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Clinical evaluation and endoscopic classification of
bronchomalacia in dogs

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Short title: Bronchomalacia in dogs

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

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

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

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

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

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

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

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

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43 Bronchomalacia (BM) refers to weakness of the bronchial walls
44 due to softening of the supportive cartilage and hypotonia of
45 myoelastic elements.^{1,2} This results in a reduction in airway lumen
46 diameter, leading to a respiratory syndrome encompassing chronic
47 cough, wheezing, intermittent or continuous dyspnoea, difficulty
48 in clearing secretions, and recurrent bronchitis and pneumonia.³⁻⁵

49 Tracheomalacia (TM) refers to weakness of the tracheal wall, such
50 that the airway is softer and more susceptible to collapse. The
51 weakness may be localized to one portion or involve the entire
52 trachea. If both bronchi and trachea are involved, the term
53 tracheobronchomalacia (TBM) is used.^{6,7} As an isolated clinical
54 entity, BM is much less common than TM and TBM in human
55 medicine⁷, in contrast to its occurrence reported in veterinary
56 medicine.⁸

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

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

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

86 The aims of the present study were: 1) to retrospectively evaluate
87 the history and clinical presentation of a series of dogs with BM;
88 2) to attempt an endoscopic classification of BM by differentiating
89 between static and dynamic bronchial collapse and with the use of

90 a scoring system; and 3) to identify possible associations between
91 historical and clinicopathological data and endoscopic findings.

92 Materials and methods

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

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

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

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

131 Normal bronchial openings were described as smooth, round or
132 slightly oval in appearance, with a minimal reduction in luminal
133 diameter during phases of respiration.²⁴ Bronchial collapse was
134 defined as static if a reduction in luminal diameter persisted during
135 all phases of respiration, and as dynamic if changes in luminal
136 diameter were observed on respiration. The reduction in luminal
137 diameter was identified as flattening of the bronchial openings,

138 circumferential narrowing or distortion of their normal round
139 appearance. Collapse was reported at the left principal bronchus
140 (LPB), left cranial lobe (LB1), or left caudal lobe (LB2) and the
141 right principal bronchus (RPB), right cranial lobe (RB1), right
142 middle lobe (RB2), accessory lung lobe (RB3), or right caudal
143 lobe (RB4). Grade 1 static and dynamic collapse was visualized
144 and defined as a diameter reduction $\leq 50\%$, grade 2 collapse as a
145 diameter reduction $>50\%$ and $\leq 75\%$, and grade 3 collapse as a
146 diameter reduction $>75\%$, with contact between the dorsal and
147 ventral mucosa of the collapsed bronchus. Furthermore, type A
148 extension of static and dynamic collapse was defined as collapse
149 affecting ≤ 3 bronchi (principal left and right, lobar, segmental),²²
150 type B as collapse affecting 4-5 bronchi (principal left and right,
151 lobar, segmental),²² and type C as collapse affecting >5 bronchi
152 (principal left and right, lobar, segmental).²² Each dog was
153 classified based on the worst grade of collapse and total number of
154 airways affected. Final endoscopic scores were then obtained by
155 evaluating separately the severity and extension (grade 1, 2, 3 and
156 type A, B, C, respectively) of static and dynamic bronchial
157 collapse. Additional bronchoscopic findings including the
158 presence of airway secretions, hyperemia or nodularity were also
159 recorded.

160 BAL was performed by wedging the endoscope into 1 or 2 of the
161 smallest bronchial segments, followed by instillation and

162 continuous vacuum aspiration of 2 ml/kg of warmed, sterile saline
163 solution through the biopsy channel of the endoscope. BAL fluid
164 was processed immediately after sampling for nucleated cell count
165 using a standard haemocytometer and cytological differentiation
166 on slides stained with Wright-Giemsa stain. Cytology results were
167 classified according to the predominant cell type in the sample.²⁵

168 Statistical analysis

169 Statistical analysis was performed using a freeware statistical
170 software package.^e

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

186 TM, DBC and DBC+SBC as the dependent variables and
187 historical and clinicopathological data as the independent
188 variables. For the endoscopic score, separate logistic regression
189 models for each grade of severity (1, 2, 3) and type of extension
190 (A, B, C) were constructed in the SBC and DBC groups
191 respectively, having the grade of severity and type of extension as
192 the dependent variables and historical and clinicopathological data
193 as the independent variables. The most parsimonial final model
194 was selected, via backward elimination, with a Wald *P*-value of
195 0.05 as the removal threshold, given an acceptable log-likelihood
196 ratio test value. Model fit was evaluated by Pearson's and Hosmer-
197 Lemeshow's goodness-of-fit test. A value of $P > 0.05$ indicates
198 that the data adequately fit the model used.

