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Alternative ways of expressing forced expiratory volume in the first second and long-term mortality in elderly patients with asthma

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ABSTRACT

Background: Clinical and epidemiologic evidence on asthma in the elderly is scant. There is evidence that forced expiratory volume in the first second (FEV₁), a commonly used indicator of overall pulmonary function, might not be an independent predictor of 5-year mortality in elderly patients with asthma.

Objective: To investigate the association between FEV₁ expressed using 3 alternative methods and 5-, 10-, and 15-year mortality in a population of elderly patients with asthma.

Methods: Participants in the Salute Respiratoria nell'Anziano study were included. Asthma was diagnosed at baseline according to spirometric and clinical data. Vital status at 15 years was assessed using death registries. FEV₁ was expressed as percentage of predicted, divided by height cubed, and as a multiple of the sex-specific first percentile. The association between FEV₁ and mortality was evaluated using Cox proportional hazard models.

Results: Two hundred patients were studied (52% women, mean age 73.1 years, standard deviation 6.2 years). All FEV₁ measurements were associated with mortality at unadjusted analysis. After correction for potential confounders, no association was found between FEV₁ and 5-year mortality. Only FEV₁ as a multiple of the sex-specific first percentile was independently associated with 10-year (hazard ratio 0.35, 95% confidence interval 0.14–0.87) and 15-year (hazard ratio 0.38, 95% confidence interval 0.19–0.79) mortality.

Conclusion: Although extensively used, FEV₁ expressed as percentage of predicted does not seem to be the best predictor of mortality in elderly patients with asthma. Although no spirometric index can predict 5-year mortality in this population, FEV₁ as a multiple of the sex-specific first percentile should be considered when longer-term prognostic stratification is needed.

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Introduction

Asthma is estimated to affect approximately 300 million people worldwide,¹ with a prevalence ranging from 1% to 18% of the population in different countries^{2,3} and increasing in recent years.⁴ At the same time, the impact of asthma on mortality and morbidity has decreased, as if this disease were becoming less severe over time. Greater diagnostic accuracy and better care are the likely explanations for these findings.¹ In elderly patients, the estimated prevalence of asthma is 6.5%,⁵ and this disease represents an important clinical challenge. This notwithstanding, most of the

available clinical and epidemiologic evidence on this disease refers to young or young adult populations.³ The lack of data on asthma in the elderly may be due to the difficulty in recognizing asthma in this population, which is often undiagnosed, because the boundary between asthma and chronic obstructive pulmonary disease (COPD) is frequently uncertain in older patients.⁶ Even the canonical criterion of full reversibility of bronchial obstruction does not always apply to elderly patients with asthma.⁶ Furthermore, asthma in the elderly is heterogeneous in nature because patients diagnosed with this disease in the first decades of life coexist with patients who develop asthma in the sixth or seventh decade.⁷ In 2007, the authors evaluated the factors associated with 5-year mortality in patients at least 65 years old with asthma and found that asthma was associated with increased risk of death.⁸ Mortality,

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however, was related mainly to nonrespiratory factors, such as age, depression, smoking, and malnutrition, but not to forced expiratory volume in the first second (FEV₁) or forced vital capacity (FVC).⁸ The lack of association between decreased FEV₁ expressed as percentage of predicted (FEV₁PP) and mortality may seem counterintuitive because FEV₁ is considered a general indicator of severity of pulmonary dysfunction.⁹ A possible explanation for this finding is that the use of predicting equations in the elderly population may be a suboptimal method to standardize the FEV₁ and alternative methods of expressing FEV₁ seem to predict mortality better than FEV₁PP in a broad population.¹⁰ In patients with COPD, for example, FEV₁ expressed as a multiple of the sex-specific first percentile (FEV₁Q) of sample distribution seems to be more informative about prognosis compared with FEV₁PP.¹¹

Against this background, the authors took the opportunity of completing their 15-year follow-up of the Salute Respiratoria nell'Anziano (SaRA; Respiratory Health in the Elderly) study to evaluate the association between spirometric data and mortality at different follow-up times. The objectives of this analysis were to compare the prognostic significance of different methods of standardizing FEV₁ with regard to mortality at 5, 10 and 15 years in elderly patients with asthma.

