

PHYSIOLOGY

## Correlation between Perceived Asthma Control and Thoraco-Abdominal Asynchrony in Primary Care Patients Diagnosed with Asthma

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**Objective.** Thoraco-abdominal asynchrony (TAA), the discordant movement of the abdomen and thorax, may impact upon health-related variables. Here, we investigated the extent to which TAA is associated with health-related variables, particularly perceived asthma control and quality of life. **Methods.** Ambulatory respiratory data from 43 patients diagnosed with asthma and 43 healthy age and sex-matched controls were recorded over 4 hours. Phase relation (Ph Rel Total), the percentage of time that the effects of rib cage (RC) and diaphragmatic movement result in opposite effects on intra-thoracic volume, quantified TAA. Subjects completed the Mini Asthma Quality of Life Questionnaire (AQLQ), Asthma Control Questionnaire (ACQ), Nijmegen questionnaire (NQ), Hospital Anxiety and Depression Scale (HADS), Spielberger State-Trait Anxiety Inventory (STAI), and General Health Perception (GHP) subscale of the short form 36 questionnaire. Capnography profiling, breath-hold time (BHT), and standard spirometry were performed. **Results.** The time in asynchrony was significantly greater in the asthma than in the healthy control group (Ph Rel Total = 14% (interquartile range (IQR) 8.5–20.7%) versus 10.4% (IQR 7.1–14.5%),  $p = .012$ ). In patients with asthma, Ph Rel Total was weakly associated with poorer ACQ scores ( $r = 0.33$ ,  $p = .03$ ), and in the healthy control group with GHP ( $r = 0.319$ ,  $p = .037$ ). Post-hoc exploratory analysis revealed a moderate relationship in the female asthma subgroup between Ph Rel Total and AQLQ ( $r = -0.56$ ,  $p = .003$ ). **Conclusions.** TAA may be associated with decreased perceived asthma control. In healthy individuals, asynchrony may be associated with low perception of general health. Further studies are required to investigate if the reduction of TAA improves these health-related variables.

**Keywords** breathing training, perceived asthma control, respiratory pattern

### INTRODUCTION

Clinical trials of breathing training for people diagnosed with asthma have found that this intervention may improve a number of patient outcomes. These include quality of life (1, 2) asthma symptoms (3), NQ scores (2, 3), anxiety (2–4), depression (2, 3), the number of emergency room visits in patients with dysfunctional breathing (1), and possibly perception of asthma control (2). A review of the effectiveness of breathing training for patients diagnosed with asthma concluded that it should be offered to patients to help control the symptoms of asthma and improve the quality of life (5).

At present, the mechanism by which breathing training improves patient outcomes is uncertain. It has been suggested that there is a need for greater description and standardization of the elements comprising particular breathing training programs (6). Few studies measure the breathing patterns of patients undertaking breathing training or explore the relationship between breathing patterns and patient outcomes. A recent exception is a

study which found that thoracic breathing patterns were associated with dyspnea, which decreased following breathing training (7). It is important to understand the impact of breathing training on breathing patterns as this will help to develop effective breathing training programs, thereby maximizing patient outcomes and ensuring that those patients who are most likely to benefit are targeted.

In a normal breathing pattern, the rib-cage (RC) and abdomen (AB) move in synchrony with each other, expanding and retracting simultaneously, optimizing tidal volume. Thoraco-abdominal asynchrony (TAA) is the discordant movement between these compartments. The highest degree of TAA is when RC and abdominal movements occur in opposite directions (paradoxical breathing).

Although it has previously been reported that TAA is higher in patients with asthma than in healthy controls (8), the role of TAA in asthma is unclear. One of the challenges of investigating this topic is that dysfunctional breathing patterns may be intermittent. This study therefore recorded ambulatory breathing patterns using the LifeShirt™ System (9) (Vivometrics, Inc., Ventura, CA, USA) over a period of approximately 4 hours. This enabled the average

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level of TAA over the course of this time period to be included in the analysis.

We hypothesized that primary care patients with asthma have significantly higher levels of TAA than age- and sex-matched controls. As previous studies have indicated that breathing training may improve asthma-related quality of life and perceived asthma control (1, 2), and it is possible that the underlying mechanism may be improvement in breathing patterns, we hypothesized that TAA is associated with poor asthma quality of life and perceived asthma control. Lastly, to contribute to the wider debate concerning the conceptualization of “dysfunctional breathing”, we explored the relationship between TAA and a range of screening tools used to detect dysfunctional breathing (NQ scores, baseline end-tidal carbon dioxide ( $E_T\text{CO}_2$ ) levels, capnography profiling, and breath-hold time).

