Current Bronchodilator Responsiveness Criteria Underestimate Asthma in Older Adults

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BACKGROUND: Asthma is common in older adults and is confirmed by demonstration of variable expiratory air-flow limitations, typically evaluated by spirometric assessment of bronchodilator responsiveness. However, many patients with clinically suspected asthma and documented air-flow obstruction do not exhibit a post-bronchodilator response that meets or exceeds current established guidelines. We investigated if extending the time from bronchodilator administration to assessment of bronchodilator response increases the yield of spirometry for the diagnosis of asthma in older adults. METHODS: This was a cross-sectional study. The subjects were nonsmokers, ≥ 60 y old, and with suspected asthma. Subjects were characterized as (1) those with a positive bronchodilator response on the 30-min post-bronchodilator spirometry, (2) those with a positive bronchodilator response on the 60-min post-bronchodilator spirometry, and (3) those without a positive bronchodilator response but with a positive methacholine challenge test. Factors associated with a late response to bronchodilator were evaluated by using bivariate analysis and by multivariate analysis by using a logistic regression model. RESULTS: This study enrolled 165 subjects. Of these, 81 (49.1%) had a positive bronchodilator response on 30-min post-bronchodilator spirometry; 25 (15.2%) had a positive bronchodilator response on the 1-h post-bronchodilator spirometry; and 59 (35.8%) had no positive bronchodilator response but had a positive methacholine challenge test. On multivariable regression analysis, those with a higher baseline percentage of predicted FEV_1, higher scores on a standard asthma control test, and wheezing and/or cough after exercise were more likely to either have a late bronchodilator response or no bronchodilator response. CONCLUSIONS: Our study showed that a late positive response to bronchodilator use was more common than previously presumed in older subjects with suspected asthma. Pulmonary function testing laboratories should consider routinely reassessing spirometry at 1 h after bronchodilator use if the earlier assessment did not reveal a significant response. *Key words: asthma; aging; older adult; bronchodilator effect; albuterol; lung diseases; spirometry.* [Respir Care 2020;65(8):1104–1111. © 2020 Daedalus Enterprises]

Introduction

There are epidemiological data that demonstrate the high burden of asthma, not only for children and younger adults but also for older adults. The prevalence of asthma in the United States in 2017 was 7.0% for those ages ≥65 y old.[1] Unfortunately, this age group accounts for a disproportionally higher rate of asthma deaths compared with other age groups.[2] Worldwide, asthma is believed to be underdiagnosed and undertreated.[3] In a population-based study, underdiagnoses were present in more than half of the adults with asthma, and it was more common in those > 64 y.[4]

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An accurate diagnosis of asthma can be a challenging task.[5] A defining feature of asthma is the presence of variable expiratory air-flow obstruction. The initial recommended test to demonstrate variable expiratory air-flow obstruction is spirometry with bronchodilator response assessment. The Global Strategy for Asthma Management and Prevention report[6] indicates that bronchodilator reversibility is to be assessed 10–15 min after short-acting bronchodilator administration, whereas the American Thoracic Society (ATS)/European Respiratory Society (ERS) Task Force Report: Standardization of Lung Function Testing[7] states that bronchodilator reversibility is to be assessed at 15 min. In our clinical practice, we noted that, for many older patients being evaluated for asthma, a positive bronchodilator response was not demonstrated within 30 min but was present 60 min after short-acting bronchodilator administration. Such clinical observation can have important implications for clinical practice if our findings are confirmed by well-designed studies. The late response to bronchodilators could be particularly common in older adults due to physiologic changes associated with aging and long-term chronic disease burden.[8-13]

In this study, we hypothesized that, in a substantial proportion of older adults with asthma, a positive bronchodilator response would not be present within 30 min but would be present 1 h after short-acting bronchodilator administration. The primary aim of this study was to determine the proportion of older adults for whom bronchodilator response is negative at 30 min and positive at 1 h after short-acting bronchodilator administration (late response). The secondary aim was to assess factors associated with late response to short-acting bronchodilators. Some of the results of these studies were previously reported in the form of an abstract.[14]

QUICK LOOK

Current knowledge

Standard protocols for diagnosing asthma include spirometry with bronchodilator response assessment 10–15 min after short-acting bronchodilator administration. For older adults, clinical observations revealed 10–15 min is not always adequate to see a bronchodilator response.