199 Results

200 Between June 1, 2010 and September 30, 2011, 59 dogs had a
201 bronchoscopic diagnosis of BM with or without TM. The study
202 population (n=59) consisted of dogs from 22 different breeds and
203 21 mixed-breed dogs. Breeds accounting for at least 3 cases were
204 miniature Poodle (n=5), Yorkshire terrier (n=5), Pugs (n=4) and
205 Epagneul Breton (n=3). Thirty dogs were male (4 neutered) and 29
206 were female (17 spayed). The median age was 11 years (range 2-
207 16). Three dogs were aged between 2 and 4 years at presentation,
208 25 between 5 and 10 years, and 31 were more than 10 years old.
209 The median body weight was 10 kg (range 2.5-60 kg). Twenty-

210 five dogs weighed 10 kg or less, 23 between 11 and 20 kg, 8
211 between 21 and 30 kg, and 3 more than 30 kg. The median BCS
212 was 7 (range 3-9). Of the 48 dogs with a BCS >5, 31 had a BCS
213 ≥ 7 . Forty dogs lived indoors, 8 outdoors, and 11 indoors/outdoors.
214 Thirty-three dogs were from households where smoking had
215 regularly occurred indoors in the past year. Chronic cough was the
216 chief complaint in all dogs; the duration was <6 months in 33 dogs
217 and ≥ 6 months in 26. Radiographic diagnosis of an abnormal
218 pulmonary pattern was made in 40/59 dogs, with bronchial and
219 bronchointerstitial patterns found in 23/40 and 13/40 dogs,
220 respectively. In the remaining 4 dogs, an interstitial pattern (2), an
221 alveolar pattern (1) and bronchiectasis (1) were identified. Static
222 radiography was considered supportive of tracheal collapse in 4/59
223 dogs. There was no radiographic evidence of bronchial collapse.
224 The VHS was ≤ 9.7 (normal, 8.5-10.7)²⁶ in all 52/59 dogs in which
225 it was measured.
226 Of the 32 dogs with concurrent heart disease, 22 were classified as
227 ISACHC Class I, of which 8/22 Class Ia and 14/22 Class Ib, 9 as
228 ISACHC Class II, and 1 as ISACHC Class III. Doppler
229 echocardiography demonstrated pulmonary hypertension in 6/59
230 dogs.
231 BM without tracheal involvement was identified on bronchoscopy
232 in 28/59 dogs (48%), and BM + TM in 31/59 (52%), of which 22
233 (71%) with a dynamic type of bronchial collapse. TM was

234 primarily associated with movement of the dorsal tracheal
235 membrane, and BM with dorsoventral flattening of the bronchial
236 wall. Among the dogs with TM, grade I tracheal collapse was
237 present in 9/31 (29%), grade II in 14/31 (45%), grade III in 7/31
238 (23%), and grade IV in 1/31 (3%). Overall, 2 dogs (3%) were
239 affected by static bronchial collapse (SBC) alone, 35 (59%) by
240 dynamic bronchial collapse (DBC) alone, and 22 (37%) by both
241 static and dynamic bronchial collapse (DBC+SBC). Concurrent
242 static collapse of 1-3 lobar bronchi was documented in 9/59 dogs
243 (15%); concurrent dynamic collapse of 1-6 lobar bronchi was
244 documented in 22/59 (37%). In 1 of these dogs both static and
245 dynamic lobar bronchial collapse was identified. Segmental static
246 and dynamic airway collapse was documented in 15/59 (25%) and
247 in 35/59 (59%) dogs respectively.

248 Overall, collapse of the left cranial lobe bronchus was most
249 commonly identified (22/59 dogs, 37%), followed in descending
250 order by collapse of the left caudal (16/59, 27%), right cranial
251 (14/59, 24%), right caudal (12/59, 20%), right middle (10/59,
252 17%), and accessory lung lobe bronchus (8/59, 14%). Table 2
253 reports the final endoscopic score; the number of dogs in the
254 different categories for static and dynamic collapse has been listed.
255 All categories of severity and extension of SBC and DBC were
256 represented, except for grade 3 type B SBC. With regard to DBC,

257 20 dogs were scored 3C, the most severe and extensive type of
258 collapse.