## METHODS

The Health Studies Research Ethics Committee at Buckinghamshire Chilterns University College and the Local Research Ethics Committee in Mid and South-West Buckinghamshire gave approval for this study (REC/709).

### *Inclusion/Exclusion Criteria*

All subjects were aged between 18 and 65 years. Patients in the asthma group had a current diagnosis of asthma, were on their general practice's asthma list, and had a current asthma-related prescription (either  $\beta_2$ -agonists or inhaled corticosteroids). Subjects were excluded if they smoked, were currently prescribed oral corticosteroids, or had significant comorbidity. Subjects were not required to withhold asthma medication. The criteria for healthy subjects were identical to those of the asthma group, with the prerequisite that they had never received a diagnosis of asthma.

### *Recruitment Methods*

Patients with a diagnosis of asthma and healthy subjects were recruited from three sites (two general practices and one University) in Buckinghamshire between April and September 2004. Using, in alphabetical order, the practice's asthma database, invitation letters were sent to 400 primary care patients with a general practitioner (GP) diagnosis of asthma. Control subjects, without a diagnosis of asthma, were recruited via posters displayed in GP waiting rooms of participating general practices and on the University campus.

### *Measurements*

**Ambulatory Respiratory Data.** These data were collected using the LifeShirt System (9), which enabled ambulatory breathing patterns to be measured. This method avoided the measurement of respiratory variables via a mouthpiece, which may increase hyperventilation and respiratory drive (10).

The LifeShirt System measures breathing patterns by means of two respiratory inductive plethysmography (RIP)

bands. These are arrays of sinusoidally arranged electrical wires that detect movement, embedded in a lightweight vest worn by the subject. The RIP bands in the LifeShirt System are positioned around the RC and AB. Magnetic information from the RIP bands was transformed into waveforms and stored on a flashcard in a small computer attached to the system. These waveforms were then downloaded to the analysis software (VivoLogic®, VivoMetrics, Inc.). Respiratory measures are calculated from the measurement of expansion and contraction of the RIP bands. Calibration of the RIP signals was performed by qualitative diagnostic calibration followed by fixed volume calibration using least squares regression (11).

The following measures were recorded and derived as advised by the manufacturer (11). Median (i.e., minute to minute) phase relation of the entire breath (Ph Rel Total) was used to measure TAA. This is percentage of time that the effects of RC and diaphragmatic movement result in opposite effects on intra-thoracic volume (12). This measure is repeatable in both patients with a diagnosis of asthma and healthy controls (13). Minute ventilation was obtained using the volume calibrated signal to give the volume of each tidal breath, with the minute ventilation being the summed volume of each tidal breath within a given minute. Other ambulatory respiratory variables were measured (see Table 2). Subjects were instructed to perform their normal daily tasks and to return after approximately 4 hours.

**Lung Function.** Spirometry values were measured using the Pneumotrac PC-based Spirometer (v4.22) (Vitalograph Ltd., Buckingham, UK) using American Thoracic Society standards (14). Weight and height were recorded.

**Self-Reported Health-Related Variables.** All subjects completed the HADS (15), the STAI (16), and the GHP (17). Patients with asthma completed the AQLQ (18) and the ACQ (19).

All subjects completed the NQ. This is a checklist of symptoms validated for use with otherwise healthy patients to indicate hyperventilation syndrome (HVS) (20). Although NQ was not validated for use with patients with asthma, it has previously been used to investigate the presence of symptoms of HVS in patients with a diagnosis of asthma (21).

**Capnometry Profiles.** Capnometry profiles can detect the presence of occasional or chronic hyperventilation. These were measured via a double-pronged nasal cannula attached to the CapnoTrainer (v1), using the CapnoTrainer software (v1.2) (Better Physiology Ltd., Boulder, CO, USA). Subjects were seated and requested to breathe through their nose with mouth closed, while baseline  $E_T\text{CO}_2$  levels were recorded for 5 minutes. The mean  $E_T\text{CO}_2$  value was recorded. Subjects were then requested to increase the rate and depth of their breathing until  $E_T\text{CO}_2$  fell to 2.66 kPa (20 mmHg), at which point subjects were instructed to resume normal breathing, and the  $E_T\text{CO}_2$  recording continued for a further 10 minutes,

with the  $E_T\text{CO}_2$  returning to within the normal range of 4.0–5.7 kPa (22). The time taken to return to the resting  $E_T\text{CO}_2$  level and the ratio of  $E_T\text{CO}_2$  at 3 minutes post hyperventilation to the resting  $E_T\text{CO}_2$  level were included in the analysis (23).

