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Does the computed tomographic appearance of the lung differ between young and old dogs?

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Abstract

In computed tomographic (CT) images of humans, decreased lung attenuation, bronchial dilation and/or thickening, air trapping, cysts, and thickened interlobular septa have been associated with increasing age. To determine if there are differences in the CT appearance of the lungs of young and old dogs that could affect interpretation of diagnostic studies, pulmonary CT images of dogs with conditions unrelated to the thorax were reviewed retrospectively in a case-control study. CT studies of 42 young dogs (range 0.3-4.8 years) and 47 old dogs (range 9-15.1 years) were jumbled and reviewed by an observer blinded to dog age. CT was performed under sedation in 62 (70%) dogs and under general anesthesia in 27 (30%). Heterotopic bone was more prevalent (62% versus 14%) in old dogs. Lung collapse was significantly associated with old age, greater body weight, and anesthesia. There were no significant differences in median lung attenuation or occurrence of ground glass pattern, cysts, bronchial thickening, bronchial dilation, or degree of tracheal calcification. No examples of reticular pattern, emphysema, pleural thickening or septal thickening were observed in any dog. Despite previous studies describing age-related changes in the radiographic appearance of the lungs of old dogs, it appears that there are minimal observable differences in CT images. Old dogs are more likely to have visible foci of heterotopic bone and may be more prone to lung lobe collapse than young dogs, but neither of these differences should contribute to misdiagnosis of pulmonary disease.

Introduction

Age-related changes in the morphology of the lung have been described in humans[1], dogs[2,3], and rats.[4] A prominent age-related feature observed in dogs was accumulation of macrophages containing dust and pigment in the respiratory bronchioles and alveolar openings.[2] It was hypothesized that exposure to dust and reduction in function of the mucociliary escalator over time resulted in accumulation of dust and pigment in the lungs,[2] but this was not confirmed. There was also an increase in the relative volume ('volume density') of alveolar ducts, progressive calcification of the bronchial cartilage, and increased size of the bronchial glands.[2] Minimal emphysema was observed and fibrosis was sparse, mainly associated with foci of pneumonitis.[2]

Correlations between morphologic changes in the lungs and the radiographic appearance of the lung were described in 100 aged dogs that had no pathologic evidence of pulmonary or cardiovascular disease.[3] Emphysema and alveolar dilatation were reported, but more emphasis was placed on findings of pleural fibrosis and interstitial fibrosis.[3] Accumulation of peribronchial collagen over time causing progressive pulmonary fibrosis has also been emphasized in studies of aging rats.[4] Together with fibrosis, thickening of the alveolar walls and calcification of bronchial cartilage in dogs were associated with radiographic signs including pleural thickening, increased linear markings, and increased opacity of the tracheal and bronchial walls.[3] Foci of heterotopic bone in the lungs of many older dogs produced small nodular opacities in radiographs.[3] Based on these findings, increased lung attenuation, pleural and septal thickening and increased prevalence of heterotopic bone may be expected in computed tomographic (CT) images of the lungs of aged dogs; however, there are no published studies of age-related changes in pulmonary CT images of dogs.

Changes associated with normal aging in the lungs of humans have been studied extensively, one aim being to avoid over-diagnosis of age-related changes as signs of clinically significant disease. Age-related changes seen in pulmonary CT images of humans include decreased lung attenuation as a result of dilatation of alveoli and/or emphysema, air-trapping, cysts, a sub-pleural reticular pattern, bronchial dilation, bronchial thickening, and thickening of interlobular septa without inflammation.[5-9] CT signs usually associated with interstitial lung disease may also be seen in healthy elderly humans, and radiologists have been cautioned not to over-interpret such findings in asymptomatic patients.[5]

The aim of the present study was to determine if there are differences in the CT appearance of the lungs of young and old dogs that could affect interpretation of diagnostic studies.