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

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

273 Results of the univariate analysis of the endoscopic scores
274 revealed that the historical and clinicopathological data that met
275 the criteria for the inclusion in the multivariate analysis were: age
276 >10 years (CI 1.084-35.72; $P = .04$) for type C extension of DBC;
277 BCS 7-9 (CI 0.27-21.13; $P = .16$) for type B extension of SBC;
278 body weight between 10 and 20 kg (CI 1.36-infinite; $P = .03$) for
279 SBC grade 1 severity; cough ≥ 6 months duration (CI 1.32-16.48;

280 $P = .02$), smoking owners (CI 0.59-45.07; $P = .18$) and
281 radiographic bronchial pattern (CI 1.12-14.01; $P = .04$) for DBC
282 grade 3 severity. Multivariate analysis showed a correlation
283 between DBC grade 3 severity and cough ≥ 6 months duration (CI
284 4.5-37.7; OR = 11.35). The goodness of fit statistic (Hosmer-
285 Lemeshow) suggested that the data adequately fit the final model
286 ($P = .24$).

287 Discussion

288 This study provides a systematic description of the concurrent
289 presence of different types of BM, with or without TM, in a
290 population of dogs with chronic cough, and explores the
291 applicability of an endoscopic scoring scheme. The occurrence of
292 BM alone or in association with TM has been described
293 elsewhere.^{5,8,17,18} As an isolated clinical entity, BM was reported in
294 87.5% of dogs with brachycephalic airway syndrome,¹⁷ in 100%
295 and in 50% of dogs examined elsewhere,^{5,8} and in 48% of the dogs
296 in the present study, most of which of small-medium size. Sixty-
297 seven percent of the dogs examined in a previous study were small
298 breed dogs,⁵ while medium and large breed dogs were common in
299 another population.⁸ Taken together, these data suggest that BM is
300 a common, increasingly recognized clinical condition in canine
301 breeds.

302 A substantial number of dogs in the present study (59%) were
303 affected by DBC alone or in association with SBC (37%), with

304 most dogs presenting with concurrent DBC and TM (71%). Only
305 two were diagnosed with SBC alone (3%). Factors contributing to
306 the association between DBC and TM are not known, though
307 similar histopathological alterations, such as atrophy of myoelastic
308 elements and cartilage, causing dorsoventral flattening of the
309 tracheal and bronchial wall along with dorsal tracheal membrane
310 movements, can be hypothesized. In contrast, the lack of SBC in
311 dogs with TM could suggest a different pathogenesis. In this
312 regard, the static collapse could result from external compression
313 or increased chronic expiratory efforts, as hypothesized
314 elsewhere.¹⁷

315 In contrast to what observed in this study, and although clear data
316 about the occurrence of DBC or SBC are largely unavailable, SBC
317 has been more frequently reported than DBC in the canine BM
318 population,^{8,18} as well as in brachycephalic dogs.¹⁷ This could
319 simply reflect either differences among dog populations or support
320 the hypothesis for the presence of two different clinicopathological
321 entities that might or might not coexist. The presence of
322 continuous forced exhalation in young brachycephalic dogs, in
323 which immature airways are more easily compressed and
324 deformed in comparison with those of adults, was hypothesized as
325 the causative mechanism for developing the static type of
326 bronchial collapse.¹⁷ However, the presence of SBC also in older,
327 non-brachycephalic dogs, as found in the present study population,

328 may reflect the existence of other pathogenetic mechanisms.
329 Furthermore, it cannot be excluded that, over time, a dynamic type
330 of bronchial collapse could evolve into a static type, thus
331 representing an initially less severe form of airway narrowing.

332 In the present study, no predilection of BM for sex or age was
333 observed. As described in previous studies,^{5,8} the majority of the
334 dogs were adult, elderly, overweight or obese, suggesting that a
335 congenital component of BM may not exist or may clinically
336 manifest over time in association with other comorbidities or
337 symptoms such as severe chronic cough and that weight gain may
338 be a contributing factor or a consequence of this condition, as
339 hypothesized elsewhere.⁵ In this regard, DBC in association with
340 SBC was more often diagnosed in dogs weighing between 20 and
341 30 kg; however, the BCS did not differ between the weight groups.

