**Mini-Review** 



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# Renal endocrine aspects of exercise-induced acute kidney injury (gym nephropathy)

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# Abstract

The important renal endocrine aspect implicated in gym nephropathy is the activation of the renin-angiotensin-aldosterone system (RAAS). Intense exercise can lead to increased sympathetic nervous system activity, resulting in the release of renin from the juxtaglomerular cells in the kidneys. Renin acts on angiotensinogen, leading to the generation of angiotensin II, a potent vasoconstrictor. Angiotensin II stimulates the secretion of aldosterone from the adrenal glands, which promotes sodium reabsorption and potassium excretion in the kidneys. The persistent activation of the RAAS in gym nephropathy may contribute to renal damage by causing vasoconstriction and promoting renal inflammation.

Keywords: Gym nephropathy, Exercise-induced nephrotoxicity, Exercise, Bodybuilding, Renin-angiotensin-aldosterone system

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# Introduction

Gym nephropathy, also known as exercise-induced acute kidney injury, is a condition characterized by the sudden onset of kidney dysfunction following intense physical activity or exercise (1,2). While the exact mechanisms underlying gym, nephropathy are not fully understood, there are several renal endocrine aspects that may contribute to its development.

# Search strategy

For this mini-review, I conducted a comprehensive search using various databases: PubMed, Google Scholar, Directory of Open Access Journals (DOAJ), Web of Science, EBSCO, Scopus, and Embase. We utilized different keywords such as gym nephropathy, exerciseinduced nephrotoxicity, exercise, bodybuilding and reninangiotensin-aldosterone system.

# Potential factors of gym nephropathy

Gym nephropathy is a multifactorial condition, and these renal endocrine aspects may interact with other factors such as individual susceptibility, pre-existing medical conditions, and hydration status. Further research is needed to fully understand the complex pathophysiology of gym nephropathy and develop effective preventive strategies (2).

# **Anabolic steroids**

The illegal use of anabolic steroids is sometimes associated with gym nephropathy. Anabolic steroids are synthetic derivatives of testosterone that can have potent effects on muscle growth. However, their use can also have adverse effects on the kidneys. Anabolic steroids can cause an increase in blood pressure and disrupt the hormonal balance in the body, potentially leading to kidney damage (3,4).

# Growth hormone and insulin-like growth factor-1

Some individuals involved in bodybuilding may misuse growth hormone and insulin-like growth factor-1 (IGF-1) to enhance muscle growth. These substances can affect the kidneys in several ways. Growth hormone can increase the production of insulin-like growth factor-binding proteins, which may lead to kidney damage. Additionally, excessive growth hormone and IGF-1 can cause enlargement of organs, including the kidneys, potentially affecting their function (5,6).

# Dehydration and diuretic use

Bodybuilders may engage in practices to reduce water retention and achieve a more defined muscle appearance. This can include excessive sweating, dehydration, and the use of diuretics. Dehydration can strain the kidneys and

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# Implication for health policy/practice/research/ medical education

Gym nephropathy (exercise-induced nephrotoxicity) refers to the kidney damage and dysfunction that can occur as a result of intense and prolonged exercise, across with excessive use of certain substances in the context of bodybuilding or weightlifting.

impact their function. Diuretics, when misused or taken in excessive amounts, can also put additional stress on the kidneys (7,8).

It is important to note that gym nephropathy is not limited to these endocrine aspects, and other factors such as overexertion, high-protein diets, and dietary supplement use may also contribute to kidney damage (9,10).

While the main mechanisms behind gym nephropathy are still being studied, there is evidence to suggest involvement of renal endocrine aspects. The suggesting parameters are the following mechanistic impacts:

# Renin-angiotensin-aldosterone system (RAAS) Activation

Intense exercise can lead to activation of the RAAS, which plays a crucial role in regulating blood pressure and fluid balance. The release of renin from the kidneys stimulates the production of angiotensin II, a potent vasoconstrictor that increases blood pressure (11). Angiotensin II also stimulates the release of aldosterone from the adrenal glands, promoting sodium and water reabsorption in the kidneys. Excessive activation of the RAAS can lead to vasoconstriction and reduced renal blood flow, potentially contributing to kidney injury (11,12).

