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Assessment of Aging Effects on Computed Tomographic Glomerular Filtration Rate in Dogs

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Abstract : The purpose of this study is to assess the relationship between glomerular filtration rate (GFR) and age by using dynamic computed tomography (CT) and Patlak plot analysis in dogs. Fifteen dogs were used in this study. CT-GFR study was performed under general anesthesia using propofol and isoflurane. 1 ml/kg dosage of 300 mgI/ml iohexol was administered at a rate of 3 ml/s during GFR measurement. CT-GFR was determined with a single-slice dynamic acquisition and Patlak plot analysis. The individual and global GFR values were calculated to plasma clearance per body weight (ml/min/kg). Bodyweight (mean ± SD) ranged from 2.0 to 5.7 kg (3.31 ± 1.13 kg). Age ranged from 3 years to 13 years old (7.14 ± 3.30). Mean ± SD creatinine (0.53 ± 0.34 mg/dl), phosphorus (4.1 ± 1.2 mg/dL), and albumin (3.3 ± 0.3 mg/dL) concentrations and urine protein-to-creatinine ratios (all ratios were < 0.5) were within reference ranges. Abdominal ultrasonography revealed small-sized renal calculi, mineralization, or renal cyst at eight dogs. The global CT-GFR ranges shown in this study was 2.57 to 6.60 ml/min/kg. In this study, there was no trend toward weight-adjusted CT-GFR with increasing age. We found no relationships between age-related kidney dysfunction in fifteen dogs. Small-sized renal calculi or cysts did not affect renal function in this study. However, it is thought that a large sample size may have been required to document an age effect.

***Key words* :** glomerular filtration rate, aging effect, dynamic computed tomography, Patlak plot analysis, dog.

Introduction

The best measure of renal function is the glomerular filtration rate (GFR). The decline in GFR that occurs with aging has been a source of considerable controversy in human. Therefore, studies on age-related changes of the kidney are of increasing interest in human medicine. However, few data on the influence of age on canine renal function have been published. According to the study of Laroute et al., GFR was higher in puppies than in 6 to 9-year-old dogs (8). In recent another study, there was no trend toward lower estimated GFR/kg with increasing age, however, GFR decreased with age in dogs in the smallest weight quartile only (2). A previous study examining renal function associated with aging effect was plasma clearance of iohexol and *p*-aminohippuric acid (2,8). The purpose of the study was to examine the effects of age on the rate of change in GFR using dynamic renal CT and Patlak plot analysis.

Materials and Methods

Animals

Fifteen client-owned dogs of nine different small breeds with age from 3 to 13 years were used. There were four Shih Tzu dogs, three Maltese dogs, two Miniature Poodles, a Schnauzer, a Japanese Chin, a Yorkshire terrier, a Spitz, a Mongrel dog. Thirteen female and two male dogs were involved in this study. The dogs were fasted overnight at home prior to the CT-GFR study, but they were given water *ad libitum*. All dogs were evaluated as healthy on the basis of results of physical examination, CBC (ABX Micros ABC Vet, HORIBA ABX, Cedex, France), serum biochemical analyses (Vetscan Abaxis Inc, Calif, USA), urinalyses, and a heartworm antigen test (Canine Heartworm Antigen Test Kit®, IDEXX Laboratory, Westbrook, USA). In all dogs, diagnostic radiographic examinations including radiography of the abdomen and thorax, ultrasonography of the abdomen, and echocardiography, were performed to rule out abnormalities of the kidneys. This study was approved by the Institute of Laboratory Animal Resources at Chungnam National University.

Anesthesia

A CBC was performed to determine the hematocrit before anesthesia. No premedications were given before induction of anesthesia. Anesthesia was induced by administration of propofol (6 mg/kg, IV) and was maintained by administration of isoflurane in oxygen. Heart and respiratory rates, blood carbon dioxide concentration, pulse oximetry and indirect blood

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pressure were continuously monitored during anesthesia.