Method and Materials

Ethical approval was granted by the Clinical Research Ethical Review Board at the Royal Veterinary College. For this retrospective case-control study, the medical records at the Queen Mother Hospital for Animals (QMHA) in the period 2012-2016 were searched for cases that satisfied the following inclusion criteria: dogs that had diagnosis of a non-malignant disease or condition unrelated to the thorax; had non-contrast CT images of the lung acquired using a high resolution (sharp or lung) algorithm; and were either less than 5 years old or more than 9 years old. Dogs with a history of lower respiratory signs or diagnosis of cardiovascular, mediastinal, pleural, bronchial, pulmonary disease, malignant neoplasia or systemic inflammatory disease were not included.

For each dog, age at the time of CT, gender, body weight and diagnosis were recorded. On the basis of body weight, dogs were divided in small (<10kg), medium (10-25kg), large (26-40kg), and giant (>40kg) categories. Use of sedation or anesthesia for CT was also recorded. For all sedated dogs, CT images were acquired during free breathing, whereas anaesthetised dogs had brief manual hyperventilation with CT images acquired during the subsequent expiratory pause.

As part of the inclusion criteria, all CT images were acquired using the same multi-slice scanner (MX8000 IDT, Phillips Best, The Netherlands). Studies lacking optimal settings for lung examination were excluded. For the purposes of this study, optimal settings were helical acquisition, slice thickness 2mm for small dogs and 3mm for other dogs, matrix 512x512, and high frequency ('sharp' or 'lung enhanced') reconstruction algorithm. All CT images were reviewed by a board-certified radiologist (CRL) without knowledge of the age, breed or history of the subjects. Images were reviewed in a lung window (level -500HU, width 2000HU) using a proprietary Digital Imaging in Communications and Medicine (DICOM) viewer (OsiriX 64-bit, version 5.2.2, Pixmeo, Switzerland). For each dog, the lungs were also examined using maximum- and minimum-intensity projections with slab thickness 5mm for small dogs and 8mm for other dogs. Dogs whose CT images were affected by motion blur were excluded.

CT images were evaluated for the following features: mean lung attenuation (Hounsfield units, HU) based on the median of three measurements made using a circular region of interest of minimum area 40mm^2 placed in different lung lobes and avoiding bronchi or large vessels; ground glass opacity (absent/present); reticular pattern (absent/present); emphysema (absent/present); pulmonary cysts (absent/present, diameter of largest cyst); visceral pleural thickening (absent, affecting one lobe, affecting multiple lobes); interlobular septal thickening (absent, affecting one lobe, affecting multiple lobes); bronchial thickening (none, slight, marked); bronchial dilation (median of bronchus: pulmonary artery ratio measurements in the right caudal lobe in three adjacent CT slices); degree of tracheal ring calcification (the median of three HU measurements made by placing a point sample on a tracheal cartilage ring immediately cranial to the origin of the lobar bronchi); foci of heterotopic bone (absent, affecting one lobe, affecting multiple lobes); and pulmonary collapse (number of affected lobes and distribution of collapse was recorded: lobe tip only, peripheral, bronchocentric, entire lobe). The term tip is used here to indicate the pointed extremity of a lung lobe in transverse CT images. Diagnosis of heterotopic bone was based on finding pulmonary hyperdense foci ranging from sub-millimeter rounded foci to larger irregularly-shaped densely ossified foci. Diagnosis of lung collapse was based on finding increased lung attenuation accompanied by reduced volume of the affected lung. Terminology followed recommendations for thoracic imaging by the Fleischner Society.[10]

Statistical analyses were done by a statistician (Yu-Mei Chang) using a commercial statistical software package (SPSS 22, IBM) Significance of differences in median lung attenuation, bronchus: pulmonary artery ratio and tracheal calcification between young and old dogs were tested using the Mann-Whitney test. Differences in prevalence of ground glass opacity, bronchial thickening and cysts were tested using Fisher's exact test. Differences in occurrence of heterotopic bone and body weight of dogs were tested using Kendall's tau-c test. Associations between the dependent variable lung collapse and independent variables age, body weight, and anesthesia were tested using binary logistic regression and results summarized as odds ratio (OR) and 95% confidence interval (CI). Differences with $p<0.05$ were considered significant.