What this paper contributes to our knowledge

Older adults with suspected asthma may not have a bronchodilator response within the standard 10–15 min after short-acting β-agonist administration. Up to 60 min after bronchodilator administration may be needed for a bronchodilator response in older adults.

Methods

This study used a cross-sectional design and is a secondary analysis of the parent "Asthma in Older Adults: Identifying phenotypes and factors impacting outcomes" study, which is a prospective, observational study funded by the National Institutes of Health, National Institute on Aging.[15] The study was approved by the University of Louisville Institutional Review Board (13.0419), and subjects provided written informed consent. Details about the study methods have been previously reported.[5,15] Inclusion criteria to be enrolled in the study were ages $\geq$ 60 y, physician diagnosis of asthma, and $\geq$1 positive response to 6 asthma screening questions. Individuals were excluded if they had a diagnosis of another pulmonary disease, lived in a nursing home, were a current smoker, had a $>$20 pack-year history of smoking, or smoked within the past 5 years.

The subjects underwent baseline spirometry with bronchodilator response testing in the clinical trials unit at the University of Louisville. The equipment used for lung function testing was the nSpire Koko spirometry system (Longmont, Colorado). The device was calibrated by using a 3-L syringe before subject testing, and we followed recommendations as outlined by the ATS. Spirometric reference values were obtained from the equations derived from the third National Health and Nutrition Examination Survey by Hankinson et al.[16] The subjects were required to hold short-acting β-agonists for 4 h and long-acting β-agonists for 12 h before the test. In addition, anticholinergic bronchodilators were held for a 6-h period and leukotriene receptor antagonists were held for 24 h before the test.

Enrollment pulmonary function assessments were completed by a registered respiratory therapist certified in pulmonary function testing (BLB). Baseline testing included at

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least 3 acceptable attempts based on forced exhalation of at least 6 s, and repeatability of FVC and FEV_1 within 200 mL or 10%, whichever was smaller. The subjects received 2.5 mg of albuterol mixed with normal saline solution, nebulized in a McKesson small-volume nebulizer, powered by a Schuco compressor (Allied Healthcare Products, St. Louis, Missouri), for 10 min. The subjects were then tested at 30 min after treatment completion. Both the pre- and post-bronchodilator spirometry were performed with the subjects in a sitting position while wearing nose clips. The post-treatment spirometry also consisted of at least 3 maneuvers with the same acceptability and repeatability criteria mentioned above.

A positive bronchodilator response was present if there was a post-bronchodilator increase of $\geq$12% and an absolute change of >200 mL from the baseline FEV_1 and/or FVC.[7] In those who did not have a positive bronchodilator response in the 30-min post-bronchodilator spirometry, a repeated spirometry was performed 60 min after bronchodilator, and the same criteria were used to define positive reversibility.

For all the subjects, structured data collection also included demographic information (eg, age, sex, smoking history, age at diagnosis), clinical information (eg, asthma screening questions, body mass index), number of reported comorbidities, number of medications (prescribed and over-the-counter), the 5-item Asthma Control Test,[17,18] fractional exhaled nitric oxide, total immunoglobulin E (IgE), skin prick testing, and specific IgE for 14 airborne allergens common to the Louisville, Kentucky area; total IgE; and vitamin D. The outcome of interest was positive bronchodilator response after short-acting β-agonist administration only at 1 h, which we denominated as a late response. In this study, the subjects were divided into 3 groups: (1) those with a positive bronchodilator response on the 30-min post-bronchodilator spirometry, (2) those with a positive bronchodilator response on the 60-min post-bronchodilator spirometry, and (3) those without a positive bronchodilator response but with a positive methacholine challenge test.

