pISSN 1229-845X, eISSN 1976-555X
J. Vet. Sci. (2011), **12**(4), 393-399
http://dx.doi.org/10.4142/jvs.2011.12.4.393
Received: 30 Jun. 2010, Revised: 14 Mar. 2011, Accepted: 11 Jun. 2011

JOURNAL OF
Veterinary Science

Original Article

Assessment of glomerular filtration rate with dynamic computed tomography in normal Beagle dogs

Jinhwa Chang[1], Sujin Kim[2], Joohyun Jung[1], Heechun Lee[3], Hojung Choi[5], Dongwoo Chang[4], Youngwon Lee[5], Junghee Yoon[1], Mincheol Choi[1,*]

[1]*Department of Medical Imaging, College of Veterinary Medicine, and Research Institute for Veterinary Science, Seoul National University, Seoul 151-742, Korea*
[2]*Department of Nuclear Medicine, College of Medicine and Institute of Radiation Medicine, Medical Research Center, Seoul National University, Seoul 110-460, Korea*
[3]*Department of Medical Imaging, College of Veterinary Medicine, Gyeongsang National University, Jinju 600-701, Korea*
[4]*Department of Medical Imaging, College of Veterinary Medicine, Chungbuk National University, Cheongju 361-763, Korea*
[5]*Department of Diagnostic Imaging, College of Veterinary Medicine, Chungnam National University, Daejeon 305-764, Korea*

The objective of our study was to determine individual and global glomerular filtration rates (GFRs) using dynamic renal computed tomography (CT) in Beagle dogs. Twenty-four healthy Beagle dogs were included in the experiment. Anesthesia was induced in all dogs by using propofol and isoflurane prior to CT examination. A single slice of the kidney was sequentially scanned after a bolus intravenous injection of contrast material (iohexol, 1 mL/kg, 300 mgI/mL). Time attenuation curves were created and contrast clearance per unit volume was calculated using a Patlak plot analysis. The CT-GFR was then determined based on the conversion of contrast clearance per unit volume to contrast clearance per body weight. At the renal hilum, CT-GFR values per unit renal volume (mL/min/mL) of the right and left kidneys were 0.69 ± 0.04 and 0.57 ± 0.05, respectively. No significant differences were found between the weight-adjusted CT-GFRs in either kidney at the same renal hilum (p = 0.747). The average global GFR was 4.21 ± 0.25 mL/min/kg and the whole kidney GFR was 33.43 ± 9.20 mL/min. CT-GFR techniques could be a practical way to separately measure GFR in each kidney for clinical and research purposes.

Keywords: computed tomography, dog, glomerular filtration rate

*Corresponding author
Tel: +82-2-880-1278; Fax: +82-2-880-8662
E-mail: mcchoi@snu.ac.kr

Introduction

The glomerular filtration rate (GFR) is an important indicator of renal function, monitoring progression of kidney disease, and the best way to determine an early diagnosis of subclinical renal function [33]. When there is a need to accurately determine GFR, such as when planning chemotherapy strategies with nephrotoxic agents or staging chronic renal disease in preparation for renal replacement, it may be necessary to use direct and accurate methods to measure GFR [19]. In current practice, there has been a general shift from purely anatomical imaging to a combined structural and functional approach. For example, functional computed tomography (CT) imaging of a main organ through dynamic CT scans using contrast media has been reported [8,28]. Other reports have indicated that GFR can be evaluated through advances in CT technology and application of a specific kinetic model [7,8,24]. In addition, GFR is determined by measuring the plasma clearance of a GFR marker that may be an endogenous metabolic product (*e.g.* urea or creatinine) or an exogenously administered substance [3,27]. Inulin, a 5.2 kDa polymer of fructose, is regarded as a gold standard substance for GFR determination [23]. However, inulin-based determination is a time-consuming chemical analysis and clinical availability may be limited [11]. Since the advent of using inulin for measuring GFR, new methods have been studied. There is an increasing interest in the use of iodinated contrast medium, such as iohexol, as a new alternative marker for estimating GFR in humans and animals [1,3,20].