**Breath-Hold Time.** BHT was measured at functional residual capacity. This is also called the “control pause” and is used by Buteyko practitioners to detect chronic hyperventilation. Subjects wore a nose clip and BHT was measured using a stopwatch. A BHT of 10 seconds or less is thought by Buteyko practitioners to indicate a “serious hyperventilation problem” (24).

### Statistical Analysis

Data analysis was performed using SPSS (SPSS Inc, Chicago, IL, USA) (version 12). As most data fields were not normally distributed, data were described using median values and IQRs (25th–75th percentiles) and group data were compared using the Mann–Whitney U-test. The relationship between Ph Rel Total and other variables was explored using Spearman’s Rho correlation coefficients. As a previous study has reported higher levels of symptoms of dysfunctional breathing in females (21), we conducted post-hoc exploratory analysis to compare these associations between male and female subjects.

Due to the paucity of literature in this area at the time the study was conducted, it was not possible to conduct a sample size calculation. However, using a nomogram for calculating sample size (25), a total sample size of 80 (40 patients with a diagnosis of asthma and 40 controls) was sufficiently large to detect a difference in Ph Rel Total of 5%.

## RESULTS

### Subject Characteristics

Data were collected on 43 patients with a diagnosis of asthma and 43 healthy control subjects. The two groups were matched by age and gender. The asthma group had significantly lower percentage of predicted forced expiratory volume in 1 second ( $FEV_1\%$  predicted) ( $p = .002$ ), GHP ( $p = .001$ ), and breath-hold times ( $p = .002$ ), and significantly higher NQ scores ( $p < .001$ ) than the control group (Table 1). Although the asthma group had significantly higher scores on the HADS depression scale than the control group ( $p = .042$ ), the mean scores for this scale were below the diagnostic threshold.

The ambulatory data for the asthma group were recorded for slightly longer in the asthma than in the control group (median values were 249 (IQR 219–281) minutes versus 225 (IQR 186–247) minutes, respectively). Subjects in the asthma group had significantly higher levels of Ph Rel Total ( $p = .012$ ), minute ventilation ( $p = .004$ ), and breaths per minute ( $p = .045$ ) than those in the control group (Table 2). Levels of activity (as measured by the median accelerometer motion indicator) were similar in both groups.

Spearman’s correlation coefficients for the relationship between Ph Rel Total and health-related correlates in the asthma and control groups are shown in Table 3. There were statistically significant but weak correlations between Ph Rel Total and ACQ scores ( $r = 0.33$ ,  $p = .03$ ) in the asthma group. Ph Rel Total was weakly associated with GHP in the control group ( $r = 0.319$ ,  $p = .037$ ) but not in the asthma group ( $r = -0.21$ ,  $p = .186$ ).

TABLE 1.—Demographic and clinical features of subjects.

|                                                                                         | Asthma ( $n = 43$ ) | Healthy ( $n = 43$ ) | $p$ -Value |
|-----------------------------------------------------------------------------------------|---------------------|----------------------|------------|
| Age (years)                                                                             | 46 (40–58)          | 48 (38–55)           | .650       |
| Ethnicity (Caucasian/Black)                                                             | 42/1                | 42/1                 |            |
| Gender (male/female)                                                                    | 17/26               | 17/26                |            |
| Inhaled bronchodilators/inhaled bronchodilators and corticosteroids                     | 11/32               | 0                    |            |
| BMI ( $\text{kg m}^{-2}$ )                                                              | 25.9 (23.6–29.4)    | 25.1 (22.6–26.9)     | .176       |
| Health related variables                                                                |                     |                      |            |
| FEV <sub>1</sub> /FVC                                                                   | 0.76 (0.64–0.84)    | 0.79 (0.74–0.83)     | .218       |
| FEV <sub>1</sub> % predicted                                                            | 91.8 (78.4–103.1)   | 106.7 (93.4–116.3)   | .002       |
| FVC% predicted                                                                          | 108.2 (90.25–118.2) | 103.6 (93.5–116.2)   | .855       |
| GHP                                                                                     | 65 (42–77)          | 75 (67–90)           | .001       |
| STAI                                                                                    | 33.3 (23.3–36.7)    | 30.0 (23.3–36.7)     | .234       |
| HADS anxiety                                                                            | 7 (6–8)             | 6 (5–8)              | .205       |
| HADS depression                                                                         | 2 (1–4)             | 1 (1–3)              | .042       |
| AQLQ                                                                                    | 5.9 (5.3–6.4)       | n/a                  |            |
| ACQ                                                                                     | 1.0 (0.4–1.7)       | n/a                  |            |
| Screening tools for “dysfunctional breathing”                                           |                     |                      |            |
| NQ                                                                                      | 19 (12–25)          | 10 (6–16)            | <.001      |
| $E_T\text{CO}_2$ levels (kPa)                                                           | 5.1 (4.8–5.4)       | 5.2 (4.8–5.6)        | .663       |
| Capnography profile: the recovery time following hyperventilation to 2.66 kPa (seconds) | 50 (30.0–96.3)      | 70 (35–130)          | .345       |
| Breath-hold time from functional residual capacity (seconds)                            | 21.6 (17.1–26.7)    | 28.6 (21.1–35.4)     | .002       |

