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Original Investigation

Obstructive and Restrictive Lung Function Measures and CKD: National Health and Nutrition Examination Survey (NHANES) 2007-2012

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Background: Prevalence and factors associated with obstructive and restrictive lung function in people with chronic kidney disease (CKD) are unknown.

Study Design: Cross-sectional and longitudinal analyses.

Setting & Participants: Participants aged 40 to 79 years from NHANES (National Health and Nutrition Examination Survey) 2007 to 2012 who underwent spirometry testing.

Predictor: CKD (estimated glomerular filtration rate [eGFR] >15-<60 mL/min/1.73 m^2 or urinary albumin-creatinine ratio ≥ 30 mg/g).

Outcomes: Restrictive lung function (defined as $FEV_1/FVC \geq 0.70$ and baseline FVC < 80% predicted), obstructive lung function (defined as $FEV_1/FVC < 0.70$ based on postbronchodilator spirometric results), and mortality data (available for 2007-2008 and 2009-2010 survey periods).

Results: 7,610 participants (CKD = 1,338; non-CKD = 6,272) were included. Prevalences of obstructive lung function adjusted to the mean age of 55 years and 50% men in the CKD and non-CKD groups were 15.6% and 13.3%, respectively ($P = 0.2$). Similarly, adjusted prevalences of restrictive lung function in the CKD and non-CKD groups were 9.8% and 6.7%, respectively ($P = 0.01$). Presence of albumin-creatinine ratio ≥ 30 mg/g was associated with obstructive (OR, 1.42; 95% CI, 1.07-1.88) and restrictive lung function (OR, 1.43; 95% CI, 1.01-2.03) in the entire study cohort. eGFR < 60 mL/min/1.73 m^2 was associated with higher odds of obstructive lung function. In a multivariable Cox model, age (HR, 1.07; 95% CI, 1.04-1.11) and presence of obstructive lung function (HR, 2.68; 95% CI, 1.80-3.97), but not CKD measures, were associated with death.

Limitations: Small proportion of participants with advanced kidney disease.

Conclusions: In a representative sample of US adults, impaired lung function is common in those with and without CKD. Albuminuria was independently associated with both obstructive and restrictive lung function, and eGFR < 60 mL/min/1.73 m^2 was associated with higher odds of obstructive lung function. Older age and obstructive lung function were associated with higher likelihood of death. Further studies examining the burden of lung disease in advanced CKD are needed.

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INDEX WORDS: Lung disease; restrictive lung function; obstructive lung function; lower respiratory disease; spirometry; albuminuria; urine albumin-creatinine ratio (UACR); estimated glomerular filtration rate (eGFR); renal function; chronic kidney disease (CKD); mortality; National Health and Nutrition Examination Survey (NHANES).

Chronic lower respiratory diseases constitute the third leading cause of death in the United States.[1] Previous studies using NHANES (National Health and Nutrition Examination Survey) 2007 to 2010 reported that 79.9% of US adults had normal lung function, 6.5% had restrictive impairment, and 13.6% had an obstructive pattern of lung function.[2] They also noted minimal changes in the respective prevalences of obstructive and restrictive lung function in 2007 to 2010 versus 1988 to 1994, highlighting the sustained disease burden over the years. Similar data have been reported from other countries.[3,4] Apart from the

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morbidity burden, lung diseases are also associated with poor quality of life and repeated hospitalizations and incur higher health care costs.[4-8]

The problem of chronic kidney disease (CKD) is increasing, and patients with CKD sustain higher rates of both cardiovascular and noncardiovascular death.[9-12] The prevalences of obstructive and restrictive lung diseases in CKD remain undefined and the few available studies have reported that the prevalence of chronic obstructive pulmonary disease (COPD) is approximately 20% to 30% in the CKD population.[13,14] It is important to note that these studies included select populations (eg, patients undergoing surgery), and studies examining the prevalence of lung diseases at the population level are lacking. In this study, we aimed to define age- and sex-adjusted prevalences of obstructive and restrictive lung function in people with and without CKD in a nationally representative sample of US adults. We also studied whether kidney function measures were associated with obstructive and restrictive lung function among NHANES participants. In addition, we studied factors associated with death in the study cohort.

METHODS

Study Population

We examined data from NHANES, a nationally representative, complex, and multistage probability survey of the US civilian noninstitutionalized population conducted by the National Center for Health Statistics. The National Center for Health Statistics Ethics Review Board approved the study protocol, and each participant provided written informed consent. Participants in NHANES were interviewed in their homes and underwent a standardized physical examination in a mobile examination center. Self-reported information for demographics, socioeconomic status, health conditions, health behaviors, and routine site of health care were obtained during the interview. The examination component consisted of medical, dental, and physiologic measurements, as well as laboratory tests administered by highly trained medical personnel.

