



The Roles of Aerobic Training and Ozone Therapy Concerning Osteoarthritis and Cardiovascular Disease

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Received 2020 November 10; Revised 2020 December 12; Accepted 2020 December 22.

Keywords: Physical Activity, Osteoarthritis, Ozone Therapy

Dear editor,

Nowadays, arthritis and cardiovascular disease are common disorders among people. Arthritis is a condition which causes pain, stiffness, and swelling in joint (1). In osteoarthritis which is the most common type of arthritis, the protective cartilage among bones begins to weaken, and the bones will be worn out, causing pain in person (2). The cardiovascular disease affecting the heart or blood vessels which is usually related to a build-up of fatty deposits inside the vessels (atherosclerosis). There are many factors involved in developing osteoarthritis and atherosclerosis, some of which, such as age and genetics, are not under human control (3, 4). Some factors such as muscle weakness, inactivity, and overweight are factors which can be controlled during the life (5-8). However, studies show that subjects who suffer from these conditions for any reason can recover with proper aerobic training and ozone therapy (5, 9-11). Due to the reports, aerobic training and ozone therapy positively affect genes related to cardiovascular health in the heart tissue of rats with osteoarthritis (9). Furthermore, combined therapies with aerobic training and ozone improve some biochemical variables in cartilage tissue of rats with knee osteoarthritis (12). Aerobic training decreases the risk of ischemia-related cardiac dysfunction/death (13). Aerobic training via several mechanisms such as changes in reverse cholesterol transport elements has a positive effect on heart health and function (7, 14-17). Aerobic training (under physician supervision) can help treat osteoarthritis and reduce pain by increasing muscle and tendon function as well as weight loss (18).

Ozone is a protective layer on earth which prevents much of Sun's UV rays from reaching earth (19). Moreover, ozone has a whole new purpose today, which has nothing to do with protection from sun (20). Ozone ther-

apy has a beneficial effect for patients with ischemic heart disease, or patients who suffer from myocardia infarction (21). Ozone activates redox system which reduces pro-inflammatory cytokines, adjusts nuclear factor- κ B (NF-KB) pathway, decreases platelet aggregation and induced the release of growth factors (21). These changes are the mechanisms to explain the beneficial effect of ozone therapy on preventing and treating ischemic heart disease and post-infarct rehabilitation (21). Nowadays, Ozone therapy is so popular because it is simply applicable to cardiovascular aim which does not require surgery for osteoarthritis treatments (22). Studies show that ozone injections relieve knee pain and improve people's life quality with knee osteoarthritis (22). Joint injection of ozone appears to regenerate ligaments and is a permanent treatment for chronic pain due to osteoarthritis (23). Joint injection of ozone repairs damaged or weak connective tissue, and by repairing connective tissue, chronic pain can be completely cured. Using ozone therapy, joint injection is an injection method similar to proletharian therapy (24). Applying ozone causes damaged joint to heal much faster than traditional medication (23). This is because ozone is a highly reactive molecule that can repair the fibroblast joint when injected into the joint capsule (21). The injection is done by injecting ozone near the nerve root of affected area and affected joint to treat osteoarthritis (25). With its anti-inflammatory properties, ozone improves joint disorders such as meniscus rupture and osteoarthritis (23). Ozone therapy is relatively painless, and the patients can fully take care of their daily tasks on the same day of treatment (26). People respond to ozone therapy differently (26), the patients usually achieve more than 50% reduction in pain. Most people may need one or two sessions of treatment (27). The healing process can take several weeks. Most col-

lagen is produced after a few weeks after injection (23). In a nutshell, ozone therapy is a very safe treatment for osteoarthritis. When performed by an experienced physician, ozone therapy rarely causes adverse side effects (28). Like medical treatments, it has potential health risks associated to infection, allergic reactions, fainting, pain, bruising, and hospitalization (29). People usually experience a significant reduction in pain 24 hours after treatment which decreases over time (29). The amount of pain reduction varies from person to person, failure to respond to treatment is rare (26).

Footnotes

Authors' Contribution: AZ wrote the first draft of manuscript. HM and LM read and revised the letter.

Conflict of Interests: The authors declare that they have no conflict of interest.

Funding/Support: This study was supported by Central Tehran Branch of Islamic Azad University.

