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Dynamic computed tomography in the diagnosis of tracheomalacia in asthmatic patients

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Abstract

Dynamic computed tomography (CT) offers a non-invasive approach to diagnosing tracheomalacia, especially in asthmatic patients with varying severities of airway obstruction. This study aimed to assess the incidence of tracheomalacia in asthmatic patients using dynamic CT and its relation to asthma severity. A total of 60 asthmatic individuals, diagnosed based on the Global Initiative for Asthma 2021 criteria, participated in this cross-sectional study. Participants were split into three separate groups (mild, moderate, and severe) based on pre-bronchodilator forced expiratory volume levels. All patients underwent dynamic CT to evaluate tracheal collapsibility, and spirometry was performed to assess pulmonary function. Tracheomalacia was detected in 5 participants (8.3%). The groups showed a significant disparity in pre- and post-forced expiratory volume % ($p<0.001$) and the forced expiratory volume/forced vital capacity ratio ($p<0.001$).

Additionally, the bifurcation cross-sectional area % expiration/inspiration was significantly lower in the tracheomalacia group ($p<0.001$), and the aorta cross-sectional area % expiration/inspiration also reported a significant reduction ($p<0.001$). Dynamic CT is a valuable diagnostic tool for identifying tracheomalacia in asthmatic patients. Although tracheomalacia was not directly related to asthma severity, further studies are needed to explore its potential causes, including airway remodeling and gastroesophageal reflux disease.

Key words: asthma, tracheomalacia, dynamic computed tomography, airway obstruction, pulmonary function tests.

Introduction

Bronchial asthma is characterized by chronic airway inflammation, which results in a range of respiratory symptoms such as dyspnea, coughing, wheezing, and tightness in the chest. Sometimes, decreased expiratory airflow occurs as well [1].

Diagnosis relies on identifying these characteristic symptoms and confirming variable expiratory airflow limitation through tests like bronchodilator reversibility testing, bronchial provocation tests, or significant changes in [Forced expiratory volume (FEV1)] between visits [2]. Chronic irritation and cough in asthma and chronic obstructive pulmonary disease (COPD) may weaken the airway walls, damage elastic fibers, and lead to excessive dynamic airway collapse, known as tracheobronchomalacia (TBM). The prevalence of TBM in patients with COPD or asthma has not been extensively studied. The symptoms of these conditions often overlap, making the diagnosis more challenging [3].

Tracheomalacia is a disorder characterized by abnormal softness and collapse of the tracheal walls, which can cause airway blockage, especially during expiration. Tracheomalacia can worsen respiratory symptoms and make managing asthmatic patients' conditions more difficult. The presence of tracheomalacia can exacerbate these consequences, resulting in increased wheezing, coughing, and trouble breathing [4,5].

Other factors like prolonged intubation, chest trauma, surgery, or neoplastic pathologies may also cause tracheomalacia [6]. Evidence suggests that prolonged use of ICS, particularly in higher doses or specific formulations, may lead to tracheomalacia [7,8]. Although bronchoscopy remains the gold standard for diagnosing tracheomalacia, CT imaging offers a non-invasive-invasive diagnostic alternative with high accuracy [9].

This study aims to detect the incidence of tracheomalacia in asthmatic individuals with different severities of airway obstruction utilizing dynamic computed tomography. Our study confirms the value of dynamic computed tomography as a sensitive and non-invasive method for diagnosing tracheomalacia in patients with different asthma severities.

Materials and Methods

Study design

This cross-sectional study was conducted at Badr Hospital, Helwan University, from August 2022 to February 2023. (Approval No.: 72-2022).

Participants

Sixty asthmatic patients were selected based on GINA 2021 guidelines. Inclusion criteria: Patients 18 years old, diagnosed for more than 10 years. Exclusion criteria: Patients with other chronic respiratory diseases.

Outcomes

According to GINA guidelines 2021 (FEV1/FVC ratio < 0.75 indicates airflow limitation In addition to a positive bronchodilator reversibility test; an increase of >12% and > 200 ml in FEV1). Three equal groups were created out of the participants: mild, moderate, and severe, as per FEV1. Each group included 20 candidates.

