CHEST

Original Research

COPD

# Dynamic Expiratory Tracheal Collapse in COPD

## Correlation With Clinical and Physiologic Parameters

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***Background:*** **COPD has been described as a risk factor for excessive expiratory tracheal collapse, but its prevalence and clinical correlates have not been fully determined. The purpose of this study is to prospectively determine the prevalence of excessive expiratory tracheal collapse among patients with COPD and to test the hypothesis that clinical and/or physiologic parameters will correlate with the presence of excessive tracheal collapse.**

***Methods:*** **We studied 100 adults meeting GOLD (Global Initiative for Obstructive Lung Disease) criteria for COPD, who underwent full pulmonary function tests (PFTs), 6-min walk test (6MWT), St. George's Respiratory Questionnaire (SGRQ), and low-dose CT scan at total lung capacity and during dynamic exhalation with spirometric monitoring. We examined correlations between percentage dynamic expiratory tracheal collapse and PFTs, 6MWT distance, and SGRQ scores.**

***Results:*** **Patients included 48 women and 52 men with mean age 65 ± 7 years, $FEV_1$ 64% ± 22% predicted, and percentage expiratory collapse 59% ± 19%. Twenty of 100 participants met study criteria for excessive expiratory collapse. There was no significant correlation between percentage expiratory tracheal collapse and any pulmonary function measure, total SGRQ score, or 6MWT distance. The SGRQ symptom subscale was weakly correlated with percentage collapse of the mid trachea ($R = 0.215$, $P = .03$).**

***Conclusions:*** **Excessive expiratory tracheal collapse is observed in a subset of patients with COPD, but the magnitude of collapse is independent of disease severity and does not correlate significantly with physiologic parameters. Thus, the incidental identification of excessive expiratory tracheal collapse in a general COPD population may not necessarily be clinically significant.**

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**Abbreviations:** 6MWT = 6-min walk test; ATS = American Thoracic Society; CSA = cross-sectional area; DLCO = single breath diffusion capacity of the lung for carbon monoxide; GOLD = Global Initiative for Obstructive Lung Disease; HU = Hounsfield unit; PFT = pulmonary function test; SGRQ = St. George's Respiratory Questionnaire; TLC = total lung capacity; TM = tracheomalacia

Excessive expiratory tracheal collapse may occur due to either weakness of the supporting tracheal cartilaginous structures (tracheomalacia [TM]) or from excessive anterior bulging of the posterior membranous wall of the trachea (excessive dynamic airway collapse).[1] These related disorders are a potentially underdiagnosed cause of chronic respiratory symptoms and have been associated with a variety of risk factors, including COPD.[1-6]

The importance of assessing for excessive expiratory tracheal collapsibility has recently gained attention. Reports of selected patients with coexisting COPD and TM or excessive dynamic airway collapse have documented improved symptoms, quality of life, and functional status following central airway stabilization with silicone stents or tracheoplasty.[7,8] Although it has been reported that patients with COPD frequently have excessive expiratory tracheal collapse, the clinical significance of this finding has not previously been elucidated.[1-4]

With this in mind, the purpose of this study was first to prospectively determine the prevalence of excessive expiratory tracheal collapse among patients with COPD using low-dose CT scanning. In addition,

we sought to test whether clinical and/or physiologic parameters would correlate with the presence or absence of excessive expiratory tracheal collapse in this population.

## Materials and Methods

This study was approved by the Beth Israel Deaconess Medical Center Committee on Clinical Investigations (Protocol 2007P-000348) and performed in compliance with Health Insurance Portability and Accountability Act guidelines. Informed consent was obtained from all study participants.

### *Study Population*

From October 2008 through November 2010, we prospectively recruited subjects aged 35 to 75 years with a history of COPD to participate in a study assessing the prevalence of excessive expiratory tracheal collapse using low-dose CT scanning. Exclusion criteria included the following: (1) pregnancy; (2) presence of other risk factors for TM, including prior prolonged intubation, mediastinal radiation, tracheal surgery, or tracheal stent placement; and (3) unstable coronary artery disease, including myocardial infarction within the past 6 months or unstable angina. The study setting was a tertiary care center in a large US city with a diverse patient population.