References

- Bullock J, Rizvi SAA, Saleh AM, Ahmed SS, Do DP, Ansari RA, et al. Rheumatoid Arthritis: A Brief Overview of the Treatment. *Med Princ Pract.* 2018;**27**(6):501-7. doi: [10.1159/000493390](https://doi.org/10.1159/000493390). [PubMed: [30173215](https://pubmed.ncbi.nlm.nih.gov/30173215/)]. [PubMed Central: [PMC6422329](https://pubmed.ncbi.nlm.nih.gov/PMC6422329/)].
- Chow YY, Chin KY. The Role of Inflammation in the Pathogenesis of Osteoarthritis. *Mediators Inflamm.* 2020;**2020**:8293921. doi: [10.1155/2020/8293921](https://doi.org/10.1155/2020/8293921). [PubMed: [32189997](https://pubmed.ncbi.nlm.nih.gov/32189997/)]. [PubMed Central: [PMC7072120](https://pubmed.ncbi.nlm.nih.gov/PMC7072120/) publication of this paper].
- Shane Anderson A, Loeser RF. Why is osteoarthritis an age-related disease? *Best Pract Res Clin Rheumatol.* 2010;**24**(1):15-26. doi: [10.1016/j.berh.2009.08.006](https://doi.org/10.1016/j.berh.2009.08.006). [PubMed: [20129196](https://pubmed.ncbi.nlm.nih.gov/20129196/)]. [PubMed Central: [PMC2818253](https://pubmed.ncbi.nlm.nih.gov/PMC2818253/)].
- Abbate R, Sticchi E, Fatini C. Genetics of cardiovascular disease. *Clin Cases Miner Bone Metab.* 2008;**5**(1):63-6. [PubMed: [22460848](https://pubmed.ncbi.nlm.nih.gov/22460848/)]. [PubMed Central: [PMC2781194](https://pubmed.ncbi.nlm.nih.gov/PMC2781194/)].
- Valderrabano V, Steiger C. Treatment and Prevention of Osteoarthritis through Exercise and Sports. *J Aging Res.* 2010;**2011**:374653. doi: [10.4061/2011/374653](https://doi.org/10.4061/2011/374653). [PubMed: [21188091](https://pubmed.ncbi.nlm.nih.gov/21188091/)]. [PubMed Central: [PMC3004403](https://pubmed.ncbi.nlm.nih.gov/PMC3004403/)].
- Zarezahehmehrzi A, Rajabi H, Gharakhanlou R, Naghdi N, Azimodokht SMA. Effect of 8 weeks of Aerobic Training on Genes Expression of Hypoxia Inducible Factor HIF-1 α , Vascular Endothelial Growth Factor (VEGF) and Angiostatin in Hippocampus of Male Rats with Wistar Model. *J Shahid Sadoughi Univ Med Sci.* 2020. doi: [10.18502/ssu.v27i11.2493](https://doi.org/10.18502/ssu.v27i11.2493).
- Rahmati-Ahmadabad S, Broom DR, Ghanbari-Niaki A, Shirvani H. Effects of exercise on reverse cholesterol transport: A systemized narrative review of animal studies. *Life Sci.* 2019;**224**:139-48. doi: [10.1016/j.lfs.2019.03.058](https://doi.org/10.1016/j.lfs.2019.03.058). [PubMed: [30922848](https://pubmed.ncbi.nlm.nih.gov/30922848/)].
- Azimodokht S, Mogharnasi M, Kargar Shouroki MK, Zarezahehmehrzi AA. The effect of 8 weeks interval training on insulin resistance and lipid profiles in type 2 diabetic men treated with metformin. *J Sport Biosci.* 2015;**7**(3):461-76.
- Zandi A, Azarbayjani MA, Peeri M, Hosseini SA. The Effect of Aerobic Training and Ozone Therapy on the Levels of MFN1 and DRP1 Gene Expression in the Heart Tissue of Rats with Osteoarthritis. *Gene Cell Tissue.* 2020;**7**(4). doi: [10.5812/gct.106920](https://doi.org/10.5812/gct.106920).
- Pina IL, Apstein CS, Balady GJ, Belardinelli R, Chaitman BR, Duscha BD, et al. Exercise and heart failure: A statement from the American Heart Association Committee on exercise, rehabilitation, and prevention. *Circulation.* 2003;**107**(8):1210-25. doi: [10.1161/01.cir.0000055013.92097.40](https://doi.org/10.1161/01.cir.0000055013.92097.40). [PubMed: [12615804](https://pubmed.ncbi.nlm.nih.gov/12615804/)].
- Leggio M, Fusco A, Loreti C, Limongelli G, Bendini MG, Mazza A, et al. Effects of exercise training in heart failure with preserved ejection fraction: an updated systematic literature review. *Heart Fail Rev.* 2020;**25**(5):703-11. doi: [10.1007/s10741-019-09841-x](https://doi.org/10.1007/s10741-019-09841-x). [PubMed: [31399956](https://pubmed.ncbi.nlm.nih.gov/31399956/)].
- Asadi S, Farzanegi P, Azarbayjani MA. Combined therapies with exercise, ozone and mesenchymal stem cells improve the expression of HIF1 and SOX9 in the cartilage tissue of rats with knee osteoarthritis. *Physiol Int.* 2020;**107**(2):231-42. doi: [10.1556/2060.2020.00024](https://doi.org/10.1556/2060.2020.00024). [PubMed: [32750029](https://pubmed.ncbi.nlm.nih.gov/32750029/)].