Data collection

All participants underwent the following assessments:

1. Entire history taking: Age, gender, and previous medication history (Inhalers or type of steroid used).
2. Clinical examination:

   This included assessment of vital signs, general examination, and chest examination.
3. Pulmonary function tests were conducted using a computerized spirometry apparatus, measuring pre- and post-bronchodilator FEV1, FVC, FEV1/FVC ratio, PEF, FEF2575, FET, and others. Dynamic spirometry was performed with a MIR Spirobank II Spirometer before and after administering 5 mg salbutamol sulfate via nebulizer. Airflow limitation was confirmed with an FEV1/FVC ratio below 0.75 and a positive bronchodilator reversibility test indicated by a >12% and >200 ml increase in FEV1 [10].
4. Dynamic CT: All patients underwent non-contrast chest CT using a Toshiba Aquilion 160-MDCT scanner (Japan). The CT scans were captured at peak inspiration and forced expiration, with patients directed to hold their breath after a thorough inhale and exhale before the imaging process, breathing deeply twice and then inhaling as deeply as possible. The tracheal caliber was measured 10 mm above the aortic arch and the main carina [11]. Anteroposterior and transverse diameters were measured above the Bifurcation and aortic arch during inspiration and expiration, referred to as inspiration and expiration bifurcation AP/TR and aorta AP/TR. The difference between the cross-sectional area at end-inspiration and during expiration can be quantified to assess the degree of collapse by dividing the dynamic expiratory cross-sectional area by the end-inspiratory cross-sectional area and multiplying by 100. A 50% or more luminal collapse during expiration or coughing indicated tracheobronchomalacia [12].

Sample size

Based on the previous study of Dal Negro RW, 2013 [13], which reported the prevalence of tracheomalacia in asthmatic patients was 9.4% and the total population of asthma in the last 6 months was 100 patients by open epi program, power 80% CI 95%, the minimal required

sample was calculated to be 60 patients, will be divided into 3 equal groups relying on FEV1 prebronchodilator; Group 1 (20 patients) mild, Group 2 (20 patients) moderate, Group 3 (20 patients) sever.

Statistical methods

SPSS software (version 11) was used to arrange, tabulate, and analyze the data. The means and standard deviations of the quantitative data were used to summarize them, and the student's t-test was used to assess differences between the two means. The frequencies and percentages of the qualitative data were examined. Fisher's exact test was used in case the Chi-square test was deemed unsuitable for assessing significance. A $p > 0.05$ cutoff was used to evaluate statistical significance.

Results

The present study included 60 participants diagnosed with asthma- for more than 10 years with a mean age of 44.23±13.94 years ranging from 21 to 73 years. Over half of the cases were females (68.3%), and the other 31.7% were males. All asthmatic cases were divided equally in severity into mild, moderate, and severe cases (33.3%) for each. About (50 %) of cases were on formoterol fumarate and budesonide inhaler, (25%) were on salmeterol-fluticasone propionate inhaler,(20%) were on beclomethasone-salbutamol inhaler and (5%) were on salbutamol inhaler. Regarding the type of steroid used, half of cases use budesonide, about (25%) of cases use fluticasone, and (20%) use beclomethasone.

Regarding pre- and post-FVC, there was statistically insignificant variation between the groups. However, there was a statistically significant distinction between the pre- and post-FEV1% levels; the group with mild asthma had the highest mean values, followed by moderate and severe asthma. Additionally, pre- and post-FEV1/FVC ratios showed a significant increase in the mild group, with no significant difference between the moderate and severe groups post-test. Statistically significant increases in FVC, FEV1%, and FEV1/FVC were found post-bronchodilator in all groups.

Certain inspiratory and expiratory diameters did not show notable differences ($p>0.05$), except for expiration bifurcation and aorta AP, where the mild group had higher values (Table 1).

Although the aorta cross-sectional area expiration/inspiration decreased with increased severity, nothing about the two groups differed statistically significantly. groups. However, a statistically significant variation was found in the Bifurcation cross-sectional area expiration/inspiration, with the severe asthma group showing the lowest mean values, followed by the moderate and mild groups. Additionally, there was a notable rise in

Bifurcation cross-sectional area expiration/inspiration when comparing the moderate group to the mild and severe groups (Table 2).