Methods

Sample

From January 1996 through July 1999, 1,970 outpatients were recruited from 24 departments of geriatrics or respiratory medicine within the context of the SaRA study. This is a multicenter Italian project investigating various aspects of chronic airway diseases in the elderly population (≥ 65 years of age) attending pulmonary or geriatric outpatient clinics. Study researchers underwent a centralized training course on the rationale and practice of spirometry. Trainees also received instruction about problems peculiar to geriatric patients and geriatric evaluation techniques, with particular attention to impairment of cognitive capacity and functioning. A detailed description of the quality implementation and control program is available elsewhere.¹² All patients at least 65 years old attending the pneumology or geriatric ambulatories of 24 participating institutions from January 1996 through July 1999 were enrolled in the study. The patients were approached by the attending physician and then referred to the study researcher, who performed the evaluation while taking into account the medical records. General exclusion criteria of the SaRA study were severe hepatic failure (Child grades B and C), severe renal failure (plasma creatinine level >2 mg/dL), severe cognitive and/or sensory impairment, hospitalization for any reason within the previous 6 months, and malignant neoplasms.⁶ Data from individual centers were collected by a coordinating center at the Cattedra di Malattie dell'Apparato Respiratorio of the University of Palermo (Palermo, Italy), which also was responsible for quality control, retrieval, and final processing of the data. The study design was approved by the ethical committees of the participating institutions. Details on the SaRA project are available elsewhere.⁶

From the SaRA dataset, the authors selected those patients with a diagnosis of asthma ($n = 233$), defined as an FEV₁ greater than 80% of predicted, a history of wheeze in the preceding year, and no history of chronic cough and sputum; or an FEV₁ less than 80% of predicted, FEV₁ increase at least 12% after fenoterol 100 μ g, and no history of chronic cough and sputum; or an FEV₁ less than 80% of predicted, an FEV₁ increase less than 12% after bronchodilator, history of wheeze in the past year, and no history of chronic cough and sputum.⁶

This definition included patients with no response to bronchodilators but with classic symptoms of asthma. This choice is

justified because of the high prevalence of “fixed” obstruction in elderly patients with asthma.¹³

Excluded were patients with missing height information ($n = 3$). Information on vital status at 15 years was available for 200 of the remaining patients (86%).

Measurement of Variables

All centers were equipped with an identical fully computerized water-sealed Stead-Wells spirometer (Baires System; Biomedin, Padua, Italy) that met the American Thoracic Society recommendations for diagnostic spirometry.¹⁴

This population was described in terms of age and sex, history of smoking (never vs ever smoker), health-related quality of life measured using the St George Respiratory Questionnaire, comorbidity using the Charlson index,¹⁵ and other available variables potentially affecting mortality: overweight (body mass index >29 kg/m²), underweight (body mass index <22 kg/m²), and diagnosis of cardiovascular or cerebrovascular diseases. The presence of cognitive decline was evaluated using the Mini-Mental State Examination,¹⁶ and mood status was evaluated using the Geriatric Depression Scale.¹⁷ Functional status was evaluated using the 6-minute walking test (6MWT).¹⁸ Spirometric variables taken into account were FVC, FEV₁/FVC, and 3 different measurements of FEV₁: (1) FEV₁PP¹⁹ (to maintain consistency with the authors' previous classification of patients, Enright normal spirometric standards were used); (2) FEV₁ standardized by height cubed (FEV₁ht³); and (3) FEV₁ divided by the sex-specific first percentile of the FEV₁ distribution derived from a large population: 0.5 L for men and 0.4 L for women (FEV₁Q).¹⁰ This index approximates to the number of remaining turnovers of a lower survivable limit of FEV₁.

