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Safety of Long-Term Creatine Supplementation in Relation to Kidney, Liver, and Skeletal Muscle Function and Reported Adverse Effects: A Narrative Review

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Abstract

Background: Despite robust evidence supporting the ergogenic and therapeutic benefits of creatine, safety concerns regarding long-term supplementation—particularly regarding kidney, liver, and muscle health—persist.

Aim: This narrative review evaluates the safety of long-term creatine supplementation on renal, hepatic, and skeletal muscle function, as well as reported adverse events.

Materials and Methods: A narrative analysis of 22 scientific publications (randomized controlled trials, systematic reviews, observational studies, and experimental models) was conducted across healthy, athletic, aging, female, and clinical populations.

Results: At recommended dosages, long-term creatine supplementation causes no clinically significant renal or hepatic impairment. Observed increases in serum creatinine reflect physiological turnover rather than renal dysfunction. Creatine is well-tolerated by skeletal muscle and supports muscle mass maintenance, particularly in older adults. Reported adverse effects are mild and transient, primarily involving gastrointestinal discomfort or short-term body mass changes.

Conclusions: Current evidence confirms the safety of long-term creatine supplementation when used appropriately. Further research is warranted in populations with pre-existing renal or hepatic conditions.

Key words: creatine supplementation; safety; renal function; hepatic function; skeletal muscle; adverse events

1. Introduction

In recent years, interest in creatine supplementation has also expanded beyond exercise performance to glycemic control and cognitive health, as demonstrated in recent reviews published in the *Journal of Education, Health and Sport* (JEHS) [21,22]. Creatine is one of the best-studied dietary supplements and is widely used in competitive sports, recreational physical activity, and selected clinical populations. Its effectiveness in improving exercise performance, muscle strength, and fat-free mass has been confirmed in numerous experimental and clinical studies [1,10]. In recent years, there has also been increasing interest in the potential use of creatine in the prevention and treatment of sarcopenia, metabolic diseases, and conditions associated with chronic muscle weakness [2,14].

Despite its widespread use, concerns regarding the safety of long-term creatine supplementation have persisted for many years. The most frequently raised concerns relate to the potential negative effects of creatine on kidney and liver function, as well as possible adverse effects on skeletal muscle and the gastrointestinal tract [2,5]. Some of these concerns stem from the

interpretation of increased serum creatinine as a marker of impaired renal function, although creatinine is a physiological byproduct of creatine metabolism [3,10].

The methodological heterogeneity of studies, including those involving healthy individuals, athletes, and patients with chronic diseases, has contributed to inconsistent opinions regarding the safety of creatine [5,19]. Therefore, a structured review of the literature is warranted to comprehensively evaluate the safety of long-term creatine supplementation, with particular emphasis on its effects on kidney and liver function, skeletal muscle, and reported adverse effects.

2. Methodology

This study is a narrative review based on the analysis of twenty published scientific articles, including meta-analyses, systematic reviews, randomized controlled trials, population-based studies, and experimental animal models. The review included studies evaluating the safety of creatine supplementation and its effects on kidney, liver, and skeletal muscle function, as well as publications analyzing reported adverse events. The included studies involved healthy individuals, athletes, older adults, women, and selected clinical populations.

The analyzed publications examined creatine supplementation using various dosing regimens and intervention durations, ranging from several weeks to several years. Due to the heterogeneity of study designs and methods used to assess safety, a quantitative meta-analysis was not performed, and the results are presented as a qualitative synthesis of the available evidence.

3. Results

3.1. Effects of long-term creatine supplementation on kidney function

The analysis of available studies indicates that long-term creatine supplementation does not lead to clinically significant impairment of kidney function in healthy individuals. Meta-analyses and systematic reviews including randomised and observational studies have shown no significant changes in glomerular filtration rate or creatinine clearance, despite observed increases in serum creatinine concentrations [2,3,18,19].

