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

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Abstract

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

Study Design—Cross-sectional and longitudinal analyses

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Supplementary Material

Note: The supplementary material accompanying this article (doi:_______) is available at www.ajkd.org

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

Predictor—CKD (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 ≥0.70 and baseline FVC <80% predicted), obstructive lung function (defined as FEV1/FVC <0.70 based on post-bronchodilator spirometric results), and mortality data (available for 2007–2008 and 2009–2010 survey periods).

Results—7,610 participants (CKD=1338; Non-CKD=6272) were included. The prevalences of obstructive lung function adjusted to the mean age of 55 years and 50% male 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/1.73m^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/1.73m^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.

Keywords

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) 2007–2010 reported that 79.9% of US adults had normal lung function, 6.5% had restrictive impairment, and 13.6% had obstructive pattern of lung function [2]. They also noted minimal changes in the respective prevalence of obstructive and restrictive lung function in 2007–2010 versus in 1988–1994, highlighting the sustained disease burden over the years. Similar data have been reported from other countries [3, 4]. Apart from the 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 rising and patients with CKD sustain higher rates of both cardiovascular and non-cardiovascular deaths [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) was approximately 20%–30% in the CKD population[13, 14]. It is important to note that these studies included selected populations (e.g. patients undergoing surgery), and studies examining the prevalence of lung diseases at the population level are lacking. In this study, we aimed to define the age- and sex-adjusted prevalences of obstructive and restrictive lung function in people with and without CKD among a nationally representative sample of US adults. We also studied whether kidney function measures were associated with obstructive and restrictive lung function among the NHANES participants. In addition, we studied the 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, non-institutionalized population conducted by the National Center for Health Statistics. The National Centers 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 on demographics, socioeconomic status, health conditions, health behaviors and routine site of healthcare were obtained during the interview. The examination component consisted of medical, dental, and physiological measurements, as well as laboratory tests administered by highly trained medical personnel.

We combined data from the NHANES 2007–2008, 2009–2010, and 2011–2012 cycles for this analysis, and 7,610 participants who met the following criteria were included: aged 40–79 years, underwent medical examination, were not pregnant, completed spirometry examination with acceptable quality of data (A, B, C), and who were neither on dialysis nor had estimated glomerular filtration rate (eGFR) < 15ml/min/1.73 m^2, and who had urine albumin-creatinine ratio (UACR) data available. The NHANES spirometry data with quality A exceeds American Thoracic Society (ATS) data collections standards, B meets ATS data collection standards, and C is potentially usable but does not meet all ATS standards. In addition, subjects who reported a diagnosis of chronic bronchitis or emphysema and did not complete the spirometry testing due to being on supplemental oxygen and fulfilled all other criteria listed above 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 1–4 were included (eGFR >15-<60 ml/min/1.73 m^2 or UACR of ≥30 mg/g). The eGFR was calculated according to the CKD-EPI (CKD Epidemiology Collaboration) equations, using calibrated creatinine[15]. The UACR was calculated from spot urine albumin and creatinine samples and dichotomized at 30 mg/g.

Comorbidities—Diabetes was defined as self-reported if ever told by a doctor that the participant 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, anti-asthmatics, and inhalers.

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

Spirometry—During NHANES 2007–2012, spirometry was offered to participants aged 6 to 79 years with the exclusion of participants with the following: 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 three survey periods. Participants were asked to provide three acceptable maneuvers. For purposes of this study, Global Initiative for Chronic Obstructive Lung Disease classification of COPD severity based on post-bronchodilator spirometric results was used along with a modified version taking into consideration only baseline pre-bronchodilator 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% to <80% predicted), and mild obstructive impairment (FEV 1/FVC <0.70 and FEV 1 ≥80% predicted). Restrictive impairment was defined as the presence of FEV 1/FVC ≥0.70 and FVC <80% predicted.

