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Chronic Proton Pump Inhibitor Use in Physically Active Individuals: Implications for Micronutrient Status, Bone Health and Physical Performance

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ABSTRACT

Background. Proton pump inhibitors (PPIs) are widely used in the treatment of acid-related gastrointestinal disorders. While generally safe in short-term therapy, increasing evidence suggests that long-term use may adversely affect micronutrient status and bone metabolism, which may be particularly relevant for physically active individuals.

Aim. The aim of this review is to summarize the current evidence regarding the effects of chronic PPI use on micronutrient status and bone health, and its potential indirect influence on physical performance in physically active individuals.

Material and methods. A narrative review of peer-reviewed literature (2006–2025) was conducted, including systematic reviews, meta-analyses, and observational studies. The

qualitative synthesis focused on PPI pharmacodynamics, micronutrient (iron, vitamin B12, calcium, magnesium) homeostasis, musculoskeletal outcomes, and physical performance, with an emphasis on biological plausibility.

Results. Long-term PPI therapy leads to sustained gastric acid suppression, which may impair the absorption of key micronutrients, including iron, vitamin B12, calcium, and magnesium. Evidence suggests associations between chronic PPI use and iron deficiency, altered vitamin B12 status, hypomagnesemia, and reduced calcium bioavailability. These disturbances may negatively affect oxygen transport, neuromuscular function, energy metabolism, and bone mineral density. Observational studies indicate a modest increase in fracture risk and potential impairment in physical performance; however, findings remain inconsistent and are influenced by confounding factors such as comorbidities and baseline nutritional status.

Conclusion. Chronic PPI use may contribute to subtle but clinically relevant disturbances in micronutrient status and bone health, potentially affecting physical performance, particularly in physically active individuals. Given the predominantly observational nature of available evidence, these associations should be interpreted cautiously. Regular reassessment of long-term PPI therapy and monitoring of nutritional and skeletal health may be warranted. Further well-designed prospective studies are needed to clarify causal relationships and better define the impact of PPIs on physical performance outcomes

Keywords: proton pump inhibitors, physical performance, micronutrients, iron deficiency, vitamin B12, magnesium, calcium, bone health

1. Introduction

Proton pump inhibitors (PPIs) are among the most widely prescribed medications worldwide. Recent systematic data indicate that nearly one-quarter of the adult population uses these agents [1]. PPIs constitute the cornerstone of pharmacotherapy for acid-related upper gastrointestinal disorders, including gastroesophageal reflux disease (GERD), peptic ulcer disease, Helicobacter pylori eradication, and functional dyspepsia [2].

Although proton pump inhibitors are generally considered safe and well tolerated during short-term therapy, accumulating evidence suggests potential adverse effects associated with their long-term use. In the literature, there is no universally accepted definition of long-term proton pump inhibitor (PPI) use. A scoping review by Haastrup et al. [3] demonstrated substantial variability, with definitions ranging from more than 2 weeks to over 7 years, although the most commonly used thresholds were ≥6 months and ≥1 year. In a clinical context, long-term use

may be considered as therapy extending beyond 4–8 weeks, depending on the indication, whereas for research purposes, a duration of ≥6 months has been proposed, particularly in pharmacoepidemiological studies.

Reported risks include increased susceptibility to pneumonia and enteric infections (e.g., *Clostridioides difficile*), a higher incidence of bone fractures, possible associations with gastric neoplasia, and impaired absorption of essential micronutrients, particularly magnesium, iron, calcium, and vitamin B12 [2, 4]. However, the long-term safety of PPIs remains a subject of ongoing debate, with inconclusive information across the literature. Most available data are derived from observational studies rather than randomized controlled trials and should therefore be interpreted with caution due to potential confounding factors. Consequently, in clinical decision-making, potential harms should be evaluated considering the level of evidence, strength of association, and biological plausibility [2]. While such metabolic and absorptive alterations may be of limited clinical relevance in the general sedentary population, their implications could be more pronounced in physically active individuals due to increased physiological demands. In this subgroup, even subtle disturbances in micronutrient availability or bone metabolism may negatively affect training capacity, recovery or overall physical performance.

