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# Serum creatinine as an indicator of lean body mass in vegetarians and omnivores

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Growing numbers of Americans are adopting vegetarian or vegan diets. While risk for some chronic conditions may be lower when following these diets, concern remains over the ability to consume adequate amounts of various nutrients, notably, protein. Knowing that serum creatinine is a reliable marker of muscle mass, this study examined the relationships between serum creatinine, lean body mass (LBM), handgrip strength, and protein intake in healthy vegetarian ( $n = 55$ ) and omnivorous ( $n = 27$ ) adults. Significantly higher protein intakes (+31%), LBM (+7%), serum creatinine (+12%) and handgrip strength (+14%) were observed for the omnivore participants compared to vegetarian participants. Positive correlations ( $p < 0.001$ ) were noted between creatinine and LBM ( $R^2 = 0.42$ ), creatinine and handgrip strength ( $R^2 = 0.41$ ), protein intake and LBM ( $R^2 = 0.29$ ), and handgrip strength and LBM ( $R^2 = 0.69$ ). These data show that serum creatinine concentrations were lower in vegetarian women and men in comparison to their omnivorous counterparts and that serum creatinine concentrations correlate with LBM and strength in healthy adults, regardless of diet.

## KEYWORDS

vegetarian, creatinine, lean body mass, muscle, grip strength

## Introduction

In recent years vegetarian diets have increased in popularity. A 2020 Harris Poll reported that 4% of men and 7% of women surveyed over 18 years of age in the United States identified as vegetarians, with half of those identifying as vegan (1). While these diets are often, but not exclusively, associated with decreased risk for cancer (2–4), cardiometabolic diseases (3–5), diabetes (6), and obesity (7–9), the possibility of micronutrient inadequacies, including iron, vitamin B12, and vitamin D remain a concern. Furthermore, although energy intakes tend to be similar, protein intake is often significantly lower for vegetarians when compared to omnivores (10–14). This can be concerning as protein intakes are directly linked to muscle mass and strength (15–17). Following ingestion, protein is digested to component amino acids, which are rapidly absorbed. The increase in plasma amino acid concentrations, particularly the essential amino acid leucine, stimulates muscle protein synthesis (18, 19). In comparison to animal proteins, plant proteins contain lower amounts of leucine (20); moreover, plant protein is 10–20% less bioavailable due to antinutrient factors present in these foods (11, 21). Clinical trials have demonstrated that the rate of muscle protein synthesis is less for

plant-based versus animal-based protein (22, 23). Indeed, decreased lean body mass (LBM) and reduced handgrip strength has been reported in vegetarians (24, 25). Since handgrip strength is an indicator of health-related quality of life irrespective of age and gender (26–28), it is important to consider this quality in vegetarians.

Serum creatinine, a normal waste product of muscle metabolism, has been shown to be a reliable marker of muscle mass since it is continually produced and filtered through the kidney (29, 30). However, many factors can impact serum creatinine levels, most notably declining kidney function. At the nephron, creatinine is filtered through the glomerulus and is not reabsorbed by the tubule; hence, elevations in serum creatinine can be utilized as a proxy for renal function. Since serum creatinine is generated from muscle, concentrations are impacted by age, sex, and body size. Equations have been developed using serum creatinine to estimate the glomerulus filtration rate (GFR) while controlling for these common confounding factors, and currently, the CKD-EPI Collaboration (Chronic Kidney Disease Epidemiology Collaboration) equation is considered the most accurate GFR measurement for clinical use (29), and GFR values  $<90$  ml/min/1.73 m<sup>2</sup> indicate declining kidney function. However, serum creatinine is influenced by other factors as well including medications, chronic illness, nutritional status and diet (31), all of which need to be considered when utilizing this measure.

Several investigators have reported lower serum creatinine concentrations in vegetarian populations in comparison to omnivores (32, 33). However, a comparison between serum creatinine, LBM, and strength based on diet adherence in a healthy adult population has not been reported. Therefore, the purpose of this investigation was to examine the relationship between serum creatinine, LBM, and handgrip strength in healthy, non-athlete vegetarian and omnivore women and men. We hypothesized that serum creatinine would be positively associated with LBM and handgrip strength in both genders, with omnivores exhibiting higher levels of creatinine, LBM, and handgrip strength than vegetarians.

