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Measuring asthma control in group studies: do we need airway calibre and rescue β_2-agonist use?

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Collection of airway calibre and β_2-agonist data in large clinical trials and epidemiological surveys is sometimes difficult and may be an inefficient use of resources. The aim of this study was to determine whether the omission of the forced expiratory volume in 1 sec (FEV_1) and β_2-agonist questions from the seven-item Asthma Control Questionnaire (ACQ) alters its measurement properties and validity.

In an observational study, 50 adults with symptomatic asthma attended the clinic at 0, 1, 5 and 9 weeks to complete the ACQ and other measures of asthma status.

All patients completed the study and provided complete data sets. Omission of the FEV_1 and β_2-agonist questions from the ACQ made minimal difference to the reliability, responsiveness, and both cross-sectional and longitudinal validity of the instrument. Omission of the FEV_1 question significantly lowered the summary score ($P<0{\cdot}0001$) but omission of the β_2-agonist question did not alter it ($P>0{\cdot}05$).

In group studies, both the FEV_1 and β_2-agonist questions may be omitted from the ACQ without changing the validity or the measurement properties of the instrument. Lowering of the summary score by the omission of the FEV_1 question means that data from this abbreviated form cannot be combined with or compared to data collected using the full questionnaire.

Key words: asthma; questionnaire; measurement; clinical trials; epidemiological surveys.

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Introduction

The Asthma Control Questionnaire (ACQ) was developed and validated to measure the clinical status both of patients participating in research studies and those being seen as individuals in clinical practice (1). It has seven questions covering all the criteria (symptoms, airway calibre and rescue β_2-agonist use) deemed necessary by international guidelines committees for determining the adequacy of asthma control (2–5).

To improve efficiency, simplify data collection and reduce costs in large clinical trials and epidemiological surveys, it would be convenient if the questions concerning airway calibre and rescue β_2-agonist use could be omitted. In addition, in some multi-national studies, estimates of airway calibre and inhaled β_2-agonist use are not available. The aim of this analysis was to determine whether the questions concerning β_2-agonist use and airway calibre can be removed from the ACQ for large studies without altering the validity and the measurement properties of the instrument.

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Methods

The database for this analysis was generated during the validation of the ACQ (1). In brief, 50 adults (17–70 years) with current symptoms of asthma were enrolled in a 9-week, observational study, with clinic visits at enrollment and after 1, 5 and 9 weeks. At each visit, prebronchodilator spirometry was measured and patients completed the ACQ, the self-administered version of the Asthma Quality of Life Questionnaire (AQLQ) (6) and the Medical Outcomes Survey Short Form-36 (SF-36) (7). In addition, patients scored five asthma symptoms that had not been selected for the ACQ (1). For 1 week before each clinic visit, patients recorded prebronchodilator peak expiratory flow (PEF) each morning. At each follow-up visit, a clinician rated change in the patient's asthma control since the previous clinic visit (+7 = a very great deal better, 0 = no change, −7 = a very great deal worse) (8). The clinician was blinded to the ACQ data and used only spirometry, diary, AQLQ

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and SF-36 data plus a consultation with the patient. The study was approved by the McMaster University Faculty of Health Sciences Ethics Committee. All patients signed an informed consent.

ASTHMA CONTROL QUESTIONNAIRE

The development and validation of the ACQ is described in detail elsewhere (1). The ACQ contains seven questions, five of which concern symptoms and activity limitations, one on FEV_1% predicted and one on short-acting β_2-agonist use. Patients are asked to recall their symptoms and β_2-agonist use during the previous week. FEV_1% predicted is the value recorded in the clinic at the time the questionnaire is completed. All seven questions are scored on a 7-point scale (0 = good control, 6 = poor control) and the overall score is the mean of the seven responses.

STATISTICAL ANALYSIS

The aims of the statistical analysis were to determine whether the abbreviated instruments are valid measures of asthma control and to compare their measurement properties with those of the original ACQ.

Differences in scores between the complete seven-item ACQ and the three abbreviated versions (symptoms alone, symptoms plus FEV_1 and symptoms plus β_2-agonist use) were examined using a paired *t*-test. Pearson correlation coefficients were used to examine associations between the ACQ and the abbreviated versions. As described in detail elsewhere (1), testing the measurement properties of the instruments required defining a group of patients who remained clinically stable between clinic visits (weeks 1–5 and weeks 5–9) and another group who experienced change in their asthma control. For each time period, we categorized each patient using the clinician's global rating of change: stable group = scores of -1, 0 or $+1$; unstable group = scores of -7 to -2 and $+2$ to $+7$ (8).

Discriminative properties (9)

Reliability was determined from patients in the stable group. If a patient was stable between both weeks 1–5 and weeks 5–9, a single observation was selected using a random number generator. Reliability was estimated as the within-subject standard deviation and related to the total standard deviation as an intra-class correlation coefficient (ICC). For cross-sectional validity, we used data from the second clinic visit (week 1) and made *a priori* predictions concerning the degree of correlation we should expect with other measures of health status if the instruments truly measure asthma control. The predictions were based on results from previous studies.