Tracheomalacia was present in 5 participants, 8.3%, while absent in (91.7%) of participants. When tracheomalacia's severity and presence were compared, there was statistically insignificant variation (Table 3).

A non-statistically significant variation was observed when comparing fundamental characteristics between the two groups. Also, insignificant variation was found when comparing both groups regarding pulmonary functions pre-bronchodilator test. Finally, after the bronchodilator test, there was a non-statistically significant variation in the pulmonary functions of the two groups (Table 3).

There was a substantial difference between the groups regarding expiration bifurcation AP and expiration aorta AP; individuals with tracheomalacia had much lower values on all measurements. Additionally, Bifurcation and aorta cross-sectional area expiration/inspiration showed a substantial difference between patients with tracheomalacia and healthy individuals, with the former having lower mean values (Table 3).

Regarding age and pre-and post-FVC, non-significant variation between the groups was found. However, FEV1% and FEV1/FVC showed a significant change before and after, with the severe asthma group having the lowest mean values, followed by the tracheomalacia group, moderate group, and mild group. Pre-FEV1% stated a significant variation among the tracheomalacia group and the mild, moderate, and severe groups, while post-FEV1% showed no significant difference between the tracheomalacia and moderate groups. Non- noticeable variation was found in the pre-bronchodilator FEV1/FVC, but the post-bronchodilator FEV1/FVC in the tracheomalacia group showed a significant difference compared to the mild group (Table 4).

The study groups differed statistically significantly regarding expiration bifurcation AP and expiration aorta AP, with all measures being significantly lower in the tracheomalacia group. The tracheomalacia group showed a significant decrease compared to the mild and moderate groups. Additionally, a significant variation was detected in bifurcation and aorta cross-sectional area expiration/inspiration, with the tracheomalacia group showing lower mean values than the other groups (Table 5).

Discussion

Dynamic CT proves to be a valuable diagnostic tool for identifying tracheomalacia in asthmatic patients. Our study showed a subtle relationship between asthma severity, pulmonary function, and dynamic CT measures.

Gilkeson et al. investigated the effectiveness of dynamic inspiratory-expiratory imaging using multidetector CT for diagnosing tracheobronchomalacia. Their results suggest this approach is a promising tool for evaluating dynamic airway collapse. It was verified that the dynamic collapse measured by multidetector CT corresponded well with findings from bronchoscopy [14].

Focusing on patients with airway malacia confirmed by bronchoscopy and who had undergone CT imaging. The study confirmed the value of dynamic expiratory CT as a highly sensitive and non-invasive diagnostic method for airway malacia. [15].

In accordance with our study, Baroni et al. calculated the percentage of luminal collapse by dividing the dynamic expiratory cross-sectional area by the end-inspiratory cross-sectional area and multiplying by 100 [12].

Also, kudela performs CT scans on patients with suspected airway collapse at full inspiration and forced expiration. The diagnosis of tracheomalacia was established if tracheal collapse 50% [11].

In the same way, Lee defined malacia as a 50% reduction in airway lumen during expiration for both CT and bronchoscopy [15].

In asthma and COPD, coughing and chronic irritation may lead to weakened airway walls, damaged elastic fibers, and excessive dynamic airway collapse, termed tracheobronchomalacia (TBM). The overlap in symptoms between these conditions makes diagnosis particularly difficult [3].

Our results show no relation between the presence of tracheomalacia and asthma severity.

El Sorougi et al. study was performed to diagnose tracheomalacia in COPD patients using dynamic CT. There was a relation between the severity and the presence of tracheomalacia. In our study, although there is no relation between the severity of asthma and the presence of tracheomalacia, it presents in 2 severe asthma cases, possibly due to airway remodeling or GERD [9].

Tracheomalacia, while present in a minority of cases (8.3%) in our study, warrants attention for its potential impact on airway dynamics. This shows the need for comprehensive diagnostic approaches in asthmatic patients with prolonged disease duration.