According to the World Health Organization (WHO) 2020 guidelines on physical activity and sedentary behaviour, adults should engage in 150–300 minutes of moderate-intensity, or 75–150 minutes of vigorous-intensity aerobic physical activity per week, or an equivalent combination, with additional muscle-strengthening activities recommended on two or more days per week [5]. Physical activity can occur in various domains, including leisure, transportation, occupational, and household activities, and should be performed regularly throughout the week to achieve health benefits.

The aim of this study is to synthesize current evidence on the potential effects of long-term PPI therapy on physical performance, with particular emphasis on the development of micronutrient deficiencies (e.g., magnesium, iron, vitamin B12) and alterations in bone metabolism in physically active individuals.

2. Material and methods

Literature Search Strategy

A comprehensive narrative review was conducted to identify studies examining the relationship between chronic proton pump inhibitor (PPI) use, micronutrient status, bone health, and

physical performance. The primary electronic databases searched included PubMed/MEDLINE, Scopus, Web of Science, and Google Scholar. The search covered articles published from January 2006 to early 2025 in order to capture both foundational mechanistic studies and the most recent clinical evidence.

Search Terms and Keywords

To ensure a comprehensive retrieval of studies, combinations of the following Medical Subject Headings (MeSH) and free-text terms were used:

- Intervention: "proton pump inhibitors", "PPI", "omeprazole", "pantoprazole", "acid-suppressive therapy"
- Outcomes (nutritional and skeletal): "micronutrient deficiency", "iron malabsorption", "vitamin B12", "cobalamin", "hypomagnesemia", "calcium absorption", "bone mineral density", "fracture risk"
- Population/context: "physical performance", "exercise capacity", "athletes", "physical activity", "sports medicine", "muscle fatigue", "neuromuscular function"

Inclusion and Exclusion Criteria

Studies were included if they were peer-reviewed, published in English, and directly addressed the pharmacodynamic effects of PPIs on the homeostasis of iron, vitamin B12, calcium, or magnesium. Priority was given to systematic reviews, meta-analyses, prospective cohort studies, retrospective observational studies, and relevant case-control studies.

Studies were excluded if they focused exclusively on pediatric populations, short-term PPI use (defined as <4 weeks without chronic intent), or solely on gastrointestinal efficacy without evaluating metabolic, nutritional, or musculoskeletal outcomes.

Data Synthesis

Due to the heterogeneity of the available evidence—particularly the limited number of randomized controlled trials involving athletes using chronic PPI therapy—a qualitative synthesis approach was applied. The evidence was assessed in terms of biological plausibility, underlying physiological mechanisms, and its potential impact on physical performance and recovery.

3. Mechanism of action

Proton pump inhibitors (PPIs) are lipophilic weak bases that function as inactive prodrugs. Owing to their lipophilic properties, they are readily absorbed into the systemic circulation and preferentially accumulate in the highly acidic secretory canaliculi of gastric parietal cells. In

this environment, PPIs undergo protonation and are converted into their active sulfenamide form [6].

Once activated, the drug covalently binds to cysteine residues of the H^+/K^+-ATPase enzyme system (the "proton pump"), forming stable disulfide bonds. This interaction results in irreversible inhibition of the final step of gastric acid secretion. Because the blockade is irreversible, acid production can resume only after the synthesis of new H^+/K^+-ATPase molecules, which explains the prolonged duration of action of PPIs despite their relatively short plasma half-life [6,7].

The primary physiological consequence of this mechanism is profound and sustained suppression of both basal and stimulated gastric acid secretion, leading to a significant elevation of intragastric pH. While this iatrogenic hypochlorhydria represents the intended therapeutic effect in acid-related disorders, it concurrently modifies the gastrointestinal environment necessary for optimal ionization and absorption of pH-dependent micronutrients.