CT-based glomerular filtration rate (CT-GFR)

Dogs were placed in dorsal recumbency on a CT table, and an automated CT power injector was connected to the catheter in the cephalic vein. Computed tomography was performed by use of a single-slice CT scanner (GE CT single-detector CT scanner, General Electric Medical System, Yokogawa, Japan). General renal CT protocols included 3 steps; baseline precontrast imaging, single-slice dynamic imaging, and postcontrast volume scan. To minimize motion artifacts, obtain optimal image quality, and achieve optimal results, all scans were performed following hyperventilation. Initial precontrast and postcontrast volume scan of both kidneys and the abdominal aorta were performed by use of helical mode, 120 kVp, 100 mA, 3-5 mm slice thickness, a pitch of 1.0. The matrix size was 512 * 512 with a display field of view of 25 cm. In the precontrast imaging, the exact location of each kidney was identified and the region for the dynamic scan was determined. Single-slice dynamic CT was performed at 1 region with 5 to 10-mm thick slices of the both renal hili at 1.5-second intervals for 2 minutes. A 1 ml/kg dosage of a 300 mg/ml solution of iohexol was administered at 3 ml/s via the automated power injector and related software.

Measurement of CT-GFR

The CT-GFR for both kidneys was estimated by the use of Patlak plot analysis (10,12,13). For CT-GFR calculation, the aortic and renal parenchymal attenuation curves and the HU values of the ROIs were required. A circular aortic ROI (Fig 1) was located inside the aortic lumen at the level of the renal hilus by use of the manufacturer's CT functional software. The average HU value within the aortic ROI before administration of contrast media was subtracted from each HU value after administration of contrast media, which thus provided a corrected aorta HU value. In the same way, ROIs were manually drawn around the left and right kidneys (Fig 1). The borders of the ROIs were drawn as close to the periphery of the renal parenchyma as possible, excluding main vessels and fatty tissue. A main feature of Patlak plot analysis is that the amount of contrast medium in the renal tissue is proportional

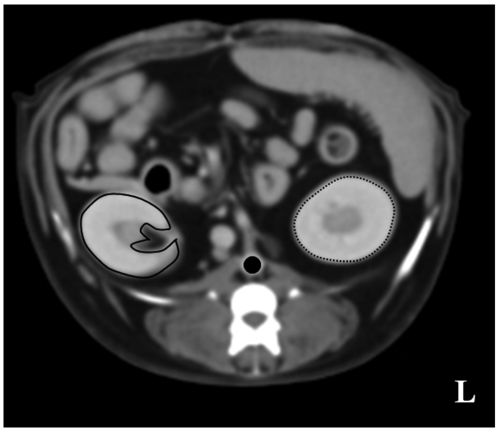

Fig 1. Single-slice dynamic CT image centered at the bilateral renal hili obtained from a dog during the parenchymal phase after injection of iohexol. The black line indicates the ROI of the right kidney, the dotted line indicates the ROI of the left kidney, and the black circle indicates the ROI of the aorta. L = Left.

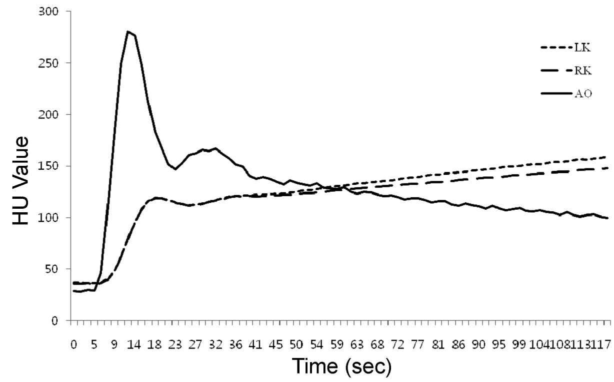

Fig 2. Graph of the time-attenuation curves that depict the iohexol concentration in the aorta and both kidneys in a dog.

