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# Kidney Function and Extreme Endurance Races: Risks, Mechanisms, and Preventing Strategies

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**Abstract**

**Background:** The increasing popularity of ultra-endurance sports emphasizes the need for a deeper understanding of their health implications, particularly the impact on kidney function. Given the kidneys' crucial role in waste filtration, fluid and electrolyte balance, and their close connection to the physiological demands of intense physical activity, it requires detailed investigation from this perspective.

**Purpose:** The objective of this study is to present the current state of knowledge on the topic of kidney function in the context of ultra-endurance sports. It examines the risk factors, underlying mechanisms, and potential strategies for preventing renal injuries associated with these specific types of physical activities.

**Findings:** Ultra-endurance sports present significant risks to kidney health, including acute kidney injury (AKI) estimated to affect approximately 40% of participants, rhabdomyolysis and dehydration, which are often compounded by additional factors such as gastrointestinal distress and the use of non-steroidal anti-inflammatory drugs (NSAIDs). There is a need for improved diagnostic criteria to detect acute renal injury in this population, with novel biomarkers such as neutrophil gelatinase-associated lipocalin (NGAL), kidney injury molecule-1 (KIM-1), and cystatin C showing promise. A multifaceted preventive approach including strategies such as mandatory pre-event screening, the use of personal monitoring devices, proper hydration and nutrition, adequate race preparation, and the avoidance of NSAIDs is crucial to mitigate these risks and maintain renal health in ultra-endurance athletes.

**Keywords:** ultra-endurance sports, acute kidney injury (AKI), rhabdomyolysis, non-steroidal anti-inflammatory drugs (NSAIDs)

## Introduction

Ultra-endurance sports are typically defined by two main criteria: duration, involving events lasting more than 6 hours, or distance, exceeding the standard marathon length of 42.195 kilometers [1,2]. Such sports may include running or walking, often in mountainous or desert environments, long-distance swimming or cycling, or a combination of different disciplines such as long-distance triathlons. The magnitude of physical exertion and demands placed on athletes can be extreme, both because of the challenging external conditions and because of the distance involved, which is often up to more than 100 kilometers [3].

The increasing popularity of ultra-endurance races, observed and proven by studies [4], indicates the need for a deeper understanding of their physiological effects and health implications. While it has been widely proven that physical activity has benefits for overall health and life expectancy, the question remains whether, in the case of ultra-athletes, the benefits outweigh the costs and potential risks [5].

Performing prolonged and demanding physical activities, such as ultra-endurance sports, imposes physiological challenges on the organism at multiple levels. Many medical issues

may occur during these competitions, varying from mild to potentially life-threatening conditions.
Several studies have shown that they can lead to complications such as dehydration, exercise-associated hyponatremia, heat stroke, rhabdomyolysis, damage to the cardiovascular system, musculoskeletal system, respiratory system, gastrointestinal tract or kidneys, including acute kidney injury (AKI) [5-7].
Among these, particular attention should be dedicated to kidneys, considering their role in waste filtration, electrolyte balance, and fluid regulation - crucial for athletes to maintain long-time performance [8]. The aim of this narrative review is to present the current state of knowledge on the topic of kidney function in the context of ultra-endurance sports. This study evaluates risk factors, pathophysiology and possible prevention mechanisms regarding renal injuries occurring during these specific types of physical activity.