Statistical Analysis

Categorical variables are presented as count and percentage, whereas continuous variables are presented as means, SDs, and minimum and maximum values. The association between factors and a late response to bronchodilator was evaluated by using the chi-square or Fisher exact tests for categorical variables and analysis of variance for continuous variables. The Bonferroni post hoc analysis was applied for significant analysis of variance findings. Multivariable ordinal logistic regression was used to assess the effect of potential predictors, which were chosen a priori based on possible biologic plausibility, on a late response to bronchodilator use. The asthma screening question that addressed symptom improvement with asthma treatment was removed from the model due to a quasi-complete separation of data points and failure of the model to converge. A score test was conducted to check the proportional odds assumption. Statistical software SAS version 9.4 (SAS Institute, Cary, North Carolina) was used for all statistical analysis, and an alpha level of 0.05 was used to determine statistical significance.

Results

This study enrolled 165 subjects with suspected asthma. Of those, 81 (49.1%) had a positive bronchodilator response on 30-min post-bronchodilator spirometry; 25 (15.2%) had a positive bronchodilator response at the 1-h post-bronchodilator spirometry; and 59 (35.8%) had no positive bronchodilator response but had a subsequent positive methacholine challenge test result. The subjects were primarily female (72.7%), white (76.4%), completed at least 1 year of college (79.4%), and retired (70.3%). Their mean $\pm$ SD age was 68.0 $\pm$ 6.0 y. The characteristics of the subjects according to their bronchodilator reversibility status are provided in Tables 1 and 2. The subjects who had no bronchodilator reversibility at 30 or 60 min were more likely to be employed. Individuals who had bronchodilator reversibility at 60 min had significantly more comorbidities than those who had no reversibility or had reversibility at 30 min. There were no significant differences between the groups with regard to demographic characteristics, asthma screening questions, age of asthma diagnosis, body mass index, vitamin D, atopy, pack-years ever smoked, the number of medications, or fractional exhaled nitric oxide. There was a trend toward a lower total IgE in those with no bronchodilator reversibility at 30 or 60 min.

Significant differences were identified among the 3 groups for all baseline and 30-min post-bronchodilator pulmonary function tests, except for post-bronchodilator FVC % predicted. In addition, there were significant differences among the groups with the Asthma Control Test scores. Those with positive bronchodilator response at 30 min had significantly lower baseline FEV_1% predicted and FEV_1/FVC compared with the group with a positive bronchodilator response at 60 min, and those without bronchodilator reversibility (Fig. 1). Post-bronchodilator FEV_1% predicted and FEV_1/FVC followed the same pattern. Those with positive bronchodilator responses at 30 min had significantly lower Asthma Control Test scores compared with only the methacholine challenge test group.

Results of multivariable modeling indicated that FEV_1% predicted at baseline and the Asthma Control Test score were the only significant predictors of late or no bronchodilator response (Table 3). An increase in baseline FEV_1% predicted was associated with an increase in the odds of late or no bronchodilator response compared with response

Table 1. Demographic Characteristics of Older Adults With Asthma and Stratified by Time of BDR: Categorical Variables

Categorical Variable	BDR at 30 Min, *n* (valid %) (*n* = 81)	BDR at 60 Min, *n* (valid %) (*n* = 25)	No BDR (positive MCT results), *n* (valid %) (*n* = 59)	Total, *n* (%) (*N* = 165)	*P*
Sex					.74
Females	57 (70.4)	18 (72.0)	45 (76.3)	120 (72.7)	
Males	24 (29.6)	7 (28.0)	14 (23.7)	45 (27.3)	
Race					.46
White	61 (75.3)	18 (72.0)	47 (79.7)	126 (76.4)	
Black	16 (19.8)	4 (16.0)	10 (16.9)	30 (18.2)	
American Indian or Alaskan native	3 (3.7)	3 (12.0)	1 (1.7)	7 (4.2)	
Asian	0	0	1 (1.7)	1 (0.6)	
Mixed race	1 (1.2)	0	0	1 (0.6)	
Education					.46
High school or less	19 (23.5)	3 (12.0)	12 (20.3)	34 (20.6)	
Some college or college graduate	62 (76.5)	22 (88.0)	47 (79.7)	131 (79.4)	
Employment					.02
Employed for wages	16 (19.8)	8 (32.0)	25 (42.4)	49 (29.7)	
Retired or unemployed	65 (80.2)	17 (68.0)	34 (57.6)	116 (70.3)	
Asthma symptoms (yes)					
Had an asthma attack or recurrent wheezing	72 (88.9)	21 (84.0)	49 (83.1)	142 (86.1)	.58
Troublesome cough at night	45 (55.6)	18 (72.0)	34 (57.6)	97 (58.8)	.34
Wheeze or cough after exercise	58 (71.6)	19 (76.0)	43 (72.9)	120 (72.7)	.91
Wheeze, cough, chest tightness after exposure to airborne allergens and/or pollutants (*n* = 164)	75 (92.6)	23 (95.8)	55 (93.2)	153 (93.3)	.86
Colds "go to chest" and/or take >10 d to clear up	59 (72.8)	20 (80.0)	41 (69.5)	120 (72.7)	.61
Symptoms improve with asthma treatment	77 (95.1)	24 (96.0)	56 (94.9)	157 (95.2)	.98
Atopy (*n* = 164)					.42
Not atopic (negative SPT results and sIgEs ≤ 0.35 kU/L)	14 (17.3)	7 (28.0)	14 (24.1)	35 (21.3)	
Atopic (any positive SPT result and/or any sIgE > 0.35 kU/L Categorical variable)	67 (82.7)	18 (72.0)	44 (75.9)	129 (78.7)	