Once enrolled in the study, participants underwent pulmonary function tests (PFTs). All tests were administered according to American Thoracic Society (ATS) and European Respiratory Society guidelines and included prebronchodilator and postbronchodilator spirometry, single breath diffusion capacity of the lung for carbon monoxide (Dlco), and plethysmographic determination of total lung capacity (TLC) and its subdivisions.[9] Participants who met GOLD (Global Initiative for Obstructive Lung Disease) criteria for COPD (compatible history and symptoms along with postbronchodilator $FEV_1/FVC \leq 0.7$) were included in the study population.[10]

### *Study Procedures*

Participants underwent the following series of study procedures: a respiratory-specific quality-of-life instrument, 6-min walk test (6MWT), and low-dose paired inspiratory-dynamic expiratory CT imaging. These tests are described in detail in the following sections.

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*Respiratory-Specific Quality-of-Life Instrument:* St. George's Respiratory Questionnaire (SGRQ), a validated, 50-item instrument with three separate scales (symptoms, activity, and impact on daily life), was administered to each participant. Scores range from 0 to 100, with higher scores indicating worse health status.[11] Additionally, participants were screened for the presence or absence of a chronic cough (> 8 weeks in duration).

*6-min Walk Testing:* The 6MWT was performed according to ATS guidelines along a 100-foot (30 m) distance marked by cones and was supervised by a respiratory physiologist.[12] The total distance covered at the end of 6 min was recorded for each subject. During the final 30 s of the 6MWT, participants were administered the multidimensional dyspnea profile to assess the level of dyspnea during exercise.[13] This validated instrument may be administered in a variety of settings, including during exercise.

*Low-Dose, Paired Inspiratory-Dynamic Expiratory CT Imaging:* All participants were imaged according to a standard protocol using a 64-detector-row scanner (LightSpeed VCT; General Electric Co). A previously validated low-dose technique was used, using the following parameters: 80 mA, 120 kVp, 0.625-mm detector collimation, 0.5-s gantry rotation time, and pitch of 1.375.[14]

Prior to scanning, initial scout topographic images were obtained to determine the area of coverage, which included the entire lungs. Helical scanning was performed in the craniocaudal direction for both end inspiratory (TLC) and dynamic expiratory scans (obtained during a forced expiratory maneuver). The end-inspiratory scan was performed first in all cases. For both sequences, images were reconstructed at 2.5-mm thickness with 1.25-mm reconstruction intervals and transferred to a Picture Archiving Communication System (Centricity, version 3.1; General Electric Co) for analysis and interpretation. These parameters were selected based on multidetector CT scan protocols validated by bronchoscopy for assessing tracheal collapsibility.[14-16] The total scanning time for each volumetric acquisition of the entire lungs was approximately 2.5 s.

### *CT Imaging Breathing Maneuvers*

A respiratory physiologist was present to monitor subjects during CT imaging studies and coach participants during both phases of the examination. While on the CT imaging table, participants were instructed in breathing maneuvers following a script.[17] To practice the breathing maneuvers for end inspiratory (TLC) imaging, the subjects took a deep breath to reach maximal inspiration, held their breath at TLC for approximately 6 s, and then expired fully for several seconds. To practice the breathing maneuvers for dynamic expiratory imaging, participants took a deep breath and then blew out hard and fast (as they did during FVC maneuvers in the PFT laboratory). Participants practiced these maneuvers while on the CT imaging table, breathing through a mouthpiece while wearing nose clips. Prior to the TLC and dynamic expiratory maneuver CT imaging sequences, the physiologist placed the mouthpiece and nose clips on the participant. He then directly observed a spirometric tracing, coaching the patient through the TLC respiratory maneuver while the CT image was acquired for the breath hold. Following CT imaging acquisition at TLC and while still connected to the mouthpiece, subjects exhaled completely into the spirometer, generating a volume time trace used to verify adequate breath hold volume (indicated by an expired volume ≥ 90% of the largest FVC measured in the PFT laboratory). During the dynamic expiratory maneuver, the spirometry trace was directly observed to assure CT scan acquisition during forceful exhalation. Maneuvers judged inadequate with respect to lung volume or forceful exhalation were immediately repeated. $FEV_1$ was determined from the spirometric

tracing and compared with the $FEV_1$ measured during PFT as an index of adequate effort.

*CT Image Interpretation*

An experienced, fellowship-trained thoracic radiologist prospectively interpreted each scan. All examinations were interpreted using a Picture Archiving Communication System workstation with standard lung (level, −650 Hounsfield units [HU]; width, 1,500 HU) and soft tissue (level, 50 HU; width, 350 HU) window display settings. For each imaging sequence, measurements were obtained at two standard levels: 1 cm above the aortic arch (mid-trachea) and 1 cm above the carina (lower trachea). Using a previously validated technique, the cross-sectional area (CSA) of the airway lumen was measured by tracing the inner wall of the airway with an electronic tracing tool.[14,16,18] The percentage expiratory luminal collapse was calculated as: % luminal collapse = 100 × (1 − [luminal area at dynamic expiration/luminal area at end-inspiration]).

