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Clinical evaluation and endoscopic classification of bronchomalacia in dogs

E. Bottero, C. Bellino, D. De Lorenzi, P. Ruggiero, A. Tarducci, A. D'Angelo, P. Gianella

From the Department of Veterinary Sciences, University of Turin, Via L. Da Vinci 44, 10095 Grugliasco (TO), Italy (Bellino, D'Angelo, Tarducci, Gianella); Poliambulatorio Veterinario Argentina, via Levà 58, Arma di Taggia (IM), Italy (Bottero); Veterinary Hospital "I Portoni Rossi", Via Roma 57, Zola Predosa, Bologna (De Lorenzi); Centro Veterinario Specialistico, Via S. Giovannini 51-53, 00137, Roma (Ruggiero)

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Key words: Bronchi; Canine; Respiratory endoscopy; Airway collapse; Chronic cough

Abbreviations:

BAL bronchoalveolar lavage

BCS body condition score

BM bronchomalacia

DBC dynamic bronchial collapse

ISACHC International Small Animal Cardiac Health Council

LPB left principal bronchus (LPB)

LB1 left cranial lobe

LB2 left caudal lobe

RPB right principal bronchus

RB1 right cranial lobe

RB2 right middle lobe

RB3 accessory lung lobe

RB4 right caudal lobe

SBC static bronchial collapse

TBM tracheobronchomalacia

TM tracheomalacia

VHS vertebral heart size

Corresponding author: Paola Gianella

Department of Veterinary Sciences

University of Turin, Via L. Da Vinci, 44 10095 Grugliasco (TO) - Italy

Tel.++39 011 6709074 Fax ++39 011 6709083

e-mail: paola.gianella@unito.it

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Background: Little information is available about the association between bronchomalacia and historical or clinicopathological data. Also, studies applying an endoscopic classification scheme that differentiates between static and dynamic bronchial collapse and based on a scoring system are lacking.

Objectives: To describe the clinical presentation of bronchomalacia in dogs, to classify endoscopic findings, and to evaluate associations between historical, clinicopathological data, and endoscopic findings.

Animals: 59 client-owned dogs with an endoscopic diagnosis of bronchomalacia

Methods: In this retrospective study, medical records were analyzed and video documentation was reviewed to assign a score to endoscopic findings. Univariate analysis was performed on categorical variables organized in contingency tables, and a stepwise logistic regression model was used for multivariate analysis.

Results: Of the 59 dogs included in the study, two were affected by static bronchial collapse (SBC), 35 by dynamic bronchial collapse (DBC), and 22 by both SBC and DBC. The association between SBC and DBC was more frequently seen in the dogs with higher body weight, pulmonary hypertension, a bronchial type of radiographic pattern and nodularity at endoscopic examination.

Thirty-one dogs presented with tracheomalacia and bronchomalacia; an association emerged between these concurrent disorders in dogs living indoors. Multivariate analysis of the endoscopic scores showed a correlation between DBC severity and cough duration.

Conclusion and clinical importance: Results of this study provide evidence for two different types of bronchial collapse. Endoscopic scoring scheme has proved to be promising in the BM classification, although further evaluation of its applicability in larger canine populations is needed.

Bronchomalacia (BM) refers to weakness of the bronchial walls due to softening of the supportive cartilage and hypotonia of myoelastic elements.[1,2] This results in a reduction in airway lumen diameter, leading to a respiratory syndrome encompassing chronic cough, wheezing, intermittent or continuous dyspnoea, difficulty in clearing secretions, and recurrent bronchitis and pneumonia.[3-5] Tracheomalacia (TM) refers to weakness of the tracheal wall, such that the airway is softer and more susceptible to collapse. The weakness may be localized to one portion or involve the entire trachea. If both bronchi and trachea are involved, the term tracheobronchomalacia (TBM) is used.[6,7] As an isolated clinical entity, BM is much less common than TM and TBM in human medicine[7], in contrast to its occurrence reported in veterinary medicine.[8]

The precise cause of malacia in humans is not fully understood, although several etiopathogenetic factors have been proposed, including congenital conditions,[9] endotracheal intubation,[10] long-term ventilation,[11] closed-chest trauma,[12] chronic airway irritation and inflammation,[13,14] malignancy,[15] asthma,[3] mechanical anatomic factors,[4] and thyroid diseases.[16] In veterinary medicine, similar causative factors have also been hypothesized,[5,8,17] although the role of airway inflammation or cardiomegaly has yet to be confirmed.[8,18]