## Subjects and methods

This study is a secondary analysis of a cross-sectional data set gathered from healthy, non-obese adults (body mass index [BMI]  $>18.5$  and  $<30$  kg/m<sup>2</sup>) to examine associations between indicators of bone health, bone mineral density, and diet adherence (vegetarian vs. omnivore) (34). Participants (27 omnivores and 55 vegetarians), aged 19–50 y, were recruited from the Phoenix metropolitan area using university list serves, connections with local vegetarian groups and farmers markets, and social media. Participants were healthy and free of chronic diseases by self-report; not taking prescription medications with the exception of oral contraceptives; not

competitive athletes or training for an endurance event; and, if female, not recently pregnant. These exclusion criteria were designed to control covariables known to impact bone mineral density, but they were also relevant to this secondary analysis with a focus on lean body mass. Participants were classified as “vegetarian” if they reported never eating meat, fish, or poultry over the preceding year. “Omnivores” were classified as eating at least 3 servings of meat, fish, and/or poultry per week over the preceding year. Omnivores who reported less than 3 servings of flesh foods weekly [e.g., flexitarians or “meat-avoiders” (35)] were excluded from participation. All participants provided written consent and the study was approved by the Institutional Review Board at Arizona State University.

A 24-h diet recall was conducted by a trained nutrition professional using the multiple pass method, and diet data were analyzed using the Food Processor software (version 7.71; ESHA Research, Salem, OR, USA). Physical activity levels were estimated by validated questionnaire and reported as metabolic equivalents (METs) (36). A venous blood sample was collected following a 12-h fast, and serum was extracted for the creatinine analyses (Jaffé method, COBAS C311, Roche Diagnostics International Ltd, Switzerland). Glomerular filtration rate (GFR) was calculated using the CKD-EPI equation (29). Height was measured using a stadiometer, and body mass was recorded using a calibrated scale (model TBF-300A, Tanita Corporation, Tokyo, Japan). Dual energy X-ray absorptiometry (DEXA) (GE Lunar iDXA, Chicago, IL, USA) was used to measure LBM by a trained X-ray technician. Dominant arm handgrip strength was measured in triplicate while seated with the elbow flexed at 90 degrees and a neutral wrist position using a handheld dynamometer (Takei Scientific Instruments, Niigata-City, Japan). Three consecutive measures were taken, and the mean score was used for analyses.

## Statistical analyses

For this secondary analysis, relationships between dietary protein, serum creatinine, strength, and LBM in omnivore vs. vegetarian participants were examined by gender. Data not normally distributed based on the Kolmogorov–Smirnov test were transformed prior to analyses (LBM only). Following a significant multivariate analysis, univariate analyses were used to assess differences between means while controlling for covariates. Pearson correlations were used to identify relationship between variables, and multiple regression analyses were utilized to determine the predictive value of variables for LBM and handgrip strength. Statistical analyses were performed using SPSS version 24 (IBM, Armonk, NY, USA), and  $p \leq 0.05$  was considered significant. Data are reported as mean  $\pm$  SD.

## Results

The study sample ( $n = 82$ ) was composed of 55 vegetarians (67%) and 58 women (71%) (Table 1). Gender, BMI, energy intake, and physical activity did not vary between the diet groups; however, the vegetarian group was older on average than the omnivorous group ( $32.5 \pm 8.8$  and  $27.2 \pm 6.7$  y respectively;  $p = 0.008$ ). In subgroup analyses, the vegetarian men were less active than their omnivorous counterparts ( $41.1 \pm 25.6$  and  $74.9 \pm 49.0$  METS respectively;  $p = 0.036$ ); hence, age and physical activity were controlled in the remaining analyses.

All variables tested were significantly impacted by diet type (Table 2). Significantly higher protein intakes (+31%), LBM (+7%), serum creatinine (+12%) and handgrip strength (+14%) were observed for the omnivore participants compared to vegetarian participants ( $p > 0.05$ ; Table 2). Additionally, the diet related differences for serum creatinine and handgrip strength were observed within gender groups. There were no significant relationships between serum creatinine and energy intake ( $r = -0.131$ ;  $p = 0.289$ ) or alcohol intake ( $r = -0.010$ ;  $p = 0.934$ ) among the participants. The average GFR measure was raised for the vegetarian participants relative to the omnivorous participants (+8%;  $p = 0.002$ ), and this diet related difference was also observed within genders.

