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Quantitative CT Evaluation for Lung Volume and Density in Dogs

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Abstract : In this study, we analyzed the computed tomography (CT) measurements of lung volume and density in dogs with relation to body weight, age, sex, and breed. The multi-detector CT examination of the thorax was performed on dogs without respiratory or cardiovascular diseases. Three-dimensional reconstruction of CT images facilitated measurement of lung volume and density. There was a statistical significant correlation between body weight and lung volume ($p < 0.0001$). Lung density significantly decreased with an increase in body weight ($p = 0.0078$). However, no correlation was seen between these lung parameters and either sex or age of the dogs. In conclusion, this study shows that body weight is an important factor to consider when interpreting total lung volume and density values measured by quantitative CT. We highlight the need for further study using quantitative CT in identifying the potential effects of sex, age, and disease status on these parameters.

***Key words* :** lung density, lung volume, dogs, CT.

Introduction

Quantitative computed tomography (CT) is increasingly used in volumetric measurements of body organs such as the liver, kidneys, and prostate in both human and animals (10,12,20). Quantitative measurements have also been performed in humans with the normal respiratory system, and with the presence of pulmonary pathology such as emphysema, increased airway diameter and airway wall thickness, and expiratory air trapping (7,18,21). In human medicine, measurement of normal lung volume by quantitative CT is considered to be a useful method for evaluation of total lung capacity compared to pulmonary function testing (14). Many reports in the human medical literature showing correlation between CT measurements of normal lung volume and density, and age, sex, and body weight or length (7,6,15,23).

Quantitative CT evaluation of lung volume and density in dogs is feasible (3). However, the small sample size preclude the establishment of a normal value of canine lung volume and density. The purpose of this study was to measure the normal canine lung volume and density measurements obtained from multidetector CT images and evaluate the effect of age, sex, body weight, and breed on the lung factors.

Materials and Methods

Client-owned dogs that underwent CT examinations for reasons other than cardiorespiratory problems at the veterinary hospital of Chungnam National University between January 2012 and March 2013 were included in this study. Dogs were excluded in this study if they had any cardiopulmonary related clinical signs at the time of imaging study, abnormal CT findings associated cardiopulmonary system, and abnormalities causing a severe increase in abdominal pressure, such as extremely large abdominal masses or massive abdominal effusion. The study was approved by the Institutional Laboratory Animal Care and Use Committee of Chungnam National University.

All dogs were fasted for 24 hours before general anesthesia for the CT examinations. A 22G intravenous indwelling catheter was placed in a cephalic vein and anesthesia was induced with propofol ($\text{Anepol}_{\text{Inj}}^{®}$, Hana Pharm, Hwasung, Korea; 5-6 mg/kg, i.v.) and maintained with isoflurane (Ifran®, Hana Pharm, Hwasung, Korea; 1.5 MAC, inhalation). The entire thoracic cavity, from the level of the 6^{th} cervical vertebra to the 3^{rd} lumbar vertebra, was performed, with dogs in prone or sternal positions using multidetector CT (Asteion 4®, Tochigi, Toshiba, Japan). The CT examinations were performed with the following settings: X-ray tube voltage of 150 kV at a maximum of 120 mAs; gantry rotation time 0.75/sec; and, scan thickness 2 mm with beam collimation pitch of 1. In order to avoid motion artifacts from respiratory movements, positive pressure ventilation of 10-15 cmH_2O was used to temporarily maintain a state of breath-holding, allowing images to be obtained at peak inspiration.

The CT data acquired were reconstructed with 2-mm-thick slices at 0.16-mm intervals, using commercially available software (Rapidia®, Infinitt, Seoul, Korea). Only precontrast images were used in this study. Lung volume and density were measured from the 3D reconstruction of the lung (11). After the background was removed from the images using 3D growing, the trachea was also removed using the tolerance technique. Threshold limits of −200 to −1024 HU were applied to exclude the soft tissue surrounding the lung, and

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the large vessels within the lung from the reconstructions. Total lung volume (TLV) and mean lung density (MLD) for each dog were obtained from this automatic segmentation.

