THE EFFECT OF AEROBIC EXERCISE ON TNF-α IN OLDER ADULTS

Donabella Fortuna Santosa¹, Nila Wahyuni²

¹ Anti-aging Medicine Program, Faculty of Medicine, Universitas Udayana, 80234, Denpasar, Indonesia ² Physiology Department, Faculty of Medicine, Universitas Udayana, 80234, Denpasar, Indonesia Email: belladonafs@gmail.com

ABSTRACT

The aging process is often accompanied by a non-specific condition of chronic inflammation. The elevated levels of various inflammatory biomarkers in the bloodstream, including TNF- α . Some studies showed that TNF- α levels in older adults significantly decreased after aerobic exercise. This literature review evaluates the aerobic exercise efficacy on TNF- α in older adults. The literature review will analyze the effect of aerobic exercise on TNF- α levels found in older adult patients. Google Scholar, ResearchGate, and Mendeley were used as the search engine. The keywords were aerobic exercise, TNF- α & older adults. We analyzed seven articles in total. A significant effect of aerobic exercise on inflammatory markers was proved by TNF- α improvement. The change in TNF- α level was varied and analyzed with other clinical progress such as cardiovascular, endocrine, and other research parameters. Aerobic exercise can be an alternative way to reduce the inflammatory process in older adult patients.

Keywords: aerobic exercise; TNF-a; older adults

INTRODUCTION

Based on World Health Organization (WHO) data, all countries must guarantee that their health and social systems are ready to profit from demographic shifts. The population of older adults is larger than it was previously. According to the United Nations, an older person is as a person who is over 60 years of age.¹ Between 2015 and 2050, the worldwide population over 60 will nearly be doubled, rising from 12% to 22%.² According to data from the Central Bureau of Statistics Indonesian National Socio-Economic Survey for March 2022, 10.48 percent of the population is aged, with an older adults dependence ratio of 16.09. This means that for every aged person, around 6 people of productive age (15-59 years) provide support. Women outnumber men (51.81 percent versus 48.19 percent), and there are more older adults in cities than in rural regions (56.05 percent versus 43.95 percent). 65.56 percent of the older adults are classed as young (60-69 years), 26.76 percent as medium (70-79 years), and 7.69 percent as old (80 years and above).³

Immunosenescence is linked to aging. The aging process is often accompanied by a nonspecific condition of chronic inflammation, which is indicated by elevated levels of various inflammatory biomarkers in the bloodstream, such as CRP, IL-18, TNF- α , and IL-6. Research has consistently revealed that activated immune function and inflammation are among the top pathways up-regulated with aging, as reported in various studies.⁴

Irrespective of age, chronic inflammation, commonly known as "inflamm-aging," significantly contributes to developing and advancing various chronic ailments, including obesity, cardiovascular diseases, and neurodegenerative disorders. Furthermore, it influences their progression and complications.⁴⁻⁹ Exercise should be increased to prevent aging complications.¹⁰ Some studies showed that TNF- α levels significantly decreased after aerobic exercise.¹¹ Reducing chronic inflammation in aging thus will reduce age-related morbidity and mortality. The previous publication about aerobic exercise efficacy to decrease elderly TNF- α should be reviewed. So, this study aimed to explore the effects of aerobic exercise on TNF- α in older adults.

METHODS

This literature review was conducted using Google Scholar, ResearchGate, Science Direct, and PubMed. Journals and preliminary research papers are also used in the literature review process with the keywords "Aerobic Exercise, TNF- α , and Older Adult"

Aerobic exercise efficacy on TNF- α in older adults (age > 60 years old) with or without specific conditions are explored with the keywords as the inclusion criteria. The literature search yielded 28.900 articles. There were seven trusted articles which sample were older adult age in accordance with the inclusion criteria of literature publication years 2013-2023. Indonesian or English was used. Non-full-text literature is excluded.

