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LETTER TO THE EDITOR

Response to letter regarding "Evaluation of bronchial narrowing in coughing dogs with heart murmurs using computed tomography"

Dear Editor,

Thank you for giving us the opportunity to respond to the letter of Szatmári et al, because this letter illustrates several noteworthy points about veterinary clinical research in general and our study in particular.

The authors seem to have misunderstood our objectives and results. The statistical analysis used in our study is complex and might need further explanation. The question that our study aimed to answer was whether an enlarged heart can be responsible for compressing the surrounding bronchi in dogs. Proving causality is difficult and often requires a series of clues.[1] A previous study has shown that comparing dogs with bronchomalacia but no cardiomegaly and dogs with bronchial narrowing and cardiomegaly failed to answer the question of causality.[2] It showed that bronchial narrowing potentially caused by bronchomalacia or compression by an enlarged heart likely looked similar and cannot be differentiated using radiography, fluoroscopy, or endoscopy.[2]

Our objective was to approach the problem differently by studying one criterion of causality: the biological gradient.[1] Our proposal was that if the heart was responsible for bronchial compression, a gradient of narrowing should be seen. If the heart is not or barely enlarged, bronchial narrowing should be absent or minimal, and the larger the heart, the narrower the bronchi would be. To explore this hypothesis, it therefore was logical to include not only dogs with enlarged left atria, but also dogs in stage B1 of myxomatous mitral valve disease (MMVD; ie, without cardiomegaly). As we investigated the effect of heart enlargement on the surrounding bronchi, we aimed at including any heart disease that could cause cardiomegaly, and not restrict ourselves to a single disease (ie, MMVD). It seems intuitive that the compressive effect of cardiomegaly on the surrounding bronchi would be similar in MMVD and dilated cardiomyopathy, as shown in human medicine.[3] Evaluating this gradient required objective measures of bronchial diameter, which was not possible by radiography, fluoroscopy, or endoscopy but could be achieved using computed tomography (CT). Indeed, radiography is a very unreliable method to determine principal or primary lobar bronchial diameter, explaining why comparing CT to radiography was not intended in our study. The narrowest bronchial diameter was identified on CT by scrolling through transverse plane images to find the frame with the narrowest diameter. Computed tomography also allowed us to assess this gradient relationship without the confounding effect of general anesthesia. Because the dogs were all awake, injection of contrast was not performed, because it would have caused variable movements of the dogs and, therefore, increased the expense and time of the data collection period. Use of contrast was deemed unnecessary, because we believe that the anatomical relationship of the left atrium to the aorta, trachea bifurcation and, therefore, the most proximal aspects of the principal bronchi is dependable and consistent.

To limit the number of statistical analyses and the risk of false positive results, we decided first to identify which bronchi were narrowed in the group of dogs with heart disease. This was the only purpose of the control group. Hence, the control group only included dogs without cardiovascular disease that underwent thoracic CT. Table 1 in our article presents demographic information about the dogs of the control group and statistical comparison with the group of dogs with heart disease.[4]

Our results confirmed a gradient association between heart size (estimated by vertebral heart scale and left atrial-to-aorta ratio) and bronchial narrowing, with the bronchi becoming narrower as heart size increased. Looking more closely at the results, the gradient was highest for left caudal bronchus (LB2) and left principal bronchus (LPB), which are the bronchi located just dorsal to the left atrium (Figure 1). It therefore seems logical that these bronchi would be the most narrowed bronchi associated with an enlarged left atrium. Looking at Figure 1, it also appears obvious that the left atrium is in close vicinity not only to the left-sided bronchi, but also to right-sided ones. It is in especially close vicinity to the right principal (RPB), right middle (RB2), and right caudal (RB4) bronchi, which were the bronchi identified as significantly narrowed in dogs with cardiomegaly in our study.[4] Even without using IV contrast injection, the left atrium can be identified on CT, as shown in Figure 1C. In Figure 1C, it can easily be appreciated how an enlarged left atrium can compress both the left-sided and the right-sided bronchi. This finding also has been described in human medicine, as discussed in our article.[4-6]

We feel the questions and comments regarding bronchial stenting or characteristics of heart murmur are not constructive. Szatmári et al indicate that we suggest bronchial stenting "as possible treatment"

