The Effects of Creatine snd Protein Supplements on Cystatin C and Serum Creatinine Levels Among Male Weight Training Enthusiasts Aged 20-35 Years in Surabaya Gymnasiums

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Abstract.

Protein and creatine supplementation is commonly used to enhance resistance training performance. Long-term and high-dose intake may influence renal function through renal hyperfiltration that affect glomerular filtration rate (GFR). This study aimed to examine the association between protein and creatine supplementation and renal function assessed by estimated glomerular filtration rate (through cystatin c and creatine serum), among male resistance training practitioners in Surabaya. A quantitative analytical comparative study with a cross-sectional design was conducted. The study population consisted of males aged 20–35 years who actively engaged in resistance training. Participants were classified into supplement users and non-users. Serum cystatin C and creatinine levels were measured using an automated clinical chemistry analyzer and eGFR values were calculated using CKD-EPI equations (2012 and 2021). Statistical analyses were performed to compare eGFR values between groups. Data normality was assessed using the Shapiro–Wilk test, and between-group comparisons were conducted using independent sample t-tests. Normal data distribution was confirmed (p > 0.05). Across all CKD-EPI equations, the non-supplement group consistently demonstrated higher mean eGFR values compared with the supplement group. The magnitude of these differences was small, with Cohen's d values ranging from 0.265 to 0.278, indicating minimal practical significance. Independent sample t-tests revealed no statistically significant differences in eGFR between supplement users and non-users using CKD-EPI 2021 (p = 0.309), CKD-EPI 2012 with race coefficient (p = 0.285), or CKD-EPI 2012 without race coefficient (p = 0.292).

Keywords*: Protein; creatine; supplement; gym; cystatin C; creatinine; estimated glomerular filtration rate and resistance training.*

I. INTRODUCTION

Weight training significantly alters the physiology of the cardiovascular, respiratory, and neuroendocrine systems, contributing to the prevention of chronic diseases through metabolic enhancement and neurobiological repair (van der Laan et al., 2016; Alm et al., 2019). Although laboratory examinations are often considered expensive, invasive, and requiring scheduled monitoring (Flynn et al., 2025), the use of biomarkers is crucial for athletes to optimize performance and prevent serious risks such as rhabdomyolysis or subclinical renal stress (Kumar et al., 2022). Biomarkers serve as objective indicators to assess the body's response to physical activity; however, their interpretation must be conducted comprehensively, as levels are influenced by various personal factors such as age, gender, and hydration status (Manasia & Narimasu, 2016; Lee et al., 2017).In the effort to monitor renal health, selecting the appropriate biomarker is key to calculating the Glomerular Filtration Rate (GFR). While the use of creatinine is more affordable, its accuracy is often distorted by muscle mass and the use of supplements such as creatine, which can yield false-positive results (Ozkurt et al., 2023).

In contrast, Cystatin C offers higher accuracy as it is not influenced by diet or muscle mass; thus, "Cystatin C should replace creatinine as the new minimum standard for eGFR measurement," in accordance with the Kidney Disease: Improving Global Outcomes (KDIGO) guidelines (Winter, 2019). This becomes particularly important considering the natural decline in renal function with age, where kidney mass begins to decrease starting at age 50 and GFR declines by approximately 5–10% per decade (Chapman et al., 2021). Therefore, the use of combined biomarkers is highly recommended to obtain a more accurate and safe overview of physiological health for those actively engaged in weight training.

II. METHODS

This study employs a quantitative approach with a comparative analytical method to evaluate differences in renal function parameters without providing interventions to the subjects. Using a cross-sectional study design, all data were collected at a single point in time to compare variables including cystatin C levels, serum creatinine, and estimated glomerular filtration rate (eGFR). The primary focus of the statistical analysis in this study is directed toward comparing eGFR values between the supplement-user group and the non-supplement-user group to identify the influence of additive substance consumption on the renal filtration profile of the population.

Population and Sample

This research focuses on a subject group of young adult males aged 20–35 years with a history of intensive physical activity, specifically those who are active and consistent in weight training and have been consuming creatine and protein supplements for at least the past three months. The sample size was determined using the quota sampling method with a minimum target of 60 participants (Dahlan, 2019; Sullivan, 2022). This sampling strategy was designed to ensure accurate representation of the target population. To maintain data validity, strict inclusion criteria were established, including the subject's age range (with a 1-year tolerance), documented training consistency, and a minimum of three months of protein and creatine supplement use. Conversely, exclusion criteria were applied to eliminate confounding factors, such as subjects with amputations that could extremeley alter creatinine levels, participants with unusual training intensities (far from the median), and individuals taking medications that could affect renal filtration function.