Note: All results are median (interquartile range: 25th–75th percentiles) unless categorical variable.

BMI, body mass index; Ph Rel Total, median phase relations of the entire breath; FEV<sub>1</sub>/FVC, ratio of forced expiratory volume in 1 second to forced vital capacity; FEV<sub>1</sub>% predicted, percentage of predicted forced expiratory volume in 1 second; FVC% predicted, percentage of predicted forced vital capacity; GHP, General Health Perception subscale of the short form 36 questionnaire (low scores = maximum impairment); STAI, State Trait Anxiety Inventory (clinical cutoff point = 40; high scores = maximum impairment); HADS, Hospital Anxiety and Depression Scale (8–10 possible anxiety/depression, >10 probably anxiety/depression); AQLQ, Asthma Quality of Life Questionnaire; ACQ, Asthma Control Questionnaire (high scores = maximum impairment); NQ, Nijmegen questionnaire (high scores = maximum impairment);  $E_T\text{CO}_2$ , end-tidal carbon dioxide; n/a, not applicable.

TABLE 2.—Descriptive data for ambulatory respiratory variables.

|                                       | Asthma ( <i>n</i> = 43) | Healthy ( <i>n</i> = 43) | <i>p</i> -Value |
|---------------------------------------|-------------------------|--------------------------|-----------------|
| Ambulatory recording length (minutes) | 249 (219–281)           | 225 (186–247)            | .024            |
| Ph Rel Total (%)                      | 14.0 (8.5–20.7)         | 10.4 (7.1–14.5)          | .012            |
| VE (L/min)                            | 11.6 (8.8–19.3)         | 8.7 (6.5–11.6)           | .004            |
| pSigh (%)                             | 4 (2–7)                 | 5 (3–7)                  | .316            |
| BR (bpm)                              | 21.1 (18.9–23.8)        | 19.4 (17.9–22.7)         | .045            |
| Ti/Ttot                               | 0.4 (0.37–0.42)         | 0.4 (0.37–0.41)          | .402            |
| %RC                                   | 80 (62–95)              | 81 (67–91)               | .846            |
| F/Vt                                  | 33.9 (26.4–45.4)        | 41.6 (32.2–47.5)         | .127            |
| AccM                                  | 0.5 (0.5–0.7)           | 0.5 (0.4–0.6)            | .255            |

Note: All results are median (interquartile range).

Ph Rel Total, median phase relations of the entire breath; VE, minute ventilation; pSigh, percentage of sighs of total breaths every 15 minutes; BR, breaths per minute; Ti/Ttot, inspiratory time/total respiratory cycle length (the inspiratory duty cycle); %RC, percentage of rib cage contribution to tidal volume; F/Vt, frequency of breathing/total tidal volume ratio (an index of rapid shallow breathing, reflecting the work of breathing); AccM, accelerometer motion indicator (the minute by minute median motion component of the accelerometer).