In addition to performing measurements at these levels, the entire imaged trachea was visually assessed on both sequences to ensure that there was not a localized segment in the trachea that demonstrated substantially greater collapse compared with the sites of standardized measurement. Based on previously published work using the same methodology in a diverse group of 51 healthy control subjects with normal pulmonary function, excessive expiratory tracheal collapse was defined as > 80% expiratory reduction in tracheal luminal CSA.[19]

*Statistical Considerations*

Our target sample size was 100 participants. This study population size provides > 90% power to demonstrate a relationship between the percentage expiratory tracheal collapse measured at CT scan and various clinical and physiologic parameters, as long as $R^2$ is ≥ 0.10.

Sample characteristics are presented as means and SDs for continuous variables and counts and proportions for nominal and ordinal variables. Normal distribution of continuous variables was examined by the Kolmogorov-Smirnov one-sample test prior to calculating Pearson correlation coefficients to assess correspondence of central airway collapse with anthropometric and functional characteristics. Characteristics of subjects who did and did not meet criteria for excessive expiratory tracheal collapse were compared by unpaired *t* test for continuous variables and by $\chi^2$ or Fisher exact probability analysis for ordinal and categorical variables.

## Results

### *Study Population*

The final study population included 48 women and 52 men with a mean age of 65 ± 7 years. Patient demographics, including age, height, weight, and BMI, are provided in Table 1.

Functional characteristics of the study population (including FVC, $FEV_1$, $FEV_1$/FVC, DLCO, GOLD-stage distribution, and 6MWT results) are documented in Table 2, along with SGRQ scores. A majority of participants (74%) had moderate to severe COPD (GOLD stages II-IV).

### *Tracheal CSA Measurements*

Cross-sectional luminal area measurements at end-inspiration, dynamic expiration, and percentage expiratory reduction in CSA for the mid-trachea (1 cm above the aortic arch) and lower trachea (1 cm above the carina) are displayed in Table 3. The mean CSA of the mid-trachea decreased from 283 ± 66 $mm^2$ at end inspiration to 113 ± 56 $mm^2$ during forced expiration. The mean percentage expiratory reduction in mid-tracheal lumen CSA for all participants was 59% ± 19% and was similar for men and women (58% ± 20% and 60% ± 17%, respectively; $P = .61$). Corresponding measurements for the lower trachea were: 276 ± 63 $mm^2$ at end inspiration; 107 ± 56 $mm^2$ during forced expiration; and 61% ± 18% expiratory reduction, with no significant difference between men and women (61% ± 20% and 61% ± 17%, respectively; $P = .94$).

**Table 1—*Descriptive Characteristics of the Study Population***

| Characteristic | Women (n = 48) | Men (n = 52) | Total (N = 100) |
|---|---|---|---|
| Age, y | 65 (7) | 65 (7) | 65 (7) |
| Height, m | 161 (7) | 175 (7) | 168 (10) |
| Weight, kg | 79 (20) | 92 (17) | 86 (20) |
| BMI, kg/$m^2$ | 30 (8) | 30 (5) | 30 (6) |

Data are presented as mean (SD).

### *Correlation With Functional Characteristics*

There was no significant correlation between percentage expiratory tracheal collapse and any pulmonary function measure, total SGRQ score, or 6MWT distance. Both the SGRQ symptom ($R = 0.215$, $P = .030$) and activity ($R = 0.199$, $P = .048$) subscales were weakly correlated with percentage collapse of the mid-trachea. However, there was no significant difference in percentage expiratory tracheal collapse

**Table 2—*Functional Characteristics of the Study Population***

| Measure | Women | Men | Total |
|---|---|---|---|
| FVC, % predicted | 86 (22) | 81 (18) | 84 (20) |
| $FEV_1$, % predicted | 69 (20) | 59 (24) | 64 (22) |
| $FEV_1$/FVC | 56 (9) | 49 (13) | 52 (12) |
| DLCO, % predicted | 72 (20) | 66 (23) | 69 (22) |
| 6MWT, m | 391 (110) | 429 (133) | 411 (123) |
| SGRQ, total score | 40 (20) | 37 (21) | 38 (20) |
| SGRQ symptoms | 47 (24) | 44 (25) | 45 (24) |
| SGRQ activity | 55 (23) | 51 (24) | 53 (23) |
| SGRQ impact | 29 (21) | 26 (23) | 27 (22) |
| GOLD stage | | | |
| I mild | 33 | 19 | 26 |
| II moderate | 54 | 46 | 50 |
| III severe | 10 | 27 | 19 |
| IV very severe | 2 | 8 | 5 |

Data are presented as mean (SD) or %. 6MWT = 6-min walk test; DLCO = single breath diffusion capacity of the lung for carbon monoxide; GOLD = Global Initiative for Obstructive Lung Disease; SGRQ = St. George's Respiratory Questionnaire.