Mortality data—NHANES Linked Mortality public use files are available for continuous NHANES periods 2007–2008 and 2009–2010. The 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, comorbidities and spirometry data (FEV1 and FVC) were compared between participants with and without CKD using t-tests for continuous variables and Rao-Scott chi-square tests for categorical variables. We studied the prevalence rates of obstructive and restrictive lung function in those with and without CKD in two different ways: a) using baseline spirometry results only, and b) using baseline and post-bronchodilator spirometry results. These prevalence estimates were adjusted to the mean age and sex percent in our cohort. Approximately half of the subjects eligible to participate in the post-bronchodilator test did not complete the test. Therefore, to estimate the prevalence of lung disease using both the pre and post bronchodilator results while accounting for the missing post-bronchodilator data, we used a re-weighting scheme described by Tilert et al.[18]. Briefly, the examination weights of the post-bronchodilator responders were adjusted to equal the weight totals of all subjects eligible for post-bronchodilator test by using the inverse of a propensity score for responding. The propensity score included the following variables: age, gender, race, self-reported COPD, current asthma and number of years smoked. We also estimated the prevalence of obstructive and restrictive lung disease adjusted to the mean age and sex percent for various subgroups of interest: age <65 versus ≥65 years, males vs. females, white race vs. other, smoker vs. none and overweight and obese vs. those with normal BMI. We evaluated the interaction between CKD and each of these factors and when the interaction term was significant, stratified estimates were obtained.

We used a logistic regression analysis to examine the factors associated with obstructive and restrictive lung function among participants using the baseline spirometry evaluation. In addition, we studied the factors associated with obstructive and restrictive lung function in those with and without kidney disease. The following factors were considered in the multivariable logistic model: age, sex, race, smoking, BMI, diabetes, hypertension, eGFR (as a continuous measure), and UACR. Our visual inspection of logit plots for log-transformed UACR vs. obstructive lung function (using raw unweighted data) suggested a non-linear relationship with increased risk of obstructive disease only at higher levels of log-transformed UACR. Hence, we chose to report the associations using a clinical meaningful cut-off- UACR ≥30 mg/g. We also ran a separate logistic regression analysis by considering eGFR as a categorical variable (eGFR ≥90 ml/min/1.73 m^2, 60–89 ml/min/1.73 m^2, and <60 ml/min/1.73 m^2). Post-bronchodilator results were not used in the logistic models because approximately half of the subjects who were eligible for the post bronchodilator spirometry test did not complete it leading to a large amount of subjects missing data that might result in biased associations.

To evaluate the association between kidney disease measures, impaired lung function and mortality, we fit a Cox proportional hazards model including lung function (normal lung function, obstructive lung function, and restrictive lung function), eGFR, albuminuria, age, sex, race (white vs. non-white), diabetes, hypertension and smoking (current or past vs. never). We also tested two-way interactions between a) obstructive lung function and each of eGFR (each 5 ml/min/1.73 m^2 lower) and UACR ≥30 mg/g, and b) between restrictive lung function and each of eGFR (each 5 ml/min/1.73 m^2 lower) and UACR ≥30 mg/g in the adjusted model. Two cycles 2007–2008 and 2009–2010 with available mortality data were included in this analysis.

All analyses were performed using survey procedures with SAS version 9.4 for Unix (SAS Institute Inc, Cary, North Carolina), which account for the sampling design of NHANES and appropriately weight participants in statistical models. Graphs were produced using R version 3.0.1 (The R Foundation for Statistical Computing, Vienna, Austria). Medical examination weights were used in all analyses. Weights were modified as described above only for the analysis to estimate prevalence of lung disease including post-bronchodilator results.

Results

Participant Characteristics

Mean age of the study population was 55 years and the CKD group was older than the non-CKD group (62 vs. 54 years; Table 1). The CKD group had a higher proportion of former/current smokers, comorbid conditions such as diabetes and hypertension, and also had higher BMI. The FEV1 and FVC (% predicted) were lower in those with CKD. Other characteristics of the study population are outlined in Table 1.