Bronchoscopy is the gold standard for diagnosis in humans and animals,[5,8,17,19,20] with the left cranial lung lobe affected more frequently in brachycephalic and non-brachycephalic dogs.[5,17,18] In human medicine, two different forms of dynamic airway obstruction are distinguished: BM and excessive dynamic airway collapse (EDAC).[6] These entities might or might not coexist; however, they are rarely described in terms of extent, severity, location and associated anomalies because their understanding has been limited over the years by uncertainties about their definition, diagnosis and management. Furthermore, comparison between studies and different therapeutic protocols has been hampered for want of a standard method to quantify the severity of airway collapse.[6]

For these reasons, quantitative or morphometric bronchoscopy has been proposed,[21] but owing to a lack of resources, time, information, or technical limitations, it has seldom, if ever, been used. In veterinary medicine, despite the recent increasing recognition of BM in dogs,[5,8,18] studies addressing functional classes of airway narrowing, as well as an endoscopic systematic classification, are lacking.

The aims of the present study were: 1) to retrospectively evaluate the history and clinical presentation of a series of dogs with BM; 2) to attempt an endoscopic classification of BM by differentiating between static and dynamic bronchial collapse and with the use of a scoring system; and 3) to identify possible associations between historical and clinicopathological data and endoscopic findings.

Materials and methods

The medical records of dogs with an endoscopic diagnosis of BM between June 2010 and September 2011 were retrospectively reviewed. Information gleaned from the medical records included breed, sex, age, body weight, body condition score (BCS), lifestyle, presence of smoking owners, cough duration, type of thoracic radiographic pattern, radiographic evidence of tracheal and bronchial collapse, vertebral heart size (VHS), ISACHC heart failure classification, presence of pulmonary hypertension, and cytology of the bronchoalveolar lavage (BAL) fluid.

Bronchoscopic examination was performed under general anesthesia in all dogs. A 5-minute preoxygenation period was used. Dogs weighing ≤ 15 kg were not intubated; a stable plane of anesthesia was maintained with a constant rate infusion of propofol at 0.1-0.4 mg/kg/min or intermittent boluses. Oxygen was delivered through the working channel of the bronchoscope or by use of jet ventilation. Dogs weighing > 15 kg were intubated after endoscopic tracheal examination and maintained on gas anesthesia. Balanced isotonic crystalloid fluids were administered IV to all dogs; ECG, blood pressure and pulse oximetry were constantly monitored. During recovery, supplemental oxygen was provided as needed.

All bronchoscopic procedures were performed in standardized fashion by two of the authors (E.B., P.R.).[22] Flexible video endoscopes (5.9 mm x 110 cm[a] and 4.9 mm x 60 cm[b]) were used. Videotaping was done with a digital video converter[c] connected to a FireWire 800-equipped Mac computer.[d] Video documentation for each dog was independently reviewed by two authors (E.B., P.G.) in a blind, separate fashion in order to grade and map airway collapse and assign an endoscopic score. A discussion to reach a consensus opinion was done only in cases of divergent opinion.

The study population was composed of dogs with BM, with or without endoscopically detectable TM, and was divided into three subgroups according to the type of bronchial airway collapse (dynamic [subgroup 1], static + dynamic [subgroup 2], static [subgroup 3]). Tracheal collapse (cervical and/or intrathoracic) was graded as proposed by Tangner and Hobson.[23] The canine endobronchial map was used for lower airways examination and identification.[22]

Normal bronchial openings were described as smooth, round or slightly oval in appearance, with a minimal reduction in luminal diameter during phases of respiration.[24] Bronchial collapse was defined as static if a reduction in luminal diameter persisted during all phases of respiration, and as dynamic if changes in luminal diameter were observed on respiration. The reduction in luminal diameter was identified as flattening of the bronchial openings, circumferential narrowing or distortion of their normal round appearance. Collapse was reported at the left principal bronchus (LPB), left cranial lobe (LB1), or left caudal lobe (LB2) and the right principal bronchus (RPB), right cranial lobe (RB1), right middle lobe (RB2), accessory lung lobe (RB3), or right caudal lobe (RB4). Grade 1 static and dynamic collapse was visualized and defined as a diameter reduction ≤50%, grade 2 collapse as a diameter reduction >50% and ≤75%, and grade 3 collapse as a diameter reduction >75%, with contact between the dorsal and ventral mucosa of the collapsed bronchus. Furthermore, type A extension of static and dynamic collapse was defined as collapse affecting ≤3 bronchi (principal left and right, lobar, segmental),[22] type B as collapse affecting 4-5 bronchi (principal left and right, lobar, segmental),[22] and type C as collapse affecting >5 bronchi (principal left and right, lobar, segmental).[22] Each dog was classified based on the worst grade of collapse and total number of airways affected. Final endoscopic scores were then obtained by evaluating separately the severity and extension (grade 1, 2, 3 and type A, B, C, respectively) of static and dynamic bronchial collapse. Additional bronchoscopic findings including the presence of airway secretions, hyperemia or nodularity were also recorded.