RESULTS

Seven studies found that aerobic exercise reduced TNF- α in older persons. Aerobic exercise was scheduled for one to eight months. The number of participants ranged between 36 and 80, with an average age of 65 years.

No	Author	Participants Condition	Grouping and Intervention	Duration (Weeks/ months) & Frequency	Result & conclusion
1	Wanderley, 2013. ¹²	50 older adults aged >60 years old	Aerobic training (n=20) vs resistance training (n=11) vs control group (n=19)	8 months Three times per week 50 minutes for each	Reduce hs-CRP and resting systolic and diastolic blood pressure $(-9.2\pm9.8\%$ and $-8.5\pm9.6\%)$
2	Kader <i>et al.</i> , 2018. ¹¹	60 older sedentary people aged 61-67 years old	Group A, n=30 (supervised aerobic exercise intervention group) vs Group B, n=30 (resistance exercise group)	session 6 months Three times per week	TNF-α, IL-6, and CRP levels decreased. IL-10 increase
3	Dos Anjos et al., 2016. ¹³	43 women aged 65 years or older, with Diabetic Mellitus type 2	Aerobic training program, grouping consists of pre- intervention vs post- intervention.	70 days 3 x 10 weekly sessions which were five minutes of warming up and 40 minutes of core exercise	No significant different level of inflammatory markers such as soluble tumor necrosis factor receptors 1 and 2, and interleukins 6 and 10.
4	Windsor, 2018. ¹⁴	30 older adults aged 60 to 86	Lower fit group (n=16) vs higher fit group (n=14)	30 days Three trial visits spaced by 3-10 days, each with 90 minutes of recuperation	No changes in TNF-α level
5	Kader <i>et al.</i> , 2016. ¹⁵	40 Alzheimer patients who were 65-75 years old	Treadmill aerobic exercise group (n=20) vs control group (no intervention, n=20)	Two months Three sessions/week for 2 months	Serum IL-6 and TNF-α significantly decreased

Table 1. The effect of aerobic exercise on TNF- α in older persons.

6	Kader <i>et al.</i> , 2019. ¹⁶	80 older adults aged 61-66 years old	Group A, n=40 (supervised aerobic exercise intervention group) vs Group B, n=40 (resistance exercise group)	6 months Three times per week for six months either walking or running	The mean value of inflammatory markers (TNF-α, IL-6, ICAM-1, VCAM-1, E- selectin) were significantly decreased, except for IL-10
7	Kader <i>et al.,</i> 2019. ¹⁷	50 older adults aged 61-67 years old with sleep difficulty	Group A, n=25 (supervised aerobic exercise intervention group) vs Group B, n=25 (control group)	6 months40 min aerobic session3 times every week for 6 months	The mean values of TNF- α and IL- 6 decreased significantly and the mean value of IL-10 significantly increased in group A, the differences were significant compared to control group.

DISCUSSION

This evaluation comprised seven articles. Aging is the leading cause of cardiovascular disease, with higher levels of pro-inflammatory mediators and endothelial dysfunction. Aerobic exercise training may be beneficial.¹⁸ The performance of exercise has a direct impact on the cellular immune system, whereby the adrenergic signalling during exercise can mobilise cytotoxic immune cells into circulation.¹⁹ Furthermore, combined exercise has a substantial influence on muscular strength, lipid and apolipoprotein profile, and inflammatory status, all of which revert to baseline values following aerobic exercise intervention.²⁰

Kader, 2018 studied sixty sedentary Saudi older adults participated in the exercise intervention (aerobic exercise or resistance exercise randomly) for 6 months, and the study found that both aerobic and resistance exercise can decrease TNF- α , IL-6, and CRP levels, and increase IL-10 levels, but Kader stated that aerobic exercise training is more appropriate to modify the inflammatory markers among the older adults.¹¹