Prevalence Estimates of Obstructive and Restrictive Lung Function

Global Initiative for Chronic Obstructive Lung Disease Criteria—The prevalences of obstructive lung function adjusted to the mean age of 55 years and 50% male in the CKD and non-CKD groups were 15.6% (95% confidence interval [CI], 12.4%–18.8%) and 13.3% (95% CI, 11.6%–15.0%), respectively (p=0.2; Figure 1). Age- and sex-adjusted prevalences of restrictive lung function in the CKD and non-CKD groups were 9.8% (95% CI, 7.6%–11.9%) and 6.7% (95% CI, 5.7%–7.8%), respectively (p=0.02; Figure 1). Among the non-CKD group, age- and sex-adjusted prevalences of mild, moderate and severe obstructive lung function were 7.8% (95% CI, 6.4%–9.3%), 4.3% (95% CI, 3.5%–5.2%), and 0.6% (95% CI, 0.1%–1.1%) respectively, while among those with CKD, they were 7.4% (95% CI, 4.5%–10.3%), 5.7% (95% CI, 3.1%–8.3%) and 1.0% (95% CI, 0%–2.3%). While adjusting to the mean age of 55 years and 50% males, 0.5% (95% CI, 0.3%–0.7%) of the non-CKD group was on supplemental oxygen and could not complete the spirometry testing (and therefore not categorized for severity). There were 2.0% (95% CI, 1.0%–2.9%) of participants with CKD on supplemental oxygen. Prevalence rates of obstructive and restrictive lung function based on UACR and eGFR are presented in Table 2. Prevalence of obstructive and restrictive lung faction for different subgroups of interest are presented in table S1.

Baseline Spirometry Data Only—When using baseline spirometry only, a similar higher burden of obstructive and restrictive lung function among CKD was also noted.

Factors Associated With Obstructive Lung Function

Older age, smoking status, lower eGFR and albuminuria were associated with higher odds of obstructive lung function, and female gender, being Non-Hispanic black or Mexican-American or other Hispanic and higher BMI were significantly associated with lower odds of obstructive lung function in the study population (Table 3). In a model with eGFR as a categorical variable, eGFR 60–89 ml/min/1.73 m^2 (odds ratio [OR], 1.14; 95% CI, 0.91–1.42) and <60 ml/min/1.73 m^2 (OR, 1.25; 95% CI, 0.94–1.65) were not significantly associated with obstructive lung function compared to those with eGFR ≥ 90 ml/min/1.73 m^2. In an analysis restricting to CKD and non-CKD groups separately, these same factors were significantly associated with obstructive lung function in both groups (age, blacks and

Mexican-Americans and other Hispanic, smoking status, and BMI) except for the following: hypertension was significantly associated with obstructive lung function only in the CKD group and female gender was associated only in the non-CKD group (Table S2).

Factors Associated With Restrictive Lung Function

Older age, current smoking status, higher BMI, presence of diabetes and albuminuria were significantly associated with higher odds of having restrictive lung function. Lower eGFR was significantly associated with lower odds of restrictive lung function in the entire study population (Table 4). This inverse association between eGFR and restrictive lung function existed only when age was included in the model. In a separate analysis restricted to those aged 60–79 years (most with eGFR < 60 ml/min/1.73 m2 were in this age category), such an inverse association was not noted. In a model with eGFR as a categorical variable, eGFR 60–89 ml/min/1.73 m^2 (OR, 0.77; 95% CI, 0.57–1.03) and <60 ml/min/1.73 m^2 (OR, 0.79; 95% CI, 0.48–1.28) were not significantly associated with restrictive lung function compared to those with eGFR ≥ 90 ml/min/1.73 m^2.

In analysis restricting to CKD and non-CKD groups separately, higher BMI and presence of diabetes were each significantly associated with higher odds of restrictive lung function. Hypertension was only associated with higher odds of restrictive disease among CKD subjects. In the non-CKD cohort, older age and current smoking status were associated with higher odds of restrictive lung function (Table S3).

Factors Associated With Mortality

There were 5,174 study participants from NHANES 2007–2008 and 2009–2010 cycles who had mortality data. During a median follow up of 33 months, 141 participants died. Older age and obstructive lung function were significantly associated with increased mortality (Table 5). Even though there was a trend, the association between UACR ≥30 mg/g and mortality was not statistically significant. We did not find a significant interaction between albuminuria and obstructive or restrictive lung disease. We also did not find a significant interaction between eGFR and obstructive or restrictive lung function.