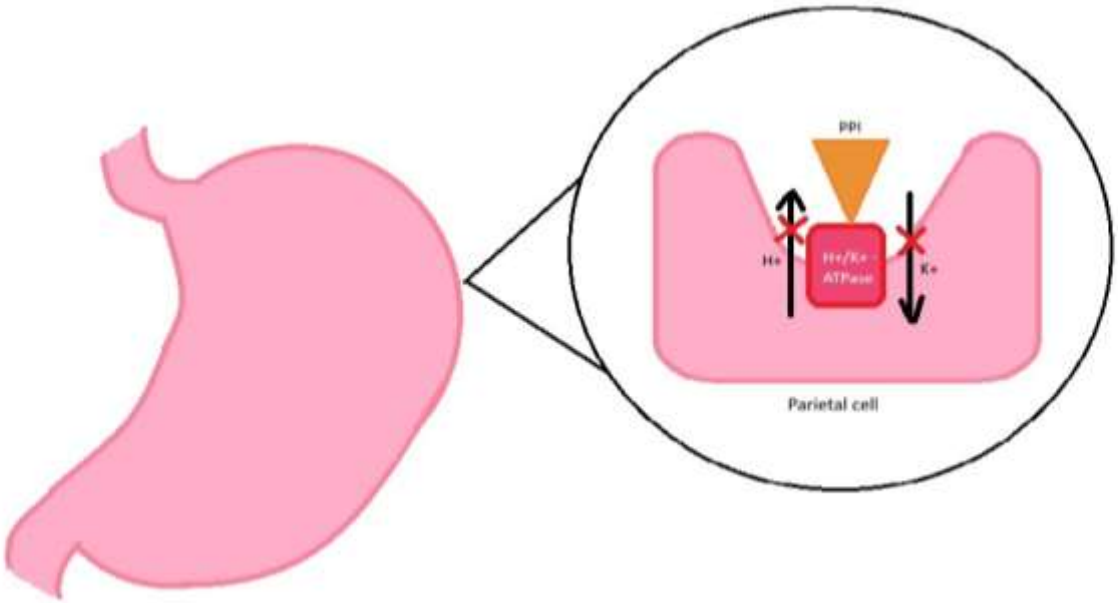

Fig. 1. Schematic representation of the proton pump inhibitor (PPI) mechanism of action.

4. Hematological and Neurological Consequences of PPI Use: Iron and Vitamin B12

4.1. Iron

Mechanisms of Iron Absorption: Heme vs Non-heme Pathways

Dietary iron is consumed in two primary forms: heme and non-heme iron [8, 9]. Heme iron is primarily derived from animal-based food sources, such as red meat, poultry, and fish. It

benefits from a highly efficient and distinct carrier-mediated uptake mechanism. It is absorbed into the intestinal enterocytes and subsequently metabolized by the enzyme heme oxygenase to release free iron [8]. Because of this unique molecular pathway, heme iron absorption is highly efficient and largely unaffected by dietary inhibitors or the pH of the gastric environment [9].

In contrast, non-heme iron, typically found in plant-based foods, fortified products, and standard oral supplements, exists predominantly in the insoluble ferric state (Fe^{3+}) [8,10]. Gastric acid plays an essential physiological role in dissolving these non-heme iron salts and facilitating the reduction of Fe^{3+} to the more soluble ferrous state (Fe^{2+}), a prerequisite for transport via divalent metal transporter 1 (DMT1) in the duodenum and proximal jejunum [8,10].

Clinical Evidence and the Challenge of Confounding Factors

Building on this mechanistic rationale, clinical studies and systematic evidence have linked chronic PPI use to iron deficiency and anemia [11,12]. However, these findings must be interpreted with caution, as they are derived predominantly from observational and retrospective studies and are therefore susceptible to residual confounding [11,12].

The gastrointestinal conditions necessitating long-term acid suppression, such as peptic ulcer disease, erosive gastritis, or concomitant NSAID use, are themselves frequently associated with occult gastrointestinal bleeding, further complicating causal attribution [12]. Accordingly, it remains difficult to determine whether iron deficiency in these patients results primarily from PPI-induced malabsorption or from chronic blood loss related to the underlying pathology [11,12].