TABLE 3.—Correlation between Ph Rel Total and health-related variables for asthma and healthy control subjects.

|                              | Asthma group ( <i>n</i> = 43) |                 | Control group ( <i>n</i> = 43) |                 |
|------------------------------|-------------------------------|-----------------|--------------------------------|-----------------|
|                              | Spearman's Rho                | <i>p</i> -Value | Spearman's Rho                 | <i>p</i> -Value |
| FEV <sub>1</sub> /FVC        | 0.21                          | .182            | −0.053                         | .735            |
| FEV <sub>1</sub> % predicted | −0.25                         | .106            | 0.293                          | .057            |
| FVC% predicted               | 0.04                          | .791            | −0.61                          | .713            |
| GHP                          | −0.21                         | .186            | 0.319                          | .037            |
| STAI                         | 0.21                          | .175            | −0.154                         | .323            |
| HADS anxiety                 | −0.14                         | .376            | 0.065                          | .678            |
| HADS depression              | 0.19                          | .233            | −0.057                         | .715            |
| AQLQ total                   | −0.23                         | .142            | —                              | —               |
| AQLQ subscales               |                               |                 |                                |                 |
| Symptoms                     | −0.29                         | .058            | —                              | —               |
| Environmental stimuli        | −0.14                         | .364            | —                              | —               |
| Emotional functioning        | −0.28                         | .070            | —                              | —               |
| Activity limitation          | −0.13                         | .416            | —                              | —               |
| ACQ                          | 0.33                          | .030            | —                              | —               |

Ph Rel Total, median phase relations of the entire breath; FEV<sub>1</sub>/FVC, ratio of forced expiratory volume in 1 second to forced vital capacity; FEV<sub>1</sub>% predicted, percentage of predicted forced expiratory volume in 1 second; FVC% predicted, percentage of predicted forced vital capacity; GHP, General Health Perception subscale of the short form 36 questionnaire (low scores = maximum impairment); STAI, State Trait Anxiety Inventory (clinical cutoff point = 40; high scores = maximum impairment); HADS, Hospital Anxiety and Depression Scale (8–10 possible anxiety/depression, > 10 probably anxiety/depression); AQLQ, Asthma Quality of Life Questionnaire; ACQ, Asthma Control Questionnaire (high scores = maximum impairment).

TABLE 4.—Correlation between Ph Rel Total and screening tools to detect dysfunctional breathing in asthma and healthy control subjects.

|                                                              | Asthma ( <i>n</i> = 43) |                 | Healthy ( <i>n</i> = 43) |                 |
|--------------------------------------------------------------|-------------------------|-----------------|--------------------------|-----------------|
|                                                              | Spearman's Rho          | <i>p</i> -Value | Spearman's Rho           | <i>p</i> -Value |
| NQ                                                           | 0.08                    | .624            | 0.03                     | .829            |
| Resting E <sub>T</sub> CO <sub>2</sub>                       | 0.03                    | .850            | 0.13                     | .412            |
| Recovery time following hyperventilation to 2.66 kPa         | −0.17                   | .292            | 0.22                     | .152            |
| Breath-hold time from functional residual capacity (seconds) | −0.184                  | .245            | 0.138                    | .385            |

Ph Rel Total, median phase relations of the entire breath; NQ, Nijmegen questionnaire (high scores = maximum impairment); E<sub>T</sub>CO<sub>2</sub>, end-tidal carbon dioxide.

Although subjects in the asthma group reported significantly more symptoms of dysfunctional breathing on the NQ compared to healthy controls (Table 1), there were no significant correlations between Ph Rel Total and the NQ (Table 4). Neither was Ph Rel Total related to resting E<sub>T</sub>CO<sub>2</sub> levels, recovery time following hyperventilation, or breath-hold time from functional residual capacity (the control pause).

#### Post-Hoc Exploratory Subgroup Analyses

This was conducted to investigate if there were any differences between genders. Descriptive data are shown in

Table 5. The female subjects with asthma had a significantly lower median Ph Rel Total ( $p = .047$ ) and AQLQ ( $p = .002$ ) scores, and significantly higher NQ ( $p = .002$ ) and ACQ ( $p = .037$ ) scores than the male subjects with asthma.

There was a significant correlation between Ph Rel Total and AQLQ scores in females ( $r = -0.565$ ,  $p = .003$ ), but not in males ( $r = -0.342$ ,  $p = .179$ ) with asthma (Figure 1). This confirms the findings for the group (Table 3; AQLQ total) for this relationship.