Results

CT images of 42 young dogs (age range 0.3-4.8 years) and 47 old dogs (age range 9-15.1 years) were reviewed. All dogs were scanned in sternal recumbency. Characteristics of young and old dog groups are summarized in Table 1. CT features observed in young and old dogs are summarized in Table 2. Heterotopic bone was more prevalent (62% versus 14%; $p<0.001$) in old dogs.

Signs of lung collapse were identified in 40 (46%) dogs. Based on regression analysis, occurrence of lung collapse was significantly associated with age (OR 3.7, CI 1.4-9.5, p=0.007), body weight (OR 1.9, CI 1.1-3.3, p=0.02), and anesthesia (OR 3.1, CI 1.1-8.8, p=0.03). Lung collapse affected the right middle lobe in 22 dogs, left cranial lobe in 21 dogs, right cranial lobe in 18 dogs, left caudal lobe in 7 dogs, accessory lobe in 6 dogs, and right caudal lobe in 4 dogs. Lung collapse affected a single lobe in 21 (24%) dogs and multiple lobes in 19 (22%) dogs. In 58/68 (85%) affected lobes collapse was limited to the tip of the lobe, in 7 (1%) lobes it was bronchocentric, and in 3 (5%) lobes it was peripheral (figure 1).

There were no significant differences in median lung attenuation or occurrence of ground glass pattern, cysts, bronchial thickening, bronchial dilation, or degree of tracheal calcification between young and old dogs. Cysts were found in 6 (7%) dogs; these were solitary in 3 dogs and multiple (2-9) in 3 dogs, and the largest ranged in size from 2-11mm diameter (figure 2). No examples of reticular pattern, emphysema, pleural thickening or septal thickening were observed in any dog.

Discussion

In this study there were minimal observable differences between the lungs of young and old dogs. Heterotopic bone was more prevalent in old dogs, which agrees with previous observations.[3] Lung collapse was also observed more frequently in old dogs, although the underlying reason for this difference cannot be determined by the present study. For physiological reasons, the right middle lobe is most prone to collapse in the dog.[11] In the present study, collapse of the right middle lobe and the right and left cranial lobes occurred with similar frequencies. In the majority of dogs, lung collapse affected only the tip of the lobe. Reduced collateral ventilation because of subclinical disease, such as chronic bronchitis with excessive mucus production, is liable to exacerbate lung collapse.[12,13] The increased tendency for lung collapse in older dogs could reflect an increasing prevalence of subclinical lung disease over their lifetime. The observation that lung collapse was more frequent in dogs that had CT under general anesthesia than in dogs that were sedated could reflect the use of high inspired pO_2 for anesthesia, which has also been associated with a higher prevalence of lung collapse than when using moderate inspired pO_2 (‘medical air’).[14] It is uncertain why lung collapse was more frequent in larger dogs. It is known that intermittent positive pressure ventilation to minimize lung collapse is required more frequently in large dogs than small dogs or cats[15], and this may reflect the larger gravitational gradient that occurs within the lung of larger patients, as observed in anesthetized horses.[16]

There were no significant differences in median lung attenuation or occurrence of ground glass pattern, cysts, bronchial thickening, bronchial dilation, or degree of tracheal calcification between young and old dogs. These results are in contrast with those of a previous study in which the lungs of old dogs had radiographic signs including pleural thickening, increased linear markings, and increased opacity of the tracheal and bronchial walls.[3] Although the results of CT in one group of dogs cannot be compared directly with results of radiography in a different group of dogs, it seems likely that CT would have detected signs of pleural thickening, increased linear markings and increased opacity of the tracheal and bronchial walls had they been present. In fact, based on ability to directly measure lung attenuation using CT and other canine studies that found increased sensitivity of CT for lung lesions[17,18], CT might be expected to reveal more age-related changes than radiography. Therefore, the relative lack of CT signs in the present study could reflect a true difference in the condition of the lungs of the dogs used in these respective studies, possibly reflecting different genetic or environmental factors. If so, this could limit the generalizability of our results, which may not be applicable in other locations.

