Letter to the Editor

What is the optimal large airway size reduction value to determine malacia: exploratory bronchoscopic analysis in patients in Mounier-Kuhn syndrome

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Excessive airway collapse (EAC) has been increasingly identified as a respiratory condition associated with several symptoms and morbidities. However, we observe a huge variability in the way of diagnosing this entity, often using different techniques. We propose a diagnostic method using bronchoscopy (1).

EAC is characterized by trachea and/or bronchi huge collapse, and occurs mainly during expiration (2,3). During expiration occurs an increase in intrathoracic pressure and supporting structures (musculature and cartilage) of central airways, leading to essential balance, which maintains the patency of tracheal and bronchial lumen (4).

Whenever there is pathological involvement of these structures a collapse can be observed (3).

EAC comprises two entities: excessive dynamic airway collapse (EDAC) and tracheomalacia (TM). In EDAC there is an excessive narrowing of the posterior trachea and/or bronchi promoted by membranaceous posterior wall due to weakness of its musculature. TM is characterized by a pathological movement of the entire tracheal structure, involving both muscles and cartilaginous rings. When it extends to the bronchi, it is referred as tracheobronchomalacia (TBM) (5,6).

TM or TBM may affect the airway either diffusely or segmentally (2,3,5). It is classified according to appearance of the trachea in crescent (anteroposterior narrowing), lateral (lateral narrowing) and circumferential (both anteroposterior and lateral narrowing) (2,3,6). Congenital forms manifest predominantly in childhood, and can be related to other respiratory tract conditions, such as Mucopolychondritis or Mounier-Kuhn syndrome (SMK). Acquired forms are related to traumatic or inflammatory injuries and idiopathic when the cause is unknown (3,5,6).

The recognition of these entities is important since it may be responsible for the existing respiratory symptoms, its worsening or the onset of new symptoms. It may be often confounding with other diseases, such as chronic bronchitis, bronchiectasis, asthma, and chronic obstructive pulmonary disease. The predominant signs and symptoms are cough, abundant tracheobronchial secretion, dyspnea and wheezing (7).

Diagnostic tests include bronchoscopy and computerized tomography scan of the chest (CT). Bronchoscopy is capable of assessing both the anatomical and the dynamic changes of the airway (2,3,6). Classically, the diagnosis is established when there is a 50% decrease in the tracheobronchial cross sectional area (8), although the use of this parameter remains controversial. The definition of the pathological collapse ranges from 35% to 80% of the airway area as shown in studies focused on the definition of pathological collapse (*Table 1*).

Most studies use chest CT scan for measuring the cross-sectional area of the trachea and/or bronchi at maximal inspiration and forced expiration. Some use spirometric monitoring and measured the forced vital capacity (FVC) to ensure maximum expiration. These studies show variations in the normal the values. However, there were different methods and techniques used for measuring, in addition of sample size discrepancies as well as different regions were analyzed.

It is therefore important to define what is really crucial to define excessive collapse. Considering that not all that

Table 1 Definition of the pathological collapse

Author (year)	Study	Evaluation Method	Evaluation site	Participants	N	Results, expiratory reduction (%)
Rayl 1965 (9)	Does not inform	Bronchography (in cough)	Trachea and bronchi	Chronic Lung Diseases	100	> 50% in all cases
Jokinen *et al.* 1977 (10)	Does not inform	Bronchoscopy	Trachea and bronchi	TBM	93	>50% in 44 cases; 50–75% in 38 cases; >75% in 12 cases
Stern *et al.* 1993 (11)	Prospective	Chest CT (insp and forced exp)	Trachea	Healthy Volunteers	10	Average 35% (11% to 61%)
Hein *et al.* 2000 (12)	Prospective	Dynamic chest CT (insp and forced exp and cough)	Trachea	Suspected TBM	8	Average 36% (11% to 49%). Cough: average 71% (60% to 80%)
Gilkeson *et al.* 2001 (13)	Does not inform	Dynamic chest CT (insp and forced exp)	Trachea and bronchi	Suspected TBM	13	>50% in all cases
Aquino *et al.* 2001 (14)	Retrospective	Chest CT (insp and forced exp)	Trachea	TBM	10	>18% in the upper trachea 28% in the middle trachea: TM 89–100% probability
Zhang *et al.* 2003 (15)	Retrospective	Dynamic helical chest CT (insp and forced exp)	Trachea and bronchi	TBM and control	20	>50% in all cases with TBM <50% on all controls
Boiselle *et al.* 2009 (16)	Prospective	Dynamic chest CT (insp and forced exp and spirometric monitoring	Trachea	Healthy Volunteers	51	Mean 54.34%±18.6%; upper trachea mean 56.14%±19.3%; lower trachea >50% reduction in 78% participants; Limit + high (>80%) reduces false positive rate
Litmanovich *et al.* 2010 (17)	Retrospective	Dynamic chest CT (insp and forced exp and spirometric monitoring	Main and intermediate bronchi	Healthy Volunteers	51	RMB average: 66.9%±19%; LMB Average: 61.4%±16.7%; >50% reduction in 73% participants
Boiselle *et al.* 2012 (18)	Prospective	Dynamic chest CT (insp and forced exp and spirometric monitoring	Trachea	COPD	100	Average 59%; 80% in 20% participants
O'Donnell *et al.* 2012 (19)	Prospective	Chest CT (insp and forced exp and spirometric monitoring	Trachea	COPD	67	≥80% in 22.4% participants
Ciet *et al.* 2016 (20)	Prospective	Chest CT (insp and forced exp and spirometric monitoring	Main and intermediate bronchi	Healthy Volunteers	50	Mean 55% (±19%) trachea; 60% (±20%) in RMB; 62% (±19%) in LMB

CT, computed tomography; Insp, Inspiration; Exp, Expiration; TBM, Tracheobronchomalacia; COPD, chronic obstructive pulmonary disease; TM, tracheomalacia; RMB, right main bronchus; LMB, left main bronchus.