Implications for Physical Performance and Aerobic Capacity

Although such subtle disturbances in iron homeostasis may be of limited clinical relevance in sedentary individuals, they carry significant implications for physically active populations. Iron plays a central role in aerobic metabolism, serving as an essential component of hemoglobin and myoglobin and facilitating oxygen delivery and utilization in skeletal muscle [13,14]. Even subclinical depletion of iron stores prior to the development of overt anemia has been shown to reduce oxygen-carrying capacity and impair exercise performance [13,14]. Given the fundamental role of oxygen in oxidative ATP synthesis, compromised iron status may

consequently lead to reduced maximal oxygen uptake (VO_2max), diminished endurance capacity, increased fatigue, and impaired post-exercise recovery [13,14].

Fig. 2. Proposed scheme linking chronic PPI use to physical performance via potential iron malabsorption.

4.2. Vitamin B12 (Cobalamin)

The Role of Gastric Acid and Pepsin

Another essential vitamin connected to physical performance is cobalamin. It functions as an indispensable coenzyme for macronutrient metabolism, specifically involving fats and amino acids [15]. It is a vital component for both cellular energy generation and DNA replication [15, 16]. Additionally, it provides critical neurotropic support required for the structural and functional integrity of the central and peripheral nervous networks [15,16].

Dietary cobalamin is predominantly bound to animal-derived proteins and requires a highly acidic gastric environment with active pepsin for its initial release [17]. Once liberated, free vitamin B12 undergoes a complex journey, ultimately binding to intrinsic factor (IF) to ensure proper intestinal absorption [17]. However, long-term PPI therapy markedly reduces gastric acid secretion [18]. This reduction impairs the acid-dependent release of vitamin B12 from dietary proteins [17,18]. Consequently, chronic PPI users may develop food-bound cobalamin malabsorption despite preserved intrinsic factor secretion [17, 18].

Clinical Evidence and the Heterogeneity of Study Results

Similar to the challenges observed with iron absorption, the clinical evidence regarding proton pump inhibitor (PPI)-induced vitamin B12 deficiency remains highly heterogeneous [18,19]. Although a biologically plausible mechanism links PPI-induced hypochlorhydria with impaired cobalamin assimilation, real-world clinical findings are often inconsistent [18]. Some observational studies report an increased risk of deficiency associated with prolonged therapy, particularly when treatment exceeds two years [18,20]. Conversely, other investigations demonstrate minimal or no clinically significant effect on serum vitamin B12 levels among standard chronic PPI users [19]. The strongest associations have been described predominantly in patients receiving high-dose, long-term therapy, such as those treated for Zollinger–Ellison syndrome [19, 20]. This lack of universal consensus suggests that while a pharmacological risk exists, the development of overt deficiency likely depends on drug dosage, duration of therapy and individual baseline vitamin B12 status and body stores [18, 20].

Implications for Neuromuscular Function and Physical Performance

Cobalamin is crucial for myelin synthesis and maintenance, thereby supporting proper nerve impulse conduction and normal neuromuscular function [16]. Observational data suggest that suboptimal B12 status may be associated with functional decline, particularly in older adults. In a two-year prospective cohort study, B12 insufficiency was associated with an increased incidence of low physical performance and sarcopenia in women, whereas no significant association was observed in men [15]. Additionally, narrative evidence indicates that altered B12 status may be bidirectionally related to frailty syndrome, potentially interacting with its musculoskeletal and neuropsychiatric components; however, the available literature remains heterogeneous and largely observational [21].

Beyond neuromuscular considerations, adequate vitamin B12 is essential for erythropoiesis and hemoglobin synthesis. In elite track and field athletes, serum B12 concentrations showed a weak but statistically significant positive association with hemoglobin levels, increasing up to approximately 400–500 pg/mL and plateauing beyond ~700 pg/mL [22]. As clinical deficiencies were not present and exercise performance was not directly assessed, conclusions regarding ergogenic effects cannot be drawn, although maintaining adequate B12 status appears relevant for optimal hematological parameters [22].