Statistical Methods

Using Cox proportional hazard models, the unadjusted risk was calculated for mortality at 5, 10, and 15 years in relation to the demographic, clinical, and functional characteristics reported earlier. To calculate the de-confounded risk for mortality, multivariable Cox proportional hazard models were used, including variables associated with mortality at unadjusted analysis. Three

Table 1

General characteristics of the population (N = 200)

Women, n (%)	104 (52)
Age (y), mean $\pm$ SD (range)	73.2 $\pm$ 6.2 (65–91)
College education, n (%)	11 (5.5)
Ever smoked, n (%)	110 (55.6)
Body mass index >29 kg/m ² , n (%)	64 (32)
Body mass index <22 kg/m ² , n (%)	22 (11)
Charlson index >1 , n (%)	32 (16)
Cardiovascular diseases, n (%)	43 (21.5)
Cerebrovascular diseases, n (%)	9 (4.5)
Diabetes, n (%)	25 (12.5)
6MWT, percentage predicted, mean $\pm$ SD (range)	76.5 $\pm$ 29.3 (11.1–181.2)
Cognitive impairment, n (%) ^a	26 (13.1)
Depressed mood, n (%) ^b	80 (41.5)
SGRQ, mean $\pm$ SD (range)	34.8 $\pm$ 19.8 (0–92.8)
FVC, mean $\pm$ SD (range)	2.5 $\pm$ 0.9 (0.7–4.9)
FEV ₁ , mean $\pm$ SD (range)	1.5 $\pm$ 0.6 (0.46–3.68)
FEV ₁ PP, mean $\pm$ SD (range)	65.6 $\pm$ 23.7 (24–140)
FEV ₁ ht ³ , mean $\pm$ SD (range)	0.4 $\pm$ 0.1 (0.12–0.72)
FEV ₁ Q, mean $\pm$ SD (range)	3.4 $\pm$ 1.3 (1.1–7.4)
FEV ₁ /FVC, mean $\pm$ SD (range)	62.5 $\pm$ 14.9 (29.6–101.4)

Abbreviations: 6MWT, 6-minute walk test; FEV₁, forced expiratory volume in first second; FEV₁ht³, forced expiratory volume in first second divided by height cubed; FEV₁PP, percentage predicted for forced expiratory volume in first second; FEV₁Q, forced expiratory volume in first second as a multiple of sex-specific first percentile; FVC, forced vital capacity; SD, standard deviation; SGRQ, St George Respiratory Questionnaire.

^aMini-Mental State Examination score <24 .

^bGeriatric Depression Scale score ≥ 5 .

Table 2
Unadjusted hazard ratios for mortality

	HR for 5-y survival	HR for 10-y survival	HR for 15-y survival
Sex (male)	1.52 (0.83–2.75)	1.51 (0.97–2.33)	1.41 (0.99–2.01)
Age (5-y increment)	1.55 (1.25–1.92)	1.6 (1.36–1.89)	1.54 (1.34–1.77)
Ever smokers	1.61 (0.86–3.02)	1.81 (1.14–2.87)	1.82 (1.25–2.64)
Body mass index >29 kg/m ²	0.31 (0.13–0.73)	0.44 (0.25–0.76)	0.61 (0.41–0.91)
Body mass index <22 kg/m ²	3.13 (1.55–6.35)	3 (1.74–5.2)	2.41 (1.46–3.98)
Charlson index >1	1.7 (0.84–3.45)	2 (1.19–3.34)	1.9 (1.22–2.95)
Cardiovascular diseases	1.68 (0.88–3.21)	1.73 (1.07–2.81)	1.76 (1.18–2.63)
Cerebrovascular diseases	2.27 (0.81–6.35)	1.7 (0.69–4.2)	1.04 (0.42–2.55)
Diabetes	1.4 (0.62–3.14)	1.33 (0.72–2.45)	1.15 (0.68–1.94)
Cognitive impairment ^a	3.79 (2.01–7.17)	3.09 (1.84–5.19)	3.06 (1.95–4.81)
Depression ^b	3.91 (1.99–7.7)	2.37 (1.5–3.73)	1.4 (0.97–2.01)
SGRQ (4-point increment)	1.11 (1.05–1.17)	1.08 (1.04–1.13)	1.06 (1.02–1.1)
6MWT (10% increment)	0.87 (0.78–0.97)	0.89 (0.83–0.97)	0.93 (0.87–0.99)
FEV ₁ /FVC (5% increment)	0.87 (0.78–0.96)	0.88 (0.82–0.95)	0.89 (0.84–0.95)
FVC/SD	0.79 (0.57–1.11)	0.79 (0.62–1)	0.83 (0.68–1.01)
FEV ₁ PP/SD	0.65 (0.48–0.89)	0.69 (0.55–0.86)	0.72 (0.6–0.87)
FEV ₁ ht ³ /SD	0.55 (0.39–0.77)	0.58 (0.45–0.74)	0.63 (0.52–0.76)
FEV ₁ Q/SD	0.51 (0.36–0.73)	0.56 (0.43–0.72)	0.62 (0.51–0.76)

