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Effects of ambient temperature on lung function in patients with chronic obstructive pulmonary disease: A time-series panel study

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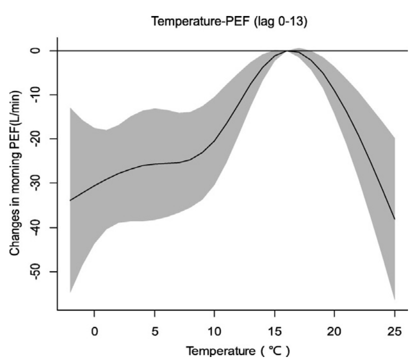
HIGHLIGHTS

- This is a time-series panel study with intensive daily lung function measurements.
- The associations between daily temperature and PEF were inverted U–shaped.
- Both low and high temperatures were significantly associated with reduced PEF.
- No apparent associations were observed for temperature and FEV_1.

GRAPHICAL ABSTRACT



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ABSTRACT

Background: Limited evidence concerns the associations between ambient temperature and lung function and the results are mixed.
Objective: To evaluate the associations between temperature variations and daily fluctuations in pulmonary function in chronic obstructive pulmonary disease (COPD) patients.
Methods: We designed a time-series panel study of 28 male urban COPD patients with repeated daily lung function measurements from December 2012 to May 2013 in Shanghai, China. We used a linear mixed-effect model combined with a distributed lag model to estimate the cumulative effects of temperature on morning/evening pulmonary function tests (PFTs), including peak expiratory flow (PEF) and forced expiratory volume in 1-s (FEV_1), while adjusting for within-subject correlations, individual characteristics, time trends and air pollution levels.
Results: We obtained a total of 8618 pairs of morning PFTs and 8528 pairs of evening PFTs. The associations between daily mean temperature and PEF were inverted U-shaped with both low and high temperatures significantly reducing morning and evening PEF. Compared with the referent temperature (16 °C), the low temperature (1st percentile, −1 °C) would result in cumulative decreases of 32.20 L/min in morning PEF and 21.15 L/min in evening PEF over lags of two weeks. The corresponding decrements at the same lag associated

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with high temperature (99th percentile, 25 °C) were 38.10 L/min in morning PEF and 27.08 L/min in evening PEF. There were no statistically significant changes in morning or evening FEV_1.

Conclusions: This time-series panel study provided robust evidence that both low and high temperatures were significantly associated with decrements in pulmonary function, particularly in PEF.

1. Introduction

Chronic obstructive pulmonary disease (COPD), characterized by persistent airflow restriction and chronic airway inflammation, is a major respiratory disease worldwide. In recent decades, COPD is projected to rank third worldwide in terms of mortality by 2020 (Lopez-Campos et al. 2016). Pulmonary function tests (PFTs) are essential for the diagnosis and management of COPD and a meaningful decrease in lung function can manifest an important change in the development of COPD, such as an acute exacerbation (Tseng et al. 2013; Vestbo et al. 2013). Thus, the identification of risk factors leading to lung dysfunction in COPD patients may be helpful to protect them from an acute exacerbation of COPD.

A number of epidemiological studies have documented significant associations of both low and high ambient temperatures with mortality or morbidity outcomes from various diseases including respiratory diseases (Basu 2009; Guo et al. 2013; Ye et al. 2012). However, the mechanisms by which a change in ambient temperature adversely affects the respiratory system remain uncertain. As key indicators for predicting the risks of COPD, parameters of PFTs have been associated with ambient temperature in several studies, but the results are inconsistent. Some suggested that a higher temperature could reduce lung function (Collaco et al. 2011; Li et al. 2014; Wu et al. 2014; Zhang et al. 2015), but others reported reverse findings (Donaldson et al. 1999; Li et al. 2015; McCormack et al. 2017; Pierse et al. 2013).