Research Variables

This study integrated the analysis of independent variables consisting of biochemical parameters, namely serum Cystatin C levels (mg/L) and serum creatinine levels (mg/dL), as well as clinical calculation instruments using the 2012 and 2021 versions of the CKD-EPI formula. All these variables were used to determine the dependent variable, which is the estimated Glomerular Filtration Rate (eGFR) in units of mL/min/1.73 m², to accurately evaluate the subjects' renal function.

Operational Definition of Variables

Table 4.1. Operational Definition of Variables

Variable	Operational Definition	Measurement Tool	Scale
Serum Cystatin C Levels	The concentration of Cystatin C in blood serum, measured in mg/L.	Laboratory examination	Ratio
Serum Creatinine Levels	The concentration of creatinine in blood serum, measured in mg/dL.	Laboratory examination	Ratio
Estimated Glomerular Filtration Rate (eGFR)	The eGFR value based on the CKD-EPI Cystatin C and creatinine formulas, measured in mL/min/1.73 m².	CKD-EPI 2021 & 2012 Formulas	Ratio

The operational definitions in this study encompass the measurement of serum Cystatin C levels (mg/L) and serum creatinine levels (mg/dL) through clinical laboratory examinations, as well as the determination of the estimated Glomerular Filtration Rate (eGFR) (mL/min/1.73 m²), calculated using the 2012 and 2021 CKD-EPI formula instruments. All three variables are measured using a ratio scale, enabling precise quantitative comparative analysis to assess the subjects' renal function based on the biomarker concentrations found in the blood.

Research Instruments

The data acquisition procedure in this study is conducted through two main instrumental stages: biochemical examination and clinical calculation. The variables for serum cystatin C and creatinine levels are obtained automatically using an autoanalyzer device through a clinical chemistry system to ensure the accuracy of laboratory results. Subsequently, these data are processed to obtain eGFR values by applying the 2012 CKD-EPI and 2021 CKD-EPI formulas using standardized medical calculators on the MDCalc website.

Research Location and Time

This research will be conducted at the Ciputra University Clinical Laboratory, Surabaya, focusing on the examination of participants' blood samples to obtain the necessary biochemical data. The entire series of research activities, ranging from data collection to analysis, is scheduled to take place over six months, from June to November 2025.

Data Analysis

The data analysis process in this study begins with data processing and presentation in the form of tables and graphs using Microsoft Excel, followed by in-depth statistical analysis using SPSS version 30 software. The initial stage of analysis involves the Shapiro–Wilk normality test chosen because the sample size is below 50 subjects per group and the Levene homogeneity test to ensure that the variance of eGFR values between the supplement-user and non-user groups is equivalent. Data are considered to meet the requirements if the significance value is ($p > 0.05$). Data that are normal and homogeneous will be further analyzed using the parametric independent sample t-test with a significance level of ($p \leq 0.05$). However, if these assumptions are not met, the analysis will shift to the non-parametric Mann Whitney test to guarantee the validity of the hypothesis testing results (Dahlan, 2019; White, 2020; Sullivan, 2022).

III. RESULT AND DISCUSSION

This study successfully collected data from 60 male participants in Surabaya who are active in weight training, after screening 100 potential candidates based on strict inclusion and exclusion criteria. Laboratory data showed variations in serum creatinine and cystatin C levels, which were influenced by individual profiles such as age, dosage, and duration of supplement use (Ko et al., 2020; Ozkurt et al., 2023). The eGFR calculation results using the 2012 CKD-EPI formula showed values that tended to be higher when including the Black race coefficient, while the 2021 CKD-EPI formula produced values that fell in the midpoint of the 2012 version's calculation range. Based on questionnaire screening results, the majority of supplement users consumed protein in the range of 60–80 grams/day and creatine at 3–6 grams/day, with dominant brands such as Optimum Nutrition and Crevolene.Statistical analysis using the Shapiro–Wilk test confirmed that the entire eGFR dataset was normally distributed ($p > 0.05$) with homogeneous variance based on Levene’s test. Although the non-supplement user group had a higher mean eGFR across all formula categories for example, on the CKD-EPI 2021, non-users ($M = 106.90$) vs. users ($M = 98.56$) the independent sample t-test results showed that the difference was not statistically significant ($p > 0.05$). This is further supported by low Cohen’s d values (0.265–0.278), indicating that the use of protein and creatine supplements in subjects actively weight training in this study does not have a major clinical impact on the decline of renal filtration function compared to those who do not use supplements.

