Research Article

Pulmonary Function Trajectories Preceding Death Among Older Adults: A Long-Term Community-Based Cohort Study

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Abstract

Background: Poor pulmonary function (PF) has been linked to mortality, but the timing of PF changes before death remains unclear. We aimed to examine the association between PF and mortality and identify different PF trajectories precedes death.

Methods: Within the Rush Memory and Aging Project, 1438 participants without chronic obstructive pulmonary disease were followed for up to 22 years. PF was assessed annually using a composite score (tertiled as low, medium, and high) based on forced vital capacity (FVC), forced expiratory volume in 1s (FEV1), and peak expiratory flow (PEF). Survival status was observed during the follow-up period. Data were analyzed using Cox regression, Laplace regression, and mixed-effect models.

Results: During the follow-up, 737 (51.25%) participants died. Compared to high PF, the hazard ratio (95% confidence interval [CI]) of mortality was 1.35 (1.05, 1.72)/1.63 (1.25, 2.12) for medium/low PF. The median survival time (95% CI) was shortened by 0.80 (0.01–1.61)/1.72 (0.43–3.01) years for participants with medium/low PF, compared to high PF. In multiadjusted trajectory analysis, the significant differences between decedents and survivors occurred at 7 years before death for composite PF (mean difference [95% CI]: 0.14 [0.02–0.25]), 6 years for FEV1 (0.21 [0.08–0.33]) and FVC (0.21 [0.08–0.34]), and 8 years for PEF (0.21 [0.06–0.37]), and became greater thereafter.

Conclusion: Poor PF is associated with elevated mortality and shortens survival for nearly 2 years. An acceleration in PF decline tends to occur 7 years before death. Poor PF, together with its decline, might be a predictor of mortality among community-dwelling older adults.

Keywords: Cohort study, Mortality, Pulmonary function, Trajectory

Aging is accompanied by a decline in pulmonary function (PF) and an increase in heterogeneity in individual trajectories (1). In order to evaluate respiratory health comprehensively, PF can be assessed using a composite measure, including forced expiratory volume in 1s (FEV1), forced vital capacity (FVC), and peak expiratory flow (PEF) (2–4). Among older adults, monitoring pulmonary health to detect impaired PF and changes in PF may have implications for maintaining general health (5–7).

Several population-based longitudinal studies have shown that poor PF, as assessed by a single PF indicator, strongly predicts mortality (8–12). However, single PF indicators, like FEV1 (the volume of air exhaled with force for 1 second), FVC (the maximum amount of air that can be exhaled after a maximum inhalation), and PEF (the maximum speed of expiration), evaluate PF from different dimensions, and these indicators are usually evaluated jointly in clinical diagnosis (13). FEV1 and FVC reflect mostly intrinsic PF...
characteristics, while PEF reflects both PF and respiratory muscle strength (14). Thus, a composite measure including FEV1, FVC, and PEF could yield a more-stable measure of PF, allowing earlier detection of lung impairment, before the occurrence of irreversible respiratory damage (15–17). In the process of death, an accelerated functioning decline has been observed (18). Moreover, a small number of studies have shown that accelerated physiological aging of the lungs (ie, modifications in elastic recoil and thorax compliance) begins at the age of about 50–55 years and with different trajectories, which are associated with subsequent health conditions (19–21). However, long-term patterns in PF trajectory among community-dwelling older adults remain unclear, particularly in the years preceding death.

In this study, we aimed to (a) examine the association of PF and its long-term changes with mortality and (b) identify the changes in PF trajectory preceding death using data from a community-based cohort study of older adults with annual follow-up.

### Method

#### Study Design and Participants

The Rush Memory and Aging Project (MAP) is an ongoing longitudinal cohort study of common chronic conditions of old age (22). The study participants in MAP were recruited from continuous care retirement communities, senior and subsidized housing, church groups, and social service agencies in Chicago and North-Eastern Illinois, USA (22). A comprehensive clinical evaluation, neurological examination, and extensive cognitive tests were performed with each participant at the time of enrollment and thereafter (23).

