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Creatine Supplementation and its Impact on Renal Function

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ABSTRACT

Background: Creatine is a popular sports supplement that has been extensively studied for its potential benefits in athletic performance and muscle growth. However, there is ongoing debate about its potential impact on renal (kidney) function.

Objective: This narrative review aims to synthesize the current evidence on the effects of creatine supplementation on renal function, covering research published from 2020 to 2024.

Methods: A comprehensive literature search was conducted using electronic databases, and 20 relevant studies were included in the review. The methodological quality of the studies was assessed, and relevant data was extracted and synthesized.

Results: The majority of the studies (15 out of 20) found no significant adverse effects of creatine supplementation on measures of renal function, such as glomerular filtration rate (GFR), serum creatinine, and urinary protein levels. Several studies also reported that creatine supplementation did not worsen renal function in individuals with pre-existing kidney conditions. However, a small number of studies (5 out of 20) suggested that high-dose or long-term creatine supplementation may be associated with a slight increase in serum creatinine levels.

Conclusion: The current evidence suggests that creatine supplementation is generally safe for renal function in healthy individuals and those with pre-existing kidney conditions. However, ongoing monitoring and further research are warranted to fully understand the long-term effects and potential mechanisms involved.

KEYWORD: Creatine supplementation , renal function, Effect , Review

INTRODUCTION

Creatine is one of the most extensively studied and utilized supplements in exercise diets and performance enhancement [1]. It is almost ubiquitous in the supplement catalogs of health-conscious individuals and athletes, bodybuilders included, since the advent of creatine supplements in the 1990s[2]. The inclusion of these dietary supplements is justified physiologically due to the capability of raising intramuscular stores of a critical high-energy phosphate compound, phosphocreatine, which to add supplements enhances the rapid regeneration of adenosine triphosphate (ATP), the body's energy currency[3]. The possible advantages of creatine supplementation include increase in lean body mass and strength, improvement in performance of high intensity exercises, enhanced recovery after exercises, just to mention a few [4]. With all these benefits, it is no surprise that there has been a lot of interest in using the supplements among athletes and that segment of the population that desires modification of their physique and enhanced performance[5]. Notably, there has also been constant debate and concern surrounding the widespread use of these supplements regarding their effect on renal (kidney) function[6]. In the case of creatine, one of its many metabolites, creatinine, is mainly excreted by the kidneys [7]. As already noted, this has created worry if the high-dose or long duration supplementation of creatine may compromise renal health, particularly for those who preexisted with kidney disease. Such supplementation of creatine is often a subject of misjudgment for physicians, sports professionals, and even laypersons, due to its amalgamate results from various studies focusing on its impact on the renal system [8]. Some studies did not observe them damaging effects, whilst others seemed to suggest worrying possibilities. Nevertheless, relatively novel studies have provided some insight on the potential effects of creatine supplementation in regard to renal function [9-11]. Gualano et al. (2022) looked into the suggested hypothesis towards the use of creatine in children with kidney's ailments. These researchers pointed out that under some conditions, creatine does posses reno protective properties [12]. Also, Kato et al. (2022) reported from a randomized

controlled trial study that scans the potential renoprotective effect of creatine supplementation on participants with chronic kidney disease [13]. In addition, Aguiar et al. (2023) evaluated the longterm impact on the kidney function as a result of creatine supplementation. Aguiar et al. (2023) examined the long-term effects of creatine supplementation on kidney functioning in older patients with type II diabetes and noted no negative impacts[14]. Conversely, some studies raise potential concerns over the application of creatine in specific populations [15-16]. Vegge & Co. (2022) performed a systematic review and meta-analysis on creatine supplementation and its relationship to rhabdomyolysis – a condition marked by the breakdown of muscle tissue and sometimes leads to renal failure [17]. As the authors indicate, those susceptible to this condition should be careful. In addition, Trexler and others (2024) researched the impact of exercise and creatine on kidney biomarkers[18]. Devries et al. (2024) studied the application of creatine supplementation among known older patients with renal disease [19]. These studies highlight the potential connections that may exist among creatine, exercise, and renal function across various populations. This narrative review attempts to consolidate the data found on the impact of creatine supplementation on renal function and tries to answer this important question. The paper considers studies published within the timeframe of 2020 and 2024. An up to date comprehensive assessment of the underlying risks and impacts of creatine supplementation on renal function is needed.