BAL was performed by wedging the endoscope into 1 or 2 of the smallest bronchial segments, followed by instillation and continuous vacuum aspiration of 2 ml/kg of warmed, sterile saline solution through the biopsy channel of the endoscope. BAL fluid was processed immediately after sampling for nucleated cell count using a standard haemocytometer and cytological differentiation on slides stained with Wright-Giemsa stain. Cytology results were classified according to the predominant cell type in the sample.[25]

Statistical analysis

Statistical analysis was performed using a freeware statistical software package.[e]

Nominal data were expressed as frequency, percentage or both. TM, dynamic bronchial collapse (DBC) and dynamic+static bronchial collapse (DBC+SBC) were classified as being present or absent. For the endoscopic score each grade of severity (1, 2, 3) and type of extension (A, B, C) were classified as present or absent in the DBC and SBC groups, respectively. The historical and clinicopathological data were transformed into class variables (Table 1). Univariate analysis of nominal data was performed with contingency table analysis by Fisher's exact test. In addition, for each 2x2 contingency table, the odds ratio (OR) and the 95% confidence intervals of the odds ratio (95% OR^{CI}) were calculated. Variables that meet a cut-off of P <0.20 at the univariate analysis were entered into a logistic regression model for the multivariate analysis. Three separate logistic regression models, one for TM, one for DBC and one for DBC+SBC were constructed, having

TM, DBC and DBC+SBC as the dependent variables and historical and clinicopathological data as the independent variables. For the endoscopic score, separate logistic regression models for each grade of severity (1, 2, 3) and type of extension (A, B, C) were constructed in the SBC and DBC groups respectively, having the grade of severity and type of extension as the dependent variables and historical and clinicopathological data as the independent variables. The most parsimonial final model was selected, via backward elimination, with a Wald *P*-value of 0.05 as the removal threshold, given an acceptable log-likelihood ratio test value. Model fit was evaluated by Pearson's and Hosmer-Lemeshow's goodness-of-fit test. A value of $P > 0.05$ indicates that the data adequately fit the model used.

Results

Between June 1, 2010 and September 30, 2011, 59 dogs had a bronchoscopic diagnosis of BM with or without TM. The study population (n=59) consisted of dogs from 22 different breeds and 21 mixed-breed dogs. Breeds accounting for at least 3 cases were miniature Poodle (n=5), Yorkshire terrier (n=5), Pugs (n=4) and Epagneul Breton (n=3). Thirty dogs were male (4 neutered) and 29 were female (17 spayed). The median age was 11 years (range 2-16). Three dogs were aged between 2 and 4 years at presentation, 25 between 5 and 10 years, and 31 were more than 10 years old. The median body weight was 10 kg (range 2.5-60 kg). Twentyfive dogs weighed 10 kg or less, 23 between 11 and 20 kg, 8 between 21 and 30 kg, and 3 more than 30 kg. The median BCS was 7 (range 3-9). Of the 48 dogs with a BCS >5, 31 had a BCS ≥7. Forty dogs lived indoors, 8 outdoors, and 11 indoors/outdoors. Thirty-three dogs were from households where smoking had regularly occurred indoors in the past year. Chronic cough was the chief complaint in all dogs; the duration was <6 months in 33 dogs and ≥6 months in 26. Radiographic diagnosis of an abnormal pulmonary pattern was made in 40/59 dogs, with bronchial and bronchointerstitial patterns found in 23/40 and 13/40 dogs, respectively. In the remaining 4 dogs, an interstitial pattern (2), an alveolar pattern (1) and bronchiectasis (1) were identified. Static radiography was considered supportive of tracheal collapse in 4/59 dogs. There was no radiographic evidence of bronchial collapse.

The VHS was ≤ 9.7 (normal, 8.5-10.7)[26] in all 52/59 dogs in which it was measured.

Of the 32 dogs with concurrent heart disease, 22 were classified as ISACHC Class I, of which 8/22 Class Ia and 14/22 Class Ib, 9 as ISACHC Class II, and 1 as ISACHC Class III. Doppler echocardiography demonstrated pulmonary hypertension in 6/59 dogs.