All data are expressed as means ± SD. Correlation of body weight to density and volume are represented by Pearson's correlation coefficient. Relationshipas between total lung volume and mean lung density and sex were analyzed using the *t*-test. Comparisons of body weights, total lung volume and mean lung density between different breeds were assessed by use of one way ANOVA. P values < 0.05 were considered significant. Statistical analysis was performed by commercial software (GraphPad Prism v6®; Graphpad Software, La Jolla, CA, USA).

Results

A total of forty six dogs were included and a summary of the breeds, age and sex is shown in Table 1. The most common breeds were Maltese (13), Shih-Tzu (11) and Toy Poodle (6). The age ranged from 0.4 to 15 years (mean, 8.7 years) while body weight ranged from 1.4 to 30 kg (mean, 6.9 kg). The age and body weight distribution of the dogs are presented (Fig 1).

The lung density and volume were −774.2 ± 43.5 HU (range, −873.3 to −656.9, median, −779.7 HU), and 545.4 ± 553.8 mL (range, 111.1-3325 mL, median, 408.4 ml), respectively. There was a significant positive relationship between body weight and lung volume ($p < 0.0001$, $R^2 = 0.86$) (Fig 2A). Mean lung density showed a weak, but significant negative correlation with body weight ($p = 0.005$, $R^2 = 0.17$) (Fig 2B), and with total lung volume ($p < 0.0001$, $R^2 = 0.31$) (Fig 3). No significant difference in mean lung density was observed between male and female dogs (Fig 4). Although there are significant differences in the body weight of Shih-Tzus (5.72 ± 1.26 kg) compared with Toy Poodles (4.00 ± 0.26 kg) and Maltese dogs (2.97 ± 1.07 kg) ($p < 0.0001$), there was no significant difference in total lung volume and lung density between these breeds (Fig 5). There was no significant relationship between age and lung volume or lung density.

Table 1. Summary of the breeds and sex of the dogs

Breeds	No. of Dogs	F	FS	M	MC
Bichon	1				1
Chihuahua	1		1		
CS	3		2		1
Jindo	1	1			
Maltese	13	5	1	4	3
Pomeranian	1	1			
Poodle	6	2	3		1
Schnauzer	4	1	1		2
ST	11	5	2	1	3
Husky	2	1	1		
Spitz	1	1			
YT	2		1		1
Total/Mean	46	17	12	5	12

MC; male castrated, FS; female spayed, CS; cocker spaniel, ST; Shih-Tzu, YT; Yorkshire terrier

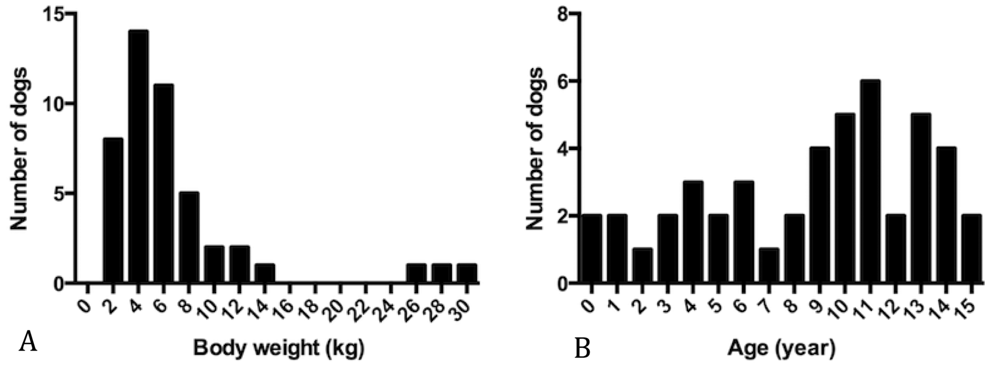

Fig 1. Bar graphs show frequency distribution of body weight (A) and age (B) of 46 dogs.

