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Assessment of Central Airways Mechanics Using Dynamic Magnetic Resonance Imaging (Cine-MRI): A Comparison to Flexible Bronchoscopy

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ABSTRACT

Background: Flexible bronchoscopy (FOB) is the current gold standard for diagnosing tracheobronchomalacia (TBM). While dynamic magnetic resonance imaging (cine-MRI) has emerged as a radiation-free alternative for TBM diagnosis, a direct comparison of its diagnostic performance with FOB has not yet been performed.

Objective: This study aimed to evaluate the diagnostic performance of cine-MRI versus FOB in detecting TBM and to assess the effect of bronchodilators on observed tracheobronchial collapse.

Methods: The study included 10 children (median age 11 years, range 8–17 years; five males) who were referred for suspected TBM. Cine-MRI was performed using a 3 Tesla GE 750 W scanner with specific sequences for static and dynamic imaging. Bronchodilator testing was conducted using 400 μg salbutamol. Children suspected of TBM underwent both FOB and cine-MRI. Cine-MRI protocol included spirometry-controlled static and dynamic sequences, pre- and post-bronchodilator administration. FOB diagnoses were made by pediatric pulmonologists, and cine-MRI assessments were independently evaluated by two trained observers, blinded to FOB results. Moreover, each child completed spirometry and a respiratory questionnaire. Descriptive statistics were used to summarize data. Diagnostic agreement and measurements repeatability were assessed using the intra-class correlation coefficient (ICC).

Results: FOB identified TBM in two children, whereas cine-MRI detected TBM in four. In three of these four children TBM was not diagnosed by FOB. Notably, no TBM was observed during static pre-bronchodilator cine-MRI assessment, but two of the four children diagnosed with cine-MRI met the diagnostic criteria of TBM only post-bronchodilation.

Conclusion: Cine-MRI, particularly post-bronchodilation shows a unique capability to detect TBM cases undetected by FOB. This may reflect its ability to perform dynamic functional measurements during active respiratory maneuvers, highlighting its potential as a valuable diagnostic tool for central airway disease in children.

Abbreviations: **2D**, Two dimensional; **3D**, Three dimensional; **4D**, Four dimensional; **BDR**, bronchodilator reversibility; **Cine-CT**, Cine-computed tomography; **Cine-MRI**, Cine-magnetic resonance imaging; **CSA**, cross sectional area; **FDA**, Food and Drug Administration; **FEV1**, forced expiratory volume in 1 s; **FOB**, flexible bronchoscopy; **FRC**, functional residual capacity; **ICC**, Intra-class correlation coefficient; ***LMA***, laryngeal mask airway; ***MPR***, multi planar reformat; ***NPV***, negative predictive value; ***PEF***, peak expiratory flow; ***PFT***, pulmonary function test; ***PPV***, positive predictive value; ***RV***, residual volume; ***SGRQ***, Saint George respiratory questionnaire; ***SPGR***, spoiled gradient echo sequence; ***TBM***, tracheobronchomalacia; ***TLC***, total lung capacity; ***TRICKS***, time-resolved imaging of contrast kinetics.

1 | Background

Assessing central airways mechanics is important for diagnosing and managing tracheobronchomalacia (TBM), a condition that is typically diagnosed by flexible bronchoscopy (FOB) [1]. TBM is not uncommon, with an estimated incidence of at least one in 2100 children (2). While most cases are congenital, TBM can be also acquired, often resulting from surgery or prolonged intubation (3) FOB is currently considered the gold standard for diagnosing TBM and assessing its severity, due to its ability to directly visualize the airway lumen during spontaneous respiration (3). However, FOB is an invasive technique and requires general anesthesia in children (2). Moreover, it does not allow for direct, objective measurements of tracheal collapse. Instead TBM severity and etiology are subjectively assessed during FOB by visually identifying abnormal airway shape and a reduction in the airway lumen exceeding 50% of the cross-sectional area during expiration [2]. This assessment using FOB has limitations, because it can be influenced by anesthetic agents, partial obstruction of the trachea by the bronchoscope, intrathoracic and airway pressures, gas-flow dynamics, optical distortion from the convex fisheye-lens, and lung volume [1]. Furthermore, FOB cannot easily replicate the dynamic changes in airway and intrathoracic pressures that occur physiologically during breathing maneuvers [1]. For these reasons, dynamic chest computed tomography (cine-CT) can be used as an alternative to assess TBM [3]. Cine-CT is quicker and less invasive than FOB and enables evaluation of tracheal collapse under static and dynamic conditions. Cine-CT can also assess mediastinal, vascular, and lung abnormalities when contrast is used, so identifying possible causes of reduced airway lumen [4]. Nevertheless, its use in children is limited due to concerns about radiation exposure [5]. Cine CT generally requires a higher radiation dose than static inspiratory CT due to the acquisition of multiple images over time, though advanced techniques like dose modulation and ECG gating can help reduce the overall exposure. Various protocols are designed to optimize the use of chest CT to reduce radiation exposure in pediatric patients. Dose reduction techniques include the use of tin filters, iterative reconstruction algorithms and adjusting mA and kV settings according to age and body weight using automatic exposure devices (AEC) [6, 7].