BM without tracheal involvement was identified on bronchoscopy in 28/59 dogs (48%), and BM + TM in 31/59 (52%), of which 22 (71%) with a dynamic type of bronchial collapse. TM was primarily associated with movement of the dorsal tracheal membrane, and BM with dorsoventral flattening of the bronchial wall. Among the dogs with TM, grade I tracheal collapse was present in 9/31 (29%), grade II in 14/31 (45%), grade III in 7/31 (23%), and grade IV in 1/31 (3%). Overall, 2 dogs (3%) were affected by static bronchial collapse (SBC) alone, 35 (59%) by dynamic bronchial collapse (DBC) alone, and 22 (37%) by both static and dynamic bronchial collapse (DBC+SBC). Concurrent static collapse of 1-3 lobar bronchi was documented in 9/59 dogs (15%); concurrent dynamic collapse of 1-6 lobar bronchi was documented in 22/59 (37%). In 1 of these dogs both static and dynamic lobar bronchial collapse was identified. Segmental static and dynamic airway collapse was documented in 15/59 (25%) and in 35/59 (59%) dogs respectively.

Overall, collapse of the left cranial lobe bronchus was most commonly identified (22/59 dogs, 37%), followed in descending order by collapse of the left caudal (16/59, 27%), right cranial (14/59, 24%), right caudal (12/59, 20%), right middle (10/59, 17%), and accessory lung lobe bronchus (8/59, 14%). Table 2 reports the final endoscopic score; the number of dogs in the different categories for static and dynamic collapse has been listed. All categories of severity and extension of SBC and DBC were represented, except for grade 3 type B SBC. With regard to DBC, 20 dogs were scored 3C, the most severe and extensive type of collapse.

On bronchoscopy, all dogs presented gross evidence of airway inflammation with hyperemia and mucus accumulation; 20 dogs presented bronchial nodules. BAL was performed in 45 dogs: cytology was normal in 7; in the remaining 38, analysis revealed neutrophilic (n=23), lymphocytic (n=1), eosinophilic (n=1), mixed neutrophilic-eosinophilic (n=12), and mixed neutrophilic-lymphocytic (n=1) inflammation. Intracellular bacteria were identified in 25 dogs. No parasitic larvae or ova were found in any of the samples examined. Culture of BAL fluid samples was not performed because of financial and logistic concerns. Fourteen dogs did not undergo BAL because of dramatic airway collapse and haemoglobin desaturation.

There were no significant associations detected for DBC by multivariate analysis (Table 3 and 4).

Results of the univariate analysis of the endoscopic scores revealed that the historical and clinicopathological data that met the criteria for the inclusion in the multivariate analysis were: age >10 years (CI 1.084-35.72; P = .04) for type C extension of DBC; BCS 7-9 (CI 0.27-21.13; P = .16) for type B extension of SBC; body weight between 10 and 20 kg (CI 1.36-infinite; P = .03) for SBC grade 1 severity; cough ≥ 6 months duration (CI 1.32-16.48;

P = .02), smoking owners (CI 0.59-45.07; *P* = .18) and radiographic bronchial pattern (CI 1.12-14.01; *P* = .04) for DBC grade 3 severity. Multivariate analysis showed a correlation between DBC grade 3 severity and cough ≥6 months duration (CI 4.5-37.7; OR = 11.35). The goodness of fit statistic (Hosmer-Lemeshow) suggested that the data adequately fit the final model (*P* = .24).

Discussion

This study provides a systematic description of the concurrent presence of different types of BM, with or without TM, in a population of dogs with chronic cough, and explores the applicability of an endoscopic scoring scheme. The occurrence of BM alone or in association with TM has been described elsewhere.[5,8,17,18] As an isolated clinical entity, BM was reported in 87.5% of dogs with brachycephalic airway syndrome,[17] in 100% and in 50% of dogs examined elsewhere,[5,8] and in 48% of the dogs in the present study, most of which of small-medium size. Sixty-seven percent of the dogs examined in a previous study were small breed dogs,[5] while medium and large breed dogs were common in another population.[8] Taken together, these data suggest that BM is a common, increasingly recognized clinical condition in canine breeds.

A substantial number of dogs in the present study (59%) were affected by DBC alone or in association with SBC (37%), with most dogs presenting with concurrent DBC and TM (71%). Only two were diagnosed with SBC alone (3%). Factors contributing to the association between DBC and TM are not known, though similar histopathological alterations, such as atrophy of myoelastic elements and cartilage, causing dorsoventral flattening of the tracheal and bronchial wall along with dorsal tracheal membrane movements, can be hypothesized. In contrast, the lack of SBC in dogs with TM could suggest a different pathogenesis. In this regard, the static collapse could result from external compression or increased chronic expiratory efforts, as hypothesized elsewhere.[17]

In contrast to what observed in this study, and although clear data about the occurrence of DBC or SBC are largely unavailable, SBC has been more frequently reported than DBC in the canine BM population,[8,18] as well as in brachycephalic dogs.[17] This could simply reflect either differences among dog populations or support the hypothesis for the presence of two different clinicopathological entities that might or might not coexist. The presence of continuous forced exhalation in young brachycephalic dogs, in which immature airways are more easily compressed and deformed in comparison with those of adults, was hypothesized as the causative mechanism for developing the static type of bronchial collapse.[17] However, the presence of SBC also in older, non-brachycephalic dogs, as found in the present study population, may reflect the existence of other pathogenetic mechanisms. Furthermore, it cannot be excluded that, over time, a dynamic type of bronchial collapse could evolve into a static type, thus representing an initially less severe form of airway narrowing.