Abbreviations: 6MWT, 6-minute walk test; FEV₁, forced expiratory volume in first second; FEV₁ht³, forced expiratory volume in first second divided by height cubed; FEV₁PP, percentage predicted for forced expiratory volume in first second; FEV₁Q, forced expiratory volume in first second as a multiple of sex-specific first percentile; FVC, forced vital capacity; HR, hazard ratio; SD, standard deviation; SGRQ, St George Respiratory Questionnaire.

^aMini-Mental State Examination score <24.

^bGeriatric Depression Scale score ≥5.

different models were built, each including a different measurement of FEV₁ and the same set of potential confounders. To allow comparison, FEV₁ measurements were rescaled by dividing them by their standard deviation (SD). In this way, the hazard ratio (HR) expresses the increase in risk associated with a 1-SD increment of the measurement taken into account.

Results

Two hundred patients meeting the inclusion criteria were identified in the SaRA study. Half (52%) were women, and the mean age was 73.2 years (SD 6.2 years). Table 1 lists the main clinical characteristics of the sample. Overall risks for mortality were 22% at 5 years, 40% at 10 years, and 62% at 15 years. In the unadjusted analysis (Table 2), the HRs for 5-year mortality were 0.65 (95% confidence interval [CI] 0.48–0.89), 0.69 (0.55–0.86), and 0.72 (0.6–0.87) for each 1-SD increase in FEV₁PP, FEV₁ht³, and FEV₁Q,

Table 3
Adjusted hazard ratios for 5-year mortality^a

	Model with FEV ₁ expressed as FEV ₁ PP, HR (95% CI)	Model with FEV ₁ expressed as FEV ₁ ht ³ , HR (95% CI)	Model with FEV ₁ expressed as FEV ₁ Q, HR (95% CI)
Sex (male vs female)	2.59 (1.11–6.06)	2.61 (1.1–6.16)	2.68 (1.12–6.42)
Age (5-y increment)	1.31 (0.97–1.77)	1.33 (0.96–1.82)	1.3 (0.94–1.79)
Body mass index >29 kg/m ²	0.42 (0.14–1.3)	0.42 (0.14–1.3)	0.43 (0.14–1.31)
Body mass index <22 kg/m ²	1.87 (0.71–4.91)	1.84 (0.7–4.83)	1.82 (0.7–4.78)
Cognitive impairment ^b	1.78 (0.69–4.59)	1.74 (0.68–4.45)	1.69 (0.65–4.36)
Depression ^c	2.97 (1.28–6.89)	2.97 (1.28–6.87)	2.97 (1.29–6.89)
SGRQ (4-point increment)	1.06 (0.99–1.14)	1.06 (0.99–1.13)	1.06 (0.99–1.13)
6MWT (10% increment)	0.98 (0.86–1.13)	0.98 (0.86–1.13)	0.99 (0.86–1.13)
FEV ₁ /FVC	0.91 (0.77–1.07)	0.93 (0.79–1.09)	0.95 (0.82–1.1)
FEV ₁ expression/SD	1.2 (0.74–1.94)	1.09 (0.64–1.83)	0.97 (0.58–1.62)

Abbreviations: 6MWT, 6-minute walk test; CI, confidence interval; FEV₁, forced expiratory volume in first second; FEV₁ht³, forced expiratory volume in first second divided by height cubed; FEV₁PP, percentage predicted for forced expiratory volume in first second; FEV₁Q, forced expiratory volume in first second as a multiple of sex-specific first percentile; FVC, forced vital capacity; HR, hazard ratio; SD, standard deviation; SGRQ, St George Respiratory Questionnaire.

^aAll models are corrected for all variables in the table.

^bMini-Mental State Examination score <24.

