International Journal of Gerontology 19 (2025) 130–135
https://doi.org/10.6890/IJGE.202507_19(3).0001

International Journal of Gerontology

journal homepage: http://www.sgecm.org.tw/ijge/

Review Article

Physical Activity in the Prevention and Treatment of Frailty among Older Adults: Potential Mechanism and Clinical Evidence – A Narrative Review

Kuan-Ting Chou [a], Yun-Ju Cheng [b], Gwo-Chi Hu [a] *

[a] *Department of Rehabilitation Medicine, MacKay Memorial Hospital, Taipei, Taiwan,* [b] *Department of Long-Term Care, College of Nursing, Asia University, Taichung, Taiwan*

ARTICLE INFO

Accepted 30 December 2024

Keywords:
physical activity,
frailty,
exercise training,
mechanism

SUMMARY

Frailty is a significant clinical syndrome associated with functional decline and increased mortality in older adults. This review focuses on the relationship between physical activity/exercise interventions and frailty. The pathophysiology of frailty, including inflammation, oxidative stress, and its impact on skeletal muscle, respiratory, cardiovascular, endocrine, and nervous systems, underscores the importance of physical activity in frailty management. Physical activity/exercise may reduce age-related oxidative damage and chronic inflammation across various systems, thereby preventing or treating the frailty phenotype and promoting healthy aging. Recent evidence demonstrates that physical activity/exercise could prevent and treat frailty-related physical impairment in the elderly. Further research is warranted to determine the optimal physical activity regimen for frailty prevention and treatment.

1. Introduction

Frailty is common in older adults and is characterized by functional decline and early mortality. With rising life expectancy and prolonged periods of physical frailty, it is crucial to understand the clinical and physiological aspects of frailty to improve prevention and management strategies. According to the International Conference on Frailty and Sarcopenia Research (ICFSR), frailty is defined as "a clinical state in which there is an increase in an individual's vulnerability for developing an increased dependency and mortality when exposed to a stressor".[1] Although the prognostic implications of frailty have been widely recognized, there is currently no consensus for its operationalization across clinical settings. Multiple validated instruments based on different conceptual approaches have been developed to measure frailty. The frailty phenotype is currently the recommended international standard for frailty identification and assessment.[2] The frailty phenotype is defined by five criteria: involuntary weight loss, exhaustion, slow gait speed, weakness, and sedentary behavior. An individual is considered frail when three or more of these components are present. Pre-frailty is identified when one or two components exist. Rockwood et al.[3] have used deficit accumulation to determine the presence of frailty by employing a frailty index, which is calculated by considering several potential age-related symptoms, signs, and diseases to assess frailty. The most cited frailty assessment tools are frailty phenotype and frailty index.

Many risk factors, such as older age, obesity, female sex, living alone, polypharmacy, malnutrition, lower vitamin D levels, and physical inactivity, were associated with older adults being more likely to experience frailty.[4]

* Corresponding author. Department of Rehabilitation Medicine, MacKay Memorial Hospital, No. 92, Section 2, Chung-Shan N. Rd., Taipei, Taiwan.
E-mail address: kung527@gmail.com (G.-C. Hu)

Frailty is associated with declines in physiological capacity across sensory, neurological, and musculoskeletal systems, which increasing the likelihood of falls, fragility fractures, and impairing activities of daily living (ADL), ultimately leading to hospitalizations and mortality.[5] Despite its potential severity, frailty is recognized as a reversible condition, and strategies have been implemented to either reverse or delay its onset and progression. Physical activity plays a central role in this regard. Physical activity is known to preserve or improve the function of many physiologic systems at abnormal levels in frail older adults.[6] Our review aimed to provide data and describe the mechanisms involved in frailty affecting specific organs and systems and to review how physical activity hinders some of those harmful mechanisms, thus improving physical function and delaying or reversing frailty. We conducted a narrative review to update the available literature on the field of the prevention and treatment of frailty based on physical activity and exercise interventions. We conducted a search on PubMed, Medline, and Cochrane Plus databases for original articles, reviews and meta-analyses. The following terms were used: [frailty]; [exercise training]; [exercise interventions]; [physical activity]; [physical exercise].