In the present study, no predilection of BM for sex or age was observed. As described in previous studies,[5,8] the majority of the dogs were adult, elderly, overweight or obese, suggesting that a congenital component of BM may not exist or may clinically manifest over time in association with other comorbidities or symptoms such as severe chronic cough and that weight gain may be a contributing factor or a consequence of this condition, as hypothesized elsewhere.[5] In this regard, DBC in association with SBC was more often diagnosed in dogs weighing between 20 and 30 kg; however, the BCS did not differ between the weight groups. While tracheal collapse is relatively common in small-breed dogs,[27] no information is available about the association between BM and medium-large-breed dogs. It is possible that, as compared to smaller-size dogs, severe chronic cough eventually associated with underlying comorbidities or more severe alterations of the bronchial cartilage and myoelastic elements could have contributed to the development of BM in the larger dogs.

TM was more often found in the dogs living indoors. This association might have been influenced by the fact that small-breed dogs, like the majority of the dogs with TM in this study population, and in which TM is relatively common,[27] are suited for indoor living. Unexpectedly, however, no significant association with chronic smoke exposure emerged. While in line with available data,[28] whether these results might have been related to less smoking among the dog owners over time is unknown and warrants further investigation.

Different abnormal radiographic patterns were identified in 68% of the dogs and a significant association emerged between the bronchial pattern and the presence of DBC+SBC. This could be explained by greater airway narrowing compared to that caused by the presence of DBC alone, thus leading to a more severe airway inflammation. In turn, the more severe airway inflammation might more likely lead radiographic infiltrates. Concurrent parenchymal pathologies cannot be excluded, however. In agreement with other reports,[5] different radiographic patterns were observed in the present study and the absence of radiographic changes did not exclude the presence of BM. Tracheal collapse was diagnosed in only 7% of the dogs and lower airway collapse in none, contrasting with other studies in which the radiographic identification of airway collapse was more accurate.[5,8]

A substantial percentage of dogs (54%) in the present study had concurrent heart disease, but no significant associations with any type of airway narrowing were found. A recent study failed to document a role of cardiomegaly in airway collapse.[18] In the dogs examined here, the available VHS values were not greater than normal, thus supporting the hypothesis that factors other than cardiomegaly might have contributed to the airway collapse.

Interestingly, an association was found between pulmonary hypertension and DBC+SBC, suggesting that the presence of the two different types of bronchial collapse might represent a severe clinicopathological entity. It should be noted, however, that no attempt was made to identify the contribution of chronic obstructive pulmonary disease or hypoxia to the development of pulmonary hypertension, in addition to that caused by an underlying heart disease.

In this population of dogs, BM was found to more commonly involve the left-side bronchi, as observed in other studies.[5,17,18] For this particular distribution, besides thoracic conformation hypothesized for brachycephalic dogs,[17] other factors such as concurrent pulmonary disorders may have played a role. In addition, compared to observations of a previous study,[8] a larger number of dogs in this study presented with smaller airway collapse in the absence of lobar bronchial collapse (49.1%). Whether a reduction in thoracic volume because of obesity or hepatomegaly might have contributed to this condition, as elsewhere suggested,[8] merits further investigation.

It is known that long-standing inflammation may lead to nodular proliferation of fibrous tissue protruding into the airway.[29] In this regard, an association was found here between nodularity at endoscopic examination and DBC+SBC, suggesting that the concurrent presence of the two different types of bronchial collapse might cause severe inflammation.

All dogs, regardless of the type and severity of airway narrowing, displayed bronchoscopic evidence of airway inflammation, and the majority showed neutrophilic inflammation, thus confirming the previously reported high percentage of inflammatory airway disease associated with BM.[5,18] No statistical differences among different types of airway narrowing and results of airway cytology were found. Intracellular bacteria were identified in 25 dogs, for which a lower respiratory tract infection was considered possible.[30] Similar to recent observations,[5] but in contrast with other studies,[8,18] our results suggests a potential association between infection and BM. However, because of the lack of BAL fluid culture, this link could not be clearly demonstrated and remains speculative at best.