We combined data from NHANES 2007 to 2008, 2009 to 2010, and 2011 to 2012 cycles for this analysis, and 7,610 participants who met the following criteria were included: aged 40 to 79 years, underwent medical examination, were not pregnant, completed spirometry examination with acceptable quality of data (A, B, and C), neither on dialysis therapy nor had an estimated glomerular filtration rate (eGFR) < 15 mL/min/1.73 m^2, and had urine albumin-creatinine ratio (UACR) data available. The NHANES spirometry data with quality A exceed American Thoracic Society (ATS) data collections standards, B meet ATS data collection standards, and C are potentially usable but do not meet all ATS standards. In addition, individuals who reported a diagnosis of chronic bronchitis or emphysema and did not complete the spirometry testing due to using supplemental oxygen and fulfilled all other criteria listed were included. Figure S1 (provided as online supplementary material) describes these details.

Measures

Kidney Disease

Participants without CKD (eGFR ≥ 60 mL/min/1.73 m^2 and UACR < 30 mg/g) and those with CKD stages 1 to 4 were included (eGFR $>$ 15-$<$60 mL/min/1.73 m^2 or UACR ≥ 30 mg/g). eGFR was calculated according to the CKD-EPI (CKD Epidemiology Collaboration) equation, using calibrated creatinine level.[15] UACR was calculated from spot urine albumin and creatinine samples and dichotomized at 30 mg/g.

Comorbid Conditions

Diabetes was defined as self-reported if the participant was ever told by a physician that he or she had "diabetes or borderline diabetes." Hypertension was defined as systolic blood pressure $>$ 140 mm Hg or diastolic blood pressure $>$ 90 mm Hg or use of antihypertensive medications. We calculated each participant's body mass index (BMI) as weight in kilograms divided by the measured height in meters squared.

Medications

Medications used to treat respiratory diseases were obtained from the prescription medication file among participants who reported using a prescription medication in the past month. Medications with primary classification as respiratory agents in the following 3 categories were included: bronchodilators, antiasthmatics, and inhalers.

Smoking

As defined in earlier studies using NHANES, we defined current smoker as a participant who had smoked 100 or more cigarettes during his or her lifetime and reported smoking currently.[2] A former smoker was defined as someone who had smoked 100 or more cigarettes during his or her lifetime and reported having stopped smoking. A never smoker was defined as someone who had not smoked 100 or more cigarettes during his or her lifetime.

Spirometry

During NHANES 2007 to 2012, spirometry was offered to participants aged 6 to 79 years with the exclusion of participants with the following conditions: current chest pain; a physical problem with forceful expiration; use of supplemental oxygen; recent surgery of the eye, chest, or abdomen; recent heart attack, stroke, tuberculosis exposure, or coughing up of blood; and history of detached retina, collapsed lung, or aneurysm.[16] Similar spirometers (Ohio 822/827 dry-rolling seal volume spirometers) and protocols were used for conducting spirometry during these 3 survey periods. Participants were asked to provide 3 acceptable maneuvers. For purposes of this study, the Global Initiative for Chronic Obstructive Lung Disease (GOLD) classification of COPD severity based on postbronchodilator spirometric results was used along with a modified version taking into consideration only baseline prebronchodilator tests.[17] We established the following categories of obstructive impairment: severe obstructive impairment (forced expiratory volume in first second of expiration [FEV_1]/forced vital capacity [FVC] < 0.70 and $FEV_1 < 50\%$ predicted), moderate obstructive impairment ($FEV_1/FVC < 0.70$ and FEV_1 50%-$<$80% predicted), and mild obstructive impairment ($FEV_1/FVC < 0.70$ and $FEV_1 \geq 80\%$ predicted). Restrictive impairment was defined as the presence of $FEV_1/FVC \geq 0.70$ and $FVC < 80\%$ predicted.

Mortality Data

NHANES linked mortality public use files are available for continuous NHANES periods 2007 to 2008 and 2009 to 2010. Follow-up time is from medical examination until December 31, 2011. Mortality status is based on a probabilistic match between NHANES and National Death Index death certificate records.

Statistical Analysis

Demographic characteristics, comorbid conditions, and spirometry data (FEV_1 and FVC) were compared between participants