Dynamic chest Magnetic Resonance Imaging (cine-MRI) can provide similar diagnostic information as cine-CT without radiation [8, 9]. Cine-MRI has been used to assess TBM both in children and adults [10], but its diagnostic performance has never been compared directly to FOB. This study aimed to evaluate the diagnostic ability of cine-MRI in both static and dynamic breathing sequences, pre and post- bronchodilator (salbutamol) administration, compared to FOB. As noted in a recent ERS statement [3], bronchodilators could potentially exacerbate airway obstruction by lowering the tone of airway smooth muscle. A secondary objective was to assess the correlation between TBM severity score determined by cine-MRI and FOB with pulmonary function tests (PFT) and respiratory questionnaire results.

2 | Materials and Methods

2.1 | Population

We prospectively enrolled children aged 8–18 years, referred to the Department of Pediatric Respiratory Medicine for suspected TBM between 2017 and 2020 (Figure 1). Inclusion criteria included a clinical indication for FOB due to suspected TBM, as determined by a pediatric pulmonologist at our tertiary care hospital after referral by a general pediatrician, and the ability to perform spirometer-controlled cine-MRI.

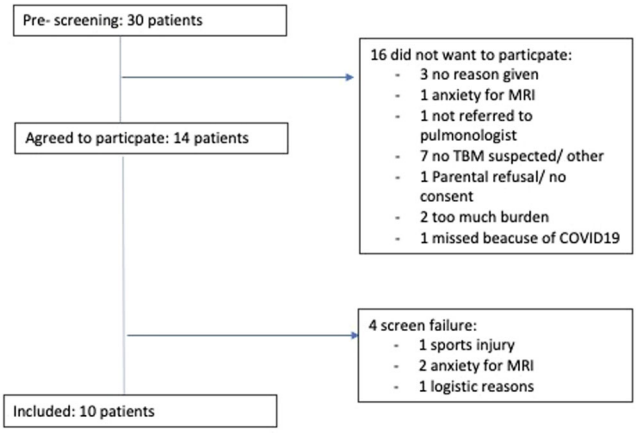

FIGURE 1 | Flowchart of patients' inclusion and exclusion. [Color figure can be viewed at wileyonlinelibrary.com]

Exclusion criteria were MRI contraindications, a time gap exceeding 3 months between cine-MRI and FOB, or a severe respiratory tract infection at the time of cine-MRI or FOB. Informed consent was obtained from parents/guardians and children aged 12 years or older. The study protocol was reviewed and approved by the local medical ethical committee of Erasmus Medical Center, Rotterdam (MEC NL57040.078.16).

2.2 | Clinical Flexible Bronchoscopy and Image Analysis

FOB was conducted as part of the diagnostic workup by experienced pediatric pulmonologists, who were blinded to cine-MRI findings. FOB was performed under general anesthesia with preserved spontaneous breathing using a laryngeal mask. Bronchoscopic procedures were performed under sedation using intravenous fentanyl at a dose of 2 μg/kg, combined with a continuous propofol infusion at 10 mg/kg/hour. Topical lidocaine was applied to the vocal cords and carina to provide local anesthesia. All procedures were conducted during spontaneous breathing, without the application of positive end-expiratory pressure (PEEP), particularly during the assessment of airway malacia. Bronchoscopies were performed exclusively by experienced bronchoscopists. In cases where the procedure was conducted by a pediatric pulmonary fellow, a senior pediatric pulmonologist was always present to supervise. Three 30-s videos were recorded at predefined distances (10, 30, 50 mm) proximal to the starting point. The starting point was defined at the level of the carina for subjects without clearly identifiable collapse, while for subjects with a collapse greater than 50%, it was established as the most proximal end of the malacic segment. This cut-off value was chosen in accordance with standard FOB practice for defining TBM [11]. The same procedure was repeated in the mainstem bronchi if a collapse greater than 50% was detected. The pulmonologist performing bronchoscopy, defined the presence of TBM (yes/no) and assigned a