5. Bone Health and Musculoskeletal Implications

5.1 Calcium

Acid-Dependent Calcium Assimilation and Bone Mineral Density

Calcium is a fundamental structural component of the skeletal system, with over 99% of its total body pool stored in the form of hydroxyapatite, providing bones with essential mechanical strength [23,24]. Bone tissue functions as a dynamic mineral reservoir, undergoing continuous remodeling to maintain calcium homeostasis in extracellular fluids [24]. For dietary calcium to be effectively absorbed and incorporated into the skeleton, it must first undergo solubilization and ionization (Ca^{2+}), processes that are facilitated by the highly acidic environment of the stomach (pH 1–3) [23]. This ionization can be impaired by anti-nutritional factors such as oxalates and phytates, which form insoluble complexes with calcium, reducing its bioavailability [23]. Additionally, pharmacologically elevated gastric pH may decrease calcium solubility and potentially limit its absorption. In response to insufficient calcium absorption, compensatory mechanisms may be activated, including increased osteoclast-mediated bone resorption [24]. Over time, impaired calcium bioavailability and absorption may contribute to a progressive decline in bone mineral density (BMD), thereby increasing the risk of osteopenia, osteoporosis, and fractures [24,25].

Physical Activity and Fracture Risk: A Non-Linear Relationship

Studies indicate that physically active individuals may exhibit a higher incidence of fractures, primarily due to increased exposure to injury [26]. However, the relationship between physical activity and fracture risk is non-linear [27]. Moderate levels of physical activity are associated with a reduced risk of certain fractures, particularly hip fractures [27], whereas both low and very high levels of activity are linked to an increased fracture risk [27]. This suggests that the effect of physical activity on bone health depends on the intensity, type, and context of activity, as well as the specific fracture site [26,27].

Acid-Suppressive Therapy, Bone Homeostasis, and the Compounding Risk in Physically Active Populations

The prolonged use of acid-suppressive medications, particularly proton pump inhibitors (PPIs), has raised significant clinical concerns regarding their long-term impact on bone health. Chronic PPI therapy induces a persistent state of hypochlorhydria, which may impair the crucial

gastric ionization of dietary calcium necessary for its absorption. Recent evidence from a case-control study by Smaoui et al. indicates that long-term PPI use is significantly associated with hypomagnesemia and concurrent hypocalcemia [28]. In response to these mineral deficits, patients may develop compensatory increases in parathyroid hormone (PTH) levels, suggesting a tendency toward secondary hyperparathyroidism, which may further contribute to bone resorption [28]. Consequently, prolonged PPI exposure has been associated with decreased bone mineral density (BMD), particularly in individuals over the age of 50, postmenopausal women, and those using high or multiple daily doses [28]. Notably, while this study confirmed a progressive decline in bone density, it did not observe a corresponding increase in vertebral or femoral neck fractures within its cohort [28]. Despite the clear biological mechanism linking PPI-induced malabsorption to reduced BMD, larger epidemiological data regarding the actual risk of fractures present a more complex picture. Several large-scale observational studies have demonstrated a modest increase in fracture risk among PPI users. Vestergaard et al. reported that PPI use within the previous year was associated with an elevated risk of overall, hip, and spine fractures, whereas histamine H2-receptor antagonists (H2RAs) were not associated with an increased fracture risk [29]. Similarly, Yu et al. found a modestly increased risk of non-spine fractures in older women using PPIs, as well as in older men who did not use calcium supplements, further highlighting the critical role of calcium availability during acid-suppressive therapy [30]. When contextualizing these findings within the paradigm of physical activity, a critical clinical hypothesis emerges. As previously noted, high-intensity physical activity subjects the skeletal system to significant mechanical stress, requiring continuous bone remodeling and an adequate supply of ionized calcium to repair micro-damages. If an active individual chronically uses PPIs, the resulting hypochlorhydria and subsequent calcium malabsorption [28] could potentially limit the structural minerals necessary for this continuous repair process. Under these conditions, the compensatory release of PTH may further contribute to bone resorption [28]. Therefore, the combination of high mechanical load from intensive training and impaired bone mineralization from PPI use may create a compounding effect. This mechanism may theoretically predispose highly physically active individuals to an increased risk of stress fractures. While current epidemiological data primarily focus on older or sedentary populations [28–30], the intersection of high-intensity exercise, mechanical skeletal load, and chronic acid suppression represents a crucial gap in the literature that warrants targeted clinical investigation.