to the integrated concentration of the contrast medium in the aorta (6,9,12). For Patlak plot analysis, we used an in-house program based on a programming language for data analysis and development software (Interactive Data Language, version 6.4, ITT Visual Information Solutions, Boulder, Colo, USA) and the time-attenuation curves of the aorta and kid-

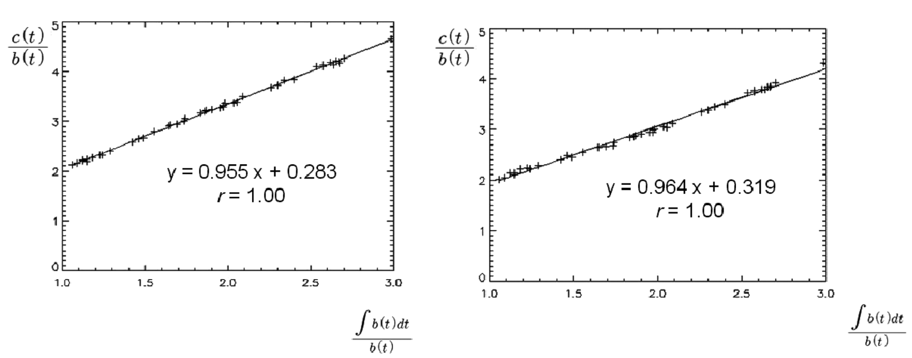

Fig 3. Patlak plot of the right kidney (A) and left kidney (B) in a dog. The slope of each line represents whole blood clearance in ml iodine/min x ml renal tissue. The y-intercept represents fractional vascular volume.

ney (Fig 2). The slope of the Patlak plot (Fig 3) for each kidney represents whole blood clearance of iodinated contrast medium per milliliter of renal tissue. The slope was corrected for pre-anesthesia hematocrit (HCT; multiplied by (1-HCT)) to obtain plasma clearance, then multiplied by renal volume and divided by the animal's weight to obtain CT-GFR in units of ml/min/kg (1,11).

Statistical analysis

Results are presented as mean ± SD. Comparison of CT-GFR values associated with aging effect was performed using a correlation analysis of statistical software (SPSS, version 17.0, SPSS Inc, Chicago, Ill, USA). A P values lower than 0.05 was considered significant.

Results

Bodyweight (mean ± SD) ranged from 2.0 kg to 5.7 kg (3.31 ± 1.13 kg). Age ranged from 3 years old to 13 years old (7.14 ± 3.30). Mean ± SD creatinine (0.53 ± 0.34 mg/dl), phosphorus (4.1 ± 1.2 mg/dL), and albumin (3.3 ± 0.3 mg/dL) concentrations and urine protein-to-creatinine ratios (all ratios were < 0.5) were within reference ranges. All electrolyte values were within the normal reference ranges. Mean urine specific gravity was 1.039 ± 0.001. There were no abnormal findings for thoracic and abdominal radiographic examinations and echocardiographic examination. However, 4 dogs older than 10 years old in all 15 dogs had very small-sized renal calculi or cysts on abdominal ultrasonographic examination. Renal calculi or cysts did not include in the CT-GFR evaluation by excluding renal calculi at region of interest and subtracting the cyst volume from total renal volume. The global CT-GFR ranges shown in this study were 2.57 to 6.60 ml/min/kg (Table 1). There was no trend toward weight-adjusted CT-GFR with increasing age. We found no relationships between age-related kidney dysfunction in fifteen dogs (Fig 4, $P = 0.58$).