subjective severity score based on lumen collapse as follows: no TBM (collapse 0%–49%), mild TBM (collapse between 50% and 69%), moderate TBM (collapse between 70% and 89%), and severe TBM (collapse greater than 90%).

Two researchers, a pediatric pulmonologist (D.C.) and a trained researcher (G.R.), who were blinded to the FOB results, extracted maximal inspiratory and expiratory frames from the recorded videos using Image J software (U. S. National Institutes of Health, Bethesda, Maryland, USA) [12]. To measure the airway surface area in the FOB images, the most distal tracheal ring that was still clearly distinguishable from the more distal black background was selected as a reference point (Supporting Information S1: Figure 2). Maximal inspiratory and expiratory frame were extracted, and airway cross-sectional areas were measured to calculate tracheal or bronchial collapse percentages [12].

2.3 | Cine-MRI Protocol and Image Analysis

All cine-MRI examinations were conducted in awake patients using a 3 Tesla GE 750W scanner (GE Healthcare, Milwaukee, WI, USA) according to the cine-MRI protocol. Sequences and scan parameters have been previously reported [10]. Static and dynamic three-dimensional (3D) airways images were acquired [13]. at total lung capacity (TLC) and residual volume (RV), with mouth pressures of 25 and 0 cm H_2O, respectively. Dynamic acquisitions involved full forced expiration from 95% of TLC to RV, with a temporal resolution of 300–500 ms, covering the trachea and main bronchi. The cine-MRI protocol was repeated after the administration of 400 micrograms of salbutamol via a metered-dose inhaler and a spacer to investigate its effect on tracheal patency. We hypothesized a worsening of the tracheal collapse after bronchodilator due to smooth muscle relaxation. Researchers, blinded to FOB results, analyzed MRI data.

Dynamic acquisitions were first evaluated in cine mode to identify the point of maximal tracheal narrowing in the sagittal plane. Then the volume showing the most severe tracheal collapse was reformatted as an axial double oblique image for lumen measurements [14]. A positive finding for TBM was defined as a $\geq 50\%$ reduction in tracheal lumen area between inspiratory and cine-MRI acquisition. Central airway dimensions were measured before and after bronchodilator inhalation using the same procedure (Figure 2) (Supporting Information S1: Figure 4).

2.4 | Pulmonary Function Tests and Respiratory Questionnaires

Spirometry was conducted according to ERS/ATS criteria [15]. Primary outcomes included forced expiratory volume in 1-s (FEV1), peak expiratory flow (PEF), and the flow-volume curves, with bronchodilator reversibility (BDR) also evaluated. In the absence of a specific questionnaire for TBM in children, a Pediatric Tracheomalacia Questionnaire was developed, incorporating elements of the S. George's Respiratory Questionnaire (SGRQ) and the ISAAC questionnaires. Higher scores indicate poorer health. The SGRQ, originally developed for chronic obstructive pulmonary disease, has been adapted for assessing TBM in adults but it has not been validated for use in pediatric populations [16, 17]. To better capture symptoms burden in children, we incorporated elements from the ISAAC questionnaire, which is designed to assess asthma-related respiratory symptoms and their impact on daily life in school-aged children—symptoms that are also commonly observed in pediatric TBM [18].

2.5 | Statistical Analysis

Descriptive statistics summarized results. Interobserver concordance for airway collapse, assessed by cine-MRI and FOB, was assessed with Intra-class correlation coefficients (ICC). While FOB was used as the gold standard to TBM diagnosis, we allowed for the possibility that cine-MRI might detect cases of TBM not identified by FOB, as forceful expiration is not feasible during FOB under anesthesia.