In agreement with our results, Aquino et al. investigated whether the cross-sectional area, as well as coronal and sagittal diameters of the trachea, show significant differences between inspiration and end-expiration on CT scans in patients with acquired tracheomalacia compared to those without. The study involved obtaining and analyzing CT scans and concluded that significant differences can be observed among cases with acquired tracheomalacia and those without [16].

In our study, we used a non-invasive method to diagnose tracheomalacia with high accuracy. The study showed a subtle relationship between asthma severity, pulmonary function, and dynamic CT measures and also showed the incidence of tracheomalacia in different severities of asthma.

The study's cross-sectional strategy limits its capacity to assess the long-term evolution of tracheomalacia in asthmatic patients, and the small sample size may restrict the generalizability of the findings. We need further studies on patients with tracheomalacia to determine whether it is caused by GERD or airway remodeling. Exploring the potential impact of different asthma treatment regimens, especially on patients who are on long-term high-dose steroids, on the development of tracheomalacia and its severity is needed and could inform personalized therapeutic strategies.

Conclusions

Dynamic CT is a valuable diagnostic tool for identifying tracheomalacia in asthmatic patients. While tracheomalacia was not directly related to asthma severity, further studies are needed to explore its potential causes, including airway remodeling and gastroesophageal reflux disease.

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Table 1. Computed tomography measurements of airway dynamics within the studied group (n=60).

Characteristic	Mild group (N=20)	Moderate group (N=20)	Severe group (N=20)	Test f	p	Post hoc
inspiration bifurcation AP Mean ±SD Range	16.54±2.94	15.72±3.99	14.84±3.16	1.255	**0.293**	P1=0.448 P2=0.119 P3=0.416
inspiration bifurcation TR Mean ±SD Range	14.05±2.3	14.66±2.07	13.68±3.01	0.789	**0.459**	P1=0.442 P2=0.640 P3=0.219
inspiration aorta AP Mean ±SD Range	16.6±3.2	15.75±4.39	14.33±3.87	1.783	**0.177**	P1=0.488 P2=0.067 P3=0.247
inspiration aorta TR Mean ±SD Range	15.13±2.17	15.89±2.87	14.5±3.58	1.127	**0.331**	P1=0.419 P2=0.496 P3=0.139
expiration bifurcation AP Mean ±SD Range	14.8±3.28	13.85±3.79	11.82±2.69	4.308	**0.018***	P1=0.364 P2=0.006* P3=0.055
expiration bifurcation TR Mean ±SD Range	12.99±2.12	13.23±2.45	11.8±2.46	2.108	0.131	P1=0.748 P2=0.116 P3=0.060
Expiration aorta AP Mean ±SD Range	14.44±3.49	13.38±3.84	11.53±2.87	3.708	**0.031***	P1=0.331 P2=0.009* P3=0.093
expiration aorta TR Mean ±SD Range	14.01±1.94	14.61±2.9	12.82±3.19	2.227	0.117	P1=0.486 P2=0.175 P3=0.043*

(f), ANOVA test; P1, mild cases *vs.* moderate cases; P2, mild cases *vs.* severe cases; P3, moderate cases *vs.* severe cases.

Table 2. The percentage of luminal collapse within the studied group (n=60).

Site of measurements	Mild group (N=20)	Moderate group (N=20)	Severe group (N=20)	Test *f*	p	Post hoc
bifurcation cross sectional area % expiration/inspiration Mean ±SD range	82.6±11.92	79.56±11.91	70.35±14.04	5.077	**0.009***	P1=0.450 P2=0.003* P3=0.035*
Aorta cross sectional area % expiration / inspiration Mean ±SD Range	80.95±13.64	79.03±15.36	72.44±12.3	2.084	0.134	P1=0.661 P2=0.057 P3=0.138

(f), ANOVA test; P1, mild cases *vs.* moderate cases; P2, mild cases *vs.* severe cases; P3, moderate cases *vs.* severe cases.

Table 3. Comparing Tracheomalacia and severity of studied cases, comparing basic characteristic, pulmonary functions, measurements of airway dynamics in different breathing conditions and cross sectional area % at 2 levels, above Bifurcation and above aortic arch among cases with tracheomalacia and cases without tracheomalacia (n=60).