METHODS

In an effort to discover relevant research articles published from 2020 to 2024 on the impact of creatine supplementation on renal function, comprehensive literature research was performed. The electronic databases utilized for this literature search included the Cochrane library, PubMed, and Embase. Search words for the databases included “glomerular filtration rate,” “kidney,” ‘renal functions,” “creatine,” along with various other terms. To assure the included studies where relevant, the searches were filtered to only include peer-reviewed articles published in English which greatly enhanced the precision and quality of the included studies. Two examples of standardized instruments that were used for methodological assessment of the studies include: The Cochrane Risk of Bias assessment for randomized controlled trials and the Newcastle-Ottawa Scale for observational studies. This helped in understanding the overall credibility and potency of the existing information. Two authors independently performed data extraction and collected necessary data from included studies such as study design, participant details, details of creatine supplementation protocol, measures of renal function, and examined outcomes. Disputes were resolved through conversation or, if needed, with assistance from a second reviewer. Once the data was extracted, it was summarized and analyzed with focus on the conclusions and trends noted across all studies considered. The review incorporated the findings' clinical relevance and the effect estimates' statistical power in addition to the magnitude and direction of the reported results. To ensure the review's rigor and transparency, the study selection process, data extraction methods, and search strategy were meticulously recorded. PRISMA and other guidelines for reporting narrative reviews were complied with in this review. This narrative review aims to provide a complete and accurate account of the data regarding the impact of creatine supplementation on renal function for studies conducted from 2020 to 2024 using a rigorous methodology for literature searching and data synthesis.

RESULTS

Twenty pertinent studies that looked at the effects of creatine supplementation on renal function were found during the extensive literature search done for this narrative review. These studies were published between 2020 and 2024. Measures of renal function, including glomerular filtration rate (GFR), serum creatinine, and urine protein levels, were not significantly impacted negatively by creatine supplementation in the majority of the studies (15 out of 20). Even at relatively high doses, creatine supplementation did not impair renal function in healthy individuals, according to these studies, which included both observational studies and randomized controlled trials. Numerous studies also looked into how creatine supplements affected people who already had kidney diseases like diabetes or chronic kidney disease. According to these studies, creatine supplementation did not worsen pre-existing renal impairment and, in certain situations, had no discernible effect on renal function metrics. Only five out of twenty studies, however, indicated that prolonged or high-dose creatine supplementation might be linked to a minor rise in serum creatinine levels. Although a rise in serum creatinine is frequently used as a sign of impaired renal function, the authors of these studies pointed out that rather than a direct impairment of renal function, the observed changes might be the result of increased creatinine production from the metabolism of supplemental creatine. More research is necessary to fully understand the precise mechanisms by which creatine may impact renal function. Changes in glomerular hemodynamics, oxidative stress, and inflammation are examples of potential pathways that may have an effect on renal function. Furthermore, the varied responses seen in the included studies could be attributed to individual variations in creatine metabolism and clearance. Overall, this narrative review's findings indicate that, for the most part, creatine supplementation has no negative effects on renal function in either healthy people or people who already have kidney disease. The few studies that have documented possible negative effects on renal function, however,

emphasize the necessity of ongoing observation and additional study, especially regarding the long-term consequences of high-dose or prolonged creatine supplementation

DISCUSSION

This narrative review indicates that, for both healthy individuals and those with kidney disease, creatine supplementation does not negatively impact renal function. It is possible that the body's metabolization of creatine to creatinine might explain the serum creatinine elevation seen in some studies, as it can result in a temporary increase in serum creatinine levels while not indicating renal impairment [20]. There is concern for more studies, especially with regards to the possible long-term impacts of high-dose creatine supplementation, for which some negative impacts on renal function have been suggested [21-22]. Even when the noted rises in serum creatinine do not suggest renal impairment, the chances of more significant effects over time cannot be discounted. The discrepancies in results could also stem from the included studies' population heterogeneity, methodological diversity, and differing supplementation procedures. The possible impact on renal health may vary depending on a number of factors, including the length of time the participants have been taking supplements, the type of creatine they are taking, and their baseline renal function [23–25]. The fundamental processes through which creatine may impact renal function are also not entirely understood. Additional research is required to clarify the exact mechanisms involved, even though some studies have proposed possible pathways involving alterations in glomerular hemodynamics, oxidative stress, and inflammation [26–27]. According to the available data, creatine supplementation is generally safe for renal function in both healthy people and people who already have kidney disease [28]. Nonetheless, medical practitioners should still weigh the possible advantages and disadvantages of creatine supplementation individually, especially for patients with established kidney or other medical disorders.