3 | Results

Out of 30 children screened, 10 eligible patients (median age 11 years, IQR 9–15; five males) were included in the study. Sixteen children declined participation for several reasons, such as MRI anxiety, parental refusal, or COVID-19 restrictions, while four children did not meet eligibility criteria (Figure 1). Table 1 summarizes the demographic, lung function and clinical characteristics of the enrolled children; Table 2 summarizes cine-MRI and bronchoscopy results.

3.1 | Intra- and Interobserver Variability

Cine-MRI measurements and objective analysis of FOB video frames showed excellent repeatability. Interobserver ICC values were 0.97 and 0.99 for static and dynamic cine-MRI measurements, respectively, and 0.88 for visual assessment of FOB video frames.

3.2 | Comparison Between FOB, FOB Image Analysis and Cine-MRI Pre-Bronchodilator

During FOB, pediatric pulmonologists identified TBM in two patients: CAM-03, with severe tracheal collapse during coughing; and CAM-06, with severe collapse during spontaneous breathing. However, the objective measurement of video frames yielded discordant results, detecting moderate tracheal collapse only in patient CAM-03 (lumen collapse of 87%), whereas patient CAM-06 had only a 35% lumen reduction, falling below the diagnostic cut-off for TBM. Pre-bronchodilator cine-MRI also identified TBM in two patients, including CAM-06 as for FOB findings and an additional patient (CAM-01), which was not detected by FOB. Importantly, TBM was only scored using the MRI sequence during dynamic respiratory maneuverer (forced expiration), a scenario not replicable during FOB. On the other hand, cine-MRI did not detect TBM in CAM03 in any