There was a significant correlation between Ph Rel Total and the ACQ scores in female ( $r = 0.403$ ,  $p = .041$ ), but not in male subjects ( $r = 0.464$ ,  $p = .061$ ) with asthma

TABLE 5.—Demographic and clinical features of subjects by gender.

|                                                                                         | Asthma ( <i>n</i> = 43) |                     |                 | Healthy ( <i>n</i> = 43) |                    |                 |
|-----------------------------------------------------------------------------------------|-------------------------|---------------------|-----------------|--------------------------|--------------------|-----------------|
|                                                                                         | Male                    | Female              | <i>p</i> -Value | Male                     | Female             | <i>p</i> -Value |
| Age (years)                                                                             | 48 (43–59)              | 43 (36–58)          | .274            | 48 (42–55)               | 47 (36–55)         | .619            |
| Ethnicity (Caucasian/Black)                                                             | 17/0                    | 25/1                | 1.0             | 17/0                     | 25/1               |                 |
| Inhaled bronchodilators/inhaled bronchodilators and corticosteroids                     | 2/15                    | 9/17                | .154            | n/a                      | n/a                |                 |
| BMI (kg m <sup>-2</sup> )                                                               | 25.3 (24.1–27.4)        | 26.0 (22.9–31.5)    | .619            | 25.6 (24.9–27.9)         | 23.5 (21.8–26.5)   | .078            |
| Thoraco-abdominal asynchrony                                                            |                         |                     |                 |                          |                    |                 |
| Ph Rel Total                                                                            | 19.8 (10.8–22.1)        | 13.4 (7.9–19.1)     | .047            | 10.0 (8.9–15.0)          | 10.5 (5.1–14.5)    | .576            |
| Health-related variables                                                                |                         |                     |                 |                          |                    |                 |
| FEV <sub>1</sub> /FVC                                                                   | 0.7 (0.6–0.8)           | 0.8 (0.7–0.8)       | .196            | 0.77 (0.73–0.81)         | 0.8 (0.74–0.84)    | .124            |
| FEV <sub>1</sub> % predicted                                                            | 84.6 (75.8–101.1)       | 92.5 (83.7–107.6)   | .441            | 106.0 (91.4–120.3)       | 106.8 (93.7–114.4) | .785            |
| FVC% predicted                                                                          | 108.2 (95.0–127.1)      | 108.5 (83.60–115.9) | .214            | 103.2 (92.4–116.2)       | 104.2 (94.4–116.4) | .786            |
| GHP                                                                                     | 67 (52–82)              | 57 (39–77)          | .147            | 72 (62–86)               | 79 (66–96)         | .418            |
| STAI                                                                                    | 27 (23–35)              | 33 (23–40)          | .172            | 30 (20–37)               | 30 (23–37)         | .632            |
| HADS anxiety                                                                            | 6 (3–8)                 | 7 (7–9)             | .017            | 7 (6–9)                  | 6 (4–8)            | .049            |
| HADS depression                                                                         | 2 (1–2.5)               | 3 (1–5)             | .112            | 2 (1–3)                  | 1 (1–2)            | .026            |
| AQLQ                                                                                    | 6.1 (5.8–6.8)           | 5.5 (4.5–6.0)       | .002            |                          |                    |                 |
| ACQ                                                                                     | 0.6 (0.4–1.4)           | 1.2 (0.6–1.8)       | .037            |                          |                    |                 |
| Screening tools for “dysfunctional breathing”                                           |                         |                     |                 |                          |                    |                 |
| NQ                                                                                      | 11.0 (8.0–22.5)         | 20.5 (18.0–26.5)    | .002            | 10.0 (6–17)              | 9.0 (6–15)         | .678            |
| E <sub>T</sub> CO <sub>2</sub> levels (kPa)                                             | 5.2 (5.0–5.5)           | 5.1 (4.8–5.3)       | .130            | 5.3 (4.9–5.6)            | 5.1 (4.5–5.4)      | .365            |
| Capnography profile: the recovery time following hyperventilation to 2.66 kPa (seconds) | 50 (29–83)              | 50 (30–115)         | .912            | 45 (38–133)              | 72.5 (35–135)      | .891            |
| Breath-hold time from functional residual capacity (seconds)                            | 23 (17–29)              | 21 (17–24)          | .468            | 31 (26–39)               | 26 (20–34)         | .075            |

BMI, body mass index; Ph Rel Total, median phase relations of the entire breath; FEV<sub>1</sub>/FVC, ratio of forced expiratory volume in 1 second to forced vital capacity; FEV<sub>1</sub>% predicted, percentage of predicted forced expiratory volume in 1 second; FVC% predicted, percentage of predicted forced vital capacity; GHP, General Health Perception subscale of the short form 36 questionnaire (low scores = maximum impairment); STAI, State Trait Anxiety Inventory (clinical cutoff point = 40; high scores = maximum impairment); HADS, Hospital Anxiety and Depression Scale (8–10 possible anxiety/depression, > 10 probably anxiety/depression); AQLQ, Asthma Quality of Life Questionnaire; ACQ, Asthma Control Questionnaire (high scores = maximum impairment); NQ, Nijmegen questionnaire (high scores = maximum impairment); E<sub>T</sub>CO<sub>2</sub>, end-tidal carbon dioxide.