As evidenced by the endoscopic score, most dogs appeared to be affected by DBC of much greater severity and extension than SBC. A possible explanation for this difference is that DBC may represent an initial form of BM, thus far more common than SBC. Furthermore, if we consider that many of the dogs here were of medium-large size, therefore with a larger bronchial tree potentially requiring higher compression forces to cause the same grade of narrowing compared to the smaller dogs, the highly severe DBC found remains surprising. It is possible that serious, chronic cough, the chief complaint in all the dogs, played a significant causative role, perhaps in association with marked alterations of the bronchial tree, especially in the medium-large size dogs.

Significant associations were found between the endoscopic score and several clinicopathological variables, thus supporting further investigation of the scheme's applicability in larger canine populations.

This study has some limitations, primarily related to its retrospective design and the relatively small sample size, considering the different types of airway narrowing addressed. The increasing recognition of this syndrome[5,8,17,18] means that a very large study population would be needed to identify significant differences between dogs with different types of airway narrowing. Another limitation is the lack of information about histological diagnosis which could have shed light on the aetiology of the different forms of airway obstruction compared here.

Finally, further studies applying the endoscopic scoring scheme are needed to compare its use in populations of dogs of different size and age. This has practical implications since, in large-breed dogs, in which deeper segments of the bronchial tree can be examined, BM might be erroneously classified as being more severe than in small-breed dogs.

The question remains as to whether the entity of cough and the presence of severe alterations of the bronchial tree could have influenced the severity of bronchial collapse and its progression from a dynamic to a static type, especially in the medium-large-breed dogs. In light of these considerations, the use of an endoscopic scoring scheme could facilitate a comprehensive approach to BM patients and eventually guide further therapeutic interventions.

Footnotes

[a] EG-270N5 Fujinon

[b] EB-270S Fujinon

[c] Canopus ADVC[110]

[d] Apple MacBook Pro-Core i7 processor 2.2 GHz 15.4-inch

[e] R, version 1.2.0, R Foundation for Statistical Computing, Vienna, Austria. Available at: www.r-project.org. Accessed Feb 6, 2012

References

1. Baxter JD, Dunbar JS. Tracheomalacia. Ann Otol Rhinol Laryngol. 1963; 72:1013–1023.

2. Nuutinen J. Acquired tracheobronchomalacia. A clinical study with bronchological correlations. Ann Clin Res 1977; 9:350–355

3. Nuutinen J. Acquired tracheobronchomalacia. Eur J Respir Dis. 1982; 63:380-387

4. Wright CD. Tracheomalacia. Chest Surg Clin North Am 2003; 13:349-357, viii

5. Adamama-Moraitou KK, Pardali D, Dai MJ, et al. Canine Bronchomalacia: a clinicopathological study of 18 cases diagnosed by endoscopy. Vet J 2012; 191:261-266

6. Murgu S, Colt H. Tracheobronchomalacia and excessive dynamic airway collapse. Respirology 2006; 11:388-406

7. Carden KA, Boiselle P., Waltz DA, Ernst A. Tracheomalacia and tracheobronchomalacia in children and adults: an in-depth review. Chest 2005; 127:984-1005

8. Johnson LR, Pollard RE Tracheal collapse and bronchomalacia in dogs: 58 cases (7/2001-1/2008). J Vet Intern Med 2010; 24:298-305

9. Mair EA, Parsons DS. Pediatric tracheobronchomalacia and major airway collapse. Ann Otol Rhinol Laryngol 1992; 101:300–309

10. Feist JH, Johnson TH, Wilson RJ. Acquired tracheomalacia: etiology and differential diagnosis. Chest 1975; 68:340–345

11. Burden RJ, Shann F, Butt W, Ditchfield M. Tracheobronchial malacia and stenosis in children in intensive care: bronchograms help to predict outcome. Thorax 1999; 54:511–517

12. Tsugawa C, Nishijima E, Muraji T, et al. A shape memory airway stent for tracheobronchomalacia in children: an experimental and clinical study. J Pediatr Surg 1997; 32:50–53

13. Johnson TH, Mikita JJ, Wilson RJ, Feist JH. Acquired tracheomalacia. Radiology 1973; 109:576–580

14. Tillie-Leblond I, Wallaert B, Leblond D, et al. Respiratory involvement in relapsing polychondritis. Clinical, functional, endoscopic, and radiographic evaluations. Medicine 1998; 77:168–176

15. Miyazawa T, Miyazu Y, Iwamoto Y et al. Stenting at the flow-limiting segment in tracheobronchial stenosis due to lung cancer. Am J Respir Crit Care Med 2004; 169:1096–1102

16. McHenry CR, Piotrowski JJ. Thyroidectomy in patients with marked thyroid enlargement: airway management, morbidity, and outcome. Am Surg 1994; 60:586–91

17. De Lorenzi D, Bertoncello D, Drigo M. Bronchial abnormalities found in a consecutive series of 40 brachycephalic dogs. J Am Vet Med Assoc 2009; 235:835-840