342 While tracheal collapse is relatively common in small-breed
343 dogs,²⁷ no information is available about the association between
344 BM and medium-large-breed dogs. It is possible that, as compared
345 to smaller-size dogs, severe chronic cough eventually associated
346 with underlying comorbidities or more severe alterations of the
347 bronchial cartilage and myoelastic elements could have
348 contributed to the development of BM in the larger dogs.

349 TM was more often found in the dogs living indoors. This
350 association might have been influenced by the fact that small-
351 breed dogs, like the majority of the dogs with TM in this study

352 population, and in which TM is relatively common,²⁷ are suited for
353 indoor living. Unexpectedly, however, no significant association
354 with chronic smoke exposure emerged. While in line with
355 available data,²⁸ whether these results might have been related to
356 less smoking among the dog owners over time is unknown and
357 warrants further investigation.

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

372 A substantial percentage of dogs (54%) in the present study had
373 concurrent heart disease, but no significant associations with any
374 type of airway narrowing were found. A recent study failed to
375 document a role of cardiomegaly in airway collapse.¹⁸ In the dogs

376 examined here, the available VHS values were not greater than
377 normal, thus supporting the hypothesis that factors other than
378 cardiomegaly might have contributed to the airway collapse.

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

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

398 It is known that long-standing inflammation may lead to nodular
399 proliferation of fibrous tissue protruding into the airway.²⁹ In this

400 regard, an association was found here between nodularity at
401 endoscopic examination and DBC+SBC, suggesting that the
402 concurrent presence of the two different types of bronchial
403 collapse might cause severe inflammation.

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

417 As evidenced by the endoscopic score, most dogs appeared to be
418 affected by DBC of much greater severity and extension than
419 SBC. A possible explanation for this difference is that DBC may
420 represent an initial form of BM, thus far more common than SBC.
421 Furthermore, if we consider that many of the dogs here were of
422 medium-large size, therefore with a larger bronchial tree
423 potentially requiring higher compression forces to cause the same

424 grade of narrowing compared to the smaller dogs, the highly
425 severe DBC found remains surprising. It is possible that serious,
426 chronic cough, the chief complaint in all the dogs, played a
427 significant causative role, perhaps in association with marked
428 alterations of the bronchial tree, especially in the medium-large
429 size dogs.

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

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

443 Finally, further studies applying the endoscopic scoring scheme
444 are needed to compare its use in populations of dogs of different
445 size and age. This has practical implications since, in large-breed
446 dogs, in which deeper segments of the bronchial tree can be

447 examined, BM might be erroneously classified as being more
448 severe than in small-breed dogs.

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

457 Footnotes

458 ^aEG-270N5 Fujinon

459 ^bEB-270S Fujinon

460 ^cCanopus ADVC¹¹⁰

461 ^dApple MacBook Pro-Core i7 processor 2.2 GHz 15.4-inch

462 ^eR, version 1.2.0, R Foundation for Statistical Computing, Vienna,
463 Austria. Available at: www.r-project.org. Accessed Feb 6, 2012

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552

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

555

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	

557 *reference values for normal BAL cell and differential count were 200-450 cells/ μ l comprising up to 5-7 \pm
 558 5% neutrophils, lymphocytes, and eosinophils, and 65-85% macrophages²⁷

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

561 ***TM endoscopically detected

562

563 **Table 2.** Severity and extension of static and dynamic bronchial collapse (endoscopic score) in 59 dogs
 564 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	

565

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

568

569 **Table 3.** Results of univariate analysis of historical and clinicopathological variables tested for the
 570 association with tracheomalacia (TM), dynamic (DBC) and dynamic+static bronchial collapse (DBC+SBC)
 571 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

572

573 *Significant association

574 BAL=bronchoalveolar lavage

575 BCS=body condition score

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

577

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

581

Study population	Historical and clinicopathological variables	OR; (95% CI)
DBC+SBC* <i>P</i> 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** <i>P</i> for Hosmer-Lemeshow goodness of fit statistic = .53	Indoor lifestyle	22.7; (4.8-176.4)

582

583 CI= 95% confidence intervals

584 OR=odds ratio

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

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

589

590

591