From 1997 to 2020, a total of 2 192 participants were annually followed up for a maximum of 22 years. We excluded a total of 754 participants due to missing follow-up data (n = 282), missing information on PF at study entry (n = 270) and follow-up (n = 434), or the presence of chronic obstructive pulmonary disease (COPD) at baseline (n = 99). This left a total of 1 438 participants remaining for the current study (Supplementary Figure 1).

The study was approved by the Institutional Review Board of Rush University Medical Center and was performed in accordance with the ethical standards laid out in the 1964 Declaration of Helsinki and its later amendments. All participants signed an informed consent and Anatomical Gift Act for organ donation before enrollment.

#### Data Collection

Information on demographic characteristics, socioeconomic status, and lifestyle factors was collected at baseline (23). Education was defined in terms of the number of years of formal schooling. Height and weight were measured at baseline while participants were wearing light clothing and no shoes. Body mass index (BMI) was calculated as weight (kg)/height (m²). Alcohol consumption was measured by the average amount of alcohol (in grams) consumed per day during the past year. Smoking status was categorized as never, former, or current smoking. Physical activity was assessed using questions adapted from the National Health Interview Survey (24). Total hours of engaging in physical activities per week during the past 2 weeks were calculated and were further categorized into higher and lower levels by the median. Global cognitive function was assessed using a battery of 19 cognitive performance tests. A composite measure of frailty was developed based on grip strength, gait speed, BMI, and fatigue. Participants in the lowest quintiles of grip strength, gait speed, and BMI were defined as frail, and any reports of fatigue were considered consistent with frailty. Participants with 0 or 1 frailty component were considered not frail, and those participants with ≥2 frail components were considered frail (25).

Diabetes was ascertained based on the self-reported medical history, glycated hemoglobin (HbA1c) ≥ 6.5%, fasting plasma glucose ≥ 126 mg/dL, random blood glucose ≥200 mg/dL or the use of diabetes medication (26). Hypertension was identified based on systolic blood pressure ≥140 mm Hg, diastolic blood pressure ≥90 mm Hg, or self-reported antihypertensive drugs use. Stroke was diagnosed by a clinician through a review of self-reported information on medical history, neurological exams, cognitive testing, and participant interviews. Heart disease was assessed based on self-reported information of medical history, including congestive heart failure, coronary, heart attack, coronary thrombosis, coronary occlusion, and myocardial infarction. Cancer was identified by self-reported medical history at an annual detailed clinical evaluation. Depression was determined by the diagnosis of the clinician or the use of antidepressive medication.

#### Assessment of PF

PF was tested using a hand-held spirometer (MicroPlus Spirometer MS03, MicroMedical LTC. Kent, UK), a method that has been used in large epidemiological studies of PF and is consistent with the standards of the American Thoracic Society (27). All participants met the acceptability criteria. The repeatability criteria were met when the second largest FEV1 and FVC were within 5% of the largest values. FVC (the maximum amount of air that can be exhaled after a maximum inhalation), FEV1 (the volume of air exhaled with force for 1 second), and PEF (the maximum speed of expiration) were measured twice at baseline and during each annual follow-up examination. The average of the 2 measurements for each parameter was calculated. Then, the raw scores of the 3 indicators were converted into z-scores using the means and standard deviations calculated from the entire cohort. Finally, a comprehensive PF score was created by averaging the z-scores of FVC, FEV1, and PEF (15), with a higher score indicating better PF. In data analysis, the composite PF score and each indicator at baseline were used as both continuous and categorical variables. The latter was trichotomized into 3 groups according to the tertiles of each indicator and the composite PF score (low, medium, and high). FEV1% predicted was calculated using the Global Lung Initiative formula standardized by age, sex, race, and height. Participants with an FEV1/FVC ratio less than or equal to 0.7 were considered to have possible COPD (28).