Given the widely reported U-, V-, or J- shaped curves for the associations between ambient temperature and respiratory mortality or morbidity (Bunker et al. 2016; Hansel et al. 2016; Ye et al. 2012), we hypothesized that both low and high temperatures could reduce lung function in male COPD patients. We therefore evaluated the short-term association between temperature and lung function in a time-series panel study among male COPD patients in Shanghai, China, which had shown negative associations between daily lung function parameters and concentrations of particulate matter with an aerodynamic diamteter ≤ 2.5 μm ($PM_{2.5}$) (Chen et al. 2017).

2. Materials and methods

2.1. Design and population

From December 10, 2012 to May 20, 2013, we performed a time-series panel study with daily measurements of lung function in Shanghai, China, which was described in our previous publication (Chen et al. 2017). Briefly, 30 male COPD patients who resided in the urban areas of Shanghai were initially recruited at Zhongshan Hospital Fudan University. They had COPD with the ratio of forced expiratory volume in 1-s (FEV_1) to forced vital capacity (FVC) <70% and FEV_1% predicted to be <80%. Individual-level confounders were collected at enrollment, including age, body mass index, education (level 1: illiteracy or elementary school; level 2: middle school; level 3: college; level 4: graduate), and smoking (status and pack-years). To account for possible influences associated with disease severity at baseline, we also collected information on the classifications of Global Initiative for Chronic Obstructive Lung Disease (GOLD). All patients received daily bronchodilator treatment (tiotropium bromide) in the morning. These patients were asked to record changes of medication use and exacerbations of COPD in a simple questionnaire. During the follow-ups, two patients quit the study, so a total of 28 subjects were finally included. The Institutional Review Board of Zhongshan Hospital Fudan University (No. 2011-205) approved the study protocol. We obtained informed written consent from every participant at enrollment.

2.2. Pulmonary function test

We requested each participant to measure lung function twice every day: morning (7 a.m. to 9 a.m.) and evening (7 p.m. to 9 p.m.). The morning test was conducted before they inhaled bronchodilators. Lung function was tested at home by using the Peak Flow Meter AM3, which can automatically record FEV_1 and peak expiratory flow (PEF). To perform a valid PFT measurement with the AM3, patients were trained by physicians at the outset of the study. Each PFT was performed three consecutive times, and this test was repeated if the range of three measurements was >5%. The best values of three valid measurements were stored in the AM3 together with the detailed time.

2.3. Environmental data

We obtained daily mean temperature and relative humidity from the Xujiahui Station of the Shanghai Meteorological Bureau. This station was located in the central urban area of Shanghai and very close to Zhongshan Hospital. To allow for adjustment of the potential confounding effects of air pollution, we obtained daily concentrations of two typical air pollutants: $PM_{2.5}$ and ozone (O_3). The air pollutant data were collected from Shanghai Environment Monitoring Center, and daily 24-h average concentration for $PM_{2.5}$ and maximum 8-h average concentration of O_3 were averaged from 9 state-controlled monitors located in the urban areas of Shanghai.

2.4. Statistical analysis

Environment and health data were linked by the date of PFTs before statistical analysis. We used the linear mixed-effect (LME) model to evaluate the associations between ambient temperature and daily variations in lung function. The model has the advantage of accounting for between-subject differences and within-subject correlations due to repeated measurements. In this study, lung function parameters were considered response variables and were entered the models without any transformation because they approximately followed normal distributions. Daily mean temperature was specified as a fixed-effect independent variable. The correlations among multiple repeated measurements were accounted for by including a random-effect intercept for each subject in the LME. Several covariates were incorporated in the models: (1) basic characteristics (age, body mass index, educational attainment, smoking status and pack-years) to account for between-subject variability; (2) a factor variable of GOLD classifications to control for possible influences of disease severity at baseline; (3) a natural spline of calendar day with 3 degrees of freedom (*df*) to adjust for the unmeasured time trends in lung function during the study period; (4) an indicator variable for day of the week to adjust for weekly temporal variation; (5) a natural spline of daily mean relative humidity with 3 *df* to adjust for its potential confounding effects; and (6) daily concentrations of $PM_{2.5}$ and O_3 to control for the potentially confounding effects of air pollution (Bunker et al. 2016; Chen et al. 2017; Wu et al.