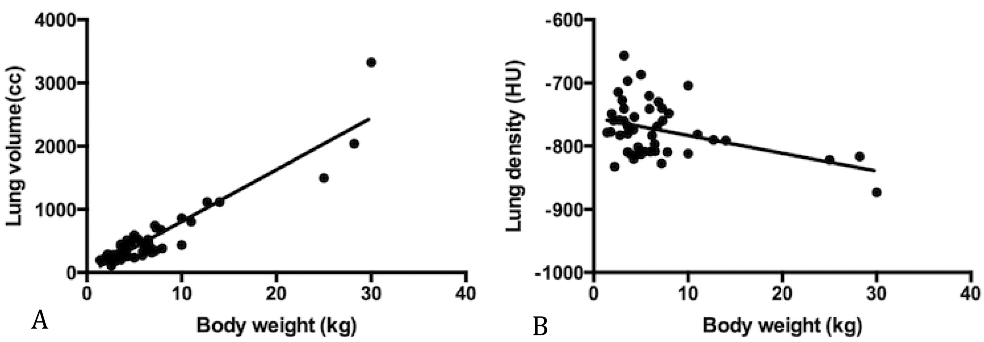

Fig 2. Relationship between body weight and total lung volume (A), and body weight and mean lung density (B) obtained on computed tomography (CT).

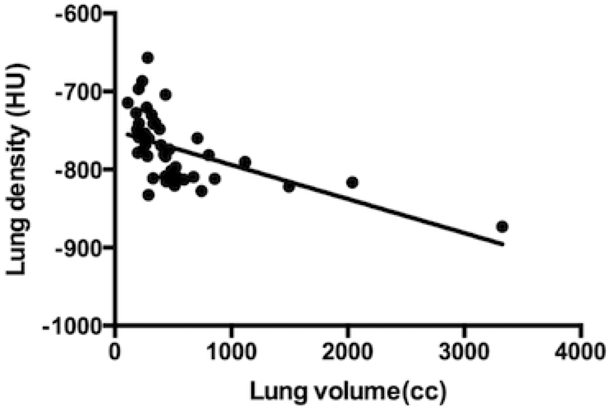

Fig 3. Scatter plot for relation between total lung volume and lung density. Mean lung density showed a negative correlation with total lung volume.

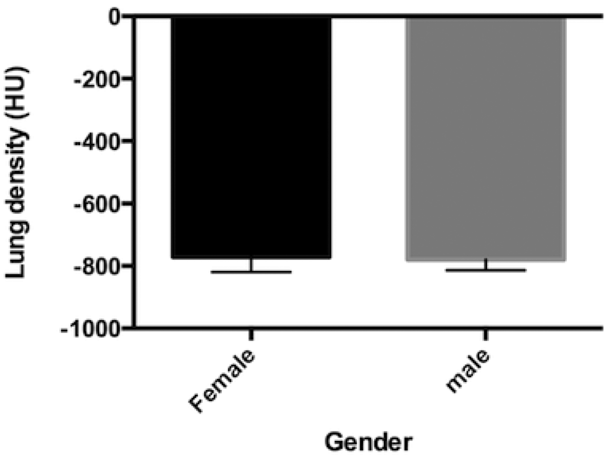

Fig 4. The comparisons of mean lung density between 29 female and 17 male dogs.

Discussion

In human medicine, numerous reports have described the use of quantitative CT examinations for measurement of lung densities and volume in both normal and various pulmonary disease conditions (5-7,9,11). In contrast, there is little published data about the application of this imaging modality to the measurement of lung parameters in animals. This study provides reference values for quantitative CT measurements of lung volume and density in dogs.

Lung density varies throughout the respiratory phase, and values may also differ depending on the type of computed tomography machines, and the patient positioning used during the procedure (3,11,13,23). Mean lung density at peak inspiration will be lower than during the expiratory phase (11). Regional differences in density also occur, for example, density is lower at the midportion of the lung lobe than at the perihilar or apical regions (16). A previous report showed that the lung density ranged from −698 to −760 HU at various lung portions in 11 beagles and 12 larger mongrel dogs under general anesthesia with spontaneous breathing. In a more recent study, the mean lung density measurements from 6 beagles maintained in full inspiration by breath-holding, was reported as −845 HU (16). The mean lung density of dogs in this present study was −774.0 ± 43.5 HU, and ranged from −873.3 to −656.9 HU (median −779.7). Our results were relatively lower than those of the former study (13), and higher than those presented in the latter (16). This discrepancy is likely to reflect the different methodologies employed in obtaining the measurements from the CT images. Whilst the other studies mentioned here used an ROI cursor with a fixed size in lung parenchyma (excluding the large vessels and airways) and lung density of older study was measured even in spontaneous breathing, we used the 3D growing method to measure mean density of whole lung by the thresholding technique (3) and also used breath-holding method to evaluate total lung capacity and to avoid respiratory motion.