^cGeriatric Depression Scale score ≥5.

respectively. Also associated with 5-year mortality were age, obesity, underweight, dementia, depression, St George Respiratory Questionnaire score, performance of the 6MWT, and the Tiffeneau index (Table 2). After correction for these potential confounders, only sex (HR for men vs women ranging from 2.59 to 2.68 depending on FEV₁ measurement included in the model) and depression (HR 2.97, 95% CI 1.3–6.9) were associated with the outcome, whereas no FEV₁ measurement was found to predict mortality (Table 3).

At 10 years, results of the unadjusted analysis confirmed the findings for 5-year mortality, but also associated smoking, comorbidity, cardiovascular diseases, and FVC with the outcome. At the adjusted analysis (Table 4), FEV₁Q was the only spirometric parameter to be associated with mortality (HR 0.35, 95% CI 0.14–0.87); among the other variables included in the model, an association with outcome was found for age (HR 1.46–1.52), smoking (HR 1.88–2.18), underweight (HR 2.11–2.22), and comorbidity (HR 2.44–2.61).

At 15 years, results of the unadjusted analysis were very similar to those obtained at 10 years. In the adjusted analysis, the role of FEV₁Q was confirmed (HR 0.38, 95% CI 0.19–0.79; Table 5). Among nonrespiratory variables, an association with mortality was found for age, smoking, comorbidity, and cognitive impairment. In the sole model adjusted for FEV₁Q, an association was found between FVC and mortality (HR 2.41, 95% CI 1.2–4.8).

Very similar results were obtained in multivariable analyses excluding those variables implicitly taken into account by FEV₁ measurements (sex and age for FEV₁PP, sex for FEV₁Q; data not shown).

Discussion

These data expand the current knowledge on the prognosis of asthma in the elderly by providing information from a population followed for 15 years with only 14% lost to follow-up. No measurement of FEV₁ was independently associated with 5-year mortality, whereas FEV₁Q was an independent predictor of 10- and 15-year mortality. The authors are unaware of other studies investigating the role of this measurement in patients with asthma, but it should be noted that, compared with FEV₁ht³ and FEV₁PP, FEV₁Q was the best predictor of mortality in different populations.¹⁰

These results are in contrast to others showing an association between FEV₁PP and mortality.²⁰ These studies, however, were performed in an adult population, and the effect of FEV₁ on mortality was attributed mostly to ensuing COPD. In contrast, the present study included elderly patients in whom the diagnosis of COPD was unlikely. Furthermore, compared with previous studies,

Table 4Adjusted hazard ratios for 10-year mortality^a

	Model with FEV ₁ expressed as FEV ₁ PP, HR (95% CI)	Model with FEV ₁ expressed as FEV ₁ ht ³ , HR (95% CI)	Model with FEV ₁ expressed as FEV ₁ Q, HR (95% CI)
Sex (male vs female)	1.63 (0.65–4.08)	1.43 (0.61–3.35)	0.87 (0.33–2.27)
Age (5-y increment)	1.52 (1.18–1.95)	1.5 (1.19–1.89)	1.46 (1.15–1.84)
Ever smoker	1.88 (0.93–3.79)	1.89 (0.93–3.84)	2.18 (1.04–4.58)
Body mass index >29 kg/m ²	0.45 (0.21–0.94)	0.47 (0.23–0.99)	0.5 (0.24–1.04)
Body mass index <22 kg/m ²	2.11 (1–4.48)	2.14 (1.02–4.52)	2.22 (1.05–4.68)
Charlson index >1	2.61 (1.16–5.88)	2.54 (1.13–5.74)	2.44 (1.07–5.58)
Cardiovascular disease	0.58 (0.26–1.29)	0.62 (0.28–1.38)	0.7 (0.32–1.56)
Cognitive impairment ^b	1.19 (0.54–2.6)	1.29 (0.59–2.8)	1.42 (0.66–3.07)
Depression ^c	1.76 (0.96–3.22)	1.71 (0.93–3.12)	1.68 (0.91–3.09)
SGRQ (4-point increment)	1.03 (0.98–1.09)	1.03 (0.98–1.09)	1.03 (0.98–1.09)
6MWT (10% increment)	1 (0.9–1.1)	1 (0.91–1.11)	1.01 (0.91–1.12)
FEV ₁ /FVC (5% increment)	0.93 (0.8–1.08)	0.97 (0.84–1.12)	1.09 (0.93–1.29)
FVC (1-SD increment)	0.91 (0.45–1.83)	1.12 (0.6–2.09)	2.27 (0.95–5.43)
FEV ₁ expression/SD	0.99 (0.51–1.9)	0.76 (0.4–1.44)	0.35 (0.14–0.87)