Biological Factors Influencing Renal Function

This study indicates that the natural decline in renal function, which typically occurs after the age of 30, was not consistently observed in the subjects. This is likely due to the narrow age range of the participants and the dominant influence of high physical activity compared to the age coefficient in the CKD-EPI formula (Kovesdy, 2022; Kamper & Strandgaard, 2017). Regarding ethnicity, the use of the 2012 CKD-EPI formula involving a race coefficient remains controversial, as its Western-based cohort data is considered less representative of the heterogeneous population in Indonesia. Consequently, the 2021 CKD-EPI formula emerged as a non-racial alternative, although it still requires further validation in Asian populations (Inker et al., 2021). Furthermore, while participants reported no comorbidities and were able to train routinely without complaints, wide variations in laboratory results persisted. This suggests limitations in detecting hidden or subclinical conditions that could potentially influence the uniformity of eGFR values if not ruled out through more comprehensive diagnostic examinations (Ozkurt et al., 2023).

Lifestyle and Gym Training

An active lifestyle combined with high protein intake (>1.5 g/kg BW/day) can trigger an adaptive renal hyperfiltration response, which may mask permanent structural damage, especially when accompanied by high salt consumption and whey protein supplements that increase uremic toxins (Oh & Nowak, 2025). In this study, subjects with protein consumption >100g showed a decrease in creatinine-based eGFR, yet their Cystatin C levels remained normal. This confirms that creatinine is more sensitive to dietary influences than to actual renal function. Beyond nutritional intake, the risk of heavy metal contamination, such as lead, in protein supplements (particularly plant-based ones) is a serious concern, as lead can trigger oxidative stress and apoptosis in renal tubular cells (WHO, 2025; Harari et al., 2018). Conversely, the use of adjuvant supplements such as levocarnitine, ashwagandha, and HMB is generally reported to be safe and even beneficial in supporting muscle metabolism and reducing renal inflammation, though caution is required for specific medical conditions, such as a history of organ transplantation (Sriperumbuduri et al., 2020; Sadeghi et al., 2024). Overall, the lack of significant difference in eGFR values between supplement users and non-users in this study may be influenced by variations in brand, dosage, and non-supplement protein intake that were not calculated longitudinally.

Study Design Factors

The primary limitation of this research lies in its cross-sectional study design, where laboratory examinations were conducted only once, thus failing to record longitudinal fluctuations in renal function. Given that eGFR values are not static, an accurate evaluation ideally requires periodic monitoring for at least three months to distinguish between temporary and permanent functional changes (Quaggin & Palevsky, 2021; Inker et al., 2021). Additionally, a sample size of 30 participants per group limits statistical power, increasing the risk of false-negative results and potentially obscuring biological significance in a heterogeneous athlete population (Dahlan, 2019; Sullivan, 2022). The use of self-reported questionnaire data also acts as a limiting factor due to potential subjective bias regarding supplement dosage reporting, body composition, and fitness levels, which collectively may affect the accuracy of the final data interpretation (Ozkurt et al., 2023).

IV. CONCLUSION AND SUGGESTIONS

Conclusion

This study concludes that although the non-supplement user group consistently demonstrated higher mean eGFR values compared to the supplement-user group, the differences were very small and neither statistically nor practically significant, as indicated by the low Cohen's d values (0.265–0.278). The consumption of protein and creatine supplements in healthy individuals who routinely engage in weight training does not exert a significant negative impact on renal function ($p > 0.05$), based on both the 2021 CKD-EPI formula ($p = 0.309$) and the 2012 CKD-EPI formula with various race coefficients. Thus, the use of protein and creatine supplements in a physically active population does not trigger a meaningful decline in renal filtration function, as the eGFR values of all subjects remained within the normal clinical range.

Suggestions

To improve data accuracy in the future, subsequent research is advised to integrate anthropometric and body composition measurements (muscle and fat mass) to validate questionnaire data. Furthermore, more stringent health screenings should be conducted including blood glucose, blood pressure, and renal ultrasound to rule out subclinical conditions such as hyperfiltration due to diabetes or hypertension (Shepherd et al., 2017; Flynn et al., 2025). The research design should ideally be expanded into a longitudinal study with at least two periodic examinations utilizing ANOVA analysis, for instance to monitor real-time renal function progression and record detailed total daily protein intake from both whole foods and supplements (Jesuthasan et al., 2022). Additionally, it is important to broaden the scope of variables to include other substances, such as anabolic steroids, which have more complex nephrotoxic impacts, with monitoring schedules tailored to the participants' usage cycles to comprehensively assess the long-term impact on the urinary system (Baggish et al., 2017; Ashouri et al., 2024).

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