**Table 3—*Tracheal Cross-sectional Luminal Area and Percentage Expiratory Collapse***

| Measure | Women | Men | Total |
|---|---|---|---|
| Area at TLC, mm² | | | |
| Mid-trachea[a] | 241 (40) | 321 (62) | 283 (66) |
| Lower trachea[b] | 232 (41) | 317 (52) | 276 (63) |
| Area during forced exhalation, mm² | | | |
| Mid-trachea | 96 (46) | 129 (60) | 113 (56) |
| Lower trachea | 90 (40) | 123 (65) | 107 (56) |
| % Expiratory collapse | | | |
| Mid-trachea | 60 (17) | 58 (20) | 59 (18) |
| Lower trachea | 61 (17) | 61 (20) | 61 (18) |

Data are presented as mean (SD). TLC = total lung capacity.
[a]Mid-trachea = 1 cm above the aortic arch.
[b]Lower trachea = 1 cm above the carina.

between those participants who screened positive for chronic cough (n = 35) compared with those who screened negative for this symptom (60% ± 16% and 59% ± 20%, respectively; $P = .88$). Similarly, the correlation between perceived shortness of breath during exercise (as measured by the multidimensional dyspnea profile) and percentage expiratory tracheal collapse was not significant ($R = 0.11$, $P = .31$). Bivariate correlation coefficients between percentage expiratory tracheal collapse and various subject characteristics are provided in Table 4.

### *Correlation With Age*

There was no significant correlation between percentage expiratory tracheal collapse and age in the entire cohort ($R = 0.17$, $P = .09$). Similarly, there was no significant correlation among subgroups of men ($R = 0.12$, $P = .40$) or women ($R = 0.24$, $P = .10$).

### *Prevalence of Excessive Expiratory Tracheal Collapse in Study Cohort*

Using a threshold of > 80% expiratory reduction in tracheal luminal CSA to define excessive expiratory tracheal collapse, 20 participants (20%) met this criterion, including 13 of 52 men (25%) and seven of 48 women (15%). With respect to disease severity, seven of 20 subjects (35%) with excessive expiratory tracheal collapse were GOLD stage III or IV, as compared with 17 of 80 subjects (21%) without excessive collapse. Neither sex nor GOLD stage differed significantly between subsets of participants with and without excessive expiratory tracheal collapse. A comparison of the characteristics of participants with (n = 20) and without (n = 80) excessive expiratory tracheal collapse is presented in Table 5. There were no significant differences in any of the functional parameters or SGRQ scores between the two subgroups. Similarly, there was no significant difference in the rating of shortness of breath during exercise between those participants with and without excessive expiratory tracheal collapse (44% ± 18% full scale and 46% ± 26% full scale, respectively, $P = .70$).

**Table 4—*Correlations of Percent Expiratory Tracheal Collapse With Selected Variables***

| Measure | Correlation Coefficient (*P* Value) |
|---|---|
| $FEV_1$, % predicted | −0.003 (.973) |
| DLCO, % predicted | −0.037 (.717) |
| 6 MWT, m | −0.023 (.827) |
| SGRQ | |
| Total | 0.196 (.052) |
| Symptom | 0.217 (.031) |
| Activity | 0.199 (.048) |
| Impact | 0.142 (.162) |

See Table 2 legend for expansion of abbreviations.

## Discussion

In this study, we observed a wide range of forced expiratory tracheal collapse among patients with COPD, with 20% of participants demonstrating excessive expiratory tracheal collapse according to a criterion based on published normative data.[19] Although there was no correlation between the magnitude of forced expiratory tracheal collapse and functional parameters, we found a weak but significant correlation with respiratory symptoms.