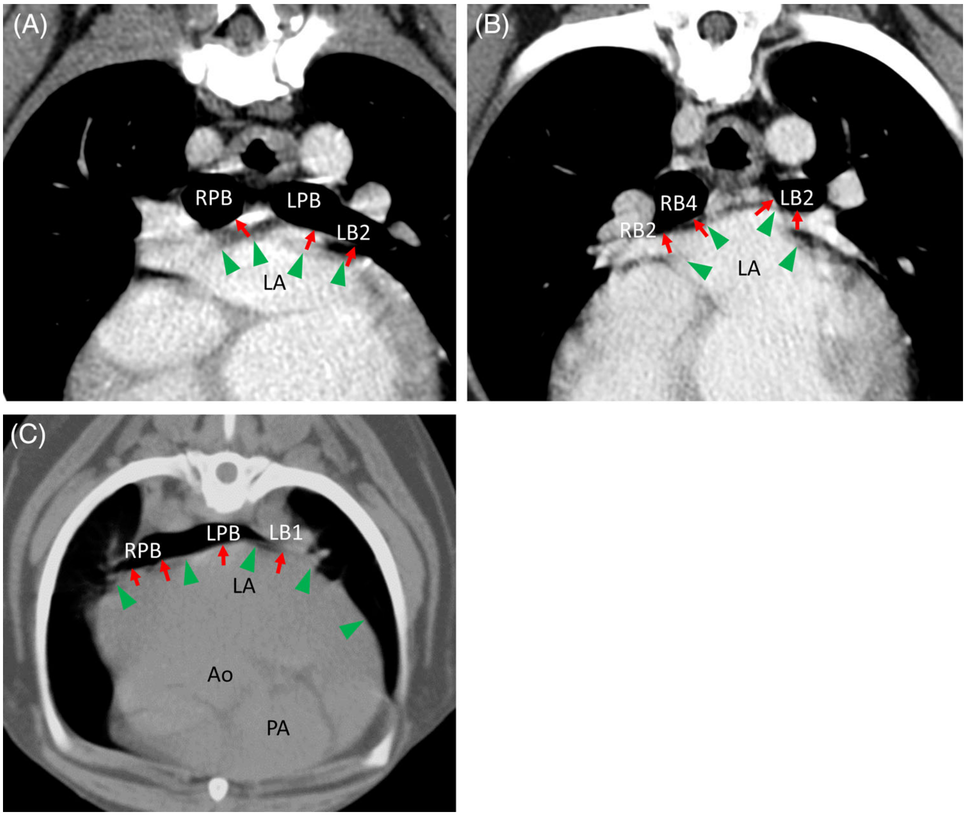

FIGURE 1 Transverse plane CT images of a dog without cardiomegaly at the level of the principal bronchi (A) and caudal bronchi (B), and a dog with cardiomegaly from Lebastard et al study[4] at the level of the principal bronchi (C). The CT images of the dog without cardiomegaly are in soft-tissue window after IV contrast injection (A, B). The CT image of the dog with cardiomegaly is in soft-tissue window without IV contrast injection (C). Note the close vicinity between the left atrium (LA, green arrow heads) and both left-sided and right-sided bronchi (red arrows). Ao, aorta; CT, computed tomography; LB1, left cranial primary bronchus; LB2, left caudal primary bronchus; LPB, left principal bronchus; PA, pulmonary artery; RB2, right middle primary bronchus; RB4, right caudal primary bronchus; RPB, right principal bronchus

based on our findings and a single case report, but fail to acknowledge our caveat that additional studies are required to investigate the potential therapeutic benefit of bronchial stenting. Because 1 criterion for causality is consistency, our study alone cannot definitively answer the question of whether cardiomegaly is responsible for surrounding bronchial compression, but it does provide an argument in favor of this hypothesis. We look forward to collaborative efforts in the future to further explore this important clinical question.

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REFERENCES

1. Fedak KM, Bernal A, Capshaw ZA, Gross S. Applying the Bradford Hill criteria in the 21st century: how data integration has changed causal inference in molecular epidemiology. *Emerg Themes Epidemiol*. 2015; 12:14.
2. Singh MK, Johnson LR, Kittleson MD, Pollard RE. Bronchomalacia in dogs with myxomatous mitral valve degeneration. *J Vet Intern Med*. 2012;26:312-319.
3. Lee JE, Oh J-H, Lee JY, Koh DK. Massive cardiomegaly due to dilated cardiomyopathy causing bronchial obstruction in an infant. *J Cardiovasc Ultrasound*. 2014;22:84-87.
4. Lebastard M, Le Boedec K, Howes M, et al. Evaluation of bronchial narrowing in coughing dogs with heart murmurs using computed tomography. *J Vet Intern Med*. 2021;35:1509-1518.
5. Cochran ST, Gyepes MT, Smith LE. Obstruction of the airways by the heart and pulmonary vessels in infants. *Pediatr Radiol*. 1977;6:81-87.
6. Kussman BD, Geva T, McGowan FX. Cardiovascular causes of airway compression. *Paediatr Anaesth*. 2004;14:60-74.