#### Mortality

Survival status was observed during the entire follow-up period. All participants agreed to organ donation and signed an Anatomical Gift Act as a condition of study entry, and the follow-up rate exceeded 90% overall with an autopsy rate in excess of 80%. Therefore, we captured virtually all deaths that occurred among study participants (29). This was supplemented by querying death records if necessary. At the time of these analyses, 100% of the vital status data were complete and up to date.

#### Statistical Analysis

Baseline characteristics of the study population by survival status were compared using chi-square tests for categorical variables and one-way analysis of variance or Wilcoxon rank-sum tests for continuous variables.
Cox proportional hazards models were used to estimate the hazard ratios (HRs) and 95% confidence intervals (CIs) for mortality associated with PF (including FEV1, FVC, and PEF). Follow-up time was calculated as the time from study entry until the date of death or the final examination. Laplace regression was used to estimate the 50th percentile difference (PD) and 95% CIs of death for FEV1, FVC, PEF, and composite PF categories separately. In the basic-adjusted model, we adjusted age, sex, and education. In the multiadjusted model, we further adjusted for baseline smoking status, alcohol consumption, physical activity, cognitive function, frailty, BMI, heart disease, hypertension, diabetes, stroke, cancer, and depression.

Trajectories of PF were ascertained using a backward timescale. That is, year 0 was the year of the last follow-up for the survivors and the year of death for the decedents. A linear mixed-effect model was performed to capture the PF trajectory and its difference between survivors and decedents. The fixed effect included PF, follow-up time (year), and their interaction. The random effect included random intercept and slope, allowing individual differences to be reflected at baseline and across follow-up. The difference in PF between survivors and decedents was estimated for each year preceding the year 0. The following were considered potential confounders and adjusted for in all analyses: age at year 0, sex, education, smoking status, alcohol consumption, physical activity, cognitive function, frailty, BMI, heart disease, hypertension, diabetes, stroke, cancer, and depression.

In sensitivity analysis, we repeated the analyses after (a) performing multiple imputations for subjects with missing values of PF or some covariates, (b) excluding participants who developed COPD (n = 128) or dementia (n = 408) during the follow-up, (c) using FEV1% predicted as PF indicator; (d) excluding participants with incident chronic diseases (n = 381), and (e) stratifying the analyses by baseline age (<75 vs ≥75 years), smoking status (smoking vs nonsmoking), and physical activity level (low vs high). p Values <.05 were considered statistically significant. All statistical analyses were performed using Stata SE 16.0 for Windows (StataCorp LLC, College Station, TX).

### Results

#### Characteristics of the Study Population

Of the 1,438 participants, 1,080 (75.10%) were women, and the mean age of the study population was 79.81 (standard deviation: 7.57) years. The z-score of PF ranged from −2.10 to 3.16 at baseline. Baseline FEV1, FVC, and PEF measures ranged from 0.38 to 3.54 L, 0.41 to 4.04 L, and 38 to 822 L, respectively. The FEV1% predicted ranged from 16.82% to 162.14% at baseline. Compared to survivors, participants who died over the follow-up were more likely to be men, older, have a lower BMI, have fewer years of education, have lower levels of alcohol consumption and physical activity, have a poorer cognitive function, and have frailty, hypertension, stroke, heart disease, diabetes, or depression (Table 1). Compared to participants with high PF, those with medium or low PF had a higher mortality rate (Supplementary Table 1). Compared to the participants who were included in the study population, those who were excluded were more likely to be male, have a lower BMI, have a poor cognitive function and PF, have frailty, and be less physically active (Supplementary Table 2).