Evaluative properties (9)

Responsiveness was examined in three ways. First, for patients in the unstable group, we determined whether the questionnaires could detect within-patient change using a paired *t*-test. Second, we assessed whether they could detect differences between stable and unstable patients using an unpaired *t*-test. Third, we calculated the responsiveness index (Δ/SDΔ) (10). To ensure that the contribution of two observations by some patients did not result in an overestimate of the precision of responsiveness, we inflated the variance by the quantity $1+(n-1)\rho$, where ρ is the ICC of the change scores and $n=2$ (number of observations per subject) (11). For longitudinal validity, we once again made *a priori* predictions based on results from previous studies.

Results

All 50 patients completed the study and provided complete data sets (Table 1).

The mean scores at the end of week 1 for the ACQ and each of the abbreviated versions are shown in Table 2. There was no evidence of any difference in scores between the ACQ and symptoms + FEV_1 (mean = 0·02; SD = 0·14; $P=0{\cdot}37$). However, both the difference between the ACQ and symptoms alone (mean = 0·26; SD = 0·37) and the difference between the ACQ and symptoms + β_2-agonist (mean = 0·20; SD = 0·28) were significant ($P<0{\cdot}0001$). Correlations between the ACQ and the abbreviated

TABLE 1. Patient characteristics

Number	50
Gender (M/F)	18/32
Age (mean : SD)	37·1 : 13·1
FEV_1% predicted pre-BD (mean : SD)	77·2 : 18·8
PEF (mean : SD)	406·3 : 107·5
Medication use	
(a) Short-acting β_2-agonists alone	12
(b) Inhaled steroids + (a)	34
(c) Long-acting β_2-agonist + (b)	3
(d) Oral steroids ± (c)	1

TABLE 2. Questionnaire scores at the end of week 1

	Mean ± SD
All questions	1·49 ± 0·66
Symptoms alone	1·23 ± 0·59
Nocturnal waking	0·58 ± 1·03
Morning symptoms	1·28 ± 0·95
Activity limitation	1·26 ± 1·16
Short of breath	1·70 ± 0·91
Wheeze	1·34 ± 0·77
Symptoms+FEV_1	1·47 ± 0·67
Symptoms + β_2-agonist use	1·29 ± 0·72

versions were high; symptoms alone: $r = 0{\cdot}87$, symptoms $+FEV_1$: $r = 0{\cdot}98$ and symptom $\pm$ β_2-agonist: $r = 0{\cdot}92$.

Reliability of the ACQ (ICC = 0·91) was very similar to that of the three abbreviated versions (symptoms $+FEV_1 = 0{\cdot}89$; symptoms + β_2-agonist = 0·90; symptoms alone = 0·89). Similarly, there was no evidence of any difference in responsiveness between the ACQ and the three abbreviated versions (Table 3), and neither was there any evidence of deterioration in responsiveness indices (ACQ = 1·06; symptoms $+FEV_1 = 1{\cdot}10$; symptoms + β_2-agonist = 1·20; symptoms alone = 1·27). The consistency of the standard deviations and the responsiveness indices (Table 3) indicate that study sample sizes will be similar for all four instruments.

Both cross-sectional and longitudinal correlations with other measures of health status were very similar for the ACQ and the three abbreviated versions (Tables 4 and 5).

Discussion

Correlations between all three abbreviated versions (symptoms alone, symptoms+ β_2-agonist use and symptoms $+FEV_1$) and the original ACQ were high, providing evidence that all three are measuring exactly the same construct (concept) as the original ACQ (criterion validity). This is further supported by the similarity of correlations, both cross-sectional and longitudinal, with other measures of health status (construct validity). The reliability and responsiveness of the three abbreviated versions of the ACQ are very similar to those of the original ACQ, suggesting that all four questionnaires have similar abilities to detect differences between patient groups in cross-sectional surveys and treatment effects in clinical trials. Thus, all three abbreviated versions are valid measures of asthma control with strong measurement properties and

TABLE 3. Responsiveness (change in score between consecutive clinic visits)

	Patients with stable asthma ($n = 36$) mean (SD*)	Patients in whom asthma changed ($n = 50$) mean (SD*)	Difference P-value
All questions	0·004 (0·25)	0·73 (0·69)**	$<0{\cdot}0001$
Symptoms alone	−0·01 (0·31)	0·88 (0·77)**	$<0{\cdot}0001$
Symptoms + FEV_1	0·01(0·27)	0·77 (0·69)**	$<0{\cdot}0001$
Symptoms + β_2-agonist use	−0·01 (0·27)	0·81 (0·66)**	$<0{\cdot}0001$

n = number of observations.
*Adjusted for multiple responses.
**$P < 0{\cdot}0001$.