Recently, it has been possible to simply and rapidly

measure GFR using dynamic CT with a Patlak plot analysis in human and veterinary medicine [1,8,20,28]. Blood clearance per unit renal volume is generally about 0.4～0.7 mL/min/mL in humans [9,28]. CT-GFR studies have been used to evaluate various diseases affecting renal function [29,30]. However, there are few published reports on the use of CT-GFR in normal dogs including the use of dynamic CT with a Patlak plot to measure CT-GFR in normal dogs and pigs [1,20]. There is also a lack of published reference data on CT-GFR values measured by functional CT in dogs. The purpose of this study was therefore to determine individual and global CT-GFR. We suggest the use of a CT-GFR technique combined triphasic renal imaging by presenting physiologic parameters obtained through aortic and renal time attenuation curves in clinically healthy Beagles.

Materials and Methods

Experimental animals

The procedures performed in the present study were approved by the Institute of Laboratory Animal Resources (ILAR) at Seoul National University, Korea. Sixteen intact male and 8 intact female Beagles 1- to 4-years-old (average age, 1.96 ± 1.00 years) and weighing 5.5 to 11.7 kg (average weight, 8.06 ± 1.53 kg) were used for the study. The dogs were housed individually in ILAR-approved facilities, fed a commercial diet (Jerony; Che-il Jedang, Korea) twice a day, and given water *ad libitum*.

All dogs were determined to be clinically normal based on physical examination, complete blood counts (CBCs), biochemical and urinalysis profiles, and heartworm antigen test results (Snap; IDEXX Laboratories, USA). Serum biochemical analyses, including ones that measured sodium, potassium, chloride, calcium, phosphorus, total protein, creatine kinase, blood urea nitrogen (BUN), creatinine, albumin, glucose, alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, gamma-glutamyl transpeptidase, amylase, and cholesterol, were performed. Using an ultrasound-guided technique, urine was collected from all dogs for urinalysis which included specific gravity measurement by a refractometer (Reichert Vet 360; Reichert, USA), routine dipstick tests (Combostick; YD Diagnostics, Korea), and sediment and cytologic examinations. General diagnostic imaging techniques using thoracic and abdominal radiography, abdominal ultrasonographic, and echocardiographic examinations were performed on all dogs.

Animal preparation and anesthesia

The animals were fasted for approximately 12 h before anesthesia. CBC was performed to determine hematocrit (HCT) levels before anesthesia. Twenty-two-gauge IV catheters (Becton-Dickinson Korea, Korea) were placed in the bilateral cephalic veins for propofol (Provive; Myungmoon Pharm, Korea) and iohexol (Omnipaque; GE Healthcare, USA) administration. No other medications were given before anesthesia induction. After inducing anesthesia with propofol (6 mg/kg, IV administration), the trachea was intubated. Anesthesia was maintained with isoflurane (Forane; Choongwae Pharm, Korea) and oxygen. The oxygen flow rate was 1 L/min, and a 1.5 to 2.0 minimum alveolar concentration of isoflurane was maintained during the CT-GFR study. Heart rate, respiratory rate, and carbon dioxide levels were monitored continuously during anesthesia. Blood pressure was measured directly or indirectly; arterial pressure was directly measured at the dorsal pedal artery or femoral artery. Indirect systolic arterial pressure was determined using a Doppler-based technique (Vet-Dop Doppler; Vmed Technology, USA). Total time spent for CT-GFR assessment was approximately 30 min from the induction of anesthesia until the conclusion of the postcontrast helical scan. The CT-GFR study was performed during a single-slice dynamic scan for 2 min after 15 to 20 min following isoflurane-induced anesthesia.

CT examination

The dogs were placed in a dorsal recumbent position on the CT table, and a CT power injector (LF CT 9000 ADV; Liebel-Flarsheim, USA) was connected to a cephalic venous cannula to control the injection rate of the contrast medium, iohexol. CT was performed with a GE CT/e (General Electric Medical System, Japan), a single-detector CT scanner. The image acquisition parameters included a helical acquisition and matrix of 512 × 512, and a 25 cm display field of view.