#### Baseline PF and Mortality

During the follow-up period (median: 7 years, interquartile range: 4–10 years), 737 (51.25%) participants died. In the multiadjusted

![Table 1. Baseline Characteristics of the Study Population by Survival Status at the End of the Follow-up](chart)

| Characteristics          | Survivors (N = 701) | Decedents (N = 737) | p    |
|--------------------------|---------------------|---------------------|------|
| Follow-up time, years    | 7.00 (4.00, 11.00)  | 7.00 (4.00, 10.00)  | —    |
| Age at baseline, years   | 76.76 ± 7.68        | 82.71 ± 6.21        | <.001|
| Female                   | 563 (80.31)         | 517 (70.15)         | <.001|
| Education, years         | 15.09 ± 3.40        | 14.65 ± 3.00        | 0.001|
| BMI, kg/m²               | 27.95 ± 5.59        | 27.06 ± 5.05        | 0.002|
| Smoking                  |                      |                     |      |
| Never                    | 396 (56.57)         | 452 (61.50)         | 0.212|
| Ever smoker              | 286 (40.86)         | 266 (36.19)         |      |
| Current smoker           | 18 (2.57)           | 17 (2.31)           |      |
| Alcohol consumption, g/day| 1.08 (0.00, 6.04)  | 0.00 (0.00, 5.28)  | <.001|
| Physical activity, hour/week| 3.00 (1.04, 5.00) | 2.25 (0.75, 4.50) | <.001|
| Frailty                  | 32.4 (5.57)         | 65 (8.82)           | 0.001|
| Cognitive function       | 0.28 (0.10, 0.59)   | −0.01 (0.46, 0.30)  | <.001|
| Hypertension             | 369 (52.64)         | 401 (54.41)         | 0.501|
| Diabetes                 | 98 (13.98)          | 112 (15.20)         | <.001|
| Heart disease            | 36 (5.14)           | 90 (12.23)          | <.001|
| Stroke                   | 40 (6.56)           | 79 (11.24)          | 0.003|
| Cancer                   | 226 (32.24)         | 241 (32.70)         | 0.852|
| Depression               | 108 (15.41)         | 142 (19.27)         | 0.054|
| Pulmonary function*      | 0.12 (−0.39, 0.68)  | −0.23 (−0.75, 0.43) | <.001|
| FEV1 (L)                 | 1.72 (1.39, 2.12)   | 1.52 (1.22, 1.93)   | <.001|
| FVC (L)                  | 1.94 (1.57, 2.35)   | 1.77 (1.41, 2.21)   | <.001|
| PEF (L/min)              | 290.50 (234.00, 350.25) | 240.00 (182.75, 318.50) | <.001|
| FEV1% predicted          | 73.04 (62.25, 86.86) | 71.10 (57.45, 88.69) | 0.004|

Notes: Values are mean ± SD, n (%), or median (interquartile range). Missing data: heart disease = 1; stroke = 125; smoking status = 3; alcohol consumption = 3; BMI = 32. BMI = body mass index; FEV1 = forced expiratory volume in 1 s; FVC = forced vital capacity; PEF = peak expiratory flow; SD = standard deviation.

*Pulmonary function was a composite score calculated by z-scores of FEV1, FVC, and PEF.
Cox model, each 1-standard deviation increase in PF was related to a decreased risk of mortality (HR: 0.73, 95% CI: 0.65–0.82). Compared to participants with high PF, the multiaed adjusted HRs (95% CIs) of mortality were 1.35 (1.05–1.72) and 1.63 (1.25–2.12) for those with medium and low PF, respectively (Table 2). This pattern of results was similar for all 3 individual PF indicators (ie, FEV1, FVC, and PEF) (Table 2).

In Laplace regression, the median survival time of participants with medium or low PF was 0.80 (95% CI: 0.01–1.61) or 1.72 (95% CI: 0.43–3.01) years shorter compared to those with high PF (Table 2 and Figure 1). Furthermore, the lowest tertile of FEV1/FVC/PEF might shorten the median survival time by 1.50 (0.31–2.68)/1.22 (0.03–2.47)/1.19 (0.03–2.34) years compared to the highest one.