The lack of association between the severity of tracheal collapse and GOLD stage of COPD in our study is consistent with the results of a previous study of 71 patients with COPD by Sverzellati et al.[20] These investigators reported a much higher prevalence of excessive expiratory tracheal collapse compared with our study (53% vs 20%); however, they used a lower threshold for diagnosis (>50%) that overlaps considerably with normative data.[18] When a similar threshold is applied to our study population, the prevalence is actually higher at 75%. Similarly, if one were to raise the threshold in their study from >50 to >75% collapse, then their prevalence would be lower than

**Table 5—*Comparison Between Subgroups With and Without Excessive Expiratory Tracheal Collapse (>80% Collapse)***

| % Tracheal Collapse | ≤ 80% (n = 80) | > 80% (n = 20) |
|---|---|---|
| $FEV_1$, % predicted | 64 (22) | 64 (25) |
| DLCO, % predicted | 70 (22) | 66 (22) |
| 6 MWT, m | 404 (127) | 439 (109) |
| SGRQ | | |
| Total score | 38 (21) | 37 (18) |
| Symptom | 44 (24) | 50 (26) |
| Activity | 52 (25) | 55 (19) |
| Impact | 28 (22) | 23 (20) |

Data are presented as mean (SD). See Table 2 legend for expansion of abbreviations.

ours (10% vs 20%). In addition, it should be emphasized that their study lacked spirometric monitoring and relied solely on breathing instructions. Thus, it is uncertain whether their recorded tracheal measurements were consistently obtained at similar points in the respiratory cycle and whether they were obtained at maximal effort. For example, low levels of expiratory effort may result in underestimation of maximal forced expiratory tracheal collapse consistent with the lower prevalence of excessive expiratory tracheal collapse (at comparable diagnostic thresholds) compared with our study.

Although we have previously published data showing a correlation between percentage expiratory tracheal collapse and age among healthy men within the 25- to 75-year-old age range,[21] we found no significant correlation of percentage expiratory tracheal collapse with age among men with COPD in this study population. The reason for this lack of correlation is uncertain, but may reflect the restricted age range of this sample (> 80% of men in this study are > 60 years of age) and/or some undefined characteristic difference between men with COPD and healthy men.

We initially anticipated that we would find additional clinical or physiologic correlates of excessive tracheal collapse in our study. The lack of such correlation fits well within the context of recent data showing a broad spectrum of forced expiratory tracheal collapse among healthy volunteers similar to our study population.[19,22] Although it has been reported that patients with COPD frequently have excessive dynamic airway collapse, the clinical significance of this finding has not been previously elucidated.[1-4] Our data suggests that the incidental identification of excessive expiratory tracheal collapse in a general COPD population may not necessarily be clinically significant in the absence of other comorbidities.

We acknowledge limitations of our study. First, our study population is relatively small, and our results should thus be validated in a larger population. Second, the distribution of severity of GOLD stages in our study population, with relatively few very severe cases, may have influenced our results. However, the complete lack of correlation between percentage expiratory tracheal collapse and functional measures suggests that neither a larger sample, nor inclusion of more patients with very severe disease, would have substantially altered our findings. Furthermore, our results are in keeping with prior published work, which included a higher percentage of patients with GOLD stages III and IV,[20] Third, the study is limited by a lack of direct respiratory pressure measurements. Although esophageal manometry measurements could have provided more direct information regarding the uniformity of expiratory efforts, several noninvasive techniques were used to ensure maximal expiratory effort. These included standardized respiratory instructions, practice maneuvers, direct observation, and spirometric monitoring. Additionally, we have reported high reliability of measurements among a subset of individuals with repeated testing over a 1-year interval.[23] Thus, it seems unlikely that our results were substantially biased by effort dependence of forced expiratory tracheal collapse. Finally, as the degree to which dynamic maximum tracheal transmural pressure would affect intrathoracic tracheal narrowing may be indicated by statically measured maximal expiratory pressure, this parameter should be part of future research endeavors in this area of investigation.

In summary, patients with COPD demonstrate a wide range of expiratory tracheal collapse, and the magnitude of collapse is independent of disease severity as categorized by GOLD stage or individual PFT parameters such as the $FEV_1$. Thus, the incidental detection of excessive expiratory tracheal collapse in a general COPD population may not necessarily be clinically relevant, especially in the absence of other comorbidities.

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*Dr Boiselle:* contributed to study concepts and design; literature search; clinical/laboratory studies; data acquisition, analysis, and interpretation; and manuscript preparation, revision/review, and final version approval.
*Dr Michaud:* contributed to study concepts, data analysis and interpretation, statistical analysis, and manuscript revision/review and final version approval.
*Dr Roberts:* contributed to study concepts, data analysis and interpretation, and manuscript revision/review and final version approval.
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