18. Singh MK, Johnson LR, Kittleson MD, Pollard RE. Bronchomalacia in dogs with myxomatous mitral valve degeneration. J Vet Intern Med 2012; 26:312-319

19. Johnson L. Tracheal collapse. Diagnosis and medical and surgical treatment. Vet Clin North Am Small Anim Pract 2000; 30:1253-1266

20. Heyer CM, Nuesslein TG, Jung D, et al. Tracheobronchial anomalies and stenoses: detection with low-dose multidetector CT

with virtual tracheobronchoscopy-comparison with flexible tracheobronchoscopy. Radiology 2007; 242:542–549

21. Rozycki HJ, Van Houten ML, Elliot GR. Quantitative assessment of intrathoracic airways collapse in infants and children with tracheobronchomalacia. Pediatr Pulmonol 1996; 21:241-245

22. Amis TC, McKiernan BC. Systematic identification of endobronchial anatomy during bronchoscopy in the dog. Am J Vet Res 1986; 47:2649-2657

23. Tangner CH, Hobson HP. A retrospective study of 20 surgically managed cases of collapsed trachea. Vet Surg 1982; 11:146-149

24. Johnson L. Small animal bronchoscopy. Vet Clin North Am Small Anim Pract 2001, 31:691-705, viii

25. Hawkins EC, DeNicola DB, Kuehn NF. Bronchoalveolar lavage in the evaluation of pulmonary disease in the dog and cat. State of art. J Vet Intern Med 1990; 4:267-274

26. Buchanan JW, Bücheler J. Vertebral scale system to measure canine heart size in radiographs. J Am Vet Med Assoc 1995; 206:194-199

27. Macready DM, Johnson LR, Pollard RE. Fluoroscopic and radiographic evaluation of tracheal collapse in dogs: 62 cases (2001-2006). J Am Vet Med Assoc 2007; 230:1870-1876

28. Hawkins EC, Clay LD, Bradley JM, Davidian M. Demographic and historical findigs, including exposure to environmental tobacco smoke, in dogs with chronic cough. J Vet Intern Med 2010; 24:825-831

29. Levitan D, Kimmel S. Flexible Endoscopy: respiratory tract. In: Lhermette P and Sobel D, eds. BSAVA Manual of canine and feline endoscopy and endosurgery. 1st ed. BSAVA; 2008: 92

30. Hirt RA, Wiederstein I, Denner EB et al. Influence of the collection and oxygenation method on quantitative bacterial composition in bronchoalveolar lavage fluid samples from healthy dogs. Vet J 2010; 184: 77-82

Table 1. Historical and clinicopathological variables recorded and tested for their association with TM, in addition to BM, dynamic bronchial collapse and dynamic + static bronchial collapse.

Historical and clinicopathological variables	Variables			
sex	male		female	
age	< 5	≥ 5 and ≤ 10	> 10	

(years)				
body weight (kg)	≤ 10	> 10 and ≤ 20	> 20 - ≤ 30	> 30
BCS (1 - 9)	1 - 5	6 - 9	7 - 9	
lifestyle	indoor	outdoor	indoor/outdoor	
smoking owners	yes		no	
duration of cough (months)	< 6		≥ 6	
radiographic pattern	normal	bronchial	bronchointerstitial	other
cardiologic examination	normal	abnormal		
pulmonary hypertension	yes		no	
BAL*	neutrophilic	eosinophilic	lymphocytic	mixed**
nodularity (endoscopic examination)	yes		no	
TM***	yes		no	

*reference values for normal BAL cell and differential count were 200-450 cells/µl comprising up to 5-7 ± 5% neutrophils, lymphocytes, and eosinophils, and 65-85% macrophages[27]

**type of mixed inflammation at cytologic analysis of BAL fluid: neutrophilic-eosinophilic; neutrophilic-lymphocytic

***TM endoscopically detected

Table 2. Severity and extension of static and dynamic bronchial collapse (endoscopic score) in 59 dogs with bronchomalacia.

	STATIC COLLAPSE								
Endoscopic score	1A	1B	1C	2A	2B	2C	3A	3B	3C
Number of dogs	7	1	2	3	2	4	3	-	2
	DYNAMIC COLLAPSE								
Endoscopic score	1A	1B	1C	2A	2B	2C	3A	3B	3C
Number of dogs	10	5	1	1	5	9	2	4	20

The numbers (1, 2, 3) indicate the grade of severity of bronchial collapse; the letters (A, B, C) refer to the extension of bronchial collapse.

Table 3. Results of univariate analysis of historical and clinicopathological variables tested for the association with tracheomalacia (TM), dynamic (DBC) and dynamic+static bronchial collapse (DBC+SBC) in 59 dogs with BM.