BDR = bronchodilator reversibility
MCT = methacholine challenge test
SPT = skin-prick test
sIgE = specific immunoglobulin E
Valid % = percent excluding missing values

at 30 min (adjusted odds ratio [aOR] 1.07, 95% CI 1.05–1.09). Further, a higher Asthma Control Test score was associated with an increase in the odds of late to no bronchodilator response compared with a response at 30 min (aOR 1.13, 95% CI 1.02–1.25). Wheezing or coughing after exercise was significant at exactly $P = .050$; those who endorsed this criterion had twice the odds of late to no bronchodilator response compared with a response at 30 min (aOR 2.35, 95% CI 1.00–5.54). No other variables were significant predictors of late to no bronchodilator response.

Discussion

Our study found that 23.6% of the older adults with suspected asthma and positive bronchodilator response did not have a response within 30 min of short-acting β-agonist administration but did demonstrate a bronchodilator response when the post-bronchodilator spirometry was obtained 60 min after the medication administration. This group with the late response to bronchodilator use comprised 15% of all older adults with confirmed asthma in our study. This finding has important implications for practice because demonstration of variable expiratory air-flow obstruction is a defining feature of asthma. As per the current guideline, the absence of positive reversibility in an individual with suspected asthma should prompt further investigation with tests that take longer or may not be available, such as twice-daily peak expiratory flow monitoring, exercise challenge test, or a bronchial challenge test.[6] Those with higher baseline FEV_1% predicted, higher Asthma Control Test score, and wheezing or coughing after exercise were more likely to either have a late response to bronchodilator or no response to bronchodilator.

Why some patients have a delayed response to β-adrenergic agonist is not clear, but a few potential explanations can be raised. First, there are data that show that poly-

Table 2. Demographic Characteristics of Older Adults With Asthma and Stratified by Time of BDR: Continuous Variables