The general renal CT protocols included three steps: baseline precontrast imaging, single-slice dynamic imaging, and postcontrast imaging. To minimize motion artifacts, obtain excellent image quality, and achieve optimal results, all scans were performed following hyperventilation to induce apnea. Initial precontrast examination of both kidneys and the abdominal aorta was performed using a helical mode with 120 kVp, 50 mA, a 3 mm slice thickness, and a 1.3 pitch. Using this procedure, the exact location of the entire kidney was identified and the region for the dynamic scan was determined. Single-slice dynamic CT was concurrently initiated with the beginning of contrast medium injection by using an automated power-injector and related software; iohexol (300 mgI/mL) was also administered at a low dosage of 300 mg/kg at the rate of 3 mL/sec. Dynamic CT was performed in one region (1 mm slice thickness) of the renal hilum of the kidney every 1.5 sec for 2 min. Following dynamic CT acquisition, both kidneys were again scanned entirely to calculate the renal volume using the same scan parameters as the initial unenhanced CT scan.

CT-GFR with a Patlak plot analysis

The Patlak plot analysis is a popular tool for estimating blood-to-tissue transfer constants from multiple time uptake data [18].

The basic concept of the Patlak plot is that the amount of contrast media in the nephron is proportional to the integrated concentration of the contrast media in the aorta during the 2 min dynamic CT scan after contrast media administration [8,28]. Q(t) is the contrast mass at time (t) in the circulation, b(t) is the blood concentration at time (t), and α represents the GFR. The mass transferred out of the blood into the renal tubules by time (t) will therefore be $Q(t) = \alpha \int_0^t b(t)dt$. If this formula is divided by V, the volume of the region of interest (ROI) under consideration, we obtain $\frac{Q(t)}{V} = \frac{\alpha}{V}\int_0^t b(t)dt$. This represents the concentration at any time (t) relative to the total concentration in the ROI filtered contrast. For example, C(t) represents the total amount of iodine in a given volume, V; therefore, $C(t) = V \times c(t)$. In this equation, C(t) is the sum of iodine in the renal blood volume B(t) and in the renal glomerular filtrates Q(t). Therefore, when $C(t) = B(t) + Q(t)$ is divided by V, it becomes $c(t) = \frac{Q(t)}{V} = \frac{B(t)}{V} + \frac{Q(t)}{V}$. If it substituted with $\frac{Q(t)}{V} = \frac{\alpha}{V}\int_0^t b(t)dt$, it becomes $c(t) = \frac{B(t)}{V} + \frac{\alpha}{V}\int_0^t b(t)dt$. B(t) is $V_B b$(t), so when substituted with $\frac{B(t)}{V}$, it becomes $\frac{c(t)}{b(t)} = \frac{V_B}{V} + \frac{\alpha}{V}\frac{\int b(t)dt}{b(t)}$. The CT value from which the background has been subtracted is then substituted for the concentrations in these equations. Components c(t) and b(t) are the CT value of the renal ROI and the aorta minus the baseline. $\frac{V_B}{V}$ is the volume of the contrast media remaining in the blood at a given time, fractional vascular volume (%, *fvv*). The Patlak plot will be linear with a slope of $\frac{\alpha}{V}$, which is the whole blood clearance rate per unit volume (mL/min/mL), and must be corrected by the HCT values to obtain the plasma clearance GFR [Slope × (1 − HCT)]. Since plasma clearance is usually reported in mL/min/kg, the results were first converted from contrast clearance per unit volume (mL/min/mL) to contrast clearance (mL/min) by multiplying by the kidney volume. Next, the contrast clearance (mL/min) was divided by the weight of the dog in kilograms to allow comparison of different GFR values in mL/min/kg units [24,30].