In 2017, Hasegawa demonstrated that endothelial dysfunction increases arterial stiffness with aging. According to a 2019 Kader research, aerobic exercise reduces ICAM-1, VCAM-1, and E-selectin more effectively than resistance training. Aging is associated with an increase in cardiovascular risks and endothelial dysfunction. Furthermore, aging promotes fat accumulation and causes an increase in arterial stiffness. The process is based on the production of proinflammatory adipokines such as tumor necrosis factor- α (TNF- α), interleukin-6 (IL-6), leptin, and adiponectin by adipose tissues. An increase in the size and quantity of adipocytes causes the level of proinflammatory mediators to rise, accelerating the course of arterial stiffness.²¹

Dos Anjos discovered no difference in inflammatory markers levels, such as soluble tumor necrosis factor receptors 1 and 2, and interleukins 6 and 10 from older people who finished the aerobic training.¹³ The impact of 10 weeks of aerobic training exercise on the inflammatory markers of 43 diabetic women was studied in this study. The individuals were assigned at random to participate in aerobic exercise three times per week for ten weeks, and the results revealed that aerobic exercise was ineffective in lowering the levels of inflammatory markers. It might be due to the study's brief intervention time.¹³

Windsor observed no significant variations in TNF- α status between consistently moderate interval and high-intensity interval exercise in older persons with higher and lower levels of cardiorespiratory fitness. ¹⁴ These findings complement Estrela et al.'s prior work in older persons, possibly because the cytokine response to exercise is reduced in older adults.²²

Some research, on the other hand, discovered beneficial alterations in TNF- α . According to the findings of Zheng et al.'s study, aerobic exercise significantly lowered inflammatory markers such

as TNF- α , C-reactive protein (CRP), and Interleukin-6 (IL-6).¹⁹ Furthermore, Kader et al. concur that aerobic exercise training can reduce TNF- and IL-6 levels while increasing IL-10 levels in fifty healthy 61-year-old men and women who have difficulties falling asleep.¹⁵

Zhao et al. found that aerobic exercise, resistance exercise, and HIIT can increase inflammation in older persons while decreasing levels of pro-inflammatory cytokines IL-6, TNF- α , and CRP. Adrenergic signaling is responsible for the release of cytotoxic immune cells during aerobic exercise.¹⁷ Aerobic exercise can improve chronic inflammatory levels in older adults, downregulate systemic inflammation, and reduce 10-year cardiovascular risk. Aerobic and resistance training together had the greatest impact on reducing tumor necrosis factor-a level in obesity.^{23,24,25}

The 40 minutes of moderate to vigorous intensity aerobic activity, 3 or 4 times a week, is recommended to reduce cardiovascular risk by reducing SBP, HDL-C, and inflammatory biomarkers in post-menopausal women. Aerobic and resistance training together had the greatest impact on reducing tumor necrosis factor-a level in obesity. Three mechanisms of aerobic exercise training as an anti-inflammatory factor are reduction in the release of adipocytokines, reduction in circulating levels of pro-inflammatory, and increase in circulating levels of T cells.^{2627, 28} Aerobic and resistance training are effective interventions in decreasing chronic inflammation, but high running can cause negative effects such as acute inflammation.^{12,29}

The present investigation is subject to multiple limitations. Regarding the specificity of intervention, it may not be possible to effectively implement blinding procedures for participants and exercise trainers in the context of aerobic exercise intervention. As a result, the occurrence of performance bias cannot be ruled out. Measurement bias could potentially arise from variations in the methods and equipment employed for TNF-alpha measurement. If the result showed no differences or increased, the hypothesis is the intensity or duration of aerobic exercise intervention was still various in several previous study

CONCLUSION

Aerobic exercise has significantly decreased the levels of TNF- α in older adults. Further studies are needed to compare cytokine responses to exercise in younger, middle age and older adults.

CONFLICT OF INTEREST

Nothing is considered a conflict of interest.