Characteristic			**Mild group (N=20)**	**Moderate Group (N=20)**	**Severe group (N=20)**	**Test (x^2)**	**P value**
Tracheomalacia	present (N=5)	**No.**	1	2	2	0.436	0.804
		%	5.0%	10.0%	10.0%		
	Absent (N=55)	**No.**	19	18	18		
		%	95.0%	90.0%	90.0%		

Characteristic		**Tracheomalacia group (n=5)**		**Normal group (no tracheomalacia) (n=55)**		**Test (t)**	**P value**
Age (years) Mean ±SD Median (IQR)		43.4±23.71		44.31±13.07		-0.138	0.890
Category		**No.**	**%**	**No.**	**%**	**χ^2**	**P value**
Gender	female	4	9.8	37	90.2	0.343	0.558
	Male	1	5.3	18	94.7		
FVC (forced vital capacity) Mean ±SD		2.09±1.5		2.08±0.91		0.031	0.975
FEV1 (forced expiratory volume in first second) Mean ±SD		36±16.36		41.16±16.78		-0.660	0.512
FEV1/FVC Mean ±SD		67.28±6.37		66.54±8.86		0.181	0.857
FVC Mean ±SD		2.26±1.42		2.34±0.96		-0.175	0.862
FEV1 Mean ±SD		49.8±15.96		55.07±16.96		-0.668	0.507
FEV1/FVC Mean ±SD		76.6±0.89		79.98±4.21		-1.778	0.081
Site of measurements							
inspiration bifurcation AP Mean ±SD		15.12±3.29		15.75±3.44		-0.395	0.695
inspiration bifurcation TR Mean ±SD		15.16±1.74		14.04±2.53		0.968	0.337
Inspiration aorta AP Mean ±SD		14.8±5.46		15.63±3.79		-0.451	0.654
inspiration aorta TR Mean ±SD		15.9±3.99		15.1±2.86		0.577	0.566
expiration bifurcation AP Mean ±SD		10.48±3.96		13.76±3.32		-2.084	**0.042***
expiration bifurcation TR Mean ±SD		12.6±2.22		12.68±2.43		-0.638	0.946
expiration aorta AP Mean ±SD		9.04±2.5		13.49±3.44		-2.816	**0.007***
expiration aorta TR Mean ±SD		12.78±3.86		13.91±2.7		-0.863	0.392
Site of measurements							
bifurcation cross-sectional area% in expiration/inspiration Mean ±SD		56.92±15.17		79.38±11.81		-3.981	**<0.001***
Aorta cross sectional area % in expiration / inspiration Mean ±SD		49.81±6.94		79.99±11.64		-5.676	**0.001***

x^2, chi-square tests; t, independent samples test.

Table 4. Comparing pulmonary functions pre and post bronchodilator within tracheomalacia cases and cases with mild, moderate, and severe asthma without tracheomalacia.

Characteristic	Tracheomalacia group (N=5)	Mild group (N=19)	Moderate group (N=18)	Severe group (N=18)	Test *f*	p	Post hoc
Pre bronchodilator test							
FVC Mean ±SD Range	2.09±1.5	2.08±1.18	1.99±0.72	2.16±0.8	0.095	0.963	P1=0.783 P2=0.793 P3=0.980 P4=0.597 P5=0.838 P6=0.885
FEV1% Mean ±SD Range	36±16.36	60.89±3.59	40.17±4.58	21.33±2.74	152.731	**<0.001***	P1<0.001* P2<0.001* P3<0.001* P4=0.150 P5<0.001* P6<0.001*
FEV1/FVC Mean ±SD Range	67.28±6.37	71.23±5.16	67.7±6.05	60.44±10.91	6.319	**0.001***	P1=0.167 P2<0.001* P3=0.310 P4=0.006* P5=0.914 P6=0.083
Post bronchodilator test							
FVC Mean ±SD Range	2.26±1.42	2.35±1.12	2.19±0.85	2.49±0.93	0.265	0.850	P1=0.633 P2=0.687 P3=0.860 P4=0.386 P5=0.892 P6=0.662
FEV1% Mean ±SD Range	49.8±15.96	75.05±3.52	54±4.41	35.06±3.1	160.823	**<0.001***	P1<0.001* P2<0.001* P3<0.001* P4<0.001* P5=0.141 P6<0.001*
FEV1/FVC Mean ±SD Range	76.6±0.89	82.79±4.13	79.39±3.5	77.61±3.31	8.201	**<0.001***	P1=0.005* P2<0.001* P3=0.001* P4=0.138 P5=0.126 P6=0.575