With LBM as the criterion variable, multiple regression analyses identified gender and serum creatinine as significant predictor variables ( $p < 0.05$ ) in a model including age ( $p = 0.396$ ), diet group ( $p = 0.316$ ) and dietary protein ( $p = 0.111$ ) [ $F_{(5,65)} = 32.094$ ,  $p < 0.001$ ,  $R^2 = 0.712$ ] (Table 3). With handgrip strength as the criterion variable, gender, diet group, and LBM, were predictor variables ( $p < 0.05$ ) in a model also including age ( $p = 0.614$ ) and dietary protein ( $p = 0.423$ ) [ $F_{(5,65)} = 44.816$ ,  $p < 0.001$ ,  $R^2 = 0.775$ ] (Table 3). Correlations between serum creatinine, LBM and handgrip strength, dietary protein and LBM, and handgrip strength and LBM were significant in the study sample ( $p \leq 0.001$ ; Figure 1), and these significant results were retained after controlling for GFR.

## Discussion

This investigation revealed that serum creatinine is significantly reduced in vegetarian women and men compared to their meat-eating counterparts. Moreover, serum creatinine was a strong, independent predictor of LBM. The vegetarian men and women tended to consume less protein than the omnivore men and women and, importantly, protein intake and LBM were directly correlated. Moreover, vegetarians in this study had significantly lower handgrip strength than their omnivore counterparts. These findings may have important physiological relevance, as LBM and handgrip strength are related to quality of life (26–28). Moreover, Srikanthan et al. reported a negative association between muscle mass and

all-cause mortality in older Americans (37). Kang et al. found a direct correlation between decreased handgrip strength and impaired mobility, increased pain and greater discomfort in both Korean men and women, with exacerbated effects as age increased, thus leading to a poorer quality of life (26). Lower levels of physical activity are associated with both a lower quality of life and with reduced handgrip strength; hence, physical activity needs to be controlled in these types of investigations (38). Herein, adults who participated in competitive sports were excluded, and the diet related differences in handgrip strength by gender remained significant controlling for age and physical activity level.

In several large cross-sectional trials, serum creatinine concentrations were significantly reduced in vegetarian populations in comparison to omnivores (32, 33). Utilizing a randomized controlled study design, Dinu et al. reported a significant reduction in serum creatinine in adults at medium-to-low risk for cardiovascular disease randomized to a hypocaloric vegetarian diet vs. a hypocaloric Mediterranean diet for 3 months ( $-0.04$  and  $+0.01$  mg/dL respectively,  $p < 0.001$ ) (39). The only dietary differences between groups were for protein and fiber; however, correlation analyses showed no significant associations between these dietary changes and change in serum creatinine. Losses in total body mass was similar between groups; however, 26% more fat mass was lost in the omnivore group in comparison to the vegetarian group suggesting a greater degree of LBM loss in the latter group, which may have contributed to the significant reduction in serum creatinine noted for this group (38). In a case report, a 65-y old male with type 2 diabetes and stage 3 kidney disease, adopted a vegetarian diet, and after four months serum creatinine concentrations fell 38% from 1.6 to 1.03 mg/dL, a reduction attributed to the loss of lean body mass (40). Kochlik et al. followed serum creatinine change in adults adhering to a meatless diet for 6 days but fed 160 g cooked chicken (e.g., approximately two servings meat equating to 35 g protein) on day 4 (41). Creatinine concentrations did not fluctuate on trial days 3, 4, 5 and 6, suggesting the dependence of plasma creatinine on muscle metabolism and not meat ingestion (41). However, Mayersohn et al. reported a 52% rise in serum creatinine 2 h after consumption of the equivalent of 225 g cooked meat (42). Animal products, primarily meat, fish, and poultry, are the sole dietary source of creatine, which is partially converted to creatinine based on the cooking method (43).