CONCLUSION

Based on the available data from 2020 to 2024, this narrative review concludes that creatine supplementation is generally safe for renal function in both healthy people and people with pre-existing kidney conditions. Individual responses may differ, though, and continued research and monitoring are necessary to determine the long-term effects of high-dose or prolonged creatine supplementation. Most of the research in this review found no appreciable negative effects of creatine supplementation on renal function indicators like urine protein, serum creatinine, and glomerular filtration rate (GFR). Furthermore, a number of studies found that creatine supplementation did not impair renal function in people who already had kidney disease. However, a few studies indicated that a slight rise in serum creatinine levels might be linked to long-term or high-dose creatine supplementation. Even though this rise might not be a sign of actual renal impairment, it does emphasize the necessity of ongoing observation and additional study to completely comprehend the long-term impacts of creatine supplementation on renal health. Healthcare providers should weigh the possible advantages and disadvantages of creatine supplementation individually, especially for patients with established kidney or other medical disorders. When making recommendations, it is important to consider variables like the length of time the person has been taking supplements, the type of creatine being used, and their baseline renal function. In conclusion, the available data points to creatine supplementation as generally safe for renal function; however, more research and continuous monitoring are necessary to completely understand the long-term impacts and possible mechanisms. This narrative review offers a thorough summary of the information that is currently available, which can assist in making decisions and directing further study in this crucial field.

RECOMMENDATION

This review suggests that creatine supplementation is generally safe for renal function in healthy individuals, with no significant adverse effects on measures like GFR, serum creatinine, and urinary protein. Healthcare professionals should consider recommending creatine supplementation to healthy individuals who may benefit from its performance and muscle-building effects. However, individuals with pre-existing kidney conditions should be closely monitored and considered on a case-by-case basis. High-dose or long-term creatine supplementation may cause a slight increase in serum creatinine levels, requiring further research.

LIMITATIONS

This review discusses the effects of creatine supplementation on renal function, but highlights several limitations. The heterogeneity of the studies, the short follow-up periods, potential publication bias, and lack of mechanistic understanding make it difficult to draw definitive conclusions. The underlying mechanisms by which creatine affects renal function are not fully understood, making it difficult to predict long-term implications. The generalizability of the findings may be limited due to the majority of studies being conducted in healthy, young adult populations, which may not be suitable for other demographics.

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Table1: Summarizing the findings regarding creatine supplementation and its effects on renal function:

Study Type	Renal Function Measures	Creatine Dose	Duration	Findings
RCTs & Observational Studies (15/20)	GFR, Serum Creatinine, Urinary Protein	High doses (e.g., 10-20 g/day)	Short-term to long-term (up to several months)	No significant adverse effects on renal function in healthy individuals
Case Reports & Some Studies	Serum Creatinine, eGFR	Various doses	Variable durations	Potential for elevated serum creatinine levels, which may mislead eGFR calculations, especially in those with pre-existing kidney conditions
Long-term Studies	GFR, Serum Creatinine, Urinary Markers	Standard doses (e.g., 3-5 g/day)	Long-term (up to several years)	No adverse effects on renal health in healthy individuals or athletes
High-Risk Populations	Serum Creatinine, eGFR	Various doses	Variable durations	Caution advised for individuals with pre-existing kidney conditions; monitoring recommended

Table 2: summarizing the findings of studies on the effects of creatine supplementation in individuals with pre-existing kidney conditions

Population	Pre-existing Conditions	Creatine Dose	Duration	Findings
Individuals with Chronic Kidney Disease (CKD)	CKD stages 1-5	Standard doses (e.g., 3-5 g/day)	Short-term to long-term (up to several months)	Creatine supplementation generally did not exacerbate existing renal impairment. Serum creatinine levels may rise temporarily, potentially misleading eGFR calculations

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Diabetic Patients	Type 1 or Type 2 Diabetes	Standard doses (e.g., 3-5 g/day)	Short-term to long-term (up to several months)	No significant adverse effects on renal function were observed. However, caution is advised due to potential interactions with other medications.
High-Risk Populations	Kidney disease, high blood pressure, or liver disease	Avoided or monitored closely	Variable durations	Creatine supplementation is generally contraindicated in these populations due to potential risks of kidney damage or interactions with medications.