- Pinckard K, Baskin KK, Stanford KI. Effects of Exercise to Improve Cardiovascular Health. *Front Cardiovasc Med.* 2019;**6**:69. doi: [10.3389/fcvm.2019.00069](https://doi.org/10.3389/fcvm.2019.00069). [PubMed: [31214598](https://pubmed.ncbi.nlm.nih.gov/31214598/)]. [PubMed Central: [PMC6557987](https://pubmed.ncbi.nlm.nih.gov/PMC6557987/)].
- Rahmati-Ahmadabad S, Shirvani H, Ghanbari-Niaki A, Rostamkhani F. The effects of high-intensity interval training on reverse cholesterol transport elements: A way of cardiovascular protection against atherosclerosis. *Life Sci.* 2018;**209**:377-82. doi: [10.1016/j.lfs.2018.08.036](https://doi.org/10.1016/j.lfs.2018.08.036). [PubMed: [30125578](https://pubmed.ncbi.nlm.nih.gov/30125578/)].
- Rahmati-Ahmadabad S, Azarbayjani MA, Farzanegi P, Moradi L. High-intensity interval training has a greater effect on reverse cholesterol transport elements compared with moderate-intensity continuous training in obese male rats. *Eur J Prev Cardiol.* 2019;2047487319887830. doi: [10.1177/2047487319887828](https://doi.org/10.1177/2047487319887828). [PubMed: [31718266](https://pubmed.ncbi.nlm.nih.gov/31718266/)].
- Ghanbari-Niaki A, Rahmati-Ahmadabad S, Zare-Kookandeh N. ABCG8 Gene Responses to 8 Weeks Treadmill Running With or Without Pistachia atlantica (Baneh) Extraction in Female Rats. *Int J Endocrinol Metab.* 2012;**10**(4):604-10. doi: [10.5812/ijem.5305](https://doi.org/10.5812/ijem.5305). [PubMed: [23843831](https://pubmed.ncbi.nlm.nih.gov/23843831/)]. [PubMed Central: [PMC3693642](https://pubmed.ncbi.nlm.nih.gov/PMC3693642/)].
- Ghanbari-Niaki A, Rahmati-Ahmadabad S. Effects of a fixed-intensity of endurance training and pistacia atlantica supplementation on ATP-binding cassette G4 expression. *Chin Med.* 2013;**8**(1):23. doi: [10.1186/1749-8546-8-23](https://doi.org/10.1186/1749-8546-8-23). [PubMed: [24267473](https://pubmed.ncbi.nlm.nih.gov/24267473/)]. [PubMed Central: [PMC4175503](https://pubmed.ncbi.nlm.nih.gov/PMC4175503/)].
- Andrade V, Padilha KG, Kimura M. [Follow-up of nurses who have finished the specialization courses in intensive care nursing]. *Rev Lat Am Enfermagem.* 1998;**6**(3):23-31. doi: [10.1590/s0104-11691998000300004](https://doi.org/10.1590/s0104-11691998000300004). [PubMed: [9752252](https://pubmed.ncbi.nlm.nih.gov/9752252/)].
- Bais AF, Lucas RM, Bornman JF, Williamson CE, Sulzberger B, Austin AT, et al. Environmental effects of ozone depletion, UV radiation and interactions with climate change: UNEP Environmental Effects Assessment Panel, update 2017. *Photochem Photobiol Sci.* 2018;**17**(2):127-79. doi: [10.1039/c7pp90043k](https://doi.org/10.1039/c7pp90043k). [PubMed: [29404558](https://pubmed.ncbi.nlm.nih.gov/29404558/)]. [PubMed Central: [PMC6155474](https://pubmed.ncbi.nlm.nih.gov/PMC6155474/)].
- Scasellati C, Galoforo AC, Bonvicini C, Esposito C, Ricevuti G. Ozone: a natural bioactive molecule with antioxidant property as potential new strategy in aging and in neurodegenerative disorders. *Ageing Res Rev.* 2020;**63**:101138. doi: [10.1016/j.arr.2020.101138](https://doi.org/10.1016/j.arr.2020.101138). [PubMed: [32810649](https://pubmed.ncbi.nlm.nih.gov/32810649/)]. [PubMed Central: [PMC7428719](https://pubmed.ncbi.nlm.nih.gov/PMC7428719/)].
- Pandolfi S, Zammitti A, Franzini M, Simonetti V, Liboni W, Valdenassi L, et al. Effects of oxygen ozone therapy on cardiac function in a patient with a prior myocardial infarction. *Ozone Ther.* 2017;**2**(1). doi: [10.4081/ozone.2017.6745](https://doi.org/10.4081/ozone.2017.6745).
- Sconza C, Respizzi S, Virelli L, Vandenbulcke F, Iacono F, Kon E, et al. Oxygen-Ozone Therapy for the Treatment of Knee Osteoarthritis: A Systematic Review of Randomized Controlled Trials. *Arthroscopy.* 2020;**36**(1):277-86. doi: [10.1016/j.arthro.2019.05.043](https://doi.org/10.1016/j.arthro.2019.05.043). [PubMed: [31679646](https://pubmed.ncbi.nlm.nih.gov/31679646/)].