Detection of the Time Point at Faster PF Decline Preceding Death
Over the follow-up period, PF tended to decline among almost all participants. The annual change of PF was −0.05 (95% CI: −0.05 to −0.04) for survivors and −0.08 (95% CI: −0.08 to −0.07) for decedents. Compared with the survivors, the decedents had a faster PF decline rate (Figure 2). In the multiaed mixed-effect model, the significant differences in PF between decedents and survivors occurred 7 years (mean difference: 0.14, 95% CI: 0.02–0.25, p = 0.017) before death and became greater thereafter (Table 3). FEV1 and FVC were higher in survivors compared to decedents starting at 6 years before death (mean difference [95% CI]: 0.21 [0.08–0.33]/0.21 [0.08–0.34]) and persisted to time 0. PEF was higher in survivors compared to decedents from 8 years before death (mean difference [95% CI]: 0.21 [0.06–0.37]) and persisted to time 0.

Sensitivity Analysis
The results were not altered largely when we repeated the analyses after (a) conducting multiple imputation for missing values of

### Table 2. Association Between Baseline Pulmonary Function (PF) and Death

| PF*          | No. of Participants | No. of Cases | HR (95% CI)† | HR (95% CI)‡ | 50th PD (95% CI)† | 50th PD (95% CI)‡ |
|--------------|---------------------|--------------|--------------|--------------|------------------|------------------|
| Composite PF score                     |                   |              |              |              |                  |                  |
| Continuous   | 1 438               | 737          | 0.64 (0.58, 0.72) | 0.73 (0.65, 0.82) | 2.06 (1.47, 2.65) | 1.25 (0.66, 2.84) |
| Categorical  |                     |              |              |              |                  |                  |
| High         | 473                 | 206          | 1.00 (Reference) | 1.00 (Reference) | 0 (Reference) | 0 (Reference) |
| Medium       | 489                 | 224          | 1.45 (1.15, 1.83) | 1.35 (1.05, 1.72) | −1.74 (−2.59, −0.89) | −0.80 (−1.61, −0.01) |
| Low          | 476                 | 307          | 2.10 (1.65, 2.69) | 1.63 (1.25, 2.12) | −3.09 (−4.27, −1.91) | −1.72 (−3.01, −0.43) |
| FEV1         |                     |              |              |              |                  |                  |
| Continuous   | 1 438               | 737          | 0.71 (0.64, 0.78) | 0.77 (0.69, 0.85) | 1.63 (0.99, 2.27) | 0.98 (0.48, 1.48) |
| Categorical  |                     |              |              |              |                  |                  |
| High         | 475                 | 205          | 1.00 (Reference) | 1.00 (Reference) | 0 (Reference) | 0 (Reference) |
| Medium       | 494                 | 241          | 1.48 (1.18, 1.85) | 1.33 (1.05, 1.69) | −1.36 (−2.17, −0.55) | −0.81 (−1.58, −0.04) |
| Low          | 469                 | 291          | 1.97 (1.55, 2.50) | 1.55 (1.19, 2.01) | −2.70 (−3.81, −1.60) | −1.50 (−2.68, −0.31) |
| FVC          |                     |              |              |              |                  |                  |
| Continuous   | 1 438               | 737          | 0.73 (0.66, 0.81) | 0.78 (0.70, 0.86) | 1.53 (0.89, −2.16) | 0.99 (0.53, −1.45) |
| Categorical  |                     |              |              |              |                  |                  |
| High         | 475                 | 217          | 1.00 (Reference) | 1.00 (Reference) | 0 (Reference) | 0 (Reference) |
| Medium       | 485                 | 232          | 1.39 (1.12, 1.72) | 1.29 (1.03, 1.62) | −1.18 (−2.04, −0.32) | −0.71 (−1.47, 0.06) |
| Low          | 478                 | 288          | 1.74 (1.38, 2.18) | 1.42 (1.11, 1.82) | −2.44 (−3.55, −1.33) | −1.22 (−2.47, 0.03) |
| PEF          |                     |              |              |              |                  |                  |
| Continuous   | 1 438               | 737          | 0.72 (0.65, 0.79) | 0.82 (0.74, 0.91) | 1.64 (1.12, −2.15) | 0.64 (0.17, −1.12) |
| Categorical  |                     |              |              |              |                  |                  |
| High         | 470                 | 319          | 1.00 (Reference) | 1.00 (Reference) | 0 (Reference) | 0 (Reference) |
| Medium       | 492                 | 222          | 1.37 (1.11, 1.70) | 1.31 (1.05, 1.64) | −1.58 (−2.50, −0.66) | −0.43 (−1.35, 0.49) |
| Low          | 476                 | 196          | 1.85 (1.49, 2.30) | 1.38 (1.10, 1.75) | −2.81 (−3.89, −1.72) | −1.19 (−2.34, −0.03) |