Abbreviations: 6MWT, 6-minute walk test; CI, confidence interval; FEV₁, forced expiratory volume in first second; FEV₁ht³, forced expiratory volume in first second divided by height cubed; FEV₁PP, percentage predicted for forced expiratory volume in first second; FEV₁Q, forced expiratory volume in first second as a multiple of sex-specific first percentile; FVC, forced vital capacity; HR, hazard ratio; SD, standard deviation; SGRQ, St George Respiratory Questionnaire.

^aAll models are corrected for all variables in the table.

^bMini-Mental State Examination score <24.

^cGeriatric Depression Scale score ≥5.

a different set of confounders was considered, making the results poorly comparable. The authors' definition of asthma included patients with "fixed" bronchial obstruction, but with symptoms of asthma. Although this might introduce a misclassification, with patients with COPD classified as having asthma, it should be noted that approximately 6% of elderly patients with asthma develop nonreversible bronchial obstruction.²¹ At any rate, this definition was used in the authors' previous study⁶ and therefore used to ensure comparability.

There are several reasons why FEV₁Q might outperform FEV₁PP in predicting mortality.

The validity of using FEV₁PP depends on the availability of predicting equations developed in a population truly representative of the one from which the sample under study has been selected, which is seldom the case. The choice of the reference equation might be a source of bias: for example, it has been shown that the commonly used equations proposed by the European Respiratory Society and European Community of Coal and Steel²² underestimate the FEV₁ compared with other reference equations²³; as a result, these equations would classify as "normal"

patients who would be classified as having a decrease of pulmonary function using other equations. Another problem with the use of predicting equations is that the coefficient of variation is age dependent, and in adults it increases considerably with age.²⁴ Therefore, the use of percentage of predicted inevitably introduces an age-related bias. Theoretically, these biases should not affect FEV₁ht³; therefore, the lack of an independent association between FEV₁ht³ and mortality does not seem to be straightforward. However, it should be noted that in elderly patients with asthma, prolonged use of corticosteroids can accelerate the age-related decrease of height. FEV₁ht³ depends heavily on this parameter, and because patients with more severe asthma are expected to be those with a greater decrease of height, a differential misclassification can ensue: patients with more severe diseases tend to have larger FEV₁ht³ values because of biased height measurement.

In this population of elderly patients with asthma, non-respiratory conditions have a major role in prognosis. This is expected in this age group because the effect of competing risk on mortality becomes considerable; therefore, general indicators of

Table 5Adjusted hazard ratios for 15-year mortality^a

	Model with FEV ₁ expressed as FEV ₁ PP, HR (95% CI)	Model with FEV ₁ expressed as FEV ₁ ht ³ , HR (95% CI)	Model with FEV ₁ expressed as FEV ₁ Q, HR (95% CI)
Sex (male vs female)	0.88 (0.45–1.73)	0.86 (0.46–1.62)	0.6 (0.3–1.24)
Age (5-y increment)	1.6 (1.31–1.96)	1.52 (1.27–1.83)	1.49 (1.24–1.8)
Ever smoker	1.92 (1.14–3.2)	1.91 (1.14–3.2)	2.05 (1.21–3.47)
Body mass index >29 kg/m ²	0.66 (0.4–1.09)	0.68 (0.41–1.12)	0.68 (0.41–1.11)
Body mass index <22 kg/m ²	1.58 (0.81–3.1)	1.63 (0.84–3.2)	1.67 (0.86–3.24)
Charlson index >1	2.11 (1.06–4.19)	2.06 (1.03–4.09)	1.98 (0.99–3.99)
Cardiovascular disease	0.82 (0.43–1.54)	0.85 (0.45–1.61)	0.86 (0.46–1.63)
Cognitive impairment ^b	2.12 (1.15–3.89)	2.17 (1.19–3.99)	2.28 (1.25–4.18)
Depression ^c	0.99 (0.61–1.61)	0.99 (0.6–1.61)	1.01 (0.62–1.66)
SGRQ (4-point increment)	1.02 (0.98–1.07)	1.03 (0.98–1.07)	1.03 (0.98–1.07)
6MWT (10% increment)	1 (0.92–1.07)	1 (0.93–1.08)	1 (0.93–1.08)
FEV ₁ /FVC (5% increment)	0.97 (0.86–1.1)	1 (0.89–1.12)	1.09 (0.95–1.26)
FVC (1-SD increment)	1.28 (0.74–2.21)	1.41 (0.87–2.27)	2.41 (1.2–4.85)
FEV ₁ expression/SD	0.78 (0.46–1.31)	0.67 (0.41–1.09)	0.38 (0.19–0.79)