As previously described, local lung densities are dependent on the region of the lung lobe, it is not surprising that the lowest lung density values are seen when mean lung density is measured at the midportion of the lung lobe when the perihilar region is not included, and when hyperinflation is induced by use of a positive pressure ventilation of 15 cm H_2O.

The same method used in this study has also been used in human medicine for measuring whole-lung mean density (6,23). In a study of 42 nonsmokers (6), the mean lung density during the inspiratory phase was −866.4 ± 15.5 HU. In another study of 92 nonsmokers, the mean lung density was measured as −846 ± 22 HU (23). These results in humans are lower than ours. Work from the seventies that looked at pulmonary arterial blood volume and tissue volume in humans and dogs showed that the human lung is generally less dense than the dog lung because lung volume is proportionally much larger than the tissue volume (17). Although the cause of the structural difference between human and canine lungs remains unclear, comparison of our results with recently published human data is consistent with these early findings.

Our results demonstrate a significant and strong positive

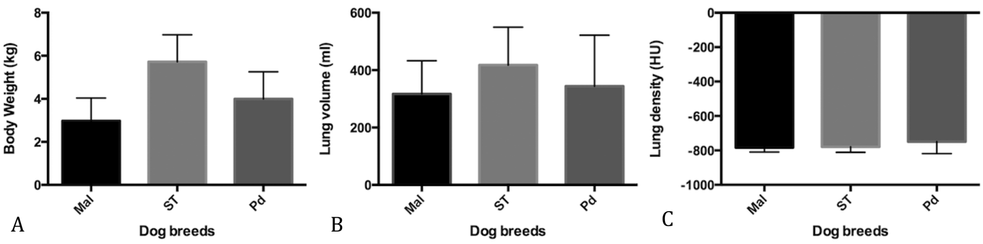

Fig 5. Bar graph showing the difference of body weights (A), total lung volume (B), and mean lung density (C) of Maltese (Mal), shih-tzu (ST), and poodle (Pd) dogs.

correlation between lung volume and body weight, similar to findings in humans (5). In dogs, interbreed variation resulted in marked differences in body weight. Therefore, any apparently interbreed differences in mean lung density, might actually relate more to the size of the dog than the breed. However, in contrast to the lung volume, in this study, mean lung density had a weak negative correlation with body weight. We could not find the significant difference of lung volume and density between three different breed dogs, although there was a significant difference between Shih-tzu dogs and Maltese or Toy Poodle dogs. It was thought that the difference of body weights between those breed dogs were not big enough to result in the difference of lung volume, because they are all small breeds. However, a previous study comparing Maltese with Pekingnese showed the significant difference of lung volume between two breeds (3).

A negative linear relationship was observed between lung volume and mean lung density of the dogs in this study. The previous human study evaluating lung densitometry also gave similar results; the larger the volume of the lung, the lower the mean lung density (6). It was suggested that the relative amount of lung tissue per unit of volume is lower in larger lungs than in smaller lungs. The recent research evaluating of respiratory system compliance and resistance in healthy dogs under general anesthesia described that body weight was linearly related to compliance of the respiratory system while resistance of respiratory system has an inverse linear relationship with body weight in dogs (2). On the other hand, as body weight increases, so do lung volume, individual alveolar volume and total compliance of the respiratory system. It is suggested that this is due to the lower pressure required to expand larger diameter alveoli with a greater compliance (2). It was also reported that their compliance values obtained from the dogs were lower than values reported in people because of the difference in size and therefore lung volume between the two species. These results also could explain the reason why our results showed not only the linear relationship between lung volume and body weight and the reverse relationship between lung volume and density but also higher mean lung density compared to humans.