ACKNOWLEDGEMENT

The author appreciates the guidance of dr. Nila Wahyuni, M.Fis. She was my supervisor for the Basic Sports Medicine course, Anti-Aging Medicine concentration of the Biomedical Science Graduate Program, Medical Faculty, Udayana University– Bali – Indonesia.

REFERENCES

- 1. Age | National Institutes of Health (NIH) [Internet]. [cited 2023 Jun 18]. Available from: https://www.nih.gov/nih-style-guide/age
- 2. Ageing and health [Internet]. [cited 2023 Apr 30]. Available from: https://www.who.int/news-room/fact-sheets/detail/ageing-and-health
- Andry Poltak L. Girsang SST, MEcDev, Rini Sulistyowati SST. MEKK, Nindya Putri Sulistyowati SST, Freshy Windy Rosmala Dewi SST, Sigit Wahyu Nugroho SAP, Karuniawati Dewi Ramadani S.Si. M, Hendrik Wilson SST, SSi, ME. Statistik Penduduk Lanjut Usia 2022 [Internet]. Jakarta; 2022. Available from: www.freepik.com
- 4. El-Kader SMA, Al-Shreef FM, Al-Jiffri OH. Impact of aerobic exercise versus resisted exercise on endothelial activation markers and inflammatory cytokines among elderly. Afr Health Sci. Makerere University, Medical School; 2019 Dec 1;19(4):2874–2880. PMID: 32127863
- Lang Y, Chu F, Shen D, Zhang W, Zheng C, Zhu J, Cui L. Role of Inflammasomes in Neuroimmune and Neurodegenerative Diseases: A Systematic Review. Mediators Inflamm [Internet]. Hindawi Limited; 2018 [cited 2023 Apr 30];2018. Available from: /pmc/articles/PMC5932495/ PMID: 29849483
- Uchoa MF, Moser VA, Pike CJ. Interactions between inflammation, sex steroids, and Alzheimer's disease risk factors. Front Neuroendocrinol [Internet]. Front Neuroendocrinol; 2016 Oct 1 [cited 2023 Apr 30];43:60–82. Available from: https://pubmed.ncbi.nlm.nih.gov/27651175/ PMID: 27651175