Attenuation measurements of tracheal rings were used in the present study as an indirect indicator of bronchial wall calcification. Tracheal rings were measured instead of bronchial walls because they are normally thicker than bronchial walls, hence any attenuation measurements will be less affected by partial volume artifact.

The process of aging occurs over a shorter period of time in dogs than in humans[1], and It is generally accepted that dogs of large and giant breeds age more rapidly than dogs of small or medium breeds. The smaller number of giant breed dogs in the aged group in the present study reflects this phenomenon. Non-contiguous age ranges were used in this study to ensure separation of young and aged dogs, which could intermingle if a heterogeneous sample of dogs were classified using a single calendar age threshold alone.

In this study, examination of the CT images included quantitative measurements and search for multiple possible lesions based on previous studies of CT signs in aged humans[5-9]; however, few examples were found of ground glass pattern, bronchial thickening or bronchial dilation, and no signs of reticular pattern, emphysema, pleural thickening or septal thickening were identified in any dog. Hence, finding any of these features in CT images of a dog with respiratory signs suggests the presence of non-age-related lung pathology that is clinically relevant.

Cysts were found in 6 (7%) dogs in this study. There is some overlap in use of the terms cyst and bulla, although in humans bulla is used for lesions greater than 1cm, and usually several cm in diameter.[10] Lung cysts (and bullae), which can be subclinical, should be distinguished from both congenital lobar emphysema[19,20] and superficial bullous emphysema, which is associated with non-traumatic (‘spontaneous’) pneumothorax.[21,22]

The main limitation of the present study was the lack of pathologic examination of lungs, which prevents histologic proof of the nature of lesions identified by CT, and allows the possibility that there were age-related lung changes that were undetected by CT. All CT studies reviewed in this study were obtained using settings suitable for clinical assessment of the lung of dogs, but more detailed assessment is possible using thinner (1mm) CT slices[23] or micro-CT[24] with histologic examination of precisely orientated lung sections. Further studies are indicated to better examine imaging-pathologic correlations in the aging canine lung. The number of dogs available for study was limited by the need to avoid including dogs likely to have had pathologic lung lesions. Use of a single observer to review the CT is also a limitation, but this is not considered to be a major problem because of the relatively homogenous nature of the study sample and use of comprehensive, pre-considered assessment criteria based on previous studies of humans.[5-9]

In conclusion, despite previous studies describing age-related changes in the radiographic appearance of the lungs of old dogs, it appears that there are minimal observable differences in CT images. Old dogs are more likely to have visible foci of heterotopic bone and may be more prone to lung lobe collapse than young dogs, but neither of these differences should contribute to misdiagnosis of pulmonary disease.

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Table 1. Characteristics of young and old dog groups

	Young dogs (n=42)	Old dogs (n=47)
Median (range) age (y)	3 (0.3-4.8)	11 (9.0-15.1)
Males/ females	28 (67%)/ 14 (33%)	31 (66%)/ 16 (34%)
Body weight range		
Small (<10kg)	10 (24%)	12 (25%)
Medium (10-25kg)	15 (36%)	20 (43%)
Large (26-40kg)	12 (28%)	13 (28%)
Giant (>40kg)	5 (12%)	2 (4%)
Diagnostic category		
Upper respiratory	19 (45%)	12 (25%)
Immune-mediated	11 (26%)	1 (2%)
Alimentary	4 (10%)	3 (6%)
Neurologic	4 (10%)	3 (6%)
Orthopedic	2 (5%)	0
Urinary	2 (5%)	2 (4%)
Benign neoplasm	0	17 (36%)
Oral conditions	0	6 (13%)
Endocrinopathy	0	3 (6%)
CT under anesthesia	12 (29%)	15 (32%)