Discussion

In a representative sample of US adults aged 40–79 years, approximately one in four adults with CKD and one in five adults without kidney disease had underlying impaired lung function based on spirometry studies. The prevalence of restrictive lung function was found to be higher in those with CKD than those without. In addition to other factors, albuminuria was independently associated with higher odds of both obstructive and restrictive lung function, whereas lower eGFR was associated with higher odds of having obstructive lung function. Factors associated with obstructive and restrictive lung function were mostly similar among those with and without kidney disease. In the entire study cohort (2007–2008, 2009–2010 survey periods), older age and presence of obstructive lung function were associated with death.

Using NHANES data, Ford *et al.* reported prevalence rates of obstructive and restrictive lung function in the general adult population of 13.5% and 6.5%, respectively[2]. Tilert *et al.*

reported a prevalence rate of 20.9% using pre-bronchodilator spirometry measurements and 14.0% using both pre- and post-bronchodilator data for obstructive lung function in the general population among those aged 40–79 years [18]. Several studies have also reported higher rates of kidney disease in those with pre-existing COPD [19, 20]. However, prevalence of impaired lung function in those with CKD using spirometry studies had previously not been defined to our knowledge. Our results suggest that age- and sex-adjusted rates of restrictive lung function are higher in those with CKD and rates of obstructive lung function are similar to those without kidney disease. Importantly, the prevalence of restrictive lung function was higher in those with albuminuria irrespective of their eGFR (Table 2). After adjustment for several confounding variables, albuminuria was associated with both obstructive (OR, 1.42; 95% CI, 1.07–1.88) and restrictive lung function patterns (OR, 1.43; 95% CI, 1.00–2.03) in this study population. Bulcun *et al.* reported that presence of microalbuminuria (defined as UACR ≥20 mg/g in men and ≥30 mg/g in women) and mean UACR are higher in patients with COPD than in those without [21]. They also reported a significant inverse relationship (using correlation analysis) of UACR with PaO_2, FEV_1%, and FVC%. Few other studies have reported similar associations [22].

Only few studies have examined the potential mechanistic causes of the observed link between albuminuria and lung disease [23]. Mechanisms relating to albuminuria and lung disease are probably multifactorial, with underlying hypoxia playing a major role. Hypoxia is associated with higher urinary protein excretion in those living at higher altitudes. Similarly, underlying hypoxia in lung disease (both with obstructive and restrictive phenotypes) could trigger inflammation and oxidative stress that contribute to the development and worsening of albuminuria [24–26]. To our knowledge, except for a study in a Korean population that reported associations between albuminuria and restrictive lung disease solely in men, such associations have not been noted [27]. While higher prevalence of restrictive lung function could be attributed to vasculitis (which contributes to interstitial lung disease) and increased extracellular volume noted in those with CKD, formal studies to explore reasons for such a higher burden are lacking. Previous studies in those with nephrotic syndrome reported subclinical pulmonary congestion, and whether such phenomenon (water accumulation in the lung interstitial space) exists in CKD merits further studies[28].

We also noted that lower eGFR was associated with obstructive lung function. This could represent an actual decline in kidney function with underlying lung disease (and its treatment) or a mere co-existence of two common comorbid conditions. The cross-sectional nature of the study precluded further analysis to address this. For unclear reasons, we noted inverse associations between eGFR and restrictive lung function patterns. In a model that did not include age and in a separate analysis restricted to those age 60–79 years, such inverse associations were not noted. Similar to others, we noted various factors to be associated with obstructive and restrictive lung function. In general, the factors associated with obstructive and restrictive lung function were similar in CKD and non-CKD groups. These data suggest the need to have a low threshold to screen patients with albuminuria and low eGFR to diagnose impaired lung function.