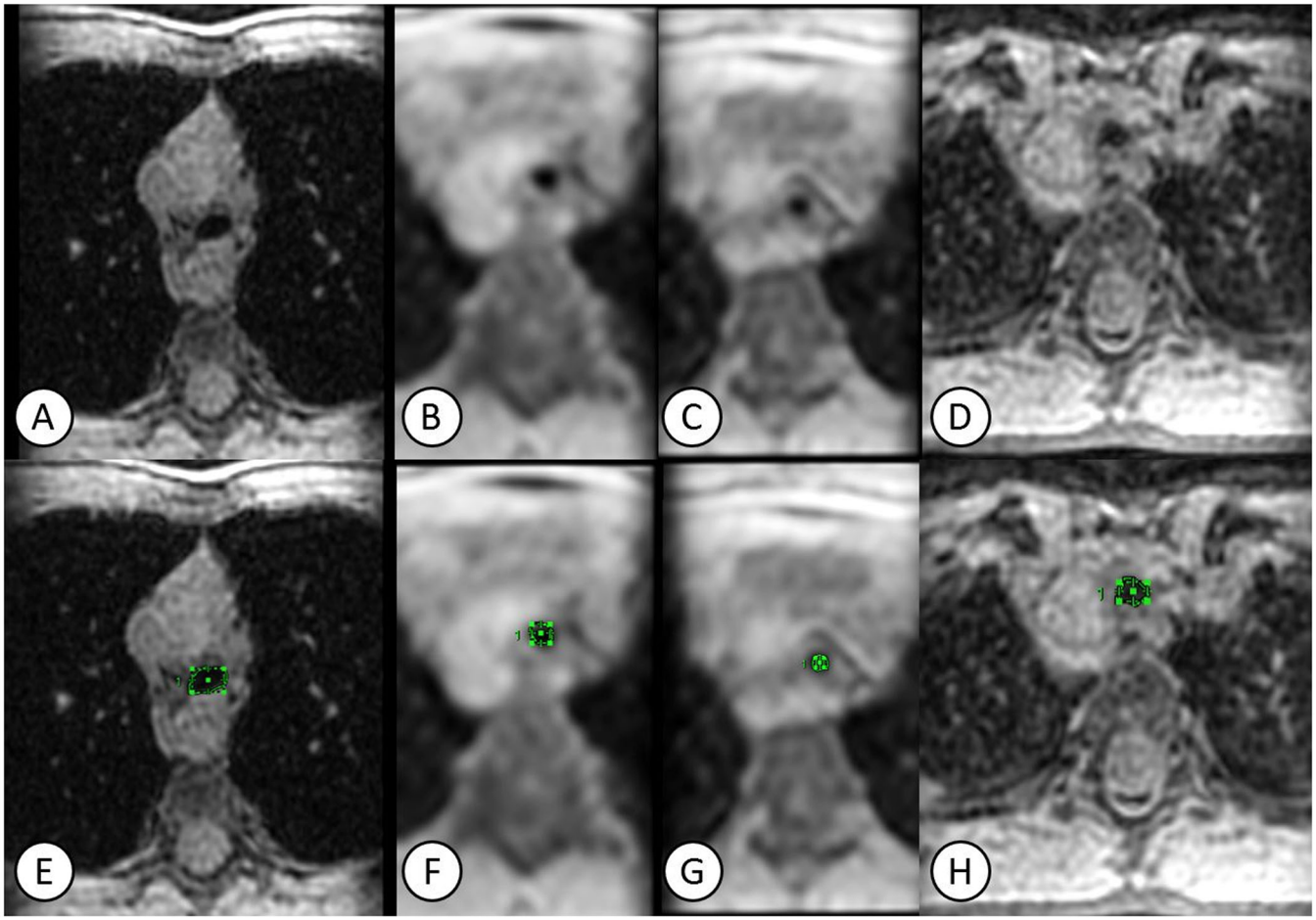

FIGURE 2 | Assessment of tracheal lumen collapse during breathing maneuvers before and after salbutamol administration in subject CAM-06. (A) Static end-inspiratory image; (B) Forced expiration pre-salbutamol (phase 11/48); (C) Forced expiration post-salbutamol (phase 16/48); (D) Static end-expiratory image. Images (E–H) show magnified regions with manual annotations. Notably, tracheal collapse increases from 36% in image B (pre-salbutamol) to 53% in image C (post-salbutamol). [Color figure can be viewed at wileyonlinelibrary.com]

of the sequences as that collapse observed during FOB was *induced by* coughing, a scenario not captured during cine-MRI.

3.3 | Comparison Between FOB and Cine-MRI After Bronchodilator

Cine-MRI post-bronchodilator identified TBM in three patients (CAM-01, CAM-02, CAM-07). Patient CAM-02 had a marginal increase in airway collapsibility (51% in post-bronchodilator vs. 49% pre-bronchodilator). Patient CAM-07 showed significant increase in airway collapsibility post-bronchodilator in both static (74 vs. 34%) and dynamic (54 vs. 19%) MRI sequences. Overall, dynamic cine-MRI sequences post-bronchodilator imaging demonstrated greater airway lumen reductions than static and pre-bronchodilator imaging, although this pattern was not consistent across all patients.

3.4 | Correlation With PFT

All the children successfully completed spirometry and bronchodilator testing. Median pre-bronchodilator FEV1 was -0.36 z-score (IQR -1.62; 0.4), and median PEF was 77% predicted (IQR 72;94). Five patients (CAM-03, CAM-06, CAM-07, CAM-08, CAM-13) had PEF values below 80% predicted. Patient CAM-06, identified as TBM-positive by both FOB and cine-MRI, had a reduced PEF (71%-predicted) but normal FEV1 (103%-predicted, 0.26 z-score) with a typical "knee"-shaped flow-volume curve indicative of TBM [7]. Similarly, patient CAM-03, identified by FOB but not by cine-MRI, had a normal FEV1 (100%-predicted, 0.04 z-score) and flow-volume curve but a reduced PEF (77%-predicted), with no changes after bronchodilator. The other three cine-MRI positive patients (CAM-01, CAM-02, CAM-07) had an obstructive (scooping) flow-volume curve, with CAM01 and CAM02 showing positive reversibility test, while CAM07 did not.

3.5 | Correlation With Symptom Questionnaire

The mean respiratory symptoms score was 10,8 (range 4–16). Symptoms included exercise-induced wheezing, breathlessness while sitting or lying, limitations in daily activities and sports, barking cough, and sleep disruption due to coughing. Patients CAM-03 and CAM-06, identified by FOB, had typical symptoms associated with TBM, such as barking cough, exercise-induced wheezing, and reduced physical exercise. The highest score

TABLE 1 | Summary of demographic, spirometry, and clinical findings.