Creatinine is generated at a constant rate from the spontaneous, non-enzymatic cyclization of creatine in muscle cells (30). Due to its steady production, and the fact it is freely filtered through the glomerulus, serum creatinine is used clinically as an indicator of kidney function, and high serum concentrations of creatinine ( $>1.4$  mg/dL) are a marker of compromised kidney function (44). In fact, acute elevations in serum creatinine are considered a potent risk factor for adverse outcomes in general in the inpatient setting (43). However, less

TABLE 1 Age, body mass index, energy intake, and physical activity by diet adherence<sup>a</sup>.

	OMN	VEG	P value
<i>n</i> (M/F)	8/19	16/39	0.267*
Age (y)	27.2 ± 6.7	32.5 ± 8.8	0.008
	Male	34.8 ± 7.9	0.003
	Female	31.6 ± 9.2	0.167
Body mass (kg)	66.8 ± 12.0	63.8 ± 11.0	0.054
	Male	72.5 ± 11.0	0.043
	Female	60.2 ± 8.9	0.205
Body mass index (kg/m <sup>2</sup> )	23.5 ± 3.1	22.4 ± 2.6	0.095
	Male	23.3 ± 2.4	0.844
	Female	22.0 ± 2.6	0.076
Energy intake (kcal)	2,153 ± 736	2,109 ± 613	0.746
	Male	2,461 ± 518	0.433
	Female	1,938 ± 589	0.828
METS (min/wk)	50.1 ± 39.0	38.8 ± 27.9	0.131
	Male	41.1 ± 25.6	0.036
	Female	39.7 ± 29.6	0.816

<sup>a</sup>Data are mean ± SD; p value for univariate analysis (gender controlled in total sample analysis); \*indicates chi square analysis; METS, metabolic equivalents.

TABLE 2 Characteristics by diet adherence<sup>a</sup>.

	OMN	VEG	P value
<i>n</i> (M/F)	8/19	16/39	0.267*
Dietary protein (g/kg)	1.48 ± 0.63	1.13 ± 0.46	0.046
	Male	1.47 ± 0.67	0.466
	Female	1.09 ± 0.45	0.262
Lean body mass (kg)	47.5 ± 11.2	44.2 ± 7.8	0.029
	Male	54.2 ± 5.7	0.010
	Female	40.1 ± 3.6	0.278
Serum creatinine (mg/dL)	0.86 ± 0.17	0.77 ± 0.12	0.002
	Male	0.89 ± 0.09	0.003
	Female	0.72 ± 0.09	0.034
GFR (mL/min/1.73 m)	104.2 ± 14.9	112.1 ± 11.8	0.002
	Male	113.1 ± 8.5	0.002
	Female	111.7 ± 13.0	0.022
Hand grip strength (kg)	29.9 ± 9.6	26.3 ± 7.7	0.005
	Male	35.8 ± 4.8	0.009
	Female	22.3 ± 4.6	0.047

<sup>a</sup>Data are mean ± SD; p value for univariate analysis (gender controlled in total sample analysis; age and physical activity controlled in all analyses); \*indicates chi square analysis. Serum creatinine reference ranges: adult men, 0.7 to 1.2 mg/dL; adult women, 0.5 to 1.0 mg/dL. GFR (glomerular filtration rate) reference range: >90 mL/min.