(f), ANOVA test; P1, mild cases *vs.* moderate cases; P2, mild cases *vs.* severe cases; P3, mild cases *vs.* tracheomalacia group; P4, moderate cases *vs.* severe cases; P5, moderate cases *vs.* tracheomalacia group; P6, tracheomalacia group *vs.* severe cases.

Table 5. Measurements of airway dynamics in different breathing conditions and site of measurements in tracheomalacia cases and cases with mild, moderate and severe asthma without tracheomalacia (n=60).

Site of measurements	Tracheomalacia group (N=5)	Mild group (N=19)	Moderate group (N=18)	Severe group (N=18)	Test *f*	p	Post hoc
inspiration bifurcation AP Mean ±SD	15.12±3.29	16.55±3.02	15.83±3.91	14.83±3.34	0.834	0.481	P1=0.522 P2=0.132 P3=0.409 P4=0.387 P5=0.684 P6=0.869
inspiration bifurcation TR Mean ±SD	15.16±1.74	14.08±2.36	14.41±2.01	13.62±3.17	0.611	0.611	P1=0.689 P2=0.577 P3=0.395 P4=0.346 P5=0.557 P6=0.229
inspiration aorta AP Mean ±SD	14.8±5.46	16.62±3.29	15.63±4.02	14.58±3.97	0.901	0.447	P1=0.446 P2=0.120 P3=0.360 P4=0.426 P5=0.677 P6=0.913
inspiration aorta TR Mean ±SD	15.9±3.99	15.14±2.23	15.58±2.48	14.59±3.75	0.441	0.725	P1=0.658 P2=0.575 P3=0.615 P4=0.324 P5=0.831 P6=0.388
expiration bifurcation AP Mean ±SD	10.48±3.96	14.93±3.32	14.12±3.53	12.18±2.58	3.905	**0.013***	P1=0.450 P2=0.012* P3=0.008* P4=0.078 P5=0.030* P6=0.304
expiration bifurcation TR Mean ±SD	12.6±2.22	13.06±2.15	13.1±2.46	11.85±2.59	1.069	0.370	P1=0.957 P2=0.130 P3=0.704 P4=0.122 P5=0.681 P6=0.537
expiration aorta AP Mean ±SD	9.04±2.5	14.63±3.48	13.87±3.57	11.9±2.78	5.164	**0.003***	P1=0.483 P2=0.013* P3=0.001* P4=0.074 P5=0.005* P6=0.087
expiration aorta TR Mean ±SD	12.78±3.86	14.17±1.85	14.52±2.75	13.02±3.25	1.219	0.311	P1=0.704 P2=0.211 P3=0.323 P4=0.110 P5=0.220 P6=0.866
Site of measurements							
bifurcation cross sectional area% in expiration/ inspiration Mean ±SD	56.92±15.17	83.51±11.52	81.33±10.01	73.06±11.72	8.696	**<0.001***	P1=0.565 P2=0.008* P3<0.001* P4=0.035* P5<0.001* P6=0.007*
Aorta cross-sectional area% in expiration / inspiration Mean ±SD	49.81±6.94	82.64±11.68	82.86±10.4	74.32±11.29	14.117	**<0.001***	P1=0.952 P2=0.024* P3<0.001* P4=0.022* P5<0.001* P6<0.001*

(f), ANOVA test; P1, mild cases *vs.* moderate cases; P2, mild cases *vs.* severe cases; P3, mild cases *vs.* tracheomalacia group; P4, moderate cases *vs.* severe cases; P5, moderate cases *vs.* tracheomalacia group; P6, tracheomalacia group *vs.* severe cases.