Image analysis

The CT-GFR of a single-kidney measured by CT was estimated using a Patlak plot [28]. For this procedure, aortic and renal parenchymal attenuation curves and Hounsfield unit (HU) values of the ROIs were acquired. A circular aortic ROI was located inside the aortic lumen at the level of the renal hilum using the manufacturer's CT functional software (Fig. 1). The unenhanced density of the aorta was calculated as the mean of three density measurements at the same enhanced aortic level in the renal hilum. The mean HU value within the aortic ROI before contrast medium administration was subtracted from each value after contrast medium administration, thus providing a corrected aorta HU value. The corrected aorta HU values reflected attenuation changes in the 2 min uptake of the contrast media.

Similarly, ROIs were 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, thus excluding main vessels and fatty tissue. The mean precontrast and postcontrast HU values were evaluated at a location adjacent to the site where the aorta was measured. The corrected HU values of the renal parenchyma, from which the precontrast HU value was subtracted from the postcontrast HU, were then analyzed. For the Patlak plot analysis, an in-house program based on IDL 6.4 development software (IDL 6.4; Interactive Display Language, USA) was used.

Experimental animals were divided into two groups based on ROI location. In group 1, the CT-GFR was measured at the renal hilum of the right kidney while the ROI in group 2 was in the left kidney. CT-GFRs along with other quantitative and functional parameters of each kidney were determined. Significant correlations among the functional parameters between the right and left kidney were then assessed. The following physiologic parameters were evaluated: baseline and postcontrast HU values in the

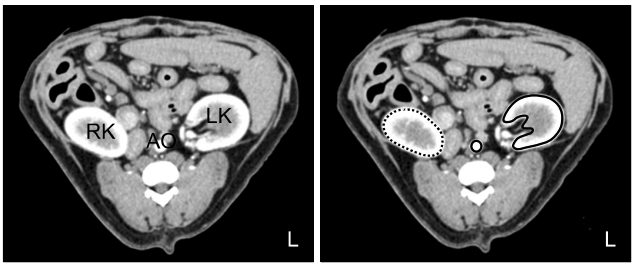

Fig. 1. Dynamic CT images centered in the left renal hilum obtained at maximal aortic enhancement with iohexol. The black circle indicates the aorta, the black line indicates the left kidney, and the dotted line indicates the right kidney. Regions of interest (ROI) are drawn around the aorta as well as left and right kidneys. Vessels and fatty tissue are excluded from the ROIs. LK: left kidney, RK: right kidney, AO: aorta.

Table 1. Precontrast and postcontrast Hounsfield unit values along with time-to-peak enhancement of the renal and aortic resions of interests

	Right kidney hilum (n = 14)	Left kidney hilum (n = 10)	*p*-value
PreAo	34.61 ± 3.94 (26.80 ~ 40.20)	32.56 ± 4.81 (24.80 ~ 39.90)	0.364
PreKd	38.20 ± 5.67 (29.80 ~ 54.80)	38.85 ± 9.24 (31.40 ~ 57.70)	0.348
PostAo	219.68 ± 63.19 (105.40 ~ 337.80)	218.11 ± 72.22 (89.19 ~ 352.20)	0.875
PostKd	129.57 ± 18.39 (109.40 ~ 174.70)	116.99 ± 31.50 (74.40 ~ 174.60)	0.192
Aopt	13.29 ± 2.75 (10.50 ~ 21.00)	13.20 ± 1.84 (9.00 ~ 15.00)	0.668

PreAo: precontrast aortic attenuation, PreKd: precontrast renal attenuation, PostAo: postcontrast aortic peak attenuation, PostKd: postcontrast renal peak attenuation, Aopt: time-to-peak enhancement of the aorta (sec). All data are expressed as the mean ± SD (range).

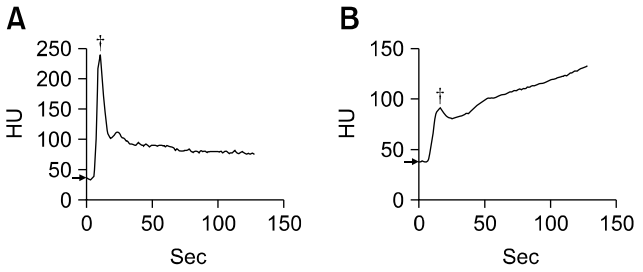

Fig. 2. Time attenuation curves (TACs) showing iohexol concentrations in the aortic blood (A) and left kidney (B) of a dog. The threshold (arrow) is the background Hounsfield unit (HU) value of the aortic (A) and renal (B) ROIs. The initial postcontrast aortic and renal peak enhancements and their times are shown (cross mark).