5.2 Magnesium

Physiological Role and Mechanisms of Absorption

Magnesium is the fourth most abundant mineral in the human body and the second most prevalent intracellular divalent cation, underscoring its fundamental role in human physiology [31]. It functions as a cofactor in more than 300 enzymatic reactions, critically regulating energy metabolism, glycemic control, and neuromuscular activity [31,32,33]. At the cellular level, magnesium predominantly exists as a complex with adenosine triphosphate (ATP), forming Mg–ATP, which is indispensable for virtually all energy-dependent biochemical processes, including muscle contraction and relaxation [31,33]. Beyond its metabolic functions, magnesium exerts significant anti-inflammatory and antioxidant effects. Adequate magnesium status has been associated with reduced circulating concentrations of C-reactive protein (CRP) and enhanced protection against oxidative stress [32,33]. Intestinal magnesium absorption is tightly regulated and occurs via two principal pathways [34]. Approximately 90% of dietary magnesium is absorbed passively through paracellular diffusion between enterocytes in the small intestine, with absorption rates increasing proportionally to luminal magnesium concentrations [34]. Under conditions of low intake, however, the body relies on an adaptive transcellular transport mechanism located primarily in the colon and distal intestine. This active pathway is mediated by transient receptor potential melastatin channels TRPM6 and TRPM7, which facilitate the uptake of divalent cations against a concentration gradient [34,35].

PPI-Induced Alterations in Magnesium Homeostasis

Chronic use of proton pump inhibitors (PPIs) is a well-recognized cause of hypomagnesemia and may lead to severe clinical manifestations, including tetany, seizures, and cardiac arrhythmias [34]. The underlying pathophysiology is multifactorial and primarily driven by PPI-induced hypochlorhydria, which disrupts both passive and active magnesium absorption pathways [35]. An increase in intestinal luminal pH reduces magnesium solubility, promoting the formation of insoluble complexes with anions such as phosphate and chloride. This process significantly limits the fraction of magnesium available for passive paracellular absorption [35]. In parallel, active transcellular transport is impaired. The TRPM6 and TRPM7 channels are highly sensitive to luminal pH and function optimally under slightly acidic conditions. PPI-induced alkalinization of the distal intestine reduces both the expression and transport efficiency of these channels, thereby diminishing magnesium uptake [34,35]. Emerging evidence also

implicates alterations in the gut microbiome. PPI therapy has been shown to reduce microbial diversity and promote the overgrowth of specific bacterial families, including *Streptococcaceae* [35]. This dysbiosis may impair the fermentation of dietary fibers, resulting in decreased production of short-chain fatty acids, which normally acidify the colonic environment and enhance magnesium solubility. Consequently, PPI-induced hypomagnesemia is often refractory to conventional oral supplementation and typically resolves only following discontinuation of the offending agent [34,35].

Implications for Physical Performance and Neuromuscular Function

Optimal magnesium status is particularly critical in physically active individuals, as physiological requirements increase with exercise intensity and duration [31,36]. Even subclinical magnesium deficiency, such as that induced by chronic PPI use, may lead to measurable impairments in neuromuscular and metabolic function. Magnesium acts as a natural calcium antagonist within muscle cells, regulating calcium influx and ensuring proper muscle relaxation. Deficiency results in increased intracellular calcium levels, impairing relaxation and manifesting clinically as early-onset fatigue, increased muscle tension, and painful muscle cramps [33,34]. In addition to its neuromuscular effects, magnesium plays a direct role in exercise metabolism. Both experimental and clinical studies demonstrate that magnesium supplementation enhances glucose availability in the brain, blood, and skeletal muscle, while delaying lactate accumulation during physical exertion [36]. Observational and interventional studies have demonstrated positive associations between magnesium status and objective performance metrics, including maximal isometric strength, quadriceps torque, handgrip strength, and vertical jump performance [36]. Furthermore, magnesium contributes to cardiovascular efficiency by modulating endothelial nitric oxide (NO) production and maintaining vascular tone [31,33]. Deficiency may impair oxygen delivery to working muscles, thereby increasing cardiovascular strain during aerobic exercise [31]. Finally, inadequate magnesium levels may compromise the body's ability to mitigate exercise-induced oxidative stress and systemic inflammation [32,33], potentially delaying recovery and reducing overall endurance capacity.