**Physiology of kidney function during exercise**

The human kidneys are a multi-tasking organ with a number of essential functions in the body, which are particularly important during long-time physical exertion. Their primary task, performed by plasma filtration, is eliminating the waste products of metabolism: urea, uric acids, creatinine, and other metabolites. They produce urine by filtrating up to 180l of blood per day [8,9]. The kidneys regulate acid-base balance by excreting acids and maintaining buffers proportions in the body, and control fluid and electrolyte balance and concentration by adjusting the rate of excretion according to the intakes of different substances [8,10]. They also play a major role in regulating blood pressure through controlling the amounts of sodium and water in the system and through secreting and interacting with hormones and vasoactive factors, such as renin, antidiuretic hormone (ADH), prostaglandins, endothelin, nitric oxide, kallikrein and bradykinin [11-13].
In addition to all of the mentioned tasks, they perform a variety of other functions, including the production of glucose from precursor molecules during gluconeogenesis [14], the synthesis of erythropoietin required for red blood cell production in the bone marrow, and the generation of the active form of vitamin D, 1,25-dihydroxyvitamin D3, also known as calcitriol [8]. Therefore, given the variety and type of their functions in the system, they are considered a crucial organ in maintaining body homeostasis [15,16].
The kidneys have several mechanisms that adapt them to physical exertion. During moderate to intense exercises, renal blood flow decreases by up to 50% - 70%, because the blood is preferentially redirected to active skeletal muscles, skin and the heart to supply their needs for oxygen and energy [17-19]. This redistribution is mediated by sympathetic nervous system activation, which induces vasoconstriction of the renal arteries, causing the decrease in renal blood flow and, consequently, temporary reduction in glomerular filtration rate (GFR) [20]. Despite the reduced GFR, the process of regulating solute and water balance is still effective, because tubular reabsorption mechanisms remain functional. Decreased blood flow in the kidneys is compensated for by enhanced tubular reabsorption of sodium and water, which relies on active transport mechanisms and changes in hydrostatic and oncotic pressures within the kidney's microcirculation [18, 20]. A major role is also played by hormonal influences: the

release of antidiuretic hormone (ADH) increases water reabsorption in the collecting ducts, and the activation of the renin-angiotensin-aldosterone system (RAAS) promotes sodium and water retention. Catecholamine hormones, such as adrenaline and noradrenaline, released during physical activity, induce vasoconstriction, further reducing renal perfusion. These adaptations enable the kidneys to maintain fluid and solute balance [17-21].
A noticeable consequence of these adaptive processes is exercise-induced oliguria, a temporary reduction in urine output occurring during physical activity [22].
This phenomenon results from the combined effects of decreased GFR and increased tubular reabsorption driven by hormonal and neural mechanisms, mentioned above. These adaptations minimize fluid loss during exertion, helping to preserve plasma volume and prevent dehydration [22, 23]. This reduction in urine production is especially important during prolonged or intense exercise, where fluid loss through sweating can be substantial [24]. All these responses demonstrate the kidneys' remarkable ability to ensure homeostasis under varying physiological demands, such as stress, reduced perfusion pressures or prolonged activity, that prevents electrolyte imbalance and dehydration.

**Acute Kidney Injury (AKI) in Endurance Athletes**

In the past decades, many researchers have attempted to define acute process of kidney damage. Following scientific consensus, previously used terminology Acute Renal Failure (ARF) has been replaced by the term Acute Kidney Injury (AKI) [25]. The definition proposed by KDIGO Guidelines in 2016 describes it as an abrupt (within hours) decrease in kidney function, which provides a comprehensive perspective and includes both injuries, referring to structural damage, and impairment, referring to loss of function [26]. The classification of acute kidney injury encompasses pre-renal AKI, acute obstructive nephropathy (post-renal AKI), and intrinsic acute kidney disorders. Since it involves the potential for structural damage, including impaired kidney function, it can potentially be the cause of chronic morbidity and increased mortality [26, 27].
Clinical diagnostic criteria rely on detecting an acute reduction in GFR, which is indicated by a rapid increase in serum creatinine (sCr) levels and/or a decrease in urine output (UO) within a specific time frame. Based on that, according to actual KDIGO criteria, AKI is defined as any of the following:

- increase in serum creatinine by 0.3 mg/dL or more within 48 hours,
- increase in serum creatinine to 1.5 times baseline or more within the last 7 days,
- urine output less than 0.5 mL/kg/h for 6 hours [26].