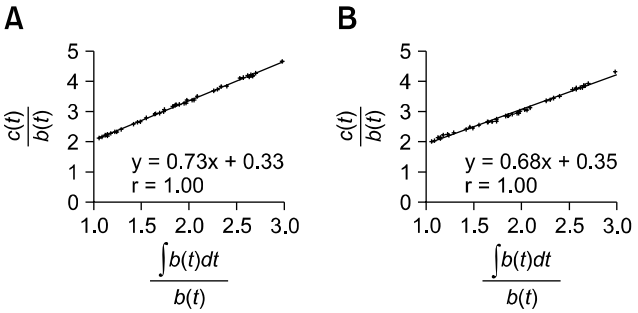

Fig. 3. Patlak plots of the right (A) and left (B) kidneys of a Beagle dog. The slope represents the blood clearance (mL/min/unit volume), and the y-intercept indicates the fractional vascular volume (%). Components c(t) and b(t) are the CT values from which the baseline has been subtracted of the renal ROI and the aorta.

aorta and renal parenchyma, time-to-peak enhancement of the ROI and time attenuation curve (TAC) patterns, and functional parameters such as slope, intercept, and CT-GFR values. Additionally, global GFR was calculated by adding right and left kidney GFR values.

Measurement of renal volume

Renal volume was calculated by measuring the cross-sectional area (cm^2) of an ROI drawn on each kidney in each CT slice. Renal volume was determined during the postcontrast helical scan. Image window width and level were set at 80 and 25 HU, respectively, for ROI determination [1]. Each of the slice areas were summed and multiplied by slice thickness (mm) to yield the renal volume (mL) [14,25].

Statistical analysis

Statistical analysis was performed using SPSS software (ver 17.0; SPSS, USA). Because of the small sample sizes, Mann-Whitney U and Wilcoxon signed rank tests were used to compare the physiologic parameters for the right and left kidneys. Functional parameters and CT-GFR of both kidneys were expressed as the mean ± SD. For all statistical analyses, *p*-values were considered significant when < 0.05.

Results

The precontrast HU values of the aorta and those of the right and left renal parenchyma were 33.75 ± 4.35, 38.20 ± 5.67, and 38.85 ± 9.24 HU, respectively (Table 1). Peak aortic enhancement occurred between 9.5 and 16 sec (13.29 ± 2.75) after iohexol injection (Table 1, Fig. 2A). During this time, the vascular phase was detected and the renal vasculature was evaluated. The aortic TAC also showed a second, lower peak at 25 ~ 36 sec. The initial peak of renal parenchymal enhancement occurred at 15 ~ 21 sec (average, 18.32 ± 3.39 sec; Table 1, Fig. 2B). This graph showed an overall gradual increase in renal parenchymal HU values following the initial enhancement peak until the end of data acquisition at 120 sec with small undulations in the renal TAC (Fig. 2B).

The slopes of the Patlak graph (Fig. 3) of the right and left kidneys were 0.69 ± 0.04 and 0.57 ± 0.05 mL/unit of volume, respectively. The CT-GFR values (mL/min/kg) of

Table 2. Results of Patlak plot analysis and computed tomography-glomerular filtration rate (GFR) values of the right and left kidneys

	Right kidney hilum	Left kidney hilum	*p*-value
Slope (mL/min/mL)	0.69 ± 0.04 (0.30 ~ 0.94)	0.57 ± 0.05 (0.33 ~ 0.84)	0.069
Intercept (%)	0.38 ± 0.02 (0.20 ~ 0.63)	0.38 ± 0.03 (0.19 ~ 0.50)	0.725
GFR 1 (mL/min)	18.28 ± 1.38(9.79 ~ 30.41)	16.67 ± 1.24 (9.82 ~ 22.12)	0.520
GFR 2 (mL/min/kg)	2.19 ± 0.17 (0.95 ~ 3.39)	2.28 ± 0.17 (1.31 ~ 3.31)	0.747
RV (mL)	26.61 ± 5.14 (21.32 ~ 37.24)	29.65 ± 5.46 (25.36 ~ 43.31)	0.074