6. Discussion

The increasing prevalence of long-term proton pump inhibitor (PPI) use represents a clinically relevant consideration in sports medicine, particularly in the context of potential nutrient-related consequences. While the therapeutic efficacy of PPIs in acid-related disorders is well

established, the present review synthesizes evidence suggesting that chronic suppression of gastric acid secretion may influence the absorption of selected micronutrients, including iron, vitamin B12, calcium, and magnesium.

A key observation emerging from the reviewed literature is that the clinical relevance of these potential deficiencies may differ depending on physiological context. In the general population, mild alterations in micronutrient status often remain subclinical. However, in physically active individuals, especially those engaged in endurance or high-intensity training, even subtle disruptions in nutrient availability may have greater functional implications. For instance, reduced iron or vitamin B12 status could theoretically affect oxygen transport and mitochondrial energy production, processes that are critical for aerobic performance and recovery. It should be emphasized, however, that direct evidence linking PPI-induced micronutrient deficiencies with measurable impairments in performance outcomes remains limited.

Similarly, disturbances in magnesium and calcium homeostasis associated with long-term PPI use may have implications for neuromuscular function and bone metabolism. Magnesium plays an important role in muscle contraction-relaxation dynamics and cellular energy processes, whereas calcium is essential for skeletal integrity. Some observational studies suggest an association between prolonged PPI use and altered bone mineral density or increased fracture risk. In physically active populations exposed to repetitive mechanical loading, these factors could potentially contribute to an elevated risk of bone-related injuries, although causality has not been firmly established.

Limitations of the Current Evidence

Several important limitations should be acknowledged. First, the majority of available data derives from observational studies conducted in older or clinical populations with multiple comorbidities, which may limit generalizability to young, healthy, or athletic individuals. Second, heterogeneity in study design, duration of PPI exposure, and outcome assessment precludes quantitative synthesis and limits the strength of conclusions. Third, there is a lack of randomized controlled trials specifically addressing the impact of chronic PPI use on physical performance, recovery, or injury risk in athletic populations.

Clinical Implications

From a practical standpoint, clinicians working with physically active individuals should remain aware of the potential, albeit not definitively established, implications of long-term PPI therapy. Prescribing decisions should consider both gastrointestinal indications and the broader

physiological context, including training load and nutritional status. Where prolonged treatment is necessary, reasonable strategies may include:

- using the lowest effective dose and clearly defined indications for continuation,
- periodic reassessment of therapy necessity,
- monitoring selected biomarkers (e.g., iron status, vitamin B12, magnesium),
- considering alternative approaches (e.g., step-down therapy) when appropriate.

At present, these recommendations should be interpreted as precautionary rather than evidence-based guidelines specific to athletic populations.

7. Conclusions

Long-term use of proton pump inhibitors may be associated with alterations in the absorption of selected micronutrients, including iron, vitamin B12, calcium, and magnesium. These nutrients are involved in processes relevant to physical performance, such as oxygen transport, neuromuscular function, and bone metabolism.

However, current evidence linking chronic PPI use with clinically meaningful impairments in physical performance or musculoskeletal health remains limited and is largely based on observational data. As such, causal relationships cannot be definitively established. The potential impact of PPIs in physically active individuals is likely influenced by multiple factors, including duration of therapy, dosage, baseline nutritional status, and individual variability.

In clinical practice, the benefits of PPI therapy should be balanced against possible long-term considerations, particularly in individuals engaged in regular or high-intensity physical activity. Periodic reassessment of treatment necessity and consideration of monitoring strategies may be appropriate in selected cases.

Further research, particularly well-designed prospective and interventional studies in physically active populations, is needed to clarify the extent to which PPI use may influence performance-related and musculoskeletal outcomes.

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Author's contribution:

Conceptualization: JT, MS, DZ

Methodology: JT, AS

Validation: JT, DZ

Resources: MS

Data curation: MS, JK

Writing — original draft preparation: JT, JK

Writing—review and editing: MS, AS

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