## **Catecholamine release**

During intense exercise, there is an increased release of catecholamines such as epinephrine and norepinephrine from the adrenal glands. These hormones help mobilize energy reserves and increase cardiac output. However, excessive catecholamine release can cause vasoconstriction in the renal arteries, reducing renal blood flow and oxygen delivery to the kidneys (13,14).

## Inflammatory response

Intense exercise can trigger an inflammatory response in various tissues, including the kidneys. Inflammatory mediators such as cytokines and chemokines can directly damage renal cells and impair kidney function. Additionally, inflammation-induced oxidative stress may further contribute to kidney injury. Furthermore, exerciseinduced oxidative stress is another factor that can affect renal endocrine function in gym nephropathy (15,16). Intense physical activity leads to an increased production of reactive oxygen species (ROS) in the body. ROS can directly damage renal cells and impair their function. It has been found that excessive ROS can disrupt the delicate balance of various renal hormones, including vasopressin and atrial natriuretic peptide (ANP) (17,18). Vasopressin is responsible for regulating water reabsorption in the kidneys, while ANP plays a role in maintaining sodium and water balance. Disruptions in the secretion or actions of these hormones due to oxidative stress may contribute to the development of kidney dysfunction in gym nephropathy (19,20).

# Fluid and electrolyte imbalance

Prolonged or intense exercise can result in significant fluid and electrolyte losses through sweating. Dehydration and electrolyte imbalances, particularly sodium depletion (hyponatremia), can disrupt normal kidney function and impair renal blood flow (21,22).

## **Rhabdomyolysis**

In rare cases, intense exercise can lead to rhabdomyolysis, a condition characterized by the breakdown of muscle tissue and the release of myoglobin into the bloodstream. Myoglobin can cause direct kidney injury by obstructing renal tubules and triggering inflammation (23,24).

# Conclusion

Gym nephropathy involves various renal endocrine aspects, including the activation of the RAAS and the disruption of renal hormonal balance due to oxidative stress. Understanding these mechanisms can help in identifying potential therapeutic targets for the prevention and treatment of gym nephropathy. However, it is important to note that further research is needed to fully understand the complex interactions between exercise, renal endocrine function, and kidney damage.

# **Conflicts of interest**

The author declares that he has no competing interests.

### **Ethical issues**

Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the author.

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#### References

- Kumar R, Kumar S, Kumar A, Kumar D, Kumar V. Exercise-Induced Rhabdomyolysis Causing Acute Kidney Injury: A Potential Threat to Gym Lovers. Cureus. 2022;14:e28046. doi: 10.7759/cureus.28046.
- Shimizu Y, Wakabayashi K, Totsuka A, Hayashi Y, Nitta S, Hara K, et al. Exercise-Induced Acute Kidney Injury in a Police Officer with Hereditary Renal Hypouricemia. Case Rep Nephrol Dial. 2019;9:92-101. doi: 10.1159/000501877.
- Albano GD, Amico F, Cocimano G, Liberto A, Maglietta F, Esposito M, et al. Adverse Effects of Anabolic-Androgenic Steroids: A Literature Review. Healthcare (Basel). 2021;9:97. doi: 10.3390/healthcare9010097.
- Ding JB, Ng MZ, Huang SS, Ding M, Hu K. Anabolic-Androgenic Steroid Misuse: Mechanisms, Patterns of Misuse, User Typology, and Adverse Effects. J Sports Med (Hindawi Publ Corp). 2021;2021:7497346. doi: 10.1155/2021/7497346.
- 5. Anderson LJ, Tamayose JM, Garcia JM. Use of growth

hormone, IGF-I, and insulin for anabolic purpose: Pharmacological basis, methods of detection, and adverse effects. Mol Cell Endocrinol. 2018;464:65-74. doi: 10.1016/j. mce.2017.06.010.