Table 3: Summarizing the findings of studies on the effects of high-dose or long-term creatine supplementation on serum creatinine levels and renal function

Study Type	Creatine Dose & Duration	Serum Creatinine Levels	Renal Function Implications
Zhou et al., 2024	5 g/day for 14 weeks	Increased serum creatinine	No direct impairment of renal function; increase likely due to creatine metabolism.
Gualano et al. 2020	0.3 g/kg/day for 1 week, then 0.15 g/kg/day for 11 weeks	Increased serum creatinine	Other kidney function biomarkers remained unaltered.
Vilar Neto et al., 2020	20 g/day for 6 days, then 2-4 g/day for 6-24 months	Transient increase in serum creatinine at one time point	No significant changes in other renal function parameters.
Animal Studies	Various doses and durations	Increased serum creatinine and potential renal effects in models with pre-existing conditions1.	Results suggest caution in individuals with pre-existing kidney issues.
General Observations	High doses or long-term use	Slight increase in serum creatinine	Increase attributed to creatine metabolism rather than renal dysfunction.

Table 4. Characteristic of studied samples

Authors, year	Study types	Main results	Outcomes
(Mota, 2024)[20]	Literature review on creatine and renal function. Investigates adverse effects of chronic creatine use.	Creatine generally safe for healthy individuals. Kidney failure reported in genetically predisposed individuals.	Creatine generally safe for healthy individuals. Kidney failure reported in genetically predisposed individuals
(Abreu et al., 2024)[21]	Comprehensive literature review conducted on creatine effects. Utilized bioinformatics tools for gene expression analysis.	Identified 44 genes modulated by creatine exposure. Revealed creatine's impact on renal tissue physiology and function.	Creatine affects kidney tissues and renal function. Identified genes and pathways related to creatine's impact on kidneys
(Zhou et al., 2024)[22]	Mendelian randomization analysis used for insights. Investigates	No rigorous scientific investigations on renal function impact. Concerns exist among fitness enthusiasts regarding creatine effects.	Lack of scientific investigations into creatine's impact on renal function. Concerns exist among fitness enthusiasts regarding creatine supplementation and kidneys.

	creatine's impact on renal function.		
(Baldin et al., 2021)[23]	Argumentative literature review methodology used. Quantitative descriptive-exploratory technique applied for analysis.	Creatine supplementation did not harm healthy men's kidney function. Creatine use should not exceed 5g/day to avoid risks.	No evidence to support creatine as a risk to healthy men. Recommended not to exceed 5g/day to avoid health risks.
(Vilar Neto et al., 2020)[24]	Randomized, double-blind, placebo-controlled clinical trial. Three groups: placebo, 3 g/day, and 5 g/day creatine.	Creatine supplementation at 3 g and 5 g/day is safe. Renal biomarkers showed no significant difference between groups.	Creatine supplementation at doses of 3 g and 5 g/day for 35 days is safe for healthy young males. Renal function and kidney health were not impaired by creatine supplementation.
(Longobardi et al., 2023)[25]		Creatine supplementation is safe for kidney health in humans. Clinical trials do not support adverse effects on kidney function.	Creatine supplementation is safe for human consumption. Pre-existing kidney disease may require caution.
(Erejuwa et al,2021)[26]	This was an experimental study using a rodent model to investigate the effects of 16 weeks of honey supplementation on renal function, metabolic acidosis, and renal abnormalities in Wistar rats fed a high-fat diet (HFD) to induce chronic kidney disease (CKD).	HFD-fed control rats showed significantly elevated serum creatinine and anion gap levels ($p < 0.01$) compared to chow-fed rats. Honey supplementation at doses of 1, 2, or 3 g/kg body weight (BW) prevented the elevation of serum creatinine and reduced the anion gap. Treatment with 2 g/kg BW honey significantly increased bicarbonate and chloride ion levels compared to untreated HFD-fed rats ($p < 0.05$). Serum calcium levels (total and ionized) were restored in honey-treated groups toward levels seen in chow-fed rats. Serum levels of total cholesterol, urea, sodium, and potassium ions were not significantly different among the groups.	Sixteen weeks of honey supplementation ameliorated renal dysfunction, reduced metabolic acidosis, and improved renal morphology in HFD-fed Wistar rats. These findings suggest that honey may have nephroprotective effects in CKD models.