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Letter to the Editor

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Dear Editor,

Thank you for the opportunity to respond to the letter from Drs. German, Batchelor, and Murtagh regarding our paper in *JVIM* on the "Relationship between lean body mass and serum renal biomarkers in healthy dogs" especially with regard to symmetric dimethylarginine (SDMA), a new serum renal biomarker for assessing glomerular filtration rate (GFR).[1] They also reviewed another paper published in *PLoS One* entitled "Feeding healthy Beagles medium-chain trigylcerides, fish oil, and cartinine offsets age-related changes in serum fatty acids and carnitine metabolites."[2] We appreciate the choice of papers to review during hospital rounds and in particular their interest in this exciting new biomarker.

The purpose of the *JVIM* paper[1] was to report the relationship between lean body mass (LBM) and serum renal biomarkers in healthy dogs. We are happy to see that there were no concerns that our data showed that serum Cr concentrations, but not SDMA concentrations are influenced by LBM, which limits serum Cr utility as a biomarker for monitoring renal function in dogs with decreased LBM. In this study, we did not report GFR using iohexol clearance. However, we have previously shown that serum SDMA is significantly correlated with GFR in cats[3–5] and in dogs.[6] The decrease in serum concentrations of SDMA in this study are consistent with an improvement in GFR.

The purpose of the original study[2] was to determine if dogs consuming a complete and balanced adult-food formula with added L-carnitine, medium-chain triglycerides (MCT), and (n-3) FA from fish oil were able to maintain total-lean-body weight, total serum protein and albumin concentrations, and achieve desired alterations in serum FA profiles and carnitine metabolite concentrations. We were able to document age-related changes in the PUFA to SFA ratio and in carnitine metabolite concentrations that could be counterbalanced by dietary enrichment with these compounds. Three test foods were prepared by Hill's Pet Nutrition, Inc. Canine Prescription Diet® k/d® was used as the control food and base formula for the two test foods. Both test foods had added L-carnitine (300 mg/kg as fed). The two test foods also had different concentrations of fatty acids, including fish oil (0.6 or 1.5% as fed). The test food with 1.5% fish oil also had added MCT from coconut oil, but reduced arachidonic acid because of a reduction in animal fat in the formulation. The reduced animal fat was replaced with plant oils (2% coconut oil and 7% corn oil). The control food (Hill's® Prescription Diet® k/d®) is a phosphorus-restricted food, however, animal feeding tests using AAFCO procedures substantiate that Canine k/d® provides complete and balanced nutrition for maintenance of adult dogs. It has lower protein (13.5% as fed), phosphorus, and sodium concentrations compared with other canine maintenance foods and contains higher levels of nonprotein calories (18.0% fat; 56.9% carbohydrate).

We reported a "time on diet effect" for total-body weight, total-fat-body weight, and serum SDMA, urea nitrogen, and phosphorus concentrations. Individual group means for SDMA concentrations across time are shown in Fig 1A. There was no formula effect so means were combined. Serum urea nitrogen also decreased in dogs from all three treatment groups, with no differences based on dietary treatment as shown in Fig 1B. It is likely that the time on test effect for serum urea nitrogen was related to the switch from the pretrial to the control/test foods, as urea concentrations were significantly decreased by 1 month. It took longer to see effects on SDMA concentration (3 months) and effects were significantly different from 3 months at 6 months. We concluded "It is interesting to speculate that this represents a dietary effect on renal function. . .Further studies are needed." Although daily food intake was calculated to maintain body weight, unintentionally dogs in all three food groups increased body weight on average of 6–8%, the increase being in total-fat-body weight. We agree that dogs were in a state of positive energy balance, although we are not suggesting that changes in renal biomarker concentrations resulted from an increase in total-fat-body weight.

Serum phosphorus concentrations increased in dogs of all three treatment groups after 1 month of food consumption, again with no differences based on dietary treatment. Changes were within the reference interval (2.2–5.1 mg/dL; Fig 1C). Further studies have been undertaken and results are in press.[7] In a new study, geriatric dogs were fed a different control food than reported here, or one of two functional foods after a switch from a pretrial food. Food compositions revealed a decrease in protein and phosphorus content, although to a lesser extent than reported here, for example, phosphorus decreased from 0.8% pretrial food to 0.7% control food or 0.6% test foods. Glomerular filtration rate was measured by iohexol clearance and increased with time on test (13.0–16.9%); dogs fed the food with highest supplemented level of bioactives had the lowest SDMA concentrations. Serum phosphorus concentrations also increased within the normal reference interval in dogs of that study ($P < .001$). There was no effect of formula and no interaction between formula and time on test. Along with our original study,[2] this new study[7] supports that changes in serum phosphorus concentrations in the reference range are not the best indicator of changes in GFR, and serum phosphorus did not move in the same direction as SDMA with a change in GFR. In the current study,[2] we did not speculate on the significance of the increase in serum phosphorus concentration, other than to say it was biologically insignificant as it remained within the reference interval throughout.