Notes: HR = hazards ratio; PD = percentile difference; CI = confidence interval; FEV1 = forced expiratory volume in 1s; FVC = forced vital capacity; PEF = peak expiratory flow.

*PF index were all standardized z-scores.
†Adjusted for age, sex, and education.
‡Adjusted for age, sex, education, smoking, alcohol consumption, physical activity, body mass index, cognitive function, frailty, heart disease, hypertension, diabetes, stroke, cancer, and depression.
baseline PF and some covariates (n = 1614) (Supplementary Table 3); (b) excluding participants with incident COPD or dementia during
the follow-up (Supplementary Tables 4 and 5); (c) using FEV1% predicted as PF indicator (Supplementary Table 6); (d) excluding parti-
cipants with incident chronic diseases (Supplementary Table 7); and (e) stratifying the analyses by age group, smoking, and physical ac-
tivity level (Supplementary Tables 8–10).

In this community-based cohort study of older adults, we found
that (a) compared to high PF (including FEV1, FVC, and PEF), low
PF is associated with a higher risk of mortality and shortens sur-
vival by nearly 2 years; (b) 18-year PF trajectories show significantly
lower PF among decedents compared to survivors in the 7 years preced-
ing death.

PF indicators such as FEV1, FVC, and PEF have been individu-
ally associated with mortality (8–12). In addition, FEV1, FVC, and
PEF have been used to evaluate the PF from different dimensions and
reflect not only lung capacity but also the resistance encountered
during breathing (15,27). Therefore, these indicators are usually
applied jointly in clinical diagnosis (30). To date, no studies have
investigated the association between comprehensive lung function
and mortality among older adults. In this study, we combined FEV1,
FVC, and PEF to more comprehensively assess PF. Our composite PF
indicator reflects pulmonary as well as some respiratory muscle con-
tributions (15,27), which may capture more aspects important for
lung health and thus affect mortality more globally. We found that
poor PF at baseline was associated with elevated mortality. These
findings suggest that baseline pulmonary health may be helpful for
identifying older adults at risk of premature death.

Emerging evidence has shown that aging is accompanied by a
decline in PF caused by physiological lung aging (31). Different tra-
jectories of individual PF may reflect exposures accumulated across
the entire life course (9,32). Throughout the life course, the PF begins
to decline at the age of approximately 25 years, with the rate of de-
cline accelerating at 50–55 years (19–21). To the best of our know-
ledge, no studies have assessed PF trajectory in community-dwelling
older adults. Here, using retrospective time-scale annual trajectory