Continuous Variable	BDR at 30 Min	BDR at 60 Min	No BDR (positive MCT results)	Total	*P*
Pulmonary function test					
Baseline					
FEV_1 % predicted	67.1 ± 19.2 (32.0, 136.0)[a]	83.4 ± 22.9 (43.0, 139.0)[b]	93.1 ± 14.4 (69.0, 132.0)[b]	78.9 ± 21.8	<.001
FVC % predicted	75.2 ± 16.6 (42.0, 126.0)[a]	83.5 ± 19.0 (48.0, 127.0)	91.6 ± 12.8 (73.0, 123.0)[b]	82.3 ± 17.4	<.001
FEV_1/FVC	0.67 ± 0.11 (0.40, 0.92)[a]	0.75 ± 0.07 (0.62, 0.89)[b]	0.77 ± 0.06 (0.64, 0.90)[b]	0.72 ±.10	<.001
30-min after bronchodilator use					
FEV_1 % predicted	81.0 ± 20.3 (42.0, 149.0)[a]	89.0 ± 24.7 (48.0, 146.0)	93.2 ± 14.3 (63.0, 123.0)[b]	86.6 ± 19.9	.001
FVC % predicted	86.5 ± 18.9 (54.0, 170.0)	85.0 ± 20.1 (48.0, 127.0)	89.7 ± 12.7 (60.0, 121.0)	87.4 ± 17.1	.41
FEV_1/FVC	0.71 ± 0.10 (0.38, 0.90)[a]	0.79 ± 0.07 (0.65, 0.91)[b]	0.79 ± 0.06 (0.61, 0.91)[b]	0.75 ± 0.09	<.001
60-min after bronchodilator use					
FEV_1 % predicted ($n = 83$)		91.5 ± 20.2 (48.0, 121.0)	96.7 ± 13.9 (69.0, 126.0)	95.2 ± 16.1	.17
FVC % predicted ($n = 83$)		87.7 ± 17.3 (51.0, 115.0)	92.9 ± 12.6 (70.0, 126.0)	91.3 ± 14.3	.13
FEV_1/FVC ($n = 83$)		0.79 ± 0.05 (0.70, 0.90)	0.79 ± 0.06 (0.65, 0.91)	0.79 ± 0.06	.74
FEV_1 % change from baseline at 30 min	22.5 ± 11.7 (12.0, 57.0)[a]	6.1 ± 4.3 (–8.0, 11.0)[b]	2.1 ± 4.3 (–11.0, 10.0)[b]	12.7 ± 13.1	<.001
FEV_1 % change from baseline at 60 min ($n = 83$)		18.6 ± 20.2 (12.0, 114.0)	3.9 ± 4.1 (–9.0, 11.0)	8.3 ± 13.3	<.001
Asthma Control Test	17.2 ± 4.6 (7.0, 25.0)[a]	18.2 ± 4.1 (9.0, 24.0)	19.2 ± 3.7 (10.0, 25.0) [b]	18.1 ± 4.3	.032
Age, y	68.4 ± 6.7 (60.4, 89.2)	67.6 ± 4.1 (60.2, 75.4)	67.5 ± 5.6 (60.1, 79.5)	68.0 ± 6.0	.63
Age asthma diagnosed, y	37.4 ± 25.4 (0.1, 76.0)	44.6 ± 19.3 (3.0, 71.0)	43.7 ± 22.6 (0.1, 78.0)	40.7 ± 23.7	.21
Body mass index, kg/m^2	32.3 ± 8.0 (16.7, 57.8)	34.5 ± 7.7 (22.3, 53.0)	32.5 ± 8.2 (20.6, 72.2)	32.7 ± 8.0	.48
Vitamin D (serum 25 hydroxyvitamin D, ng/mL) ($n = 161$)	31.9 ± 16.2(8.0, 112.0)	37.1 ± 23.4 (11.0, 124.0)	35.5 ± 13.0 (11.0, 84.0)	34.0 ± 16.5	.26
No. pack-years smoked	1.9 ± 3.8 (0.0, 17.1)	2.8 ± 5.5 (0.0, 17.5)	2.8 ± 5.7 (0.0, 20.0)	2.3 ± 4.8	.50
Total no. self-reported comorbidities	4.7 ± 2.6 (0, 12)[b]	6.3 ± 4.7 (1, 24)[a]	4.6 ± 2.2 (0, 12)[b]	4.9 ± 3.0	.036
Total no. medications (prescribed and over the counter)	10.8 ± 5.1 (2, 24)	13.5 ± 5.8 (2, 24)	11.3 ± 4.6 (2, 20)	11.4 ± 5.1	.069
F_{ENO}, ppb ($n = 159$)	32.1 ± 35.0 (5, 245)	27.0 ± 20.1 (7, 90)	22.4 ± 15.4 (5, 82)	27.8 ± 27.5	.12
Total IgE, kU/L	257.2 ± 457.7 (2.3, 2534)	208.3 ± 273.2 (2.8, 931)	111.9 ± 158.9 (2, 897)	197.9 ± 356.1	.059