TABLE 4. Cross-sectional validity (Pearson correlation coefficient)

	All questions	Symptoms alone	Symptoms + FEV_1	Symptoms +β_2-agonist use
Asthma Quality of Life Questionnaire				
Overall	0·76	0·85	0·77	0·82
Symptoms	0·75	0·85	0·74	0·85
Emotions	0·66	0·68	0·65	0·70
Activities	0·71	0·77	0·74	0·73
Environment	0·55	0·63	0·58	0·59
Generic health status (SF-36)				
Physical	0·55	0·50	0·56	0·50
Mental	0·18	0·29	0·14	0·32
Other asthma symptoms	0·42	0·56	0·41	0·56

A priori predictions:
(1) AQLQ: $r = 0{\cdot}4 - 0{\cdot}8$. The highest correction should be with the symptom domain ($r = 0{\cdot}6 - 0{\cdot}8$) and the lowest with the environmental domain ($r = 0{\cdot}4 - 0{\cdot}6$).
(2) Physical health domain of the SF-36: $r = 0{\cdot}4 - 0{\cdot}6$.
(3) The five additional asthma control symptoms: $r = 0{\cdot}4 - 0{\cdot}6$.

TABLE 5. Longitudinal validity (Pearson correlation coefficient)

	Δ All questions	Δ Symptoms alone	Δ Symptoms + FEV_1	Δ Symptoms + β_2-agonist use
Asthma Quality of Life Questionnaire				
Δ Overall	0·77	0·77	0·76	0·78
Δ Symptoms	0·79	0·79	0·77	0·81
Δ Emotions	0·64	0·62	0·63	0·63
Δ Activities	0·69	0·68	0·68	0·68
Δ Environment	0·34	0·34	0·33	0·35
Generic health status (SF-36)				
Δ Physical	0·29	0·25	0·28	0·27
Δ Mental	0·13	0·13	0·10	0·16
Δ Other asthma symptoms	0·49	0·52	0·47	0·54*

A priori predictions:
(1) Change in AQLQ: $r = 0{\cdot}4-0{\cdot}8$; the highest correlations should be with the symptom domain ($r = 0{\cdot}6-0{\cdot}8$) and the lowest with the environmental domain ($r = 0{\cdot}4-0{\cdot}6$).
(2) Change in physical health domain of the SF-36: $r = 0{\cdot}2-0{\cdot}4$.
(3) Change in the five additional asthma symptoms (cough, chest tightness, sputum, coloured sputum and clearing the throat): $r = 0{\cdot}4-0{\cdot}6$.

can be used with confidence in clinical trials and epidemiological surveys to measure asthma control.

The inclusion/exclusion of rescue β_2-agonist use makes no difference to the summary score, whereas removal of the FEV_1 question lowers the summary score significantly. This means that summary scores calculated without the FEV_1 question are perfectly valid for measuring asthma control but they cannot be combined or compared with summary scores that include the FEV_1 question.

For categorizing patients into the stable and unstable groups it would have been ideal for several clinicians, blinded to the ACQ data, to have independently assessed each patient at each clinic visit and a consensus taken as to whether each patient had changed. This was not feasible and left us with the choice of reviewing recorded data at a later date for a group decision or having one clinician make the decision at the time of the clinic visit. We selected the latter because a group decision would have had to rely heavily on recorded symptoms, β_2-agonist use and airway calibre, i.e. all the data recorded in the ACQ. The approach we took makes it less likely that spuriously high correlations resulted from ACQ data exercising undue influence on the global rating.

A limitation of this study was the relatively small sample size ($n = 50$) but was of a size comparable to other questionnaire validation studies (6, 12–14). Although the patients represented a wide range of asthma severity (Table 1), they tended to be fairly well controlled (Table 2). Since measurement properties of valid instruments tend to be consistent irrespective of the severity of the impairment (6, 12–14), the results of this study should apply to patients with more severely uncontrolled asthma. Nevertheless, confidence in the validity of the abbreviated versions of the ACQ will increase as they are evaluated in future studies.

It is important to emphasize that the results of this study only apply to the use of the ACQ in clinical trials and epidemiological surveys. They should not be interpreted to mean that spirometry and use of rescue β_2-agonist may be excluded from the estimation of asthma control in individual patients. The reason that international guidelines on the management of asthma identify that all three factors (symptoms, airway calibre and rescue β_2-agonist) (2–5) should be used to evaluate asthma control in individual patients is that there is a wide variation in the way patients manifest inadequacy of asthma control (15). The reason that we are able to omit the measurement of FEV_1 and β_2-agonist use from the assessment of asthma control in large studies is that the effect of patient heterogeneity is lost in large sample sizes.

In conclusion, we have shown that asthma symptoms alone may be used to estimate asthma control in large studies. This will help investigators wishing to improve the efficiency of data collection in large studies and for those who do not have access to estimates of airway calibre or inhaled β_2-agonist use.

Acknowledgements

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