### Table 3. Differences in Pulmonary Function (PF) Between Survivors and Decedents in the 18 Years Preceding Death

| Years Preceding Death | Composite PF Score* | FEV1* | FVC* | PEF* |
|-----------------------|---------------------|-------|------|------|
| 18                    | -0.24 (−0.56 to 0.07) | -0.04 (−0.77 to 0.01) | 0.17 (−0.37 to 0.71) | −0.39 (−0.64 to 0.14) |
| 17                    | -0.36 (−0.74 to 0.02) | -0.39 (−0.86 to 0.07) | -0.33 (−0.79 to 0.13) | −0.38 (−0.81 to 0.05) |
| 16                    | 0.17 (−0.11 to 0.45) | 0.15 (−0.18 to 0.48) | 0.09 (−0.25 to 0.44) | 0.28 (−0.07 to 0.63) |
| 15                    | 0.21 (−0.06 to 0.47) | 0.15 (−0.17 to 0.46) | 0.17 (−0.15 to 0.49) | 0.31 (−0.05 to 0.68) |
| 14                    | 0.19 (−0.03 to 0.40) | 0.28 (−0.03 to 0.52) | 0.20 (−0.05 to 0.45) | 0.10 (−0.17 to 0.36) |
| 13                    | 0.15 (−0.06 to 0.37) | 0.15 (−0.10 to 0.41) | 0.11 (−0.15 to 0.36) | 0.21 (−0.04 to 0.46) |
| 12                    | 0.04 (−0.22 to 0.30) | -0.01 (−0.31 to 0.30) | -0.02 (−0.32 to 0.28) | 0.15 (−0.15 to 0.45) |
| 11                    | -0.11 (−0.33 to 0.12) | -0.16 (−0.42 to 0.10) | -0.14 (−0.39 to 0.12) | -0.04 (−0.33 to 0.26) |
| 10                    | 0.09 (−0.08 to 0.25) | 0.10 (−0.10 to 0.29) | 0.13 (−0.06 to 0.33) | 0.04 (−0.16 to 0.24) |
| 9                     | 0.08 (−0.06 to 0.22) | 0.09 (−0.07 to 0.25) | 0.05 (−0.11 to 0.21) | 0.11 (−0.05 to 0.27) |
| 8                     | 0.11 (−0.02 to 0.23) | 0.11 (−0.05 to 0.26) | 0.01 (−0.15 to 0.16) | 0.21 (0.06 to 0.37)* |
| 7                     | 0.14 (0.02 to 0.25)* | 0.12 (−0.01 to 0.25) | 0.06 (−0.08 to 0.20) | 0.25 (0.11 to 0.38)* |
| 6                     | 0.17 (0.06 to 0.28)* | 0.21 (0.08 to 0.33)* | 0.21 (0.08 to 0.34)* | 0.12 (0.01 to 0.25)* |
| 5                     | 0.24 (0.13 to 0.36)* | 0.26 (0.13 to 0.40)* | 0.24 (0.10 to 0.37)* | 0.25 (0.12 to 0.39)* |
| 4                     | 0.24 (0.11 to 0.37)* | 0.27 (0.11 to 0.42)* | 0.25 (0.10 to 0.41)* | 0.21 (0.05 to 0.36)* |
| 3                     | 0.23 (0.11 to 0.35)* | 0.21 (0.07 to 0.35)* | 0.12 (0.03 to 0.25)* | 0.37 (0.23 to 0.51)* |
| 2                     | 0.29 (0.18 to 0.40)* | 0.31 (0.19 to 0.44) | 0.20 (0.07 to 0.32)* | 0.40 (0.27 to 0.53)* |
| 1                     | 0.36 (0.25 to 0.47)* | 0.37 (0.24 to 0.49)* | 0.25 (0.11 to 0.38)* | 0.49 (0.36 to 0.62)* |
| 0                     | 0.30 (0.14 to 0.45)* | 0.33 (0.15 to 0.51)* | 0.24 (0.07 to 0.42)* | 0.35 (0.17 to 0.53)* |
| Difference in trajectories | 0.32 (0.25 to 0.40)* | 0.34 (0.26 to 0.43)* | 0.24 (0.15 to 0.33)* | 0.41 (0.32 to 0.50)* |

Notes: CI = confidence interval; FEV1 = forced expiratory volume in 1s; FVC = forced vital capacity; PEF = peak expiratory flow.
*PF index were all standardized z-scores.
†Adjusted for age at death, sex, education, smoking, alcohol consumption, physical activity, body mass index, cognitive function, frailty, heart disease, hypertension, diabetes, stroke, cancer, and depression.
*p < .05.
analysis, we found that decedents have lower PF than survivors 7 years before death. Our findings provide a time window where monitoring and treating PF among community-dwelling older adults could be particularly important for prolonging survival.