2. Pathophysiology of frailty

Frailty is a clinical syndrome that affects multiple critical systems, including the endocrine, respiratory, and cardiovascular systems, as well as musculoskeletal systems. Among these systems, musculoskeletal system might be as a target organ of frailty processes. Musculoskeletal functioning is a key component in quantification of frailty. This condition significantly impacts the musculoskeletal system, where age-related physiological declines in muscle mass, strength, and bone mineral density are notably exacerbated.[7] Understanding the pathophysiological mechanisms underlying frailty's onset and progression to disability and mortality is crucial for developing effective treatment strategies. Aging, combined with increased oxidative damage and chronic inflammation, underpins dysfunction across multiple organ systems and contributes to the development of chronic diseases. Several frailty-related processes, including genomic instability, cell loss and death, loss of proteostasis, mitochondrial dysfunction, and altered intercellular communication, have been in some way related not only to aging itself but also to related oxidative stress and inflammation (Figure 1). Chronic inflammation is characterized by increased levels of pro-inflammatory cytokines such as interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α), and C-reactive protein (CRP), which might adversely affect function and mobility in older individuals.[8] Studies have shown that elevated cellular and molecular inflammatory mediators have inverse associations with hemoglobin concentrations, insulin-like growth factor (IGF)-1 levels, and levels of albumin, micronutrients, and vitamins.[9] Also, chronic inflammation is associated with the catabolism of skeletal muscle and adipose tissue, contributing to the nutritional compromise, muscle weakness, and multiple organ dysfunction.[10] Free radical theory of aging developed by Denham Harman connected oxidative stress with the aging process and aging-related diseases. An imbalance between pro-oxidant and antioxidant species would result in molecular and cellular damage.[11] Oxidative stress plays a crucial role in disrupting cell signaling associated with aging. The accumulation of oxidized proteins and disrupted proteostasis results in muscle loss, motor unit loss, and fragmentation of neuromuscular junctions, leading to impaired muscle innervation.[12] Oxidative stress directly contributes to frailty by disrupting the mitochondriogenic signaling pathway in skeletal muscle. Stimulating transcription factor nuclear erythroid-2 like factor-2 (Nrf2)/antioxidant response element pathway seems to play a prominent role in the response to oxidative insult and induces antioxidant defense. Consequently, the disruption of these pathways leads to reduced oxidative capacity, increased proteolysis, decreased protein synthesis, and mitochondrial dysfunction in skeletal muscle, ultimately resulting in sarcopenia, disabilities, and frailty.[13]

Physical activity is a crucial strategy for preventing or reducing frailty-related impairment by counteracting oxidative and inflammatory signaling across multiple systems.[14,15] It promotes mitochondrial biogenesis, enhances protein synthesis, optimizes myokine profile, and suppresses pro-inflammatory cytokine expression, enhancing muscle structure and function. In the vascular system, the increase in antioxidant enzymes and nitric oxide availability helps alleviate age-related vascular dysfunction and reduce the incidence of cardiovascular disease.[16] Exercise exerts potent anti-inflammatory and anti-oxidative stress effects by modulating key signaling pathways. It plays a critical role in boosting Nrf2 expression, essential for redox adaptation and protection against reactive oxygen species (ROS)-induced damage in skeletal muscle.[17] Additionally, exercise activates the IGF-1 pathway to stimulate protein synthesis and utilizes myokines to reduce protein degradation. Furthermore, it enhances the signaling of the transcription factor peroxisome proliferator-activated receptor gamma coactivator 1-alpha (PGC-1α), improving mitochondrial function and reducing nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB)-mediate inflammation.[18] These mechanisms normalize cell metabolism, improve exercise adaptation, and confer beneficial effects on skeletal muscle, cardiovascular, respiratory, and metabolic systems. Long-term exercise can ameliorate physical disability, cognitive functions, emotional well-being, social interactions, and overall quality of life in frail elderly individuals (Figure 2).[19] Frailty is, however, a reversible condition and numerous strategies have been implemented to reverse it or delay its onset and progression. Most of the successful interventions focus on exercise and physical activity intervention. Exercise interventions encompass resistance, aerobic, balance, and flexibility training, each contributing to enhanced physical functioning by im-