RV: estimated renal volume. All data are expressed as the mean ± SD (range).

the right and left kidney were 2.19 ± 0.17 and 2.28 ± 0.17, respectively. There were no statistically significant differences between these values (Table 2). The average global GFR, which is the sum of the GFR of both kidneys, was 4.21 ± 0.25 mL/min/kg while the whole kidney GFR was 33.43 ± 9.20 mL/min.

Discussion

For the present study, a single-slice dynamic CT technique, Patlak plot analysis, and a low dose of contrast medium with a propofol-isoflurane anesthetic protocol were used. We chose propofol for our study to induce anesthesia in the young healthy dogs undergoing CT-GFR because of ability of this drug to cause smooth and rapid induction and uncomplicated recovery [4]. Mean CT-GFR values of the right and left kidney were 2.19 ± 0.17 mL/min/kg and 2.28 ± 0.17 mL/min/kg, respectively. The average global GFR was 4.21 ± 0.25 mL/min/kg in the 24 clinically healthy Beagles. The CT-GFR technique used in this study may be extremely useful for assessing GFR in each kidney separately in specific clinical setting, such as prior to performing uninephrectomy in patients for testing the function of the remaining kidney and the potential risk of post-surgery kidney failure, unlike plasma or urinary clearance methods. In the study by O'Dell-Anderson *et al*. [20], the average global GFR was found to be 2.57 ± 0.33 mL/min/kg using functional CT, 4.06 ± 0.37 mL/min/kg using plasma iohexol clearance, and 4.05 ± 1.10 mL/min/kg using renal scintigraphy in eight healthy intact male dogs weighing between 14.6 and 16.5 kg. Other studies determined that the mean global GFR was 2.9 ± 0.3 mL/min/kg using plasma iohexol clearance in six healthy Beagles [17] and 3.46 ± 0.52 mL/min/kg using ^{99m}Tc-DTPA scintigraphy in 10 healthy Beagles [15]. When comparing the present CT-GFR results to those from other GFR methods, we obtained considerably higher values. This may be explained by differences by body weight, gender, and age of the experimental animals or a potential effect associated with the investigator.

Information from triphasic renal imaging could be obtained through the time attenuation curves of the aorta and renal parenchyma obtained during single-slice dynamic scanning. Triphasic renal imaging consists of the precontrast scan along with corticomedullary and nephrographic phases [5,16,26]. In present study, the corticomedullary phase was scanned during the initial cortical peak time ranging from 15 to 21 sec. The nephrographic phase and diffuse enhancement of general renal parenchyma could be obtained after approximately 40 to 50 sec when reaching the contrast media in the renal pelvis. Time-to-peak enhancement of the aorta could be also applied when performing renal angiography; by doing this, excellent visualization of the aorta and its branches is acquired [21]. Triphasic renal CT including a vascular phase is a valuable method for detecting and characterizing lesions, anatomic examination of potential kidney transplant donors, and preoperative planning for urologic surgery [6,13,32].

By performing a Patlak plot analysis during CT examination, rapid and simple GFR determination is possible within at least the first 2 min following tracer injection [2]. In particular, the best window of time for GFR calculation is 40 ~ 110 sec following aortic rise [12,31]. Our study showed that multiple time data by dynamic CT can be obtained from only one section level. This could present a drawback for cases in which a solid organ may show functional inhomogeneity or in patients with renal disease that is unevenly distributed.