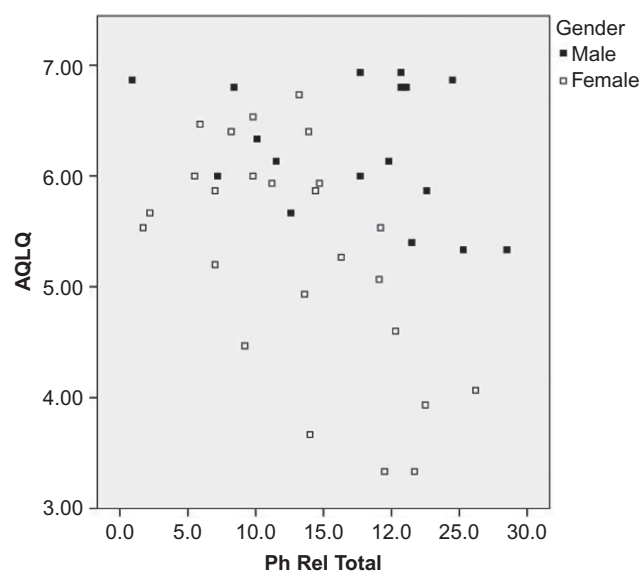


FIGURE 1.—Relationship between AQLQ and Ph Rel Total.

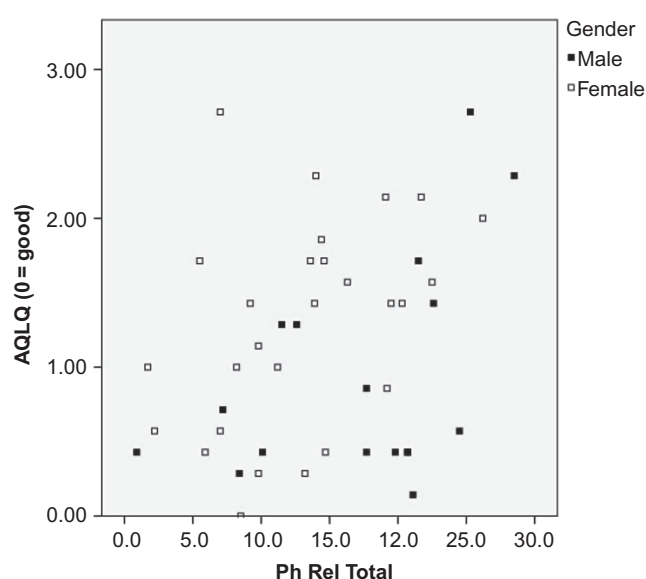


FIGURE 2.—Relationship between ACQ and Ph Rel Total.

(Figure 2). This confirms the findings for the group (Table 3; ACQ) for this relationship.

The effect of gender on the association between Ph Rel Total and the remaining health-related variables in the asthma group was investigated. There was a

significant correlation between Ph Rel Total and FEV<sub>1</sub>/FVC in the male asthma group ( $r = 0.524$ ,  $p = .031$ ), but not in the female asthma group ( $r = 0.074$ ,  $p = .721$ ), otherwise no other significant correlations were observed.

## DISCUSSION

*Main Findings*

We found that subjects in the asthma group had significantly higher levels of TAA than healthy controls, and that high levels of TAA were related to poor levels of self-reported asthma control in the asthma group and low levels of GHP in the healthy control group, but not in the asthma group. No relationship was found between measures of anxiety and depression and level of TAA. Similarly, no significant associations were found between TAA and a range of screening tools for dysfunctional breathing. Post-hoc exploratory subgroup analysis revealed that the TAA was associated with ACQ and AQLQ scores in the female but not in the male asthma group.

*Strengths and Limitations of This Study*

This study focused on median ambulatory breathing patterns over a period of approximately 4 hours. The length of ambulatory monitoring was longer in the asthma group, with a mean difference of 24 minutes, which may have biased the findings as Ph Rel Total values may be affected by motion artifacts (26).