Akin to reports from the general population, Ford and colleagues reported associations between UACR and eGFR and all-cause mortality among US adults with obstructive lung function [29, 30]. Similar results were shown in another longitudinal study, suggesting that albuminuria is associated with all-cause mortality in individuals with chronic obstructive lung disease and could be a relevant tool in identification of chronic obstructive lung disease patients with poor prognosis. It would be important to know the additional impact of underlying impaired lung function in those with CKD since both diseases are associated with cardiovascular disease [31]. Underlying lung diseases could also contribute to pulmonary hypertension and adverse outcomes in CKD [32, 33]. In this cohort, underlying obstructive lung function was associated with death. Even though there was a trend, UACR ≥ 30 mg/g was not associated with death, and CKD measures did not seem to modify the associations between impaired lung function and mortality. It is important to note that we lacked mortality data for the NHANES 2011–2012 period and the follow-up period was short. Whether presence of restrictive and obstructive lung function are associated with pulmonary hypertension, cardiovascular disease, and death in those with early and advanced CKD is unknown and merits further prospective studies using spirometry measures.

Strengths of our study include the use of a nationally representative sample with various US ethnic groups being sufficiently represented and the availability of spirometry data. We used pre- and post-bronchodilator data using the Global Initiative for Chronic Obstructive Lung Disease criteria to calculate the prevalence rates. However, important limitations need to be considered, including the cross-sectional nature of the study. Because a single UACR and creatinine measurement was used in the NHANES surveys, individuals might be falsely identified as having CKD, especially for participants with CKD of an early stage. Further, the number of participants with advanced CKD was small and whether there are any of the observed associations among individuals with more advanced kidney disease should be examined in future longitudinal studies using spirometry data. Recent reports indicate that GOLD criteria could misclassify some patients with normal lung function as those with impaired lung function[34]. Future studies should consider using Global Lung Initiative classification to diagnose impaired lung function. Finally, we did not have additional details to further attribute potential reasons for underlying restrictive lung function patterns noted in CKD and other measures of adiposity (such as waist-to-hip ratio), which also merits further investigations.

In summary, in a representative cohort of US adults, impaired lung function was more common in individuals with CKD. UACR ≥ 30 mg/g was independently associated with both obstructive and restrictive lung function and eGFR < 60 mL/min/1.73 m2 was associated with obstructive lung function. Furthermore, longitudinal studies examining the burden of impaired lung function and lung disease in those with advanced CKD are needed. Importantly, mechanisms relating kidney function and lung disease in CKD and their impact on patient-centered outcomes are warranted.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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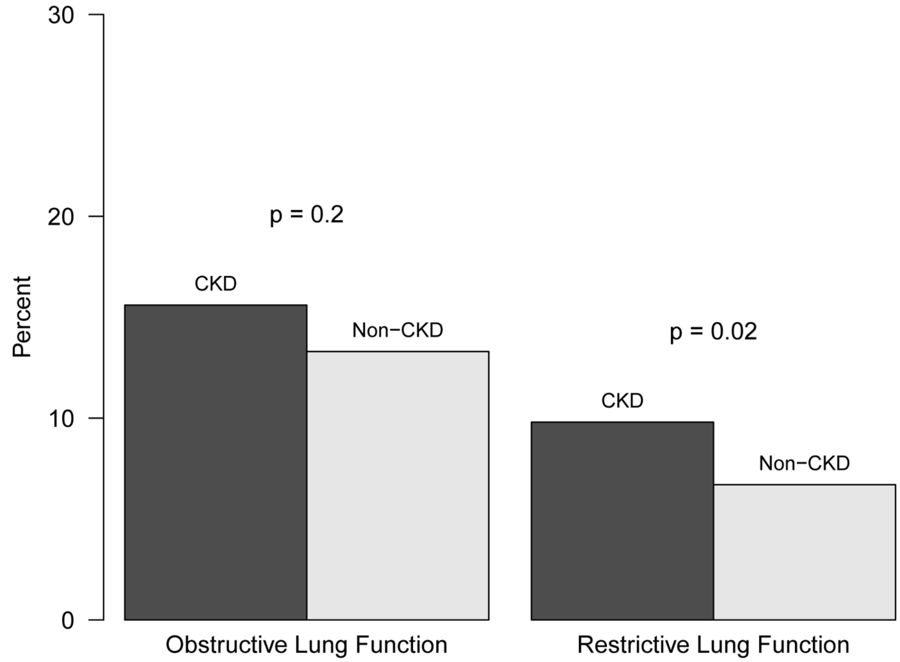

