

Impact of Asthma Exacerbations and Asthma Triggers on Asthma-related Quality of Life in Patients with Severe or Difficult-to-Treat Asthma

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What is already known about this topic? Although the association between asthma triggers and asthma exacerbations is well established, few studies have quantified the impact of these variables on asthma-related quality-of-life (QoL) or the impact of asthma exacerbation severity on QoL.

What does this article add to our knowledge? The greater severity and numbers of asthma exacerbations were significantly associated with decreases in asthma-related QoL. Poorer QoL and greater asthma exacerbation severity and frequency were significantly associated with higher numbers of asthma triggers at baseline.

How does this study impact current management guidelines? Avoidance of asthma triggers may be an effective treatment strategy to reduce exacerbation rates and improve asthma-related QoL in patients with severe or difficult-to-treat asthma, although formal interventional trials would be required to confirm this.

BACKGROUND: Few data are available that evaluate the relationship among asthma exacerbations, asthma triggers, and asthma-related quality of life (QoL).

OBJECTIVE: To evaluate the impact of asthma exacerbations and asthma triggers on QoL.

METHODS: Patients with severe or difficult-to-treat asthma, ages ≥ 13 years ($n = 2679$) from the TENOR (The Epidemiology and Natural History of Asthma: Outcomes and Treatment Regimens)

3-year observational study were included. Exacerbations were defined hierarchically in descending order of severity (hospitalization, emergency department [ED] visit, steroid burst, no exacerbation) by using data from months 6 and 12. The total number (frequency) of exacerbations was assessed. Asthma-related QoL was measured at month 12 by using the Mini-Asthma QoL Questionnaire (Mini-AQLQ); self-reported asthma triggers were collected at baseline and annually. We used 1-way ANOVA to test for differences in Mini-AQLQ domain scores across asthma exacerbation severity, the total number of asthma exacerbations, and the number of asthma triggers. **RESULTS:** A significant decrease ($P < .001$) in Mini-AQLQ domain scores was seen with increasing severity of asthma exacerbation (no exacerbation, steroid burst, ED visit, and hospitalization); symptom (5.5, 4.8, 4.3, and 4.2), activity (5.8, 5.2, 4.6, and 4.4), emotional (5.6, 5.0, 4.4, and 4.2), exposure (5.0, 4.5, 4.0, and 3.9); and overall (5.5, 4.9, 4.3, and 4.1). Increasing exacerbation frequency and the number of baseline asthma triggers also were associated with significant decreases in Mini-AQLQ domain scores. An increasing number of asthma triggers were associated with an increase in severity and frequency of exacerbations.

CONCLUSION: Avoidance of asthma triggers may reduce exacerbation rates and improve asthma-related QoL in patients with severe or difficult-to-treat asthma. Interventional studies are warranted to further explore these outcomes. © 2014 American Academy of Allergy, Asthma & Immunology (J Allergy Clin Immunol Pract 2014;2:544-52)

Key words: Severe asthma; Difficult-to-treat asthma; Allergic triggers; Quality-of-life

Asthma exacerbations are responsible for a large disease burden, including hospitalization, decline in lung function, and death.¹ It has been shown that asthma costs are directly related to patients' levels of asthma control, with the highest costs incurred in patients with severe

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Abbreviations used

BMI- Body mass index

ED- Emergency department

HCU- Health care utilization

FEV₁- Forced expiratory volume in 1 second

LSM- Least squares mean

Mini-AQLQ- Mini-Asthma Quality of Life Questionnaire

NA- Not applicable

NS- Not significant

OR- Odds ratio

QoL- Quality of life

*TENOR- The Epidemiology and Natural History of Asthma:
Outcomes and Treatment Regimens*

uncontrolled asthma.²⁻⁴ Despite the widespread dissemination of asthma guidelines, many patients have inadequately controlled disease,⁵⁻⁷ and experience frequent exacerbations of asthma.⁸⁻¹⁰ It is estimated that, during a 12-month period, approximately 40% of patients with severe asthma will require an emergency department (ED) visit compared with 20% of patients with moderate asthma and 15% of those with mild asthma.¹¹