The elevated serum creatinine levels observed in individuals supplementing with creatine result from its normal metabolism and increased substrate availability rather than from impaired renal function [10,20]. Clinical studies using reference methods for assessing kidney function, including direct measurement of glomerular filtration rate (GFR), confirm the absence of any adverse effect of creatine supplementation, even in individuals engaged in resistance training and consuming high-protein diets [3,18].

An important component of safety assessment comes from studies using modern renal biomarkers. In randomised controlled trials, no subclinical kidney injury or changes in biomarkers of tubular damage were detected, despite short-term biochemical changes that remained within reference ranges [6].

The absence of adverse effects of creatine supplementation on kidney function has also been confirmed in selected clinical populations. In patients with peripheral artery disease, no significant changes in creatinine clearance or other renal parameters were observed following creatine supplementation [12]. Furthermore, studies on creatine homeostasis in kidney transplant recipients indicate that disturbances in creatine metabolism primarily result from impaired endogenous synthesis rather than supplementation, suggesting potential clinical relevance of creatine in this patient population [16].

3.2. Effects of creatine supplementation on liver function.

The review of the analyzed studies does not provide clear evidence of hepatotoxic effects of creatine in humans. Population-based observational studies have shown that higher dietary creatine intake is not associated with an increased risk of hepatic steatosis, fibrosis, or cirrhosis [15]. Likewise, clinical trials involving long-term creatine supplementation have not demonstrated significant changes in liver enzyme activity [4,7].

Experimental studies in animal models have shown that the effects of creatine vary depending on the metabolic background. Creatine supplementation exerted protective effects in models of non-alcoholic fatty liver disease, whereas in combination with chronic alcohol exposure, it exacerbated inflammatory changes and oxidative stress in liver tissue [13]. These findings highlight the need for cautious interpretation of experimental data and the limited applicability of direct extrapolation to human populations.

In the context of chronic liver disease, literature reviews suggest that creatine may potentially support the management of sarcopenia in patients with liver cirrhosis, without clear evidence of deterioration in hepatocyte function [14].

3.3. Effects of creatine supplementation on skeletal muscle

Skeletal muscle represents the primary reservoir of creatine in the body, which is reflected in the findings of the analyzed studies. Both clinical and experimental research indicate that creatine supplementation supports the maintenance or increase of muscle mass and improves structural muscle parameters, particularly in older adults and under conditions of reduced anabolic capacity [7,9,17].

In animal models of aging, creatine supplementation attenuated muscle wasting and did not induce degenerative changes in muscle tissue or damage to the kidneys and liver [9]. In long-term human studies, including those involving postmenopausal women, no adverse muscular effects were observed, and in some cases, improvements in body composition and muscle function were reported [7].

3.4. Reported adverse effects and tolerability of creatine supplementation

Analysis of the reviewed publications indicates that creatine supplementation is generally well tolerated. The most commonly reported adverse effects included mild and transient gastrointestinal discomfort and a small increase in body mass, which is mainly interpreted as an effect of water retention [5,10].

Systematic reviews and meta-analyses, including those focused exclusively on female populations, did not demonstrate an increased risk of serious adverse events or clinically relevant impairments in kidney or liver function compared with control groups [11]. Expert consensus statements and critical reviews further emphasize that reports of dehydration, muscle cramps, or rhabdomyolysis are not supported by high-quality scientific evidence [1,10,20].

4. Discussion

The conducted literature review encompassing twenty scientific publications indicates that long-term creatine supplementation, when used at recommended doses, exhibits a favorable safety profile in healthy individuals and in most of the analyzed clinical populations. These findings are consistent across randomized controlled trials, meta-analyses, and critical reviews, which strengthens the reliability of the presented conclusions [1,2,5,10].

The most frequently raised concerns in the literature relate to the potential negative effects of creatine on kidney function. The analyzed studies clearly demonstrate that the observed increase in serum creatinine concentrations in individuals supplementing with creatine does not reflect impaired glomerular filtration but rather represents a physiological consequence of

increased creatine metabolism [3,10,18,19]. The absence of adverse renal effects of creatine supplementation has also been confirmed in studies using direct measurements of kidney function and modern renal biomarkers, which exclude the presence of subclinical renal injury [6].