Figure 1.
Age- and sex-adjusted prevalence of obstructive and restrictive lung function in patients with and without CKD

Table 1

Baseline characteristics of study participants with and without CKD

Variable[#]	Entire cohort (N=7610)	CKD (n=1338)	Non-CKD (n=6272)
Age, y	55.2±0.2	62.1±0.3	54.1±0.2
Male Sex	48.7(0.7)	46.7(1.9)	49.0(0.8)
Race/Ethnicity			
White	74.4(1.9)	71.1(2.5)	75.0(1.9)
Black	9.5(1.0)	12.7(1.8)	9.0(0.9)
Mexican American	6.0(0.9)	6.2(1.1)	5.9(0.9)
Other Hispanic	4.4(0.7)	4.5(0.8)	4.3(0.7)
Other	5.7(0.6)	5.5(1.0)	5.7(0.6)
Smoking status			
Current	19.0(0.8)	19.7(1.5)	18.8(0.8)
Former	29.9(0.9)	35.1(1.7)	29.1(1.1)
Never	51.1(0.9)	45.2(2.2)	52.1(1.0)
BMI, kg/m^2	29.2±0.1	30.7±0.3	29.0±0.1
Diabetes	13.4(0.5)	30.1(1.8)	10.7(0.5)
Hypertension	41.5(0.9)	66.2(2.0)	37.6(1.0)
Self-reported COPD	8.1(0.7)	15.3(1.8)	6.9(0.6)
Self-reported Asthma	7.6(0.6)	9.5(1.4)	7.3(0.6)
Respiratory Medication use[*]	5.8(0.5)	7.1(1.1)	5.3(0.5)
FEV1, ml	2927.3±14.5	2514.1±33.0	2991.7±15.5
FVC, % predicted	97.4±0.3	93.3±0.7	98.0±0.3
FEV1/FVC	0.75 ±0.002	0.73 ±0.004	0.76 ±0.002
eGFR (ml/min/1.73 m^2)	87.8±0.4	71.4±1.1	90.4±0.3
eGFR category			
≥90 ml/min/1.73 m^2	48.9(1.1)	26.8(1.9)	52.4(1.1)
60–89 ml/min/1.73 m^2	44.6(0.9)	25.3(2.0)	47.6(1.1)
<60 ml/min/1.73 m^2	6.5(0.4)	47.8(2.4)	0
UACR, mg/g	6.5 [4.3–11.4]	37.5 [8.7–79.4]	6.1 [4.2–9.4]
UACR ≥30 mg/g	8.4(0.5)	61.7(2.4)	0

Note: Values for categorical variables are given as weighted percentage ± standard error; for continuous variables, as weighted mean ± standard error or median [interquartile range].

[*] Reported prescription respiratory agent use (bronchodilator, anti-asthmatic, or inhaler);

[#] All variables were significantly different between CKD and non-CKD groups except for sex and asthma; UACR was tested for significance as logged values;

BMI – body mass index; CKD – chronic kidney disease as defined in Methods; COPD – chronic obstructive pulmonary disease; FEV1 – forced expiratory volume in first second of expiration; FVC -= forced vital capacity; UACR, urine albumin creatinine ratio

Table 2

Age- and sex-adjusted prevalence of obstructive and restrictive lung function based on eGFR and albuminuria*

Type of lung impairment	UACR <30mg/g	UACR ≥30mg/g
Obstructive lung function*		
eGFR ≥60 mL/min/1.73 m2	13.3 (11.6–15.0)	14.8 (9.9–19.8)
eGFR <60 mL/min/1.73 m2	16.5 (11.4–21.7)	16.2 (6.7–25.7)
Restrictive lung function**		
eGFR ≥60 mL/min/1.73 m2	6.8 (5.7–7.8)	12.3 (9.1–15.6)
eGFR <60 mL/min/1.73 m2	5.1 (1.9–8.3)	15.0 (6.5–23.5)