- Korniluk A, Koper O, Kemona H, Dymicka-Piekarska V. From inflammation to cancer. Ir J Med Sci [Internet]. Ir J Med Sci; 2017 Feb 1 [cited 2023 Apr 30];186(1):57–62. Available from: https://pubmed.ncbi.nlm.nih.gov/27156054/ PMID: 27156054
- Landman GWD, Kleefstra N, Groenier KH, Bakker SJL, Groeneveld GH, Bilo HJG, van Hateren KJJ. Inflammation biomarkers and mortality prediction in patients with type 2 diabetes (ZODIAC-27). Atherosclerosis [Internet]. Atherosclerosis; 2016 Jul 1 [cited 2023 Apr 30];250:46–51. Available from: https://pubmed.ncbi.nlm.nih.gov/27179179/ PMID: 27179179
- 9. Bonaccio M, Di Castelnuovo A, Pounis G, De Curtis A, Costanzo S, Persichillo M, Cerletti C, Donati MB, De Gaetano G, Iacoviello L, Vermylen J, Carrasco IDP, Giampaoli S, Spagnuolo A, Assanelli D, Centritto V, Spagnuolo P, Staniscia D, Zito F, Bonanni A, Lorenzet R, Mascioli A, Olivieri M, Rotilio D, Gianfagna F, Giacci M, Padulo A, Petraroia D, Marracino F, Spinelli M, Silvestri C, De Lucia F, Vohnout B, Coordinator G, Verna A, Di Lillo M, Di Stefano I, Pannichella A, Vizzarri AR, Pampuch A, Arcari A, Barbato D, Bracone F, Di Giorgio C, Magnacca S, Panebianco S, Chiovitti A, Caccamo S, Caruso V, Rago L, Cugino D, Ferri A, Castaldi C, Mignogna M, Guszcz T, Di Giuseppe R, Barisciano P, Buonaccorsi L, Centritto F, Cutrone A, Fanelli F, Santimone I, Sciarretta A, Sorella I, Plescia E, Molinaro A, Cavone C, Galuppo G, D'Angelo D, Ramacciato R, Molise ASR Del. A score of low-grade inflammation and risk of mortality: prospective findings from the Moli-sani study. Haematologica [Internet]. Ferrata Storti Foundation; 2016 Oct 31 [cited 2023 Apr 30];101(11):1434. Available from: /pmc/articles/PMC5394885/ PMID: 27742767
- Argilés JM, Busquets S, Stemmler B, López-Soriano FJ. Cachexia and sarcopenia: mechanisms and potential targets for intervention. Curr Opin Pharmacol [Internet]. Curr Opin Pharmacol; 2015 Jun 13 [cited 2023 Apr 30];22:100–106. Available from: https://pubmed.ncbi.nlm.nih.gov/25974750/ PMID: 25974750
- 11. Cvečka J, Vajda M, Novotná A, Löfler S, Hamar D, Krčmár M. Benefits of Eccentric Training with Emphasis on Demands of Daily Living Activities and Feasibility in Older Adults: A Literature Review. International Journal of Environmental Research and Public Health. 2023.
- Abd El-Kader SM, Al-Shreef FM. Inflammatory cytokines and immune system modulation by aerobic versus resisted exercise training for elderly. Afr Health Sci. Makerere University, Medical School; 2018 Mar 1;18(1):120–131. PMID: 29977265
- Wanderley FAC, Moreira A, Sokhatska O, Palmares C, Moreira P, Sandercock G, Oliveira J, Carvalho J. Differential responses of adiposity, inflammation and autonomic function to aerobic versus resistance training in older adults. Exp Gerontol. 2013 Mar;48(3):326–333. PMID: 23333772
- 14. dos Anjos DM da C, Moreira B de S, Kirkwood RN, Dias RC, Pereira DS, Pereira LSM. Effects of aerobic exercise on functional capacity, anthropometric measurements and inflammatory markers in diabetic elderly women. J Bodyw Mov Ther. Churchill Livingstone; 2017 Jul 1;21(3):509–516. PMID: 28750957
- 15. Windsor MT, Bailey TG, Perissiou M, Meital L, Golledge J, Russell FD, Askew CD. Cytokine responses to acute exercise in healthy older adults: The effect of cardiorespiratory fitness. Front Physiol. Frontiers Media S.A.; 2018 Mar 15;9(MAR).
- S.M. AEK, O.H. AJ. Aerobic exercise improves quality of life, psychological well-being and systemic inflammation in subjects with alzheimer's disease. Afr Health Sci [Internet]. 2016;16(4):1045–1055. Available from:

http://www.embase.com/search/results?subaction=viewrecord&from=export&id=L614746874

- 17. El-Kader SMA, Al-Jiffri OH. Aerobic exercise modulates cytokine profile and sleep quality in elderly. Afr Health Sci. Makerere University, Medical School; 2019 Jun 1;19(2):2198–2207. PMID: 31656505
- 18. El-Kader SMA, Al-Shreef FM, Al-Jiffri OH. Impact of aerobic exercise versus resisted exercise on endothelial activation markers and inflammatory cytokines among elderly. Afr Health Sci. 2019;19(4).
- 19. Theodorou AA, Panayiotou G, Volaklis KA, Douda HT, Paschalis V, Nikolaidis MG, Smilios I, Toubekis A, Kyprianou D, Papadopoulos I, Tokmakidis SP. Aerobic, resistance and combined training and detraining on body composition, muscle strength, lipid profile and inflammation in coronary artery disease patients. Research in Sports Medicine. Taylor and Francis Inc.; 2016 Jul 2;24(3):171–184. PMID: 27258806
- Hasegawa N, Fujie S, Horii N, Uchida M, Kurihara T, Sanada K, Hamaoka T, Iemitsu M. Aerobic exercise training-induced changes in serum C1q/TNF-related protein levels are associated with reduced arterial stiffness in middle-aged and older adults. Am J Physiol Regul Integr Comp Physiol [Internet]. 2018;314:94–101. Available from: www.ajpregu.org
- 21. Estrela AL, Zaparte A, Da Silva JD, Moreira JC, Turner JE, Bauer ME. High volume exercise training in older athletes influences inflammatory and redox responses to acute exercise. J Aging Phys Act. Human Kinetics Publishers Inc.; 2017 Oct 1;25(4):559–569. PMID: 28181836