Other classifications, such as RIFLE (Risk, Injury, Failure, Loss, End-stage) and AKIN (Acute Kidney Injury Network), provide different criteria for staging and determining the severity of acute kidney injury (AKI), but despite differences in methodology, according to all three of them AKI is diagnosed when level of serum creatinine changes (a 1.5-fold increase in serum creatinine or >25% decrease in GFR for RISK stage) or when urine output decreases to less than 0.5 mL/kg/h for 6 h. These benchmarks serve as the foundation for AKI diagnosis across the classifications, facilitating standardization of assessments [25, 28].

Participation in ultra-endurance sports is associated with significant functional and structural kidney damage, including elevated serum creatinine levels and increased renal filtration demands, and is recognized as a risk factor for the development of AKI [28-30]. Research based on urine microscopy analysis, serum creatinine levels, and levels of novel biomarkers of injury and repair, indicates that acute kidney injury in ultra-endurance athletes is primarily a consequence of structural renal damage, with acute tubular injury (ATI) being the predominant pathology [31]. It is a result of interaction of hemodynamic, metabolic, and environmental factors. Prolonged physical exertion leads to significant dehydration and hypovolemia, which reduces renal perfusion and glomerular filtration rate (GFR), predisposing the kidneys to ischemic injury [30].

Physical stress triggers the release of catecholamines (e.g., adrenaline, noradrenaline), which further exacerbate vasoconstriction, enhancing the reduction in renal blood flow [19]. Concurrently, increased muscle breakdown releases myoglobin into the bloodstream, potentially causing rhabdomyolysis, which can lead to tubular obstruction and direct cytotoxic effects on renal tissues [30]. Heat stress and elevated core body temperatures during endurance events also intensify oxidative stress and inflammation, contributing to renal injury [32].

All these mechanisms contribute to increased risk of AKI in athletes performing ultra-endurance sports, especially when combined with insufficient hydration and electrolyte imbalance usually co-existing during these activities [28].

There are also additional factors that increase the likehood of AKI in this group of athletes. The widespread use of non-steroidal anti-inflammatory drugs (NSAIDs) among ultra-endurance athletes, reported by as many as 75% of participants in some studies [33, 34], is one such factor. NSAIDs are commonly used because they facilitate event completion by reducing muscle inflammation, delaying fatigue, and improving pain tolerance. However, high doses, often at the upper limits of over-the-counter recommendations, have been shown to increase the risk of acute kidney injury and potentially impair training adaptations, reducing athletic performance [30, 35, 36]. A potential mechanism contributing to this risk is the vasoconstrictive effect of NSAIDs, which exacerbates the already diminished renal blood flow caused by prolonged exercise [37]. Moreover, NSAIDs can accelerate the progression from AKI to chronic kidney disease (CKD) [38].

Other factors associated with an elevated risk of AKI in ultra-athletes include the use of nitrate supplements, female sex, dehydration, and significant weight loss during races, often due to inadequate nutrition [30]. Evidence also suggests that shorter races, which demand higher running speeds over shorter durations, are more likely to cause AKI compared to medium- or long-distance ultramarathons [30, 39].

In addition to these factors, other physiological and pathological conditions arising during extreme sports can further increase the risk of AKI. Excessive fluid intake without adequate sodium replacement, a common practice in ultra-endurance events, can lead to exercise-associated hyponatremia (EAH). This condition disrupts osmotic balance and causes cellular swelling and dysfunction, impairing the kidneys' ability to regulate fluid balance and filtration, and increasing the risk of tubular damage and AKI [40]. Ultra-endurance sports themselves

can also cause gastrointestinal problems. Symptoms such as nausea, vomiting, diarrhea, and bloating, frequently occur during ultra-endurance events due to the combined effects of prolonged physical stress, altered circulation to the gut, mechanical factors, and nutrition [6, 41]. Reduced blood flow to the gastrointestinal tract during intense exercise results in ischemia, which compromises the integrity of the intestinal mucosa. This damage increases the permeability of the intestinal wall, allowing gram-negative bacteria and their toxic byproducts, such as lipopolysaccharides (LPS), to translocate into the bloodstream, a condition known as endotoxemia [41].