Table 1. Glomerular filtration rate assessed by dynamic renal CT and Patlak plot analysis in 15 dogs

No.	Breed	Age (Y)	Global GFR	R-GFR	L-GFR
1	Poodle	3	5.358	1.782	3.575
2	Maltese	3	6.344	3.204	3.140
3	Schnauzer	5	6.600	3.863	2.737
4	Mix	3	4.346	2.009	2.338
5	Shihtzu	5	2.593	1.460	1.133
6	Poodle	11	2.700	1.219	1.481
7	YT	13	4.064	2.093	1.972
8	Maltese	7	6.115	3.328	2.787
9	Spitz	8	5.906	2.984	2.921
10	Maltese	11	6.462	3.453	3.010
11	Shihtzu	11	4.848	2.562	2.286
12	Shihtzu	7	4.250	2.143	2.107
13	Japanese chin	6	5.451	3.119	2.332
14	Pomeranian	7	2.569	1.274	1.295
15	Shihtzu	6	2.819	1.903	0.906

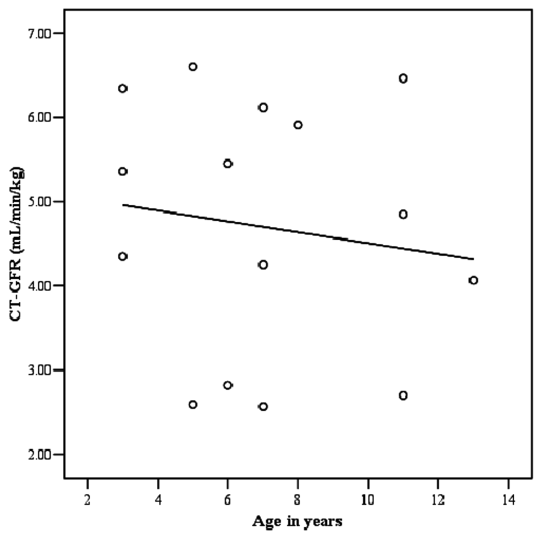

Fig 4. Relationship between estimated glomerular filtration rate (GFR)/kg body weight and age in 15 healthy dogs ($r^2 = 0.019$).

Discussion

A single-slice dynamic renal CT technique using Patlak analysis applied in present study is the alternative method to assess simultaneously renal morphology and GFR in veterinary medicine (3,11). The estimated GFR values observed in our study displayed a wide reference range, 2.57 to 6.60 ml/min/kg in various small breeds and ages. Recent published data also showed a similar reference range, 1.85 to 6.07 ml/min/kg in clinically healthy Beagle adult dogs (3). Our results demonstrate that there are no statistical significances in correlation between GFR and ages. However, there are some limitations in our study. First, the relatively small number of dogs was used depending on the anticipation of only client-owned volunteer dogs for one year. Especially, it was more difficult to evaluate renal function of geriatric dogs due to a lower anticipation compared to young adult dogs in this study. Secondly, 4 dogs older than 10 years old had abnormal findings such as very small-sized renal calculi or cysts (less than 5 mm) on abdominal ultrasonographic examination. We excluded these lesions on selecting the slice location to measure GFR. In dogs with renal cysts, renal parenchymal volumes were estimated by subtracting the renal cyst volume from the total kidney volumes, however, the size of renal cysts was too small to affect the corrected total kidney volume. According to previously reported study, the presence of simple renal cyst or characteristics of cyst was also not related to the decreased GFR (4).

In human medicine, morphological changes are noted in the human glomerulus with aging and there is an associated decrease in GFR (7). These changes include loss of cortical and interstitial volume, global glomerulosclerosis, glomerular involution and disappearance, and loss of filtration surface area (5,7). Estimated GFR in healthy humans over the age of 60 years is 20-30% lower than corresponding GFR in individuals under the age of 50 years (7). It is difficult to observe similar age-related changes in older dogs except for dogs with chronic kidney diseases. It is speculated that decreases in estimated GFR may not occur to the same extent because of the shorter life span of dogs compared with humans, despite similar histopathological changes (2). The effect on age-related kidney functions was also not apparent in the present study. However, research using CT-GFR method is needed to further validate age-related kidney function through a large sample of patients with various ages.