Note: Values given as prevalence (95% confidence interval) in percentages. Adjusted to the mean age of 55 years and 50% males

*overall p-value =0.5 and

**overall p value= 0.006;

eGFR - estimated glomerular filtration rate; UACR - urinary albumin-creatinine ratio

Table 3

Factors associated with obstructive lung function, compared to normal lung function, in entire cohort

Variable	Multivariable-adjusted OR (95% CI)
Age, per 1-y older	1.06 (1.05–1.07)
Sex, Female vs. Male	0.60 (0.48–0.74)
Race	
White	1.00 (reference)
Black	0.58 (0.47–0.71)
Mexican American	0.32 (0.25–0.40)
Other Hispanic	0.40 (0.29–0.54)
Other race	0.91 (0.55–1.52)
Smoking status	
Current	6.09 (4.79–7.73)
Former	2.47 (1.98–3.08)
Never	1.00 (reference)
BMI, per 1-kg/m^2 higher	0.96 (0.95–0.98)
Diabetes	1.00 (0.76–1.31)
Hypertension	1.13 (0.97–1.32)
eGFR, per 5-ml/min/1.73 m^2 lower	1.03 (1.01–1.06)
UACR ≥30 mg/g	1.42 (1.07–1.88)

Note: n=6780.

BMI - body mass index; CI, confidence interval; eGFR - estimated glomerular filtration rate; OR, odds ratio; UACR, Urinary albumin-creatinine ratio

Table 4

Factors associated with restrictive lung function, compared to normal lung function, in entire cohort

Variable	Multivariable-adjusted OR (95% CI)
Age, per 1-y older	1.04 (1.02–1.05)
Sex, Female vs. Male	1.01 (0.77–1.33)
Race	
White	1.00 (reference)
Black	1.11 (0.87–1.41)
Mexican American	0.82 (0.61–1.11)
Other Hispanic	1.39 (1.01–1.92)
Other race	6.78 (4.71–9.74)
Smoking status	
Current	1.67 (1.15–2.42)
Former	1.08 (0.79–1.49)
Never	1.00 (reference)
BMI, per 1-kg/m^2 higher	1.07 (1.05–1.09)
Diabetes	2.32 (1.67–3.21)
Hypertension	1.14 (0.88–1.47)
eGFR, per 5-ml/min/1.73 m^2 lower	0.96 (0.93–0.99)
UACR ≥30 mg/g	1.43 (1.01–2.03)

Note: n=5987.

CI, confidence interval; OR, odds ratio; BMI - body mass index; eGFR - estimated glomerular filtration rate; UACR - urine albumin-creatinine ratio.

Table 5

Associations of various factors with all-cause mortality, NHANES 2007–2010

Factor	HR (95% CI)	P-value
Age, per 1-y older	1.07 (1.02–1.11))	0.008
Female sex	0.86 (0.53–1.40)	0.5
White Race	0.76 (0.49–1.17)	0.2
Diabetes	1.23 (0.66–2.31)	0.5
Hypertension	1.28 (0.74–2.20)	0.4
Current or past smoker	1.47 (0.85–2.54)	0.2
Normal lung function	1.00 (reference)	
Obstructive lung function	2.68 (1.80–3.97)	<0.001
Restrictive lung function	0.96 (0.35–2.61)	0.9
eGFR, per 5-ml/min/1.73 m^2 lower	1.04 (0.94–1.16)	0.4
UACR ≥30 mg/g	1.66 (0.95–2.90)	0.08

Note: Model included age, sex, race, diabetes, hypertension, smoking status, lung function, eGFR and albuminuria.

CI, confidence interval; eGFR, estimated glomerular filtration rate; HR, hazard ratio; NHANES, National Health and Nutrition Examination Survey; UACR, urinary albumin-creatinine ratio