- 22. Zheng G, Qiu P, Xia R, Lin H, Ye B, Tao J, Chen L. Effect of aerobic exercise on inflammatory markers in healthy middle-aged and older adults: A systematic review and meta-analysis of randomized controlled trials. Frontiers in Aging Neuroscience. Frontiers Media S.A.; 2019.
- 23. Rose GL, Skinner TL, Mielke GI, Schaumberg MA. The effect of exercise intensity on chronic inflammation: A systematic review and meta-analysis. Journal of Science and Medicine in Sport. Elsevier Ltd; 2021. p. 345–351. PMID: 33153926
- 24. Monteiro-Junior RS, De Tarso Maciel-Pinheiro P, Da Matta Mello Portugal E, Da Silva Figueiredo LF, Terra R, Carneiro LSF, Rodrigues VD, Nascimento OJM, Deslandes AC, Laks J. Effect of Exercise on Inflammatory Profile of Older Persons: Systematic Review and Meta-Analyses. J Phys Act Health [Internet]. J Phys Act Health; 2018 Jan 1 [cited 2023 Apr 26];15(1):64–71. Available from: https://pubmed.ncbi.nlm.nih.gov/28771081/PMID: 28771081
- Cronin O, Keohane DM, Molloy MG, Shanahan F. The effect of exercise interventions on inflammatory biomarkers in healthy, physically inactive subjects: A systematic review. QJM. Oxford University Press; 2017 Oct 1;110(10):629–637. PMID: 28472518
- 26. Ahn N, Kim K. Can active aerobic exercise reduce the risk of cardiovascular disease in prehypertensive elderly women by improving hdl cholesterol and inflammatory markers? Int J Environ Res Public Health. MDPI AG; 2020 Aug 2;17(16):1–16. PMID: 32824020
- 27. Wang S, Zhou H, Zhao C, He H. Effect of Exercise Training on Body Composition and Inflammatory Cytokine Levels in Overweight and Obese Individuals: A Systematic Review and Network Meta-Analysis. Frontiers in Immunology. Frontiers Media S.A.; 2022. PMID: 35812437
- 28. Idorn M, Hojman P. Exercise-Dependent Regulation of NK Cells in Cancer Protection. Trends in Molecular Medicine. Elsevier Ltd; 2016. p. 565–577. PMID: 27262760
- You T, Arsenis NC, Disanzo BL, Lamonte MJ. Effects of exercise training on chronic inflammation in obesity: current evidence and potential mechanisms. Sports Med [Internet]. Sports Med; 2013 Apr [cited 2023 May 2];43(4):243–256. Available from: https://pubmed.ncbi.nlm.nih.gov/23494259/ PMID: 23494259
- Lavie CJ, Lee DC, Sui X, Arena R, O'Keefe JH, Church TS, Milani R V., Blair SN. Effects of running on chronic diseases and cardiovascular and all-cause mortality. Mayo Clin Proc [Internet]. Elsevier Ltd; 2015 Nov 1 [cited 2023 Apr 30];90(11):1541–1552. Available from: http://www.mayoclinicproceedings.org/article/S0025619615006217/fulltext PMID: 26362561