- Holt RI, Sönksen PH. Growth hormone, IGF-I and insulin and their abuse in sport. Br J Pharmacol. 2008;154:542-56. doi: 10.1038/bjp.2008.99.
- Cadwallader AB, de la Torre X, Tieri A, Botrè F. The abuse of diuretics as performance-enhancing drugs and masking agents in sport doping: pharmacology, toxicology and analysis. Br J Pharmacol. 2010;161:1-16. doi: 10.1111/j.1476-5381.2010.00789.x.
- Tidmas V, Brazier J, Hawkins J, Forbes SC, Bottoms L, Farrington K. Nutritional and Non-Nutritional Strategies in Bodybuilding: Impact on Kidney Function. Int J Environ Res Public Health. 2022 Apr 3;19:4288. doi: 10.3390/ijerph19074288.
- Martin WF, Armstrong LE, Rodriguez NR. Dietary protein intake and renal function. Nutr Metab (Lond). 2005 Sep 20;2:25. doi: 10.1186/1743-7075-2-25.
- Ko GJ, Rhee CM, Kalantar-Zadeh K, Joshi S. The Effects of High-Protein Diets on Kidney Health and Longevity. J Am Soc Nephrol. 2020;31:1667-1679. doi: 10.1681/ ASN.2020010028.
- Fountain JH, Kaur J, Lappin SL. Physiology, Renin Angiotensin System. [Updated 2023 Mar 12]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK470410/.
- Ames MK, Atkins CE, Pitt B. The renin-angiotensin-aldosterone system and its suppression. J Vet Intern Med. 2019;33:363-382. doi: 10.1111/jvim.15454.
- Paravati S, Rosani A, Warrington SJ. Physiology, Catecholamines. [Updated 2022 Oct 24]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK507716/
- 14. Zouhal H, Jacob C, Delamarche P, Gratas-Delamarche A. Catecholamines and the effects of exercise, training and gender. Sports Med. 2008;38:401-23. doi: 10.2165/00007256-200838050-00004.

- 15. Aldahr MHS, Abd El-Kader SM. Impact of exercise on renal function, oxidative stress, and systemic inflammation among patients with type 2 diabetic nephropathy. Afr Health Sci. 2022;22:286-295. doi: 10.4314/ahs.v22i3.30.
- Liao P, He Q, Zhou X, Ma K, Wen J, Chen H, et al. Repetitive Bouts of Exhaustive Exercise Induces a Systemic Inflammatory Response and Multi-Organ Damage in Rats. Front Physiol. 2020 Jun 23;11:685. doi: 10.3389/fphys.2020.00685.
- Thomas DT, DelCimmuto NR, Flack KD, Stec DE, Hinds TD Jr. Reactive Oxygen Species (ROS) and Antioxidants as Immunomodulators in Exercise: Implications for Heme Oxygenase and Bilirubin. Antioxidants (Basel). 2022;11:179. doi: 10.3390/antiox11020179.
- Simioni C, Zauli G, Martelli AM, Vitale M, Sacchetti G, Gonelli A, et al. Oxidative stress: role of physical exercise and antioxidant nutraceuticals in adulthood and aging. Oncotarget. 2018 Mar 30;9:17181-17198. doi: 10.18632/oncotarget.24729.
- Stockand JD. Vasopressin regulation of renal sodium excretion. Kidney Int. 2010;78:849-56. doi: 10.1038/ki.2010.276.
- Boone M, Deen PM. Physiology and pathophysiology of the vasopressin-regulated renal water reabsorption. Pflugers Arch. 2008;456:1005-24. doi: 10.1007/s00424-008-0498-1.
- Klingert M, Nikolaidis PT, Weiss K, Thuany M, Chlíbková D, Knechtle B. Exercise-Associated Hyponatremia in Marathon Runners. J Clin Med. 2022 Nov 16;11:6775. doi: 10.3390/ jcm11226775.
- 22. Armstrong LE. Rehydration during Endurance Exercise: Challenges, Research, Options, Methods. Nutrients. 2021 Mar 9;13:887. doi: 10.3390/nu13030887.
- 23. Parammal Alikutty J, Raj A, Soofi SK, Alkhateeb AA, Soliman AA, Al Amiri FR, et al. Rhabdomyolysis-Induced Acute Kidney Injury (AKI) in a Young Bodybuilder: A Case Report. Cureus. 2023 Feb 4;15:e34625. doi: 10.7759/cureus.34625.
- 24. Stanley M, Chippa V, Aeddula NR. Rhabdomyolysis. [Updated 2023 Apr 16]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-. Available from: https://www. ncbi.nlm.nih.gov/books/NBK448168/