Abbreviations: 6MWT, 6-minute walk test; CI, confidence interval; FEV₁, forced expiratory volume in first second; FEV₁ht³, forced expiratory volume in first second divided by height cubed; FEV₁PP, percentage predicted for forced expiratory volume in first second; FEV₁Q, forced expiratory volume in first second as a multiple of sex-specific first percentile; FVC, forced vital capacity; HR, hazard ratio; SD, standard deviation; SGRQ, St George Respiratory Questionnaire.

^aAll models are corrected for all variables in the table.

^bMini-Mental State Examination score <24.

^cGeriatric Depression Scale score ≥5.

poor health (eg, depression) or conditions with a very poor prognosis, such as cognitive impairment, may override specific indicators of organ function. This is true, for example, for patients with heart failure, in whom depression²⁵ and cognitive impairment²⁶ are independent risk factors for mortality. Interestingly, in the present study, depression outperformed cognitive impairment as a predictor of death at 5 years, but the reverse occurred at 15 years. This finding confirms that predictive models should not be used beyond their scope, that is, beyond the time span over which it has been tested. In general, these results confirm that a multidimensional approach is more appropriate to establish the prognosis of elderly patients, regardless of the “main” diagnosis.²⁷

They also show that, at variance from what applies to COPD,²⁸ FEV₁ has a minor prognostic role in asthma. However, the association of FEV₁Q with long-term mortality suggests that respiratory function also is related to survival in elderly patients with asthma and multiple morbidities and thus encourages further research on the best way of quantifying lung dysfunction in this population.

The lack of association between performance of the 6MWT and mortality deserves some comments. The 6MWT is an important prognostic indicator in COPD,²⁹ and a decrease of physical performance in general is a well-established marker of poor health in the elderly population.³⁰ Furthermore, in participants of this study without asthma or COPD, performance of the 6MWT was associated with 5-year mortality.⁸ However, few data on the prognostic significance of this indicator in elderly patients with asthma are available. Given that exercise induces bronchoconstriction in a variable, yet remarkable, proportion of patients with asthma,³¹ in this population the 6MWT can be considered a mixed measurement, partly reflecting asthma type and severity and partly reflecting general health status. This likely explains why it lacked prognostic implications. Unfortunately, the SaRA database did not include information on type of asthma, precluding a subgroup analysis.

Some limitations of this study should be considered. The relatively small sample might have had an impact on the precision of the estimates. The inspection of point estimates and associated 95% CIs shows that a lack of power might have had a greater influence on the negative results pertaining to FEV₁ht³ than those pertaining to FEV₁PP, whose HR was very close to 1. Another potential limitation arises from the fact that the first percentile used to calculate FEV₁Q was derived from an external population. Although this might introduce some bias, the authors preferred to use a centile extrapolated from a large population. More data are needed to verify the actual predictive power of FEV₁Q calculated using different normative values.

The authors' choice of classifying patients with no response to bronchodilators but with classic symptoms of asthma as having asthma might have misclassified some patients with COPD as having asthma. However, the authors tried to tailor the diagnostic criteria to the age-related changing phenotype of asthma.^{13,32} Furthermore, these patients reported wheeze as episodic, whereas it would be persistent or highly frequent in COPD. Crises of wheeze were reported to resolve with inhaled steroids and bronchodilators without requiring antibiotic therapy. These factors likely minimized the risk of misclassification.

In conclusion, FEV₁PP does not seem to be the best predictor of mortality in elderly patients with asthma. Although no spirometric index can predict 5-year mortality, FEV₁Q should be considered when longer-term prognostic stratification is needed.

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