Data are mean ± SD (minimum, maximum).
[a]differs significantly from [b]
BDR = bronchodilator reversibility
MCT = methacholine challenge test
F_{ENO} = fractional exhaled nitric oxide level
IgE = immunoglobulin E

morphisms in the gene encoding the β-2 adrenergic receptor, which belongs to the G protein-coupled receptor family, could influence the airway response to inhaled β-adrenergic medication.[19-21] Conceivably, such polymorphisms may also determine the timing of the peak bronchodilator response. Second, aging could have a physiologic impact on the bronchodilator response pattern. Experimental and human studies have shown a decreased effect of β-adrenergic agonist with increasing age.[22,23] Possible mechanisms include a reduction in both adenylate cyclase activity and of the β-adrenergic receptor affinity.[23] For example, in cardiac tissue, the density of β-receptors decreases with aging.[24] Third, other patient-related mechanisms could affect the pharmacokinetics of inhaled β-adrenergic agonist. For instance, Cazzola et al [25] considered that gastrointestinal absorption of a swallowed drug could explain the second peak plasma concentration that has been observed in individuals who inhale salmeterol. Fourth, altered pharmacokinetics of concomitant medications in the elderly may alter the β-agonist effects of albuterol or alter the β receptor sensitivity and number as observed with concurrent corticosteroid use.[26-30] Fifth, it is very difficult to determine individual β receptor up- or downregulation status in patients with asthma because of varying degrees of exposure to various inhaled bronchodilators, theophylline, and other sympathomimetic agents as well as variable genetic polymorphisms.[30-33]

The methodology for bronchodilator responsiveness assessment has been fraught with heterogeneity. Several different bronchodilators have been used. Earlier studies used drugs such as terbutaline, isoetarine, isoproterenol, and metaproterenol.[34-37] More-recent studies used albuterol

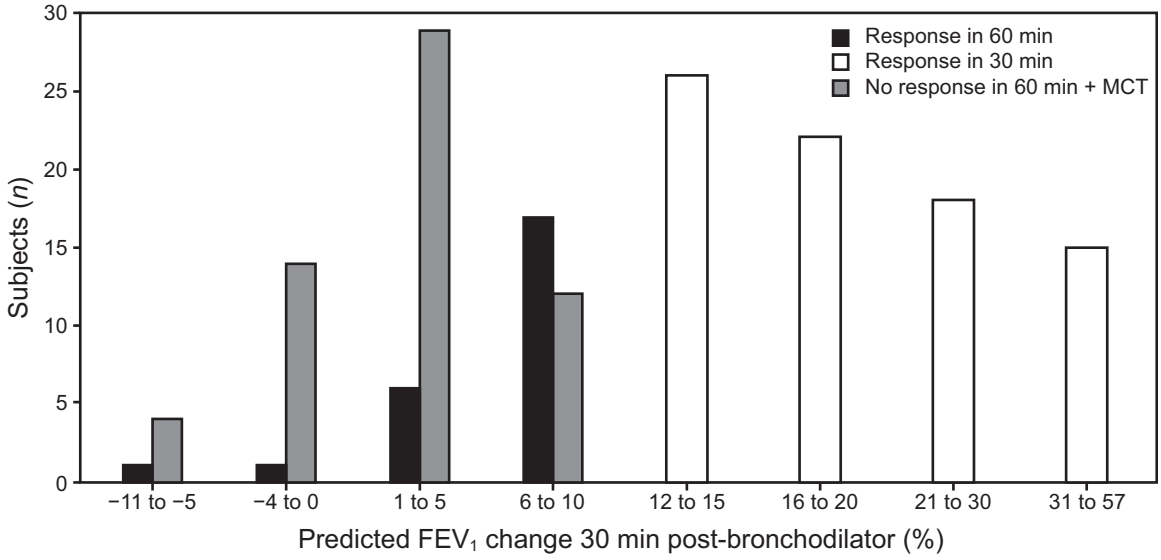

Fig. 1. FEV_1 % predicted change at 30 min after bronchodilator for the subjects with a positive bronchodilator response at 30 min ($n = 81$), at 60 min ($n = 25$), and those with a no bronchodilator response by 60 min with a positive methacholine challenge test (MCT) ($n = 59$).