Increases in the prevalence of asthma in the United States¹² have been accompanied by a rise in reports of allergen sensitivity.¹³ Although the association between asthma triggers and asthma exacerbations is well established, few studies have directly examined the individual impact of these highly interconnected variables on asthma-related quality of life (QoL) or have quantified the impact of the severity of the asthma exacerbation on QoL. In a 4-week study of 112 patients with moderate-to-severe asthma, patients who had exacerbations during the study period reported poorer QoL than those patients who did not have exacerbations.¹⁴ A further decrease in QoL was observed in patients who had been hospitalized as a result of an exacerbation. In a study of 296 patients with moderate-to-severe asthma who presented to a US ED with an asthma exacerbation, those who reported more asthma triggers had worse overall QoL scores and more frequent exacerbations, and were more likely to have been previously hospitalized for asthma and oral corticosteroids than patients who reported fewer asthma triggers.¹⁵

The Epidemiology and Natural History of Asthma: Outcomes and Treatment Regimens (TENOR) study was a large, prospective, observational cohort study of patients with severe or difficult-to-treat asthma that was initiated in 2001.¹⁶ The study assessed a broad range of clinical and patient-reported outcomes over a 3-year period. We analyzed the population of patients ages ≥ 13 years enrolled in the TENOR study to (1) assess the association between the severity of asthma exacerbations and asthma-related QoL, (2) evaluate the impact of asthma triggers on asthma-related QoL, and (3) assess the association between asthma triggers and the severity of asthma exacerbations (see Figure E1 in this article's Online Repository at www.jaci-inpractice.org).

METHODS

Patients

Patients ages ≥ 6 years with physician-assessed severe or difficult-to-treat asthma were included in the TENOR study. Asthma was considered difficult to treat based on a number of prespecified parameters, including a need for multiple asthma medications, severe exacerbations, frequent exacerbations, an

inability to avoid triggers, and complex medication regimen (multiple reasons were allowed).¹⁶ Patients with mild or moderate asthma were eligible for enrollment if their asthma was considered difficult to treat by the evaluating physician and they met the additional inclusion criteria. TENOR study enrollment criteria are shown in Figure E2 (in this article's Online Repository at www.jaci-inpractice.org).

Study design

The study design and methodology of TENOR have been published previously.¹⁶ In brief, the TENOR study was a multi-center, observational cohort study conducted over a 3-year period (2001-2004) at 283 sites across the United States, including community physicians, managed care organizations, academic centers, and group practices. A total of 4756 patients with severe or difficult-to-treat asthma who were receiving care from an allergist or pulmonologist were enrolled. TENOR study was approved by a central institutional review board and, when necessary, by the institutional review board at each site.

Data collection

After enrollment, the patients attended follow-up visits every 6 months. A range of clinical, demographic, standard laboratory, and patient-reported assessments were completed at baseline and over the 3-year follow-up period. Health care utilization (HCU) data were collected every 6 months and were based on self-reported hospitalizations, ED visits, and oral corticosteroid bursts during the 3 months before each study visit. Asthma-related QoL data were collected annually by using the validated Mini-Asthma Quality of Life Questionnaire (Mini-AQLQ),¹⁷ with lower scores indicating poorer asthma-related QoL. Data on asthma triggers were collected at baseline and annually by using a self-administered questionnaire. The patients were asked if, in the previous 12 months, they had experienced a cough, wheeze, or other symptom of asthma as a result of exposure to any of the following common asthma triggers: emotional stress, cold and/or sinus infection, pollen, animals, mold and/or dampness, or dust. The patients could check "all that apply" for this question.

Asthma exacerbations

The severity of asthma exacerbations and the total number of asthma exacerbations were evaluated for each patient by using HCU data from the month-6 and month-12 study visits (which assessed HCU during the 3 months before each visit). Asthma exacerbation severity was defined in descending order of severity: hospitalization, ED visit, steroid burst, and no exacerbation. For each patient, an asthma exacerbation was defined as the "highest" value in the hierarchy from both the month-6 and month-12 visits. The total number of exacerbations was defined as the sum of hospitalizations, ED visits, and steroid bursts from both the month-6 and month-12 visits.

Analytic cohort

Patients ages ≥ 13 years with nonmissing HCU data at month 6 and month 12, and nonmissing QoL data at month 12 were included in the analyses.

Statistical analyses

Baseline demographic and clinical characteristics were summarized by using percentages for categorical variables and mean \pm SD for continuous variables. Differences in

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