Table 2. CT features of the lungs of young and old dogs

	Young dogs (n=42)	Old dogs (n=47)
Median (range) lung attenuation (HU)	-788 (-605 to -878)	-793 (-679 to -900)
Ground glass opacity	7 (17%)	8 (17%)
Cysts	1 (2%)	5 (10%)
Bronchial thickening	5 (12%)	5 (11%)
Median (range) bronchus: pulmonary artery ratio	0.66 (0.41-1.06)	0.63 (0.40-1.46)
Median (range) tracheal calcification (HU)	224 (65-577)	236 (107-512)
Heterotopic bone		
In one lobe	3 (7%)	6 (13%)
In multiple lobes	3 (7%)	23 (49%)
Pulmonary collapse		
None	29 (69%)	20 (43%)
One lung lobe affected	9 (21%)	12 (26%)
Multiple lobes affected	4 (10%)	15 (32%)

Legend

Figure 1. Examples of pulmonary collapse. A) Collapse of the ventral tip of the left cranial lobe (arrowhead); B) bronchocentric collapse (arrowhead) affecting the right cranial lobe; C) peripheral pulmonary collapse (arrowheads) affecting the lateral aspect of the left caudal lobe.

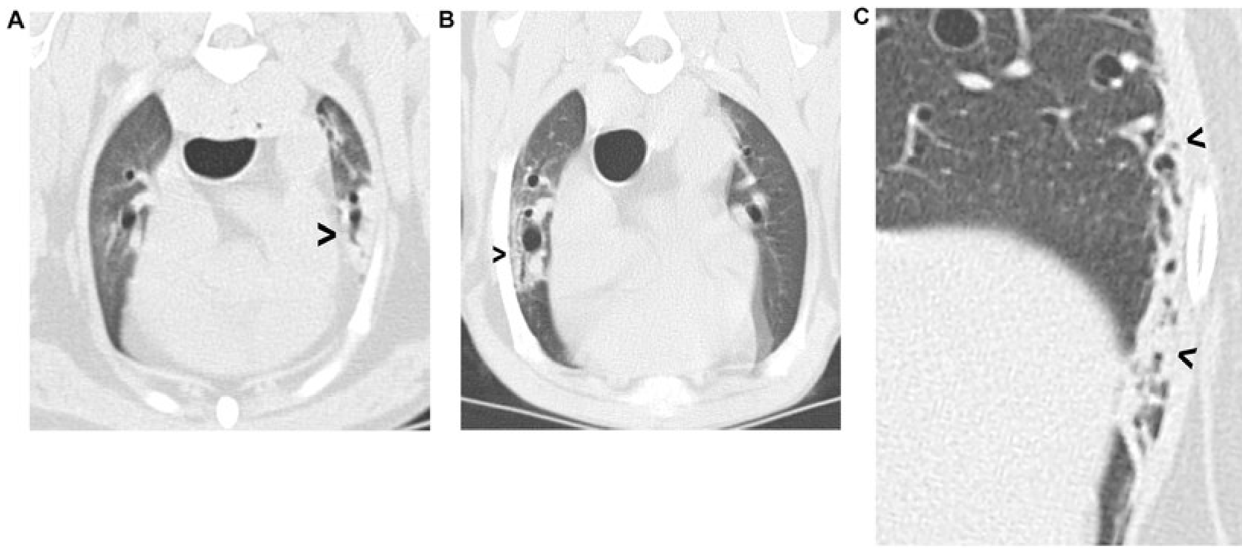

Figure 2. Examples of lung cysts. A) 10mm diameter cyst (arrowhead) in the left caudal lobe of a 1-year-old golden retriever that had CT as part of the work-up for nasal panniculitis. This was one of 3 pulmonary cysts in this dog; B) 8mm diameter cyst (arrowhead) in the right caudal lobe of a 14-year-old English springer spaniel that had CT as part of the work-up for hyperadrenocorticism.