The mechanisms through which PF may affect mortality are not well understood. One possibility is that impaired ventilation may directly contribute to mortality through the regulation of oxygenation (33). Additionally, hypoperfusion and hypoxia caused by poor PF (34) could lead to oxidative stress and inflammation (35–37), thereby increasing the risk of death (38–41). In particular, chronic inflammation and oxidative stress are also related to chronic diseases, which can accelerate mortality (42,43). Another possible explanation is that the decline in PF might be due to the accumulation of concurrent diseases, which could be the actual determinants of adverse health outcomes (38,44). Moreover, an accelerated decline in PF before death could reflect age-related increases in oxidative stress and DNA damage (44–46) and other anomalies in the physiological mechanisms of aging (47). Finally, decreased respiratory muscle strength due to frailty is closely associated with impaired PF; which in turn increases the risk of death (48). Therefore, future work should assess the combined effect of frailty and impaired PF on mortality.

Surprisingly, in the current study, we found that smoking, high blood pressure, and cancer diagnosis were not significantly associated with an elevated mortality. This might be explained by the fact that smoking status rather than cumulative tobacco was used, and that the control of hypertension was not considered. Moreover, MAP participants were volunteers that were healthier than the general population, which might have contributed to the negative associations. In accordance with other studies (49,50), we also found that smoking was significantly related to PF decline ($\beta$ [95% CI]: −0.28 [−0.49, −0.07]) over time, but depression was not ($\beta$ [95% CI]: −0.06 [−0.26, 0.15]).

Strengths of this study include the community-based cohort design with a relatively large sample size and long-term annual follow-up. Additionally, we used an aggregated indicator of PF, which provides a more comprehensive measure of respiratory function. Nonetheless, some limitations should be pointed out. First, the Rush MAP participants were volunteers, and not randomly selected from the community. Compared to the general population, the participants were better educated and scored higher on cognitive tests, characteristics that are associated with lower mortality (51). Therefore, caution is needed when our findings are generalized to other populations. In addition, some participants who dropped out of the study during the follow-up (12.86%) may have done so because of poor health conditions. This might have led to an underestimation of the observed associations. Second, there is a risk of selection bias due to missing data on some variables. However, we repeated the analyses after multiple imputations, and the results were not altered substantially. Third, although the composite PF has been validated in the MAP population, it has not been used in other study populations. However, using individual FEV1, FVC, or PEF to repeat the analysis, similar results to those from the initial analysis were shown. Further population-based longitudinal studies using the composite score are warranted. Finally, although we included a wide range of variables, some potential confounders (such as asthma) could not be adjusted for due to the unavailability of such information.

In conclusion, this study provides evidence that poor PF predicts mortality risk and substantially shortens survival. The trajectories of PF over 18 years show significantly lower PF among decedents compared to survivors in the 7 years preceding death. Our findings underscore the importance of monitoring PF and detecting PF decline early in order to prolong survival among community-dwelling older adults with targeted interventional strategies.

**Supplementary Material**

Supplementary data are available at The Journals of Gerontology, Series A: Biological Sciences and Medical Sciences online.

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**Conflict of Interest**

None declared.

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**Author Contributions**

W.X. and X.Q.: conceived idea for the study. W.X. and D.A.B.: funding acquisition. J.W. wrote the original draft, J.W.: formal analysis, J.W., J.G., and W.X.: methodology. All authors critically revised the manuscript for intellectual content and approved the final version.

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The funding source had no role in the design and conduct of the study, the collection, management, analysis, and interpretation of the data, the preparation, review, and approval of the manuscript, or the decision to submit the manuscript for publication.

**Data Availability Statement**

Data can be found and requests for MAP data can be made online at the Rush Alzheimer’s Disease Center Resource Sharing Hub (https://www.radc.rush.edu/).

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