Historical and clinicopathological variables	TM (n=31) (95% OR^{CI}; *P*)	DBC (n=35) (95% OR^{CI}; *P*)	DBC + SBC (n=22) (95% OR^{CI}; *P*)
Sex	0.34-3.34; 1	0.24-2.55; 0.8	0.38-4.17; 0.7
Age <5 years	0.00-2.13; 0.1*	0.06-85.72; 1	0.013-16.98; 1
Age ≥ 5 years and ≤ 10 years	0.29-3.29; 1	0.13-1.60; 0.3	0.57-6.74; 0.3
Age > 10 years	0.48-5.09; 0.4	0.58-6.31; 0.3	0.16-1.81; 0.3
Body weight ≤ 10 kg	2.31-32.98; <0.01*	0.72-7.84; 0.1*	0.17-1.87; 0.4
Body weight > 10 and ≤ 20 kg	0.10-1.61; 0.2	0.64-12.70; 0.2	0.04-1.30; 0.1*
Body weight > 20 and ≤ 30 kg	0.002-0.90; 0.02*	0.001-0.65; 0.05*	1.02-71.02; 0.04*
BCS ≤ 1-5 vs ≥ 6-9	0.31-6.71; 0.7	0.43-9.49; 0.3	0.08-1.94; 0.3
BCS 7-9	0.43-4.37; 0.6	0.72-7.84; 0.1*	0.17-1.87; 0.4
Indoor	4.01-216.83; <0.01*	1.10-14.96; 0.02*	0.07-1.00; 0.04*
Outdoor	0.00-0.43; <0.01*	0.01-1.18; 0.05*	1.01-71.02; 0.04*
Indoor/outdoor	0.01-0.83; 0.01*	0.10-2.31; 0.3	0.31-6.96; 0.7
Smoking owners	0.26-2.63; 0.8	0.64-7.24; 0.2	0.17-2.00; 0.4
Duration of cough < 6 months vs ≥ 6	0.34-3.48; 1	0.15-1.62; 0.3	0.79-9.10; 0.1*

months			
Abnormal radiographic pattern	0.4-4.83; 0.6	0.94-17.8; 0.04*	0.03-0.91; 0.2
Radiographic bronchial pattern	0.16-1.79; 0.3	0.07-0.85; 0.01*	1.50-20.14; 0.01*
Radiographic bronchointerstitial pattern	0.38-7.15; 0.5	0.27-5.08; 1	0.23-4.42; 1
Abnormal cardiologic examination	0.33-21.98; 0.4	0.45-2.97; 0.3	0.81-6.22; 0.3
Pulmonary hypertension	0.51-254.15; 0.2	0.002-1.14; 0.03*	1.02-512.75; 0.02*
Neutrophilic inflammation (BAL)	0.13-1.56; 0.1*	0.29-3.33; 1	0.26-3.17; 0.8
Neutrophilic-eosinophilic inflammation (BAL)	0.12-2.49; 0.5	0.33-7.64; 0.7	0.15-3.57; 1
Nodularity	0.18-2.13; 0.4	0.11-1.41; 0.1*	0.64-7.84; 0.1*
Endoscopically detectable TM	-	0.85-9.50; 0.3	0.13-1.56; 0.5

*Significant association

BAL=bronchoalveolar lavage

BCS=body condition score

OR^{CI}= odds ratio 95% confidence intervals

Table 4. Results of multivariate analysis of historical and clinicopathological variables tested for the association with tracheomalacia (TM), dynamic (DBC) and dynamic+static bronchial collapse (DBC+SBC) in 59 dogs with BM.

Study population	Historical and clinicopathological variables	OR; (95% CI)
DBC+SBC* *P* for Hosmer-Lemeshow goodness of fit statistic = .44	Body weight > 20 - ≤ 30 kg	8.4; (1.4-74.3)
	Radiographic bronchial pattern	7.0; (1.9-30.6)
	Pulmonary hypertension	25.7; (3.0-579.9)
	Nodularity	3.4; (1.5-18.4)
TM** *P* for Hosmer-Lemeshow goodness of fit statistic = .53	Indoor lifestyle	22.7; (4.8-176.4)

CI= 95% confidence intervals

OR=odds ratio

* variables removed in backward selection for DBC+SBC group: Body weight > 10 and ≤ 20 kg; Indoor lifestyle; Outdoor lifestyle; Duration of cough < 6 months vs ≥ 6 months.

** variables removed in backward selection for TM group: Age <5 years; Body weight ≤ 10 kg; Body weight > 20 and ≤ 30 kg; Outdoor lifestyle; Indoor/outdoor lifestyle; Neutrophilic inflammation (BAL).