Although the self-reported diagnosis of asthma was not confirmed by the researchers, all subjects in the asthma group had a GP diagnosis of asthma, were taking asthma medication on at least a weekly basis, and were on the general practice's asthma register. It is possible that some of these subjects may have been excluded, had an objective diagnostic test been performed using diagnostic methods outlined in national UK guidelines (27). However, we decided to take a pragmatic approach and ensure that results could be generalized to primary care patients with a GP diagnosis of asthma. This pragmatic approach has been adopted in previous evaluations of breathing training (2).

A related limitation is that the subjects in the asthma group perceived that they had relatively well-controlled symptoms, as indicated by the AQLQ and ACQ scores. This limited the range of AQLQ and ACQ scores included in the sample, and therefore possibly the range of TAA values, and robustness of the results.

The findings in the post-hoc exploratory subgroup analysis of significant associations between Ph Rel Total and FEV<sub>1</sub>/FVC in the male asthma group and with ACQ and AQLQ scores in the female asthma group should be treated with caution. It is possible that this difference between genders was due to the larger number of female subjects in the sample, who had a larger range of AQLQ scores and significantly higher ACQ and NQ scores and HADS anxiety scale, resulting in greater power in the female group. It is also of note that Ph Rel Total was significantly related to ACQ and AQLQ scores in female but not in male subjects, even though female subjects with asthma had significantly lower Ph Rel Total scores (indicating less asynchrony between the compartments) than the male subjects.

The relatively steep negative correlation slope for female subjects (Figure 1) illustrates that smaller increases in asynchrony (greater Ph Rel Total) resulted in a greater

decrease in AQLQ scores in female compared to male subjects with asthma. The reason for this discrepancy between genders is unclear. Future studies are needed to explain this finding, and deepen understanding of the role of gender in the strength of association between TAA and health-related variables.

One of the limitations of this study is that it presented a one-off snapshot of the relationship of TAA in asthma. We have no data on the repeatability of these observations in the same subjects over time and currently whether interventions would alter the relationships observed in this study. In order to do this appropriately, data from each individual could be "normalized" with reference to their baseline values and then repeatability and the effects of interventions could be more clearly observed.

*Interpretation of Findings in Relation to Previously Published Work*

Few studies have been conducted which could explain the association between Ph Rel Total and perceived asthma control. It has been reported that individuals with asynchronous motion between the upper RC and AB are less able than those with synchronous motion to obtain heart rate variability coherence (28). This reflects a decreased ability to self-regulate autonomic and cardiorespiratory homeostatic reflexes, indicating reduced physiological resilience and efficiency. It is possible that this association between TAA and autonomic nervous system regulation may result in poorer perceptions of general health, quality of life, and perceived asthma control. Further research is required to investigate if this mechanism does contribute to the relationship between TAA and these health-related variables.

The lack of a significant association between measures of anxiety and depression and level of TAA may have been because psychological well-being was high in each group. There is a strong literature, showing that psychological dysfunction is common in people with a diagnosis of asthma and is associated with poor outcomes (29). In addition, TAA has been found to increase during acute psychosocial stress (30). It would therefore be of interest to investigate the level of dysfunctional breathing patterns, including TAA, in patients with psychological morbidity and asthma.

The finding that there were no significant relationships between TAA and a range of screening tools for dysfunctional breathing echoes the previous literature. A lack of association has been reported between breathing measures in people with concerns about their breathing (31), and a randomized controlled trial of breathing training for patients with a diagnosis of asthma found that the effects of breathing training were similar between patients with positive and negative screening scores on the NQ (2).

*Implications for Future Research, Policy, and Practice*

Breathing patterns are rarely measured in randomized controlled trials of breathing training. Future trials should investigate if breathing training changes breathing

patterns, and whether dysfunctional breathing patterns are established during subsequent periods of bronchospasm. Given the popularity and range of types of breathing training currently available (e.g., physiotherapy, biofeedback, Buteyko, Transformational Breath, and Yoga), future studies should also investigate whether different types of breathing training have different effects on patients with a diagnosis of asthma. The clinical implication is that decreasing TAA may result in an increase in perceived asthma control, and possibly in quality of life.

## CONCLUSION

In this dataset, TAA was related to perceived asthma control, and in healthy individuals to GHP. It is also significantly higher in patients with a diagnosis of asthma than those without this diagnosis. The clinical implication of these findings is that decreasing TAA may result in an increase in perceived asthma control, and possibly in quality of life. Future studies should evaluate the benefit of reducing TAA in patients with a diagnosis of asthma and healthy individuals.

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## DECLARATION OF INTEREST

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this article.

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