exercise were independently related to RSP. The association of these covariates mentioned above and RSP were in agreement with previous studies [6, 8-10, 36]. As for the relationship between RSP and chronic kidney disease, RSP was reported to be common in patients with advanced chronic kidney disease and the eGFR displayed an inverted J-shaped association with FVC [29, 30]. However, this study did not show a significantly positive association between chronic kidney disease and RSP. The possible explanation may be related to that most subjects did not have advanced chronic kidney disease (2.5% in non-smokers and 2.2% in smokers). As for lipid profiles, we found  $TC/HDL-C \geq 5$  had no association with RSP in the adjusted model. A collinearity with diabetes, hypertension, and BMI may result in an insignificant association of  $TC/HDL-C \geq 5$  with RSP. Another reason may be related to that subjects with dyslipidemia may take anti-hyperlipidemic medications.

This study had several limitations. This is a cross-sectional study. The temporal relationship of tea consumption and the risk of RSP should be generated with caution. The participants enrolled are mainly from southern Taiwan. A more generalized population for further studies are needed. The questionnaires used to determine the amount and frequency of tea consumption depended on the participants' memory, and thus, the recall bias regarding the details of tea intake could not be excluded. Besides, we did not examine the effect of tea by its types. The types of tea in the questionnaires from the health checkup were green tea, oolong tea, black tea, and others. Oolong tea consumers composed the largest population among all tea drinkers. However, the types or brands of tea are miscellaneous in Taiwan and the drinking habits may change overtime. Therefore, we combined the results from all kinds of tea for this study.

## Conclusion

In summary, habitual tea drinking and tea consumption of at least 3 cup-years had a reduced odds of RSP in non-smokers but not in smokers. More studies are needed to elucidate the protective effect of tea or its extracts on RSP in both smokers and non-smokers.

## Abbreviations

RSP: Restrictive spirometry pattern

FVC: Forced vital capacity

FEV1: Forced expiratory volume in 1 second

COPD: Chronic obstructive pulmonary disease

BMI: Body mass index

TC: Total cholesterol

HDL: High density lipoprotein-cholesterol

TG: Triglyceride

CRP: C reactive protein

eGFR: Estimated glomerular filtration rate

MDRD: Modification of diet in renal disease

OR: Odds ratio

CI: Confidence interval

FFQ: Food frequency questionnaire

## Declarations

### Funding

No funding was received for this study.

### Authors' contributions

C.-Y. H. and J.-S. W. are the guarantors of this original article. Y.-C. Y., C.-J. C., J.-S. W., Z.-J. S., F.-H. L., and C.-Y. C. collected data initially. C.-Y. H. did the data analysis with the assistance of C.-J. C. and J.-S. W. The manuscript was drafted by C.-Y. H., and I.-H. W., Y.-C. Y., C.-J. C., F.-H. L., and J.-S. W. gave useful advice on this manuscript.

### Ethics declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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Tables

Table 1. Comparisons of clinical parameters between subjects with and without restrictive spirometry pattern

	Restrictive spirometry pattern		p value
	No (n=13,148)	Yes (n=1,849)	
Age, years	47.3±11.6	60.0±12.4	<0.001
Male gender	7827 (59.5)	978(52.9)	<0.001
Body mass index, kg/m <sup>2</sup>	24.3±3.5	25.3±4.0	<0.001
Body mass index <24	411 (3.1)	74 (4.0)	
24 <27	6055 (46.1)	597 (32.3)	
≥27	6682 (50.8)	1178 (63.7)	
Diabetes mellitus	1491 (11.3)	534 (28.9)	<0.001
Hypertension	2140 (16.3)	780 (42.2)	<0.001
Cerebrovascular disease	47 (0.4)	31 (1.7)	<0.001
eGFR<60	241 (1.8)	131 (7.1)	<0.001
TC/HDL-C ratio	4.3±1.6	4.5±1.5	<0.001
CRP >75 percentile	2992 (22.8)	748(40.5)	<0.001
Regular exercise	1126 (8.6)	101(5.5)	<0.001
Smoking, pack-years	3.6±11.5	4.0±13.0	<0.01*
Habitual tea drinking	3150 (24.0)	279 (15.1)	<0.001
Tea consumption, mL/day	110±242	65±191	<0.001*
FEV1, L	2.75±0.66	1.74±0.47	<0.001
FVC, L	3.34±0.79	2.10±0.56	<0.001
FEV1/FVC, %	82.5±5.4	83.2±7.0	<0.001
Data expressed as mean±standard deviations or number (%)			
*Non-parametric test			

Table 2. Multiple logistic regression models for the relationship between clinical variables and restrictive spirometry pattern in non-smoker and smoker

	Non-smoker (n=12,309)		Smoker (n=2,688)	
	Model 1	Model 2	Model 1	Model 2
Age, years				
40-64 vs 20-40	2.68 (2.16-3.33) ***	2.68 (2.16-3.32) ***	5.21 (2.91-9.30) ***	5.22 (2.92-9.33) ***
≥65 vs 20-40	11.76 (9.25-14.96) ***	11.70 (9.20-14.88) ***	22.97 (11.99-44.00) ***	22.81 (11.91-43.71) ***
Male vs female	0.77 (0.68-0.87) ***	0.77 (0.68-0.87) ***	0.90 (0.46-1.75)	0.90 (0.46-1.76)
Body mass index, kg/m <sup>2</sup>				
24 - <27 vs <24	1.12 (0.97-1.29)	1.12 (0.97-1.29)	1.04 (0.74-1.45)	1.04 (0.75-1.46)
≥27 vs <24	1.52 (1.30-1.76) ***	1.51 (1.30-1.76) ***	1.46 (1.03-2.09) *	1.47 (1.03-2.10) *
eGFR ≥ 60 vs <60	1.23 (0.95-1.64)	1.25 (0.95-1.64)	1.27 (0.67-2.43)	1.27 (0.67-2.42)
Diabetes mellitus, yes vs no	1.63 (1.41-1.69) ***	1.63 (1.41-1.88) ***	1.36 (0.99-1.86)	1.36 (0.99-1.86)
Hypertension, yes vs no	1.90 (1.67-2.16) ***	1.90 (1.67-2.16) ***	1.90 (1.42-2.55) ***	1.91 (1.42-2.56) ***
TC/HDL-C ratio ≥ 5, yes vs no	0.98 (0.85-1.12)	0.98 (0.85-1.12)	0.87 (0.66-1.16)	0.87 (0.66-1.16)
CRP >75 percentile, yes vs no	1.75 (1.55-1.99) ***	1.75 (1.55-1.98) ***	1.75 (1.32-2.32) ***	1.75 (1.32-2.32) ***
Cerebrovascular disease, yes vs no	1.77 (0.95-3.30)	1.78 (0.95-3.33)	2.60 (1.05-6.45) *	2.60 (1.05-6.45) *
Regular exercise, yes vs no	0.69 (0.53-0.89) **	0.69 (0.54-0.89) **	0.60 (0.37-0.97) *	0.60 (0.37-0.98) *
Tea consumption				
Habitual drinking vs none	0.75 (0.63-0.89) **		0.87 (0.66-1.15)	
<3 cup-year vs none		0.69 (0.46-1.05)		0.83 (0.41-1.66)
≥ 3 cup-year vs none		0.74 (0.61-0.89) **		0.82 (0.62-1.09)
*p <0.05 **p<0.01 ***p<0.001				