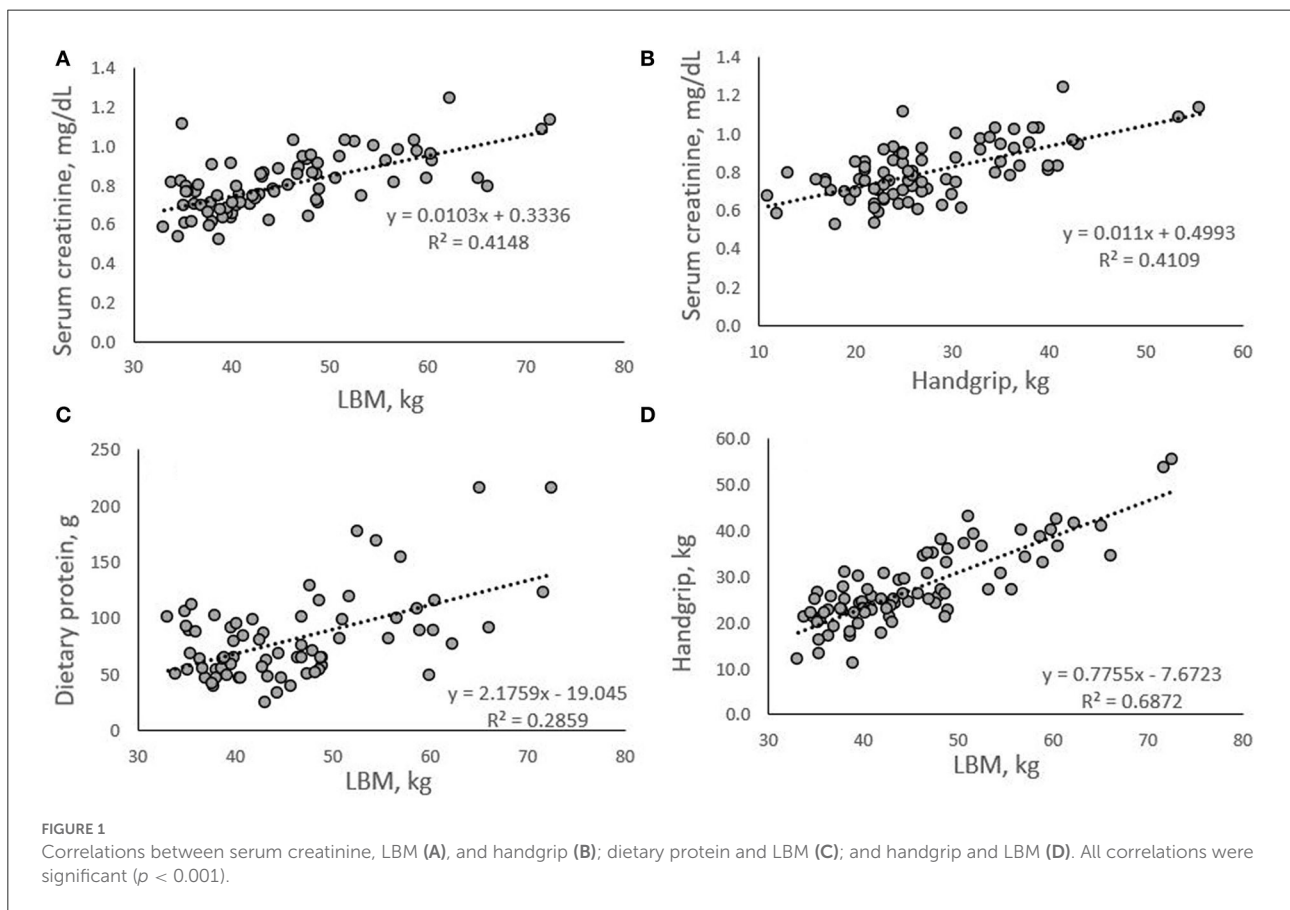
attention is directed at creatinine concentrations in the low-normal range. Low serum creatinine concentrations can indicate acute illness, severe liver disease, and the loss of muscle mass, such as in malnutrition, muscular dystrophy, or sarcopenia in older adults (45–49). Also, serum creatinine is linked to hydration status, and concentrations are lower in dehydrated states (50, 51).

In the present report, participants were young, healthy adults, screened for chronic disease, underweight and medical conditions. Thus, this report suggests that low-normal serum creatinine concentrations were linked to low LBM, reduced strength, and vegetarian diet adherence in healthy, young adults. Participants were likely well-hydrated when tested since less than 5% of the adults had serum sodium concentrations >146

TABLE 3 Multiple regression results predicting lean body mass and handgrip strength.