An important aspect is also the safety of creatine supplementation in populations at increased health risk. Studies involving patients with peripheral artery disease and kidney transplant recipients did not show deterioration of renal parameters associated with creatine supplementation, which challenges the commonly repeated concerns regarding its use in conditions of reduced renal reserve [12,16].

With regard to liver function, most analyzed clinical and observational studies did not demonstrate unfavorable changes in biochemical markers or an increased risk of liver disease associated with creatine supplementation [4,7,15]. Population-based data further confirm the neutral safety profile of creatine at the general population level. However, experimental studies suggesting a possible exacerbation of liver injury under conditions of chronic alcohol exposure should be interpreted with caution and should not be directly extrapolated to humans [13]. At the same time, observations indicating potential beneficial effects of creatine in non-alcoholic fatty liver disease and in the treatment of sarcopenia in patients with liver disease represent promising directions for future research [14].

Analysis of studies on skeletal muscle indicates that creatine is not only safe for this tissue but may also exert protective and supportive effects on the maintenance of muscle mass and function. These effects have been observed in both experimental studies and long-term clinical interventions, particularly in older adults and postmenopausal women [7,9,17]. The lack of evidence for an increased risk of rhabdomyolysis or other muscle injuries challenges commonly repeated concerns about the negative impact of creatine on the muscular system [10,20].

Reported adverse effects of creatine supplementation were mostly mild and transient, most commonly including gastrointestinal discomfort and a slight increase in body mass, mainly attributable to water retention [5,10]. Systematic reviews and meta-analyses, including those focused exclusively on female populations, did not demonstrate an increased risk of serious adverse events or organ dysfunction [11].

It should be emphasized that the analyzed studies exhibited substantial heterogeneity in terms of study design, duration of intervention, creatine dosage, and populations studied. These limitations justify caution when formulating generalized recommendations and indicate the need for further long-term studies, particularly in clinical populations with increased health risk.

5. Conclusions

Based on the conducted narrative review of twenty scientific publications, it can be concluded that long-term creatine supplementation, when used at recommended doses, exhibits a favorable safety profile in healthy individuals and in most of the analyzed clinical populations [1,2,5,10]. The available evidence does not support the existence of a clinically meaningful negative effect of creatine on kidney function. The increase in serum creatinine observed in some studies should be interpreted as a physiological consequence of enhanced creatine metabolism rather than as an indicator of renal damage, as confirmed by meta-analyses as well as studies using direct measurements of glomerular filtration rate and modern renal biomarkers [3,6,18,19].

Analysis of studies on liver function indicates a neutral effect of creatine supplementation in the general population, with no increased risk of liver disease or significant changes in biochemical parameters [4,7,15]. At the same time, experimental data suggesting potential adverse interactions between creatine and chronic alcohol consumption highlight the need for caution in certain clinical contexts [13].

With respect to skeletal muscle, creatine supplementation not only does not increase the risk of muscle injury but may exert beneficial effects on the maintenance of muscle mass and function, particularly in older adults and in conditions associated with sarcopenia [7,9,14,17]. The absence of evidence for an increased risk of rhabdomyolysis or other serious muscle complications further supports the good tolerability of creatine in long-term interventions [10,20].

Reported adverse effects of creatine supplementation are generally mild and transient, and systematic reviews and meta-analyses, including those focused exclusively on female populations, do not demonstrate an increased risk of serious adverse events or organ dysfunction [5,11].

In summary, creatine can be regarded as a dietary supplement with a high level of safety when used long-term. Nevertheless, an individualized approach to supplementation remains advisable, particularly in individuals with advanced kidney or liver disease, and further long-term studies in clinical populations at increased health risk are warranted [12,16].

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Declaration of the Use of Generative AI and AI-Assisted Technologies in the Writing Process

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