A low dose of iohexol acts in a manner pharmacokinetically similar to inulin during functional CT scanning [10]. Such a low dose of contrast medium (1 mL/kg) allows the calculation of GFR while limiting the risk of contrast medium-induced nephropathy [22]. In our preliminary study, it was possible to evaluate renal function with a dose of 0.75 mL/kg, but it was difficult to judge the renal margin to measure renal volume during the immediate postcontrast helical scan. An even lower dose of contrast medium (0.5 mL/kg) created noise on the TAC curves and the correlation coefficients from the Patlak plot were relatively low. Part of the tracer-use concept indicates that the mass of the chemical administered is so small that it does not

itself affect the function of the organ system being studied [19]. Therefore, the dose used in our study was chosen on the basis of preliminary CT-GFR examinations [20].

One drawback of our study was that the accuracy of our technique was not compared to a gold standard method, but it was already considered to be a simple alternative to GFR measurement for clinical and research purposes. Erratic breath may have also caused respiratory misregistration problems and affected CT number measurements. Additionally, the radiation burden of the patient may be significant when taking repeated CT images.

Despite these limitations associated with functional CT techniques using the Patlak plot, we recommend the use of functional CT-GFR and triphasic renal scan based on the results of our study. We were able to obtain scout, baseline, and single-slice dynamic scans using contrast media (1 mL/kg), and two postcontrast scans including cortico-medullary and nephrographic phases using additional contrast media (2 mL/kg). This technique can simultaneously provide detailed functional and morphological information and is practical for application in veterinary medicine. Further investigations are required to validate of our findings, including ones examining differences associated with age or breed-related GFR, and the application of CT-GFR for patients with various diseases.

References

1. **Alexander K, del Castillo JRE, Ybarra N, Morin V, Gauvin D, Authier S, Vinay P, Troncy É.** 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. **Blomley MJ, Dawson P.** Review article: the quantification of renal function with enhanced computed tomography. Br J Radiol 1996, **69**, 989-995.
3. **Brown SC, O'Reilly PH.** Iohexol clearance for the determination of glomerular filtration rate in clinical practice: evidence for a new gold standard. J Urol 1991, **146**, 675-679.
4. **Chang J, Kim S, Jung J, Lee H, Chang D, Lee Y, Lee I, Yoon J, Choi M.** Evaluation of the effects of thiopental, propofol, and etomidate on glomerular filtration rate measured by the use of dynamic computed tomography in dogs. Am J Vet Res 2011, **72**, 146-151.
5. **Cohan RH, Sherman LS, Korobkin M, Bass JC, Francis IR.** Renal masses: assessment of corticomedullary-phase and nephrographic phase CT scans. Radiology 1995, **196**, 445-451.
6. **Dachman AH, Newmark GM, Mitchell MT, Woodle ES.** Helical CT examination of potential kidney donors. AJR Am J Roentgenol 1998, **171**, 193-200.
7. **Dawson P.** Dynamic contrast-enhanced functional imaging with multi-slice CT. Acad Radiol 2002, **9** (Suppl 2), S368-370.
8. **Dawson P.** Functional imaging in CT. Eur J Radiol 2006, **60**, 331-340.
9. **Dawson P, Peters M.** Dynamic contrast bolus computed tomography for the assessment of renal function. Invest Radiol 1993, **28**, 1039-1042.
10. **Frennby B, Sterner G.** Contrast media as markers of GFR. Eur Radiol 2002, **12**, 475-484.
11. **Gleadhill A, Peters AM, Michell AR.** A simple method for measuring glomerular filtration rate in dogs. Res Vet Sci 1995, **59**, 118-123.
12. **Hackstein N, Heckrodt J, Rau WS.** Measurement of single-kidney glomerular filtration rate using a contrast-enhanced dynamic gradient-echo sequence and the Rutland-Patlak plot technique. J Magn Reson Imaging 2003, **18**, 714-725.
13. **Herts BR, Coll DM, Lieber ML, Streem SB, Novick AC.** Triphasic helical CT of the kidneys: contribution of vascular phase scanning in patients before urologic surgery. AJR Am J Roentgenol 1999, **173**, 1273-1277.
14. **Heymsfield SB, Fulenwider T, Nordlinger B, Barlow R, Sones P, Kutner M.** Accurate measurement of liver, kidney, and spleen volume and mass by computerized axial tomography. Ann Intern Med 1979, **90**, 185-187.
15. **Kampa N, Wennstrom U, Lord P, Twardock R, Maripuu E, Eksell P, Fredriksson SO.** Effect of region of interest selection and uptake measurement on glomerular filtration rate measured by ^{99m}Tc-DTPA scintigraphy in dogs. Vet Radiol Ultrasound 2002, **43**, 383-391.
16. **Kopka L, Fischer U, Zoeller G, Schmidt C, Ringert RH, Grabbe E.** Dual-phase helical CT of the kidney: value of the corticomedullary and nephrographic phase for evaluation of renal lesions and preoperative staging of renal cell carcinoma. AJR Am J Roentgenol 1997, **169**, 1573-1578.
17. **Laroute V, Lefebvre HP, Costes G, Toutain PL.** Measurement of glomerular filtration rate and effective renal plasma flow in the conscious beagle dog by single intravenous bolus of iohexol and p-aminohippuric acid. J Pharmacol Toxicol Methods 1999, **41**, 17-25.
18. **Miles K, Dawson P, Blomley M.** Functional Computed Tomography. 1st ed. pp. 117-132, Isis Medical Media, Oxford, 1997.
19. **Miles KA, Leggett DA, Bennett GA.** CT derived Patlak images of the human kidney. Br J Radiol 1999, **72**, 153-158.
20. **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.
21. **Rubin GD, Dake MD, Napel SA, McDonnell CH, Jeffrey RB Jr.** Three-dimensional spiral CT angiography of the abdomen: initial clinical experience. Radiology 1993, **186**, 147-152.
22. **Sanaei-Ardekani M, Movahed MR, Movafagh S, Ghahramani N.** Contrast-induced nephropathy: a review. Cardiovasc Revasc Med 2005, **6**, 82-88.
23. **Smith HW.** The Kidney: Structure and Function in Health and Disease. 1st ed. pp. 47-48, Oxford University Press, New York, 1951.
24. **Sommer FG.** Can single-kidney glomerular filtration rate be determined with contrast-enhanced CT? Radiology 2007, **242**, 325-326.