Table 3. Proportional Odds Model of Late (60 min) BDR to No BDR (Positive MCT Results) Compared With Positive 30-min BDR

Parameter	aOR (95% CI)	*P*
Baseline FEV_1% predicted	1.07 (1.05–1.09)	<.001
Asthma Control Test total	1.13 (1.02–1.25)	.02
Atopy (atopic vs not atopic)	1.36 (0.56–3.32)	.50
Age	0.96 (0.90–1.03)	.30
Age at diagnosis	1.01 (0.99–1.03)	.34
Pack-years smoked	1.03 (0.96–1.11)	.44
Fractional exhaled nitric oxide level	0.99 (0.97–1.00)	.09
Total no. medications	1.05 (0.97–1.13)	.28
No. comorbidities	1.02 (0.89–1.16)	.82
Had an asthma attack or recurrent wheezing (yes vs no)	0.97 (0.34–2.81)	.96
Troublesome cough at night (yes vs no)	1.05 (0.47–2.31)	.91
Wheeze and/or cough after exercise (yes vs no)	2.35 (1.00–5.54)	.050
Wheezing, cough, chest tightness after exposure to airborne allergens and/or pollutants (yes vs no)	1.82 (0.42–7.93)	.43
Colds "go to chest" and/or take >10 d to clear up (yes vs no)	1.17 (0.50–2.75)	.72

BDR = bronchodilator reversibility
MCT = methacholine challenge test
aOR = adjusted odds ratio

and levalbuterol.[38-40] The dose of bronchodilator has varied even within individual studies. The dose response of various bronchodilators is unique to the individual compound, and each has special pharmacokinetic considerations in older adults, which makes the 15-min reversibility standard difficult to interpret.[31,41,42] Nebulizers have been used in some studies, whereas pressurized metered-dose inhalers have been used in other studies. The definition of a positive bronchodilator response also varies. Some studies have used percent change from the predicted value, whereas others have used percent change from baseline.[36,37] All of these sources of heterogeneity in the literature were recognized in the ATS/ERS document for standardization of lung function testing.[7] Studies that followed the ATS/ERS document[7] provided further insight into the bronchodilator reversibility criteria. For instance, Hansen et al[43] showed that using the statistical test of the individual variability of spirometric measurements leads to more identification of bronchodilator response compared with the ATS/ERS criteria. A large population-based study confirmed that the 95th

percentile for percent change in FEV_1 relative to the initial value is indeed 12% for healthy never-smokers. The 95th percentile for the absolute change in the FEV_1 relative to the initial value was 284 mL.[44] The timing of post-bronchodilator assessment has not been as scrutinized and seems a less-contentious topic, as seen in the literature.

We recognize limitations in our study. It was conducted in a single academic center, which decreases its external validity. To be considered for the study, the subjects had to have a physician diagnosis of asthma, which may not be representative of what most clinicians would encounter in their practice, especially in primary care settings. It is possible that, in some subjects, an improvement in the post-bronchodilator spirometry represented normal within-subject variability. In the future, further investigation to better characterize those with a late response to short-acting bronchodilator use is warranted. For instance, it would be important to establish whether those patients with a late response have a different asthma phenotype and whether they tend to clinically respond to asthma treatments differently. In addition, it is unclear whether younger adults with asthma also have a late response, and further studies are needed to characterize their responsiveness to bronchodilation. The first assessment of bronchodilator response in our study was at 30 min. Previous expert statements have suggested assessing the bronchodilator response at 15 min.[6,7] Also, it would be important to characterize the peak pharmacodynamics effects of different short-acting bronchodilators because they may vary.

Conclusions

Our study showed that a late positive response to bronchodilator use was common in older adults with suspected asthma. Those with a higher baseline FEV_1% predicted, higher Asthma Control Test score, and wheezing or coughing after exercise were less likely to have a positive bronchodilator response at 30 min. However, no single risk factor can definitely predict those with a late response. For that reason, pulmonary function test laboratories should consider routinely reassessing spirometry at 60 min after bronchodilator if the earlier assessment did not reveal a significant bronchodilator response.

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