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Effects of creatine supplementation on postoperative wound healing: mechanisms and evidence

Efeitos da suplementação de creatina na cicatrização pós-operatória: mecanismos e evidências

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ABSTRACT

Introduction: Tissue healing and repair processes are complex and require adequate energy and nutritional supply to occur efficiently. Creatine, a nitrogenous compound widely known for its role in muscle energy metabolism and its use as an ergogenic supplement, has emerged as a potential therapeutic agent in several conditions beyond sports.

Objective: This narrative review aimed to synthesize the main information on the influence of creatine supplementation on healing and postoperative recovery.

Method: A narrative search was conducted in the PubMed, Scopus, Web of Science, and LILACS databases, using the DeCS/MeSH descriptors: Creatine, Wound Healing, Postoperative period, Tissue Repair, and Dietary supplements. Original and review articles published since 2000, in Portuguese and English, were included.

Result: Seventeen articles were selected.

Conclusion: Creatine has robust theoretical potential to aid healing and postoperative recovery, inducing favorable cellular responses and attenuating catabolism. Understanding the biological mechanisms that mediate the effects of creatine on tissue repair is essential for the development of effective nutritional intervention strategies in the perioperative period.

KEYWORDS: Creatine. Wound healing. Postoperative period. Dietary. Supplements.

Central Message

Creatine, widely known for its role in muscle energy metabolism and its use as an ergogenic supplement, has emerged as a potential therapeutic agent in several conditions, in addition to sports. Evidence indicates that metabolic stress induced by surgical procedures increases the demand for ATP, and creatine, through the phosphocreatine system, acts in the rapid regeneration of this compound.

Perspective

The mechanisms by which creatine supplementation may positively affect postoperative recovery include optimizing energy metabolism, modulating inflammation and oxidative stress, and influencing protein synthesis and cellular hydration. Surgery imposes metabolic stress that can deplete cellular energy reserves, leading to impairment of cellular function and repair processes.

RESUMO

Introdução: Os processos de cicatrização e reparo tecidual são complexos e demandam suprimento energético e nutricional adequado para ocorrerem de forma eficiente. A creatina, um composto nitrogenado amplamente conhecido por seu papel no metabolismo energético muscular e seu uso como suplemento ergogênico, tem emergido como potencial agente terapêutico em diversas condições além do esporte.

Objetivo: Revisão narrativa a fim de sintetizar as principais informações sobre a influência da suplementação de creatina nos eventos de cicatrização e recuperação pós-operatória.

Método: Realizou-se busca nas bases de dados PubMed, Scopus, Web of Science e LILACS, utilizando os descritores DeCS/MeSH: Creatine, Wound healing, Postoperative period, Tissue repair e Dietary supplements. Foram incluídos artigos originais e de revisão publicados a partir de 2000, em português e inglês.

Resultado: Foram selecionados 17 artigos.

Conclusão: A creatina possui potencial teórico robusto para auxiliar na cicatrização e recuperação pós-operatória, induzindo respostas celulares favoráveis e atenuando o catabolismo. A compreensão dos mecanismos biológicos que mediam os efeitos da creatina sobre o reparo tecidual é essencial para o desenvolvimento de estratégias de intervenção nutricional eficazes no perioperatório.

PALAVRAS-CHAVE: Creatina. Cicatrização. Período pós-operatório. Dieta. Suplementos.

Supplementary material for the articles included in this publication[1-17]

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INTRODUCTION

Adequate recovery in the postoperative period is essential for the prognosis and quality of life of patients, and is a constant challenge in clinical practice.[1] The processes of healing and tissue repair are complex and require adequate energy and nutritional supply to occur efficiently.[2] Creatine, a nitrogenous compound widely known for its role in muscle energy metabolism and its use as an ergogenic supplement.[3] has emerged as a potential therapeutic agent in several conditions beyond sports. Evidence indicates that metabolic stress induced by surgical procedures increases the demand for ATP, and creatine, through the phosphocreatine system, acts in the rapid regeneration of this compound.[4]

Surgical interventions often lead to a catabolic state, with loss of muscle mass and impaired function, in addition to a systemic inflammatory response that, if exacerbated or prolonged, can impair healing.[5] The search for nutritional strategies that can modulate these responses and optimize recovery is, therefore, of great relevance. The relationship between creatine supplementation and the optimization of postoperative recovery is multifaceted, impacting the body through several biological mechanisms.[6] It is known that, in addition to energy supply, creatine can influence cellular hydration, protein synthesis, inflammatory response, and oxidative stress, all of which are crucial processes for tissue repair and wound healing.[7,8]

This review aimed to synthesize and critically analyze the available scientific evidence on the potential effects of creatine supplementation on wound healing and tissue recovery in the postoperative period.

METHOD

This is a narrative review of the literature, carried out in the PubMed, Scopus, Web of Science and LILACS databases. The search used the following keywords (DeCS/MeSH) and their correspondents: "Creatine", "Wound Healing", "Postoperative Period", "Tissue Repair", and "Dietary Supplements". The inclusion criteria included original articles (clinical trials, observational studies, studies in animal models) and review articles (systematic, meta-analyses) published from the year 2000 to December 2023, in Portuguese and English, available in full text. Articles that did not address the topic of creatine supplementation in the context of healing or post-trauma/surgery recovery, or that focused exclusively on sports performance unrelated to injury, were excluded. The selection process followed the PRISMA[9] guidelines for identification, screening, and inclusion of studies. In total, 17 articles were selected for this review (See table in supplemental material at the end).