25. **Staron RB, Ford E.** Computed tomographic volumetric calculation reproducibility. Invest Radiol 1986, **21**, 272-274.
26. **Szolar DH, Kammerhuber F, Altziebler S, Tillich M, Breinl E, Fotter R, Schreyer HH.** Multiphasic helical CT of the kidney: increased conspicuity for detection and characterization of small (< 3-cm) renal masses. Radiology 1997, **202**, 211-217.
27. **Toto RD.** Conventional measurement of renal function utilizing serum creatinine, creatinine clearance, inulin and para-aminohippuric acid clearance. Curr Opin Nephrol Hypertens 1995, **4**, 505-509.
28. **Tsushima Y.** Functional CT of the kidney. Eur J Radiol 1999, **30**, 191-197.
29. **Tsushima Y, Blomley MJ, Kusano S, Endo K.** Use of contrast-enhanced computed tomography to measure clearance per unit renal volume: A novel measurement of renal function and fractional vascular volume. Am J Kidney Dis 1999, **33**, 754-760.
30. **Tsushima Y, Blomley MJ, Okabe K, Tsuchiya K, Aoki J, Endo K.** Determination of glomerular filtration rate per unit renal volume using computerized tomography: correlation with conventional measures of total and divided renal function. J Urol 2001, **165**, 382-385.
31. **Tsushima Y, Taketomi-Takahashi A, Endo K.** Patlak plot analysis for assessment of single-kidney glomerular filtration rate with dynamic CT. Radiology 2008, **246**, 336-338.
32. **Urban BA.** The small renal mass: what is the role of multiphasic helical scanning? Radiology 1997, **202**, 22-23.
33. **Verlander JW.** Glomerular filtration. In: Cunningham JG, Klein BG (eds.). Textbook of Veterinary Physiology. 4th ed. pp. 528-536, Saunders, St. Louis, 2007.