	Lean body mass					Handgrip strength				
	B	SE	Beta	t	p	B	SE	Beta	t	p
Gender	-12.423	1.975	-0.623	-6.290	0.000	-8.809	1.999	-0.465	-4.407	0.000
Age	0.067	0.078	0.062	0.855	0.396	-0.033	0.064	-0.032	-0.507	0.614
Diet group	-1.543	1.526	-0.079	-1.011	0.316	-2.686	1.247	-0.145	-2.154	0.035
Dietary Protein	0.034	0.021	0.138	1.615	0.111	-0.014	0.018	-0.062	-0.806	0.423
LBM						0.448	0.101	0.472	4.446	0.000
Serum creatinine	11.900	5.875	0.187	2.026	0.047					
Constant	54.766	9.862				28.655	8.634			
R <sup>2</sup>	0.712					0.775				
Adjusted R <sup>2</sup>	0.690					0.758				
	$F_{(5,65)} = 32.094^{***}$					$F_{(5,65)} = 44.816^{***}$				

\*\*\*p < 0.001.



mEq/L. The vegetarian men and women averaged creatinine concentrations below the mid-point of the reference ranges of 0.7–1.2 mg/dL for men and 0.5–1.0 mg/dL for women (52). In the men, serum creatinine was below 0.95 mg/dL in 81% of vegetarians vs. 13% of omnivores ( $p = 0.002$ ). Although not statistically significant, serum creatinine was below 0.75 mg/dL

in 67% of vegetarian women vs. 42% of omnivorous women ( $p = 0.094$ ).

Previous research indicates that creatinine can be used reliably to estimate muscle mass (30, 53) and data from the present analysis support this contention (Figure 1A). Additionally, we show a positive relationship with large effect

size between serum creatinine and handgrip strength, with serum creatinine explaining 41% of variance in handgrip strength ( $R^2 = 0.4109$ ; [Figure 1B](#)). It is known that dietary protein, and specifically the amino acid leucine, leads to the upregulation and activation of anabolic signaling systems responsible for muscle protein synthesis ([18, 19](#)). We have previously shown that in vegetarians and vegans who averaged less than the protein recommended dietary allowance (RDA) value of 0.8 g/kg/d, an increase in protein intake by 18 g per day significantly increased muscular strength in the absence of a training program ([54](#)). This novel finding suggested that increasing protein intake above the RDA when intake is low has beneficial effects on strength levels in vegetarians. It is well documented that inadequate protein intakes are associated with muscle protein breakdown, leading to catabolism and functional decline ([55](#)).

Some factors presented limitations in this study. Data were analyzed from a cross-sectional trial; therefore, causation cannot be determined. Additionally, this was a secondary data analysis, thus the study and data collection procedures were not initially designed for this specific outcome variable. There are many confounding variables that need to be considered as discussed, and although many of these variables were measured and/or controlled in this investigation, others were not. Gender significantly impacted the outcome variables and must be carefully considered when interpreting these data. Furthermore, flexitarians (e.g., meat-avoiders) were excluded from the study; hence, it is not known how occasional meat consumption may impact the outcome measures. This is an important consideration for a future trial. The renal function of participants was estimated using the calculated GFR; however, the gold standard measurement of renal function involves the injection of a tracer and its clearance by the kidneys ([56](#)). A single 24-h recall was used to estimate protein intakes. Research suggests that two to three 24-h records are needed for reasonable accuracy in estimating dietary protein ([57](#)). Future studies might include randomized controlled trials examining the impact of dietary protein on the outcome measures herein while addressing the limitations encountered in this report.

## Conclusion

This study shows that both men and women who follow an omnivore diet have significantly greater dietary protein intake, serum creatinine levels, and grip strength compared to vegetarian men and women. Additionally, the data show that creatinine is positively correlated to LBM and handgrip strength, and that dietary protein is positively correlated to LBM. These

data offer the possibility that in healthy adults, serum creatinine may be a complementary indicator of muscle mass and strength and can be utilized by practitioners and coaches, particularly for advising vegetarian clients. However, more work is warranted regarding the relevance of serum creatinine concentrations in the low-normal range in terms of LBM and functional strength, and it is important to consider gender, altered kidney function and physical activity in these assessments.

## Data availability statement

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author.

## Ethics statement

The studies involving human participants were reviewed and approved by Institutional Review Board at Arizona State University. The patients/participants provided their written informed consent to participate in this study.

## Author contributions

EB and CJ designed the secondary research, analyzed the data, wrote the manuscript, and had primary responsibility for the final content. JK and CJ designed the original research. EB conducted the secondary research and drafted the first version of the manuscript. All authors read and approved the final manuscript and provided critical comments on the manuscript.

## Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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