DISCUSSION

The mechanisms by which creatine supplementation may positively affect postoperative recovery include optimizing energy metabolism, modulating inflammation and oxidative stress, and influencing protein synthesis and cellular hydration. Surgery imposes metabolic stress that can deplete cellular energy reserves, leading to impairment of cellular function and repair processes.[1]

Biochemical and physiological mechanisms of creatine in tissue repair

The fundamental mechanisms that contribute to the potential benefits of creatine in the postoperative period are associated with several pathways. These include the primary role in the ATP-phosphocreatine system for rapid energy resynthesis in tissues with high demand, the attenuation of protein catabolism often observed after surgical procedures[9], the possible modulation of the inflammatory response[10] and the antioxidant capacity.[11] In terms of direct impact, systemic inflammation and exacerbated oxidative stress in the postoperative period can delay healing. Creatine has been shown in some contexts to reduce inflammatory markers such as TNF-α and IL-6 and protect against oxidative damage.[10,11]

Preservation of muscle mass and functional recovery

The preservation of muscle mass in the postoperative period is crucial, especially in patients undergoing major operations or requiring immobilization. Hespel et al.[1] demonstrated that creatine supplementation attenuated muscle atrophy and facilitated rehabilitation after immobilization in humans. This effect is attributed both to the improvement of energy availability to muscle fibers and to possible direct effects on the expression of myogenic factors. The loss of muscle mass not only affects mobility, but also reduces the reserve of amino acids available for the synthesis of new proteins necessary for healing. Other mechanisms related to creatine supplementation include cell volumization. Creatine attracts water into the cell, which can act as an anabolic signal, stimulating protein synthesis and inhibiting proteolysis.[12]

Creatine in the healing of specific tissues

Studies indicate that creatine supplementation may be particularly beneficial in tissues with a high metabolic rate or in regeneration. Antolic et al.[13] demonstrated in rats that creatine supplementation accelerated bone healing. Although direct transposition to humans and other tissues requires further studies, the principle of providing additional energy substrate for the cells involved in repair (osteoblasts, fibroblasts, keratinocytes) is promising. In the context of skin wound healing, direct evidence of oral creatine supplementation is still limited. However, fibroblasts, central cells in collagen production and extracellular matrix, are metabolically active and could benefit from increased ATP availability. The topical application of creatine has been explored in cosmeceuticals, suggesting improvement in skin bioenergetics[2], but oral supplementation for surgical wound healing requires specific investigation.

Dosage and safety

Considering safety, creatine supplementation is generally well tolerated in healthy subjects at recommended doses (saturation phase of ~20g/day for 5-7 days, followed by maintenance of 3-5 g/day).[3,7] However, in surgical patients, especially those with

compromised pre-existing renal function or at risk of acute kidney injury, supplementation should be considered with caution and under monitoring.[14]

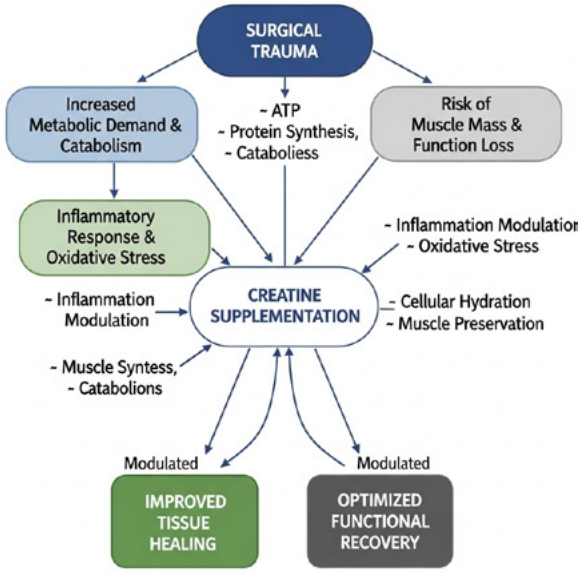

FIGURE — Potential effect of creatine supplementation on postoperative recovery.

CONCLUSION

Creatine supplementation has robust theoretical potential and some indirect evidence of benefit for postoperative recovery, particularly in attenuating muscle loss and improving function. Its mechanisms of action, centered on the optimization of cellular bioenergetics and possible anabolic and anti-inflammatory effects, are congruent with the needs of the tissue repair process. However, direct evidence on the impact of creatine on the healing of specific surgical wounds in humans is currently limited. Future research should prioritize well-controlled randomized controlled trials to elucidate the efficacy, safety, and optimal protocols of creatine supplementation in this context. If proven effective, creatine could become a valuable adjuvant tool to improve surgical outcomes.

Authors' contributions

Gabriel Mathias Vitoreti – Conceptualization, Supervision
Homero Grein Neto – Formal Analysis, Revision
Mariana Tiboni Nacamura – Investigation, Writing (revision and editing)
Luiz Eduardo Latorre Guimarães – Methodology, Project Management

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