Acknowledgement

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References

1. Alexander K, Del Castillo JR, Ybarra N, Morin V, Gauvin D, Authier S, Vinay P, Troncy E. Single-slice dynamic computed tomographic determination of glomerular filtration rate by use of Patlak plot analysis in anesthetized pigs. Am J Vet Res 2007; 68: 297-304.
2. Bexfield NH, Heiene R, Gerristen RJ, Risøen U, Eliassen KA, Herrtage ME, Michell AR. Glomerular filtration rate estimated by 3-sample plasma clearance of iohexol in 118 healthy dogs. J Vet Intern Med 2008; 22: 66-73.
3. Chang J, Kim S, Jung J, Lee H, Choi H, Chang D, Lee Y, Yoon J, Choi M. Assessment of glomerular filtration with dynamic computed tomography in normal Beagle dogs. J Vet Sci 2011; 12: 393-399.
4. Chin HJ, Ro H, Lee HJ, Na KY, Chae D-W. The clinical significances of simple renal cyst: Is it related to hypertension or renal dysfunction? Kideny Int 2006; 70: 1468-1473.
5. Darmady EM, Offer J, Woodhouse MA. The parameters of the aging kidney. J Pathol 1973; 109: 195-207.
6. Dawson P. Functional imaging in CT. Eur J Radiol 2006; 60: 331-340.
7. Hoang K, Tan JC, Derby G, Blouch KL, Masek M, Ma I, Lemley KV, Myers BD. Determinants of glomerular hypofiltration in aging humans. Kidney Int 2003; 64: 1417-1424.
8. Laroute V, Chetboul V, Roche L, Maurey C, Costes G, Pouchelon JL, De La Farge F, Bpisspif M, Lefebvre HP. Quantitative evaluation of renal function in healthy Beagle puppies and mature dogs. Res Vet Sci 2005; 79: 161-167.
9. Mankoff DA, Shields AF, Graham MM, Link JM, Krohn KA. A graphical analysis method to estimate blood-to-tissue transfer for tracers with labeled metabolites. J Nucl Med 1996; 37: 2049-2057.
10. Miles KA, Leggett DA, Bennett GA. CT derived Patlak images of the human kidney. Br J Radiol 1999; 72: 153-158.
11. O'Dell-Anderson KJ, Twardock R, Grimm JB, Grimm KA, Constable PD. Determination of glomerular filtration rate in dogs using contrast-enhanced computed tomography. Vet Radiol Ultrasound 2006; 47: 127-135.
12. Patlak CS, Blasberg RG, Fenstermacher JD. Graphical evaluation of blood-to-brain transfer constants from multiple-time uptake data. J Cereb Blood Flow Metab 1983; 3: 1-7.
13. Tsushima Y, Blomley MJ, Kusano S, Endo K. Use of contrast-enhanced computed tomography to measure clearance per unit volume: a novel measurement of renal function and fractional vascular volume. Am J Kidney Dis 1999; 33: 754-760.

개에서 연령에 따른 동적 컴퓨터단층촬영을 이용한 사구체여과율의 평가

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요 약 : 동적 컴퓨터단층촬영을 이용하여 연령에 따른 CT-GFR 수치에 대한 패턴을 살펴보기 위해 본 연구를 실시하였다. 품종이나 성별에 대한 제한 없이 다양한 연령으로 15마리의 개를 이용하였다. 혈액검사, 요검사, 영상학적 검사를 실시하여 개의 건강 상태를 확인한 후, propofol-isoflurane을 이용한 호흡마취를 실시하여 CT 촬영을 하였다. Iohexol (1 ml/kg, 300 mgI/ml)을 3 ml/s 일정한 속도로 2분간 주입하면서 1.5초 간격으로 총 80개의 영상을 촬영하여 파트락 분석을 통해 사구체여과율 (ml/min/kg)을 측정하였다. 양측 신장의 사구체여과율의 범위는 2.57-6.60 ml/min/kg이었다. 본 연구에서 연령에 따라 사구체여과율의 유의적인 차이는 확인되지 않았다.

주요어 : 사구체여과율, 연령, 동적컴퓨터단층촬영, 파트락 분석, 개