The results of these two studies support "the time on diet effect" on SDMA concentrations is the result of GFR alterations. The study in press again suggests a dietary effect in that healthy geriatric dogs fed

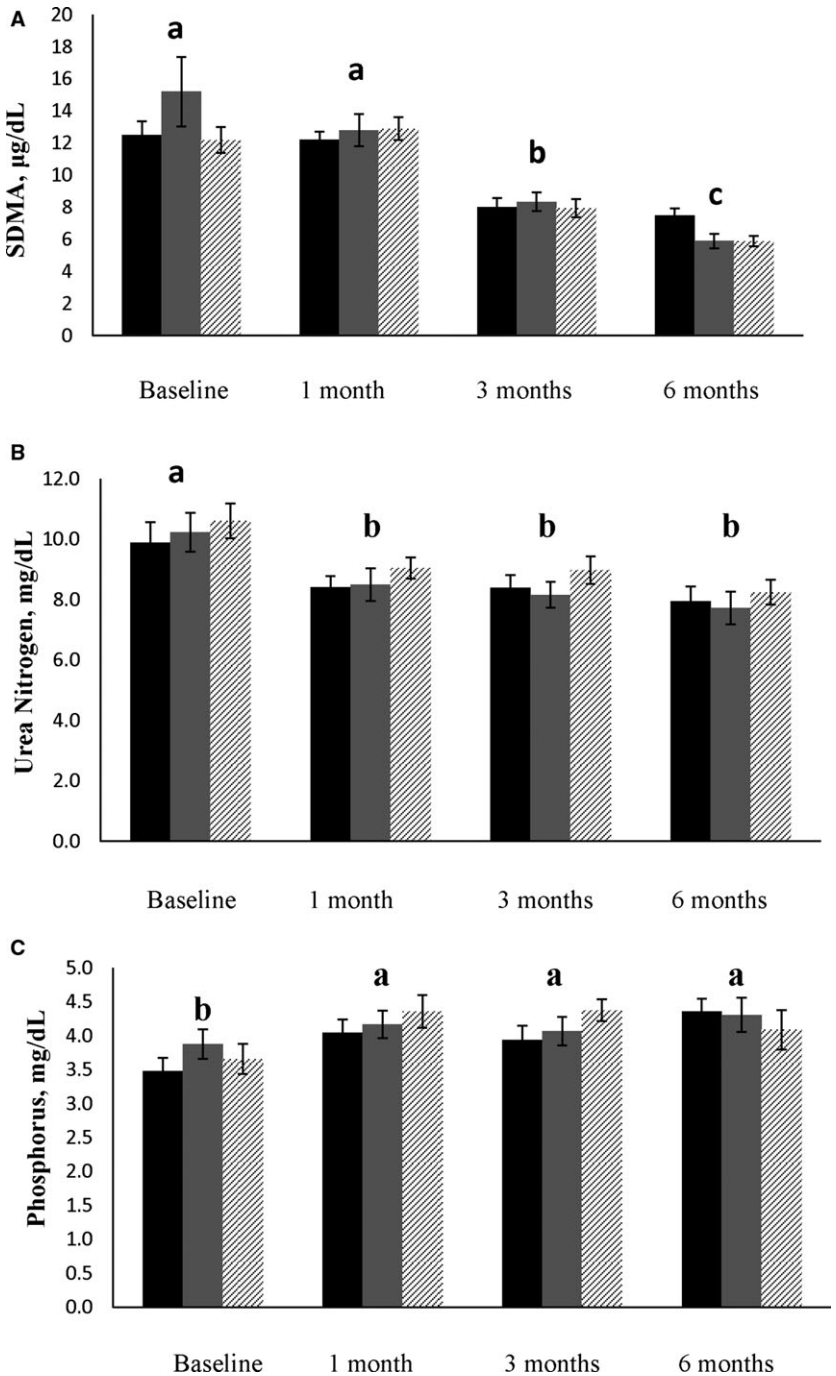

Fig 1. Serum renal biomarkers: (**A**) SDMA, (**B**) urea nitrogen, and (**C**) phosphorus concentrations of dogs at baseline (initial) and after consuming control (Prescription Diet® k/d®; black bars), test food with added L-carnitine and 0.6% fish oil (gray bars), or test food with added L-carnitine, 1.5% fish oil, and medium-chain triglycerides (striped bars) for 6 months. There was no formula effect. [a,b,c]Means with different superscripts are different between months ($P < .05$).

functional foods showed increased GFR measured by iohexol clearance and decreased SDMA concentrations. There was no concurrent change in body weight. Thus, our results are unlikely because of an effect of positive energy balance or gain in fat mass. Nonetheless, we are continuing to investigate the influence of foods with differing nutrient content on serum SDMA concentrations and on GFR in healthy geriatric dogs and cats, as well as in pets with chronic kidney disease (CKD) defined by IRIS guidelines. Now that the utility of using serum SDMA as an early indicator of compromised renal function in dogs and cats with CKD has been demonstrated, we find ourselves in the fortunate situation of being able to evaluate the benefits of early dietary interventions to improve the outcome of CKD in pets.

References

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J.A. Hall DVM, MS, PhD, DACVIM (SAIM)
Department of Biomedical Sciences, College of Veterinary Medicine, Oregon State University, Corvallis, OR

M. Yerramilli MS, PhD, E. Obare BS and M. Yerramilli PhD
The IDEXX Biotechnology Group, IDEXX Laboratories, Inc., Westbrook, ME

L.D. Melendez DVM, MS, DACVIM (SAIM) and D.E. Jewell PhD
The Pet Nutrition Center, Hill's Pet Nutrition, Inc., Topeka, KS