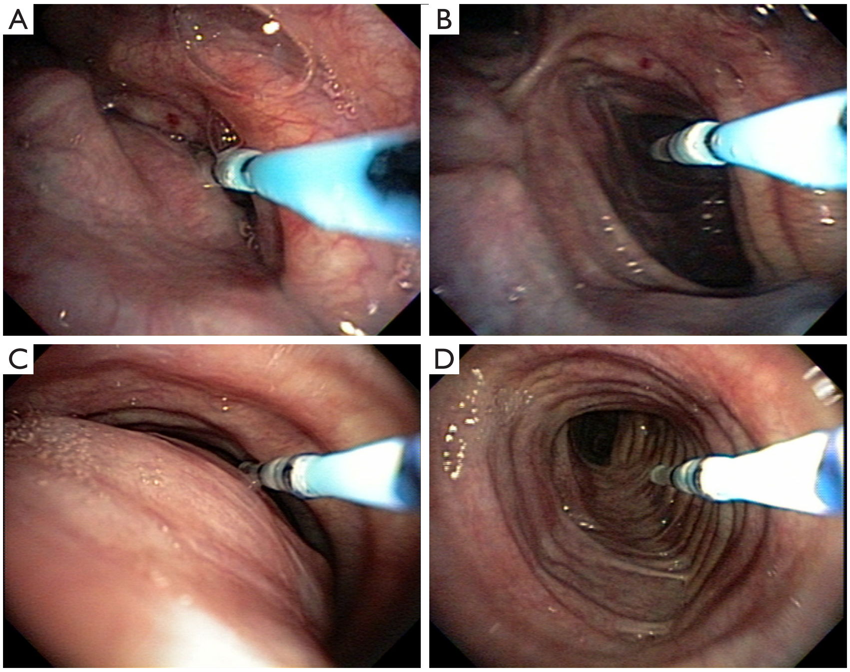

Figure 1 Bronchoscopic view of the trachea, right bronchus and the catheter (blue). (A) Right bronchus during expiration in pressure 0 cmH_2O; (B) rigth bronchus during inspiration in pressure 0 cmH_2O; (C) trachea during expiration in pressure 0 cmH_2O; (D) trachea during inspiration in pressure 0 cmH_2O.

patients with EAC have symptoms (3), and the fact that healthy individuals may have collapse of up to 80% on forced expiration (16), the values for the FVC used in chest CT as a diagnostic for pathological collapse remain unanswered.

Another issue is whether the values found during chest CT studies can actually be extrapolated to bronchoscopic analysis, once respiratory cycles are dynamically evaluated. When symptoms are aggravated or triggered by TBM, it has been shown that they may also occur with spontaneous breathing (2,3,5,6). Thus, defining the percentage value of the diagnosis of pathological collapse using findings on forced expiratory chest CT with spirometry monitoring may result in over diagnosis of TBM.

Despite being the gold standard, bronchoscopy (2,3,6) has been underutilized for the analysis of collapse and one of the limiting factors is the lack standardization of the bronchoscopic procedure. Ideally, sedation should be light in a way that the patient can interact with the examiner, but sufficient to avoid discomfort.

Airway size reduction is achieved during spontaneous and forced inspiration and expiration without spirometric monitoring (2,3). Such technical difficulty during the objective analysis yields to results that are dependent on the examiner's judgement (2,6). For an accurate quantitative measurement of the area to be analysed, the examiner is expected to know the distance between the endoscopic lens and the area of interest, keeping the tip of the bronchoscope in the same position, since any change in this distance may result in an increase (nearness) or decrease (distance) from the assessed area (21). In this context, we believe that the best assessment the diagnosis of TBM is via bronchoscopy using a standardized technique with a method that allows objective analysis of the collapse.

In order to find the best way to objectively analyse the variation between inspiration and expiration using bronchoscopy, we designed an assessment protocol to evaluate patients with MKS and TBM (1).

After sedation, we tested the response to continuous positive airway pressure (CPAP) using non-invasive mechanical ventilation (NIMV). A custom catheter was used containing distance markings in centimeters (we used a Fogarty catheter nº 3 and made markings in centimeters) that is inserted into the working channel of the bronchoscope. It is kept at a known distance between its distal end and the bronchoscope, minimizing the variation in the distance from the device to the collapse region (*Figure 1*). NIMV/CPAP titration was performed from 0 to 18 cmH_2O (started in 0 cmH_2O and gradually increases in steps by 2 cmH_2O every 10 complete cycles) (1).

The procedure was recorded digitally and the images analysed by a software (Image Processing Toolbox, Matlab®, Natick, MA) capable of evaluating and measuring airway pixel variation by means of comparing the collapse area at 0 cmH_2O with the different titrated pressures (1). The pixels measured at each titration record are proportional to the airway area when corrected for the known distance. From this analysis it was possible to define the best pressure capable to reduce the collapse.

Despite its experimental character, this methodology can be extrapolated to diagnose TBM, allowing a dynamic analysis of the airway that excludes the bias of using FVC in the diagnosis. Therefore, it allows a more realistic analysis of the dynamic variations in airway diameter, thus avoiding an overdiagnosis of pathological collapse, often made in asymptomatic patients.

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Footnote

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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