The presence of endotoxins in circulation activates systemic inflammatory pathways and generates oxidative stress, both of which contribute to tubular injury within the kidneys and impair renal function [30,41]. Collectively, these factors significantly elevate the risk of developing acute kidney injury (AKI).

**Symptoms and Diagnosis**

As acute kidney injury is a condition with complex and multifaceted potential etiology, clinical manifestations can vary, depending on the underlying cause provoking the AKI [26]. In ultra-endurance athletes, acute kidney injury often presents asymptomatically or with only mild symptoms, with athletes typically reporting minimal complaints, and it usually normalizes over the next few days [30] However, in some cases, AKI can manifest with more severe symptoms, potentially requiring hospitalization [19].

When accompanied by conditions such as hyponatremia and rhabdomyolysis, AKI in ultra-endurance athletes may present with symptoms including reduced urine output (oliguria), hematuria, and myoglobinuria - manifesting as blood in the urine or dark-colored urine. Systemic symptoms such as nausea, dizziness, vomiting, and general malaise are also common, often reflecting disturbances in fluid balance and electrolyte homeostasis. As the severity of renal dysfunction progresses, these symptoms may worsen, potentially leading to more pronounced fatigue or confusion [28, 42].

The prevalence of acute kidney injury (AKI) among ultra-endurance athletes is challenging to determine accurately. Most studies report an average incidence of approximately 40% of participants during such events, although some have documented prevalence rates as high as 80% [28, 43, 44]. This variability may stem from the absence of standardized diagnostic criteria and consistent methodologies for assessing kidney damage in ultra-endurance sports [30].

A significant challenge in the literature is identifying the most appropriate criteria for diagnosing AKI in ultra-endurance sports participants. Commonly used criteria, including KDIGO, RIFLE, and AKIN, rely on serum creatinine levels and urine output measurements. [25, 28]. However, these frameworks were originally developed for use in the general population and may not fully account for the unique physiological adaptations observed in this athletic cohort. Serum creatinine levels and urine output, while widely used, are limited in their ability to capture early or transient changes in renal function, especially in individuals undergoing significant physiological stress. Additionally, the rise in serum creatinine observed during the race could result from either a true decline in creatinine clearance or an increased

release of creatinine from muscle damage, but the relative contribution of each factor remains uncertain [45].

Emerging research highlights the need for novel biomarkers that are more sensitive and specific to the early stages of kidney injury in ultra-endurance athletes. Neutrophil gelatinase-associated lipocalin (NGAL) and kidney injury molecule-1 (KIM-1) are promising early indicators of AKI [30]. NGAL is released from renal tubular cells in response to injury, detectable in both plasma and urine within hours of damage, making it particularly valuable for early diagnosis. Similarly, KIM-1, a transmembrane protein highly upregulated in proximal tubular cells during injury, serves as a marker of tubular damage and has been correlated with the severity of AKI [30, 46].

Other novel biomarkers are also the subject of research, such as interleukin-18 (IL-18), a pro-inflammatory cytokine, released in response to renal tubular damage, which has shown diagnostic and prognostic value in AKI [46]. Cystatin C, an endogenous protein filtered by the glomerulus, is a marker of glomerular filtration rate and is less influenced by muscle mass, offering potential advantages in athletic populations with high creatinine variability due to muscle breakdown [19, 46].

The combination of these biomarkers may provide a more comprehensive assessment of kidney function and injury, enabling earlier and more accurate detection of AKI in ultra-endurance athletes. Future studies are needed to validate these markers in the context of ultra-endurance sports and to explore their incorporation into diagnostic frameworks that account for the unique physiological adaptations of this population.