23. Seyam O, Smith NL, Reid I, Gandhi J, Jiang W, Khan SA. Clinical utility of ozone therapy for musculoskeletal disorders. *Med Gas Res*. 2018;**8**(3):103-10. doi: [10.4103/2045-9912.241075](https://doi.org/10.4103/2045-9912.241075). [PubMed: [30319765](https://pubmed.ncbi.nlm.nih.gov/30319765/)]. [PubMed Central: [PMC6178642](https://pubmed.ncbi.nlm.nih.gov/PMC6178642/)].
24. Manoto SL, Maepa MJ, Motaung SK. Medical ozone therapy as a potential treatment modality for regeneration of damaged articular cartilage in osteoarthritis. *Saudi J Biol Sci*. 2018;**25**(4):672-9. doi: [10.1016/j.sjbs.2016.02.002](https://doi.org/10.1016/j.sjbs.2016.02.002). [PubMed: [29736142](https://pubmed.ncbi.nlm.nih.gov/29736142/)]. [PubMed Central: [PMC5935866](https://pubmed.ncbi.nlm.nih.gov/PMC5935866/)].
25. Li J, Li T, Li G, Liu H, Zhang X. Selective nerve root injection of ozone for the treatment of phantom limb pain: Three case reports. *Medicine (Baltimore)*. 2020;**99**(16). e19819. doi: [10.1097/MD.00000000000019819](https://doi.org/10.1097/MD.00000000000019819). [PubMed: [32312002](https://pubmed.ncbi.nlm.nih.gov/32312002/)]. [PubMed Central: [PMC7220434](https://pubmed.ncbi.nlm.nih.gov/PMC7220434/)].
26. Bocci V. The Clinical Application of Ozonotherapy. *Ozone*. 2010. p. 97-232. doi: [10.1007/978-90-481-9234-2_9](https://doi.org/10.1007/978-90-481-9234-2_9).
27. Fernández Cuadros ME, Pérez Moro OS, Albaladejo Florin MJ, Mirón Canelo JA. Ozone Improves Pain, Function and Quality of Life in Patients with Knee Osteoarthritis: A Prospective Quasi-Experimental Before-After Study. *Middle East J Rehabil Health*. 2016;**4**(1). doi: [10.17795/mejrh-41821](https://doi.org/10.17795/mejrh-41821).
28. Rowen RJ, Robins H. Ozone Therapy for Complex Regional Pain Syndrome: Review and Case Report. *Curr Pain Headache Rep*. 2019;**23**(6):41. doi: [10.1007/s11916-019-0776-y](https://doi.org/10.1007/s11916-019-0776-y). [PubMed: [31062104](https://pubmed.ncbi.nlm.nih.gov/31062104/)]. [PubMed Central: [PMC6502773](https://pubmed.ncbi.nlm.nih.gov/PMC6502773/)].
29. Elvis AM, Ekta JS. Ozone therapy: A clinical review. *J Nat Sci Biol Med*. 2011;**2**(1):66-70. doi: [10.4103/0976-9668.82319](https://doi.org/10.4103/0976-9668.82319). [PubMed: [22470237](https://pubmed.ncbi.nlm.nih.gov/22470237/)]. [PubMed Central: [PMC3312702](https://pubmed.ncbi.nlm.nih.gov/PMC3312702/)].