Whilst one report showed that mean lung density did not differ significantly between men and women (6), another study showed that total lung volume is significantly higher, and mean lung density significantly lower in men compared with women (23). Differences in environmental exposure have also been considered as a possible cause of lung parameter differences between the sexes, as males are more likely to be exposed to airborne agents in their work (7). Whilst our study showed no difference in mean lung density between male and female dogs, it is important to note that previous findings have shown that in contrast to humans, sex differences in body weight are relatively small in dogs.

In this study, changes in mean lung density with increasing age were not observed. In human medicine, several studies have reported that lung attenuation decreases with age (7,19). However, the other study performed in adults aged over 40 years described a lack of change in lung attenuation values with increasing age, which is similar to our findings (23). Several studies in infants and young children have suggested that after the age of 2 years, progressive alveolar expansion occurs with increasing lung volume (5). Similar results have been described in animal studies, which have shown, for example, that 30-day old rats had significantly higher lung densities than 800-day old rats (13). Although no significant age-related differences in lung parameters were shown in our study, these dogs were all adults except four were less than 1year-old. The potential effect of age on lung parameters measured with quantitative CT cannot be ruled out and should be investigated in subsequent studies on bigger population of young adult dogs and puppies.

The CT measurements of lung volume and density have been used for clinical practice in human medicine. For example, the quantitative CT for lung volume and density has been used as a significant parameter to evaluate lung function after lung volume reduction surgery for emphysema as well as the severity of chronic obstructive pulmonary disease (1,7,15,21,22). The analyses of lung volume and density with quantitative CT may be used for the diagnosis of pulmonary fibrosis, post-lobectomy evaluation, and chronic obstructive pulmonary diseases in veterinary medicine. In fact, the quantitative CT values of the lung lobes were measured in case studies describing CT findings in twelve West highland white terriers with idiopathic pulmonary fibrosis (8), and in a Golden Retriever with pulmonary alveolar proteinosis (4), although their measuring methods were not exactly the same with this study. Based on the results of those study, the CT values were significantly higher in idiopathic pulmonary fibrosis compared with control dogs and the dog with pulmonary proteinosis had also severely increased CT values.

Our study has several limitations. The age distribution in this study was not even because CT examinations were usually performed in the dogs with geriatric diseases like intervertebral disk diseases, tumors, metastasis check and so on. In addition, the number of large breed dogs was minimal because of their small population in South Korea. The lack of comparative information to gold standards for lung volume and function remains as an important limitation in this study.

In conclusion, this study demonstrates that the effects of the sex, age, and body weight on total lung volume and density should be taken into consideration when evaluating quantitative CT thoracic images in dogs. Studies including more various breeds of dogs, dogs of different ages, and dogs with the various respiratory diseases, are needed to further explore the degree of variation seen in lung parameters measured with quantitative CT.

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개에서 정량적 컴퓨터단층촬영을 이용한 폐용적과 폐밀도의 평가

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요 약 : 컴퓨터단층촬영을 이용하여 개에서 폐용적과 폐밀도를 측정하였으며, 체중, 나이, 성별 및 품종에 따라 분석하였다. 데이터 수집을 위해 호흡기 질환이나 심혈관계질환이 없는 개에서 수행된 흉부 컴퓨터단층촬영 영상이 사용되었으며, 전체 폐용적과 밀도의 측정을 위해 컴퓨터단층촬영 영상의 재구성 기법을 이용하였다. 폐용적은 체중이 증가할 수록 통계적으로 유의적인 증가를 보였다($p < 0.0001$). 폐밀도는 체중이 증가함에 따라 유의적으로 감소하였다($p = 0.0078$). 그러나, 폐용적과 밀도는 성별 또는 연령과 상관 관계를 보이지 않았다. 따라서, 정량적 컴퓨터단층촬영 검사로 전체 폐용적이나 폐밀도를 평가할 때 체중으로 인한 효과가 고려되어야 한다.

주요어 : 폐밀도, 폐용적, 개, 컴퓨터단층촬영