

## Symmetric dimethylarginine (SDMA): new biomarker of renal function in cats and dogs (2015)

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Filtration, specifically its magnitude (glomerular filtration rate or GFR), is the central measure of the adequacy of renal function. Furthermore, the severity of most renal diseases, including both acute kidney injury (AKI) and chronic kidney disease (CKD), is judged by their effects on GFR. Although direct measurement of GFR is widely accepted as the reference method for assessment of renal function, clinicians frequently use surrogate markers, such as blood urea nitrogen concentration or blood (plasma or serum) creatinine, to determine the adequacy of GFR. However, mild to moderate decreases in GFR are difficult to detect with these commonly used diagnostic tests. While serial evaluation of blood creatinine concentration in the same animal increases the sensitivity of this test, baseline measurements are often unavailable.

There are several species of methylated arginine produced as a byproduct of intracellular protein methylation followed by protein degradation. Of interest are the dimethylated derivatives of arginine, symmetric dimethylarginine (SDMA) and asymmetric dimethylarginine (ADMA). While ADMA is metabolized enzymatically, SDMA is eliminated primarily by renal filtration and plasma SDMA concentration has been used as an alternate biomarker for estimating GFR in people. A meta-analysis of 18 studies involving human patients showed that  $1/\text{SDMA}$  concentrations correlated highly with GFR (inulin clearance;  $r = 0.85$ ), and SDMA concentrations correlated highly with blood creatinine ( $r = 0.75$ ). Plasma SDMA concentrations are increased in cats with CKD and correlate with blood creatinine concentrations.

To date, published veterinary studies have investigated the utility of this biomarker in cats. Citations for these studies [*and conclusions of the study authors*] are provided below. Studies in dogs have demonstrated similar results. At present, the available data suggest that plasma (or serum) concentration of SDMA reflects GFR in cats and dogs, may be more sensitive than blood creatinine for early detection of CKD, and may be less affected by loss of lean body mass than blood creatinine. Clearly SDMA has utility for the diagnosis and management of dogs and cats with renal disease. But, as with any promising new biomarker, there is a need for additional studies.

### Cats

Jepson RE, Syme HM, Vallance C, Elliott J. Plasma asymmetric dimethylarginine, symmetric dimethylarginine, l-arginine, and nitrite/nitrate concentrations in cats with chronic kidney disease and hypertension. *J Vet Intern Med* 2008;22:317-324. [*Plasma SDMA concentrations were increased in cats with CKD and correlated with blood creatinine.*]

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Hall JA, Yerramilli M, Obare E, Yerramilli M, Yu S, Jewell DE. Comparison of serum concentrations of symmetric dimethylarginine and creatinine as kidney function biomarkers in healthy geriatric cats fed reduced protein foods enriched with fish oil, L-carnitine, and medium-chain triglycerides. *J Vet Intern Med* 2015;29:1036-1044. [Serum SDMA concentration was more highly correlated with GFR than serum creatinine, and, unlike creatinine, was unaffected by muscle wasting.]

Hall JA, Yerramilli M, Obare E, Yerramilli M, Jewell DE. Comparison of serum concentrations of symmetric dimethylarginine and creatinine as kidney function biomarkers in cats with chronic kidney disease. *J Vet Intern Med* 2014;28:1676-1683. [Using serum SDMA as a biomarker for CKD allowed earlier detection of CKD in cats compared with blood creatinine.]

Braff J, Obare E, Yerramilli M, Elliott J, Yerramilli M. Relationship between serum symmetric dimethylarginine concentration and glomerular filtration rate in cats. *J Vet Intern Med* 2014;28:1699-1701. [Increased serum SDMA concentrations were observed in cats with reduced renal function as determined by direct measurement of GFR. The relation between GFR and SDMA was of similar strength as the relation between GFR and blood creatinine.]

### Dogs

Nabity MB, Lees GE, Boggess M, Yerramilli M, Obare E, Yerramilli M, Aguiar J, Relford R. Correlation of symmetric dimethylarginine with glomerular filtration rate in dogs with chronic progressive renal disease. *J Vet Intern Med* 2013;27:733(Abtract). [SDMA correlated well with GFR in dogs with progressive renal disease.]

Yerramilli M, Obare E, Jewell DE, Hall JA. SDMA increases earlier than serum creatinine in dogs with chronic kidney disease (CKD). *J Vet Intern Med* 2014:1084(Abtract). [SDMA was an earlier biomarker than serum creatinine reference ranges for diagnosing CKD in dogs.]

### People

Kielstein JT, Salpeter SR, Bode-Boeger SM, Cooke JP, Fliser D. Symmetric dimethylarginine (SDMA) as endogenous marker of renal function – a meta-analysis. *Nephrol Dial Transplant* 2006;21:2446-2451. [SDMA was a reliable marker of renal function.]

Protas PT, Tenderenda-Banasiuk E, Taranta-Janusz K, Fitonowicz R, Zajac M, Wasilewska A. Is symmetric dimethylarginine a sensitive biomarker of subclinical kidney injury in children born with low birth weight? *Biomarker* 2014;19:231-235. [SDMA correlated well with GFR.]