**Prevention strategies**

Although the majority of acute kidney injury (AKI) cases among ultra-endurance athletes follow a mild or asymptomatic course, the long-term consequences and risks remain unknown, which emphasizes the need for effective prevention strategies suitable for this group [5]. Few approaches have been discussed in the literature. One proposed strategy includes mandatory pre-event screening to identify individuals at elevated risk of AKI [30]. Studies suggest that females and athletes aged <19 or >35 years are particularly vulnerable to AKI during ultra-endurance events, warranting special attention to these groups [5].

During races, advanced personal monitoring technologies such as GPS tracking and heart rate monitors could help in the early detection of potentially serious adverse events [30]. Proper hydration is another critical preventive measure. Athletes must balance fluid intake to avoid both dehydration and exercise-associated hyponatremia, as both conditions are significant contributors to AKI risk [28]. Personalized hydration plans, which consider factors like environmental conditions, individual sweat rates, and race duration, are essential to mitigate these risks [24]. Additionally, electrolyte imbalances and high-protein diets can exacerbate kidney stress during endurance events. To address this, electrolyte supplementation to maintain sodium levels is recommended, particularly in longer races, alongside adequate carbohydrate intake to sustain energy levels and reduce muscle breakdown; this strategy is crucial for preventing rhabdomyolysis, which increases the risk of AKI [47-49].

The use of non-steroidal anti-inflammatory drugs (NSAIDs) during events is another important factor. Research has shown that NSAIDs consumption exacerbates AKI risk by impairing renal perfusion, and thus, athletes should be advised to limit or avoid NSAIDs use before and during endurance races [30, 34].

Further preventive strategies should also include gradual increases in training intensity to prepare the body for extreme physical demands and acclimatization to challenging conditions such as heat or high altitudes, both of which can reduce physiological stress on the kidneys [30, 50]. A multifaceted approach, incorporating proper hydration and nutrition, avoidance of NSAIDs, targeted training, and environmental preparedness, is essential for AKI prevention. However, implementing these strategies is complex and requires collaboration between athletes, coaches, medical staff, and event organizers to develop protocols tailored to individual needs and specific race conditions.

**Conclusion**

Considering the growing popularity of ultra-endurance races, more research is needed to explore acute kidney injury in this group of athletes, including its causes, mechanisms, detection, and prevention. A key question is the true incidence of AKI - whether ultramarathon participation itself increases AKI risk or if additional factors, such as non-steroidal anti-inflammatory drug use, play a predominant role.

Studies have reported NSAIDs usage rates of up to 75% among ultramarathoners, significantly elevating AKI risk due to impaired renal perfusion [30, 33, 34].

Another critical area of investigation is whether repeated AKI episodes contribute to chronic kidney disease progression and worsen the prognosis of subsequent AKI events. Some studies suggest that multiple episodes of AKI during ultra - endurance events do not have a cumulative effect and may not increase the risk of progression to CKD or associated mortality [51] unlike findings observed in the general population [27]. However, other studies indicate that repeated AKI events could contribute to CKD development in this athletic cohort, and that more data on this topic is needed [30, 52].

Longitudinal studies exploring the long-term effects of ultra-endurance sports on kidney health are limited. There is also a need to refine AKI diagnostic criteria for this population. Current frameworks, such as KDIGO or RIFLE, rely on serum creatinine and urine output, which may not adequately reflect the physiological changes experienced by ultra-endurance athletes [25, 30]. Novel biomarkers like neutrophil gelatinase-associated lipocalin (NGAL), kidney injury molecule-1 (KIM-1) and cystatin C show promise for earlier and more specific AKI detection in this group [19, 46].

Extreme endurance racing carries significant risks to kidney health, including AKI, rhabdomyolysis, and dehydration, often compounded by additional complications such as gastrointestinal distress [5-7]. This emphasizes the urgent need for standardized guidelines on hydration, nutrition, and race preparation, alongside strategies for early detection of health problems. Customized prevention strategies, suited to individual needs and race-specific conditions, are essential to ensure athlete safety and performance [30]. A multidisciplinary approach involving athletes, coaches, and healthcare providers is critical. More research is

required to address these challenges and advance our understanding of AKI in the context of ultra-endurance sports.

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