SUBJECTS ID	AGE AT MRI (y)	SEX	PRE-BRONCHODILATOR FEV1 Z-SCORE	PRE-BRONCHODILATOR % PREDICTED PEF	POST-BRONCHODILATOR FEV1 Z-SCORE	POST-BRONCHODILATOR % PREDICTED PEF	BDR	SYMPTOMS	QUESTIONNAIRE SCORE
CAM-01	16	M	−1.77	94	−0.50	94	YES	Asthmatic symptoms not controlled, recurrent dyspnea	14/23
CAM-02	9	M	**−1.57**	n/a	−0.55	n/a	YES	Asthmatic symptoms, dyspnea	16/23
CAM-03	8	F	0.04	**77**	0.13	**77**	NO	Chronic barking cough	11/23
CAM-06	8	M	0.26	**71**	0.30	**71**	NO	Dyspnea on exertion	10/23
CAM-07	11	M	**−1.13**	**69**	−0.80	**70**	NO	Recurrent lower respiratory tract infections, pseudocroup	10/23
CAM-08	10	F	**−3.56**	**72**	**−2.82**	89	YES	Chronic recurrent cough, limited exercise tolerance	9/23
CAM-10	14	F	0.81	94	0.90	110	NO	Recurrent respiratory tract infections, asthmatic symptoms	4/23
CAM-12	17	M	1.98	144	1.90	146	NO	Recurrent low airway infections	7/23
CAM-13	11	F	−0.77	**77**	−0.44	84	NO	Chronic cough, recurrent upper respiratory tract infections	12/23
CAM-14	17	F	0.05	84	0.17	82	NO	Asthmatic symptoms, cough, dyspnea, audible breathing	15/23

Note: Patient IDs in bold indicate subjects diagnosed with TBM using cine-MRI, while the underlined ID corresponds to the subject with TBM identified only by FOB. Pathological PFT values are written in bold. Symptoms questionnaire scores were calculated out of a maximum of 23 with higher scores reflecting greater symptoms severity.

Abbreviations: Patient characteristics. BDR, Bronchodilator reversibility; FEV1, Forced expiratory volume in 1 s; ID, Patient identification number; MRI, Magnetic Resonance Imaging; PEF, Peak expiratory flow; Z-score, Standard deviation score.

TABLE 2 | Summary of cine-MRI and bronchoscopy results.

SUBJECTS	BRONCHOSCOPY		CINE- MRI			
	FLEXIBLE BRONCHOSCOPY	IMAGE J MEASURES	STATIC BREATHING SEQUENCES PRE-SALBUTAMOL	DYNAMIC BREATHING SEQUENCES PRE-SALBUTAMOL	STATIC BREATHING SEQUENCES POST-SALBUTAMOL	DYNAMIC BREATHING SEQUENCES POST-SALBUTAMOL
CAM-01	NO	8%	44%	61%	51%	31%
CAM-02	NO	6%	33%	49%	34%	51%
CAM-03	YES	87%	38%	32%	15%	25%
CAM-06	YES	35%	36%	53%	n/a	41%
CAM-07	NO	3%	34%	19%	74%	54%
CAM-08	NO	8%	40%	36%	n/a	32%
CAM-10	NO	9%	21%	35%	25%	17%
CAM-12	NO	7%	33%	38%	36%	43%
CAM-13	NO	6%	10%	11%	n/a	29%
CAM-14	NO	4%	32%	30%	n/a	23%

Note: For bronchoscopy: findings include the clinical FOB score (yes/no) and the percentage (%) of tracheal lumen reduction calculated using Image J software. For cine-MRI, all measurements represent the percentage reduction in tracheal lumen area between inspiration and expiration. These measurements were obtained for each breathing maneuver before and after salbutamol administration.

(> 12/23) was found in four patients (CAM-01, CAM-02, CAM-13, CAM-14), among these, cine-MRI identified TBM in two patients (CAM-01 and CAM-02). While typical TBM-related symptoms were more frequent in subjects with tracheal collapse exceeding 50%, these symptoms were not exclusive to this subgroup.

4 | Discussion

The primary aim of our study was to assess the diagnostic performance of cine-MRI in detecting TBM in school-aged children. Our study closely mirrors clinical practice, where diagnosing TBM remains challenging even in the presence of highly suggestive clinical symptoms. We found that cine-MRI identified three additional cases with significant airway lumen reduction that were not detected by FOB. While FOB is considered the gold standard for diagnosis TBM, its sensitivity may be reduced by procedural factors, such as the depth of anesthesia and the application of positive end-expiratory pressure (PEEP). Inadequate optimization of these parameters can result in non-physiological breathing patterns during FOB under general anesthesia, potentially leading to underdiagnosis of significant airway collapse. In our center, all pediatric FOB procedures were performed under general anesthesia using a laryngeal mask airway (LMA), which provides secure airway access, ensures adequate ventilation, and minimizes airway trauma compared to endotracheal intubation. No procedures in this cohort were performed via the nasal approach. We acknowledge that the use of an LMA may influence upper airway mechanics and alter tracheal dynamics, and this potential limitation should be considered when interpreting bronchoscopic results. For this reason, the additionally cases identified by cine-MRI were not classified as false positives. These patients had a high clinical suspicion of TBM, with FOB indication determined by a pediatric pulmonologist. Furthermore, three of the four patients identified by cine-MRI had a reduced FEV1 and/or PEF measurements, so further supporting the likelihood that these cases were true positive TBM cases rather than false findings. The higher sensitivity of cine-MRI compared to FOB in diagnosing TBM could be attributed to the advantage of dynamic respiratory imaging performed with cooperative and awake children. This approach allows cine-MRI to reveal milder tracheal collapse that might not be apparent during quiet breathing under anesthesia. Previous studies on cine-CT have similarly highlighted the importance of standardized breathing maneuvers, especially forced expiration, in enhancing TBM detection [19].

An interesting and novel finding in this study involved five patients whose airway collapse increased after bronchodilator administration, as observed in both static and dynamic cine-MRI sequences. To our knowledge, this is the first study to visually document cases of reduced airway patency after bronchodilator administration. Although TBM is not formally listed as a contraindication for the administration of albuterol (https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/020983s041lbl.pdf) these drug is frequently used in clinical practice for children with respiratory symptoms, including those ultimately diagnosed with TBM. Bronchodilators may theoretically worsen airway obstruction by reducing airway smooth muscle tone, as

mentioned in a recent ERS statement [3]. Previous studies have reported reduced PFT parameters after bronchodilators, supporting our findings. For instance, Panitch *et al.* demonstrated a 31.6% reduction in maximal forced expiratory flow rate at functional residual capacity (V′max FRC) in children with TBM after β2-agonists use [20]. Similarly, Boogaard *et al.* showed that lung function values (FEV1 and PEF) of children with TBM did not improve after bronchodilation, and in some of these patients even deteriorated, with PEF more affected than FEV1 [3]. Hofhuis *et al.* also reported that V′maxFRC in infants with malacia was not more likely to worsen after β2-agonists than in wheezy controls [21]. Our findings support the potential use of bronchodilators in TBM assessment, as these drugs may increase airway collapse and enhance diagnostic sensitivity of PFTs. This would also help shorten diagnostic delays when encountering spirometric curve values and morphologies indicative of TBM. Conversely, pharmacologic agents such as bethanechol, which increase airway smooth muscle tone, have been proposed as a potential therapeutic option for TBM. Preliminary reports from small pediatric cohorts suggest possible improvements in airway stability and symptoms relief. However, the current evidence remains limited and no large-scale pediatric trials have been conducted to date.

Despite its advantages, cine-MRI missed one case of severe TBM identified by FOB, likely because the collapse occurred only during coughing, a maneuver not included in our cine-MRI protocol. Incorporating coughing alongside forced exhalation could further increase sensitivity of our cine-MRI protocol. Intrathoracic pressure changes during forced exhalation can significantly deform the trachea and bronchi, even in asymptomatic healthy individuals. In adults, this phenomenon has led to the adoption of a higher diagnostic cut-off of 70% airway lumen reduction during expiration for TBM diagnosis on CT imaging [19]. Beyond diagnostic performance, practical considerations such as cost, scanner availability, and the need for anesthesia are important when selecting an imaging modality. Although micro-costing approaches like time-driven activity-based costing (TDABC) have been proposed to more accurately estimate procedural costs [22], our study did not include such analysis. In general, MRI incurs higher procedural charges than CT, and FOB can be even more costly when anesthesia and operating room resources are factored in. In some health systems, the primary limitation may be the opportunity cost of allocating limited MRI scanner time to this indication. Our cine-MRI protocol required approximately 20–25 min in cooperative, awake children. However, feasibility maybe reduced in younger patients, who require sedation or general anesthesia, and in such cases the benefits of avoiding radiation must be weighed against the risks and resource implications of anesthesia. A possible alternative for younger patients is the use of real-time MRI, whichenables high speed imaging without the need for sedation of anesthesia [23, 24]. Nevertheless, these considerations underscore the importance of evaluating not only diagnostic accuracy but also logistical and economic factors when ingrating advanced imaging modalities into routine clinical care. The lack of a standardized diagnostic cut-off for children complicates comparison across different imaging modalities. Considering these uncertainties, we propose that cine-MRI can serve as a complementary diagnostic tool to increase TBM detection in cooperative children. However, cine-MRI will not replace traditional FOB for all children with a suspicion for TBM, especially in younger children unable to perform the necessary breathing maneuvers. Recent studies showing the feasibility of cine-MRI in preschool children without anesthesia suggest this approach might become possible in the future [25, 26].

Our study also observed lower spirometry values in the four patients identified with TBM by cine-MRI or FOB, consistent with reports of reduced PEF in TBM [27]. While reduced PEF is not specific to TBM, it can increase clinical suspicion and should be part of a comprehensive diagnostic work-up.

It is important to acknowledge the limitations of our study, including the small sample size and low prevalence of TBM confirmed by FOB. All FOB procedures were performed under general anesthesia using LMA, with no cases conducted via the nasal approach. While the LMA offers advantages in term of airway security and reduced trauma compared to endotracheal intubation, it can potentially alter upper airway mechanics and influence tracheal dynamics; an important consideration when interpreting bronchoscopic findings. Objective analysis of FOB was performed on three standardized 30-s video clips at predefined tracheal locations rather than on the entire bronchoscopy recording. Although this standardized approach minimized interobserver variability, it may have underestimated the severity of airway collapse observed during the live procedure. Over a 3 years at our tertiary care center, only 10 cases with strong clinical suspicion of TBM met inclusion criteria, with just two ultimately receiving a clinical diagnosis of TBM. This low prevalence limited our ability to formally assess the diagnostic accuracy of cine-MRI and to draw definitive conclusions regarding its comparative sensitivity relative to FOB. While our findings suggest that FOB may have missed some clinically relevant cases, this observation should be interpreted with caution given the limited sample size and specific patient profile. Nonetheless, the study provides clinically meaningful insights, supported by key strengths: adherence to a standardized clinical care pathway, exclusive inclusion of patients with high clinical suspicion of TBM, blinded review of FOB recordings, and high interobserver agreement in cine-MRI analysis, as demonstrated by ICC values. These factors highlight the robustness of our methodology and potential clinical value of cine-MRI in evaluating airway collapse, even in children without overt symptoms.

5 | Conclusions

Our study underscores the potential value of cine-MRI as a complementary diagnostic modality for diagnosing TBM in cooperative children compared to FOB. Cine-MRI identified more cases with dynamic collapse exceeding 50%, likely due to its ability to assess airways during forced respiratory maneuvers. However, FOB successfully identified severe airway collapse induced by coughing, which was missed by cine-MRI. These findings emphasize the importance of considering both diagnostic modalities, each with its distinct strengths and limitations. Larger multicenter studies are required to confidently determine the diagnostic accuracy of both methods. It is also important to acknowledge that neither modality currently

serves as a definitive gold standard for diagnosing TBM. As research progresses and technology advances, the interplay between cine-MRI and FOB may continue to evolve, ultimately offering clinicians a more comprehensive and robust approach to diagnose TBM in pediatric patients.

Author Contributions

Giulia Roberto: writing – original draft, writing – review and editing, data curation, investigation. **Federico Mollica:** investigation, methodology, data curation. **Yifan Wang:** conceptualization, methodology. **Piotr Wielopolski:** conceptualization, methodology. **Marielle Pijnenburg:** conceptualization, methodology, supervision. **Daan Caudri:** conceptualization, investigation, methodology, data curation, supervision. **Pierluigi Ciet:** conceptualization, methodology, validation, visualization, formal analysis, project administration, data curation, supervision.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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Supporting Information

Additional supporting information can be found online in the Supporting Information section.
sup 0001 Fig2. sup-0002-figure4 Capture300. sup-0003-TBM scoring sheet. sup-0004-Vragenlijst kinderen 12 17 jr V1 0 3mar2016. sup-0005-Vragenlijst ouders v kinderen 7 12 jaar V1 0 03mar2016. sup-0006-Vragenlijst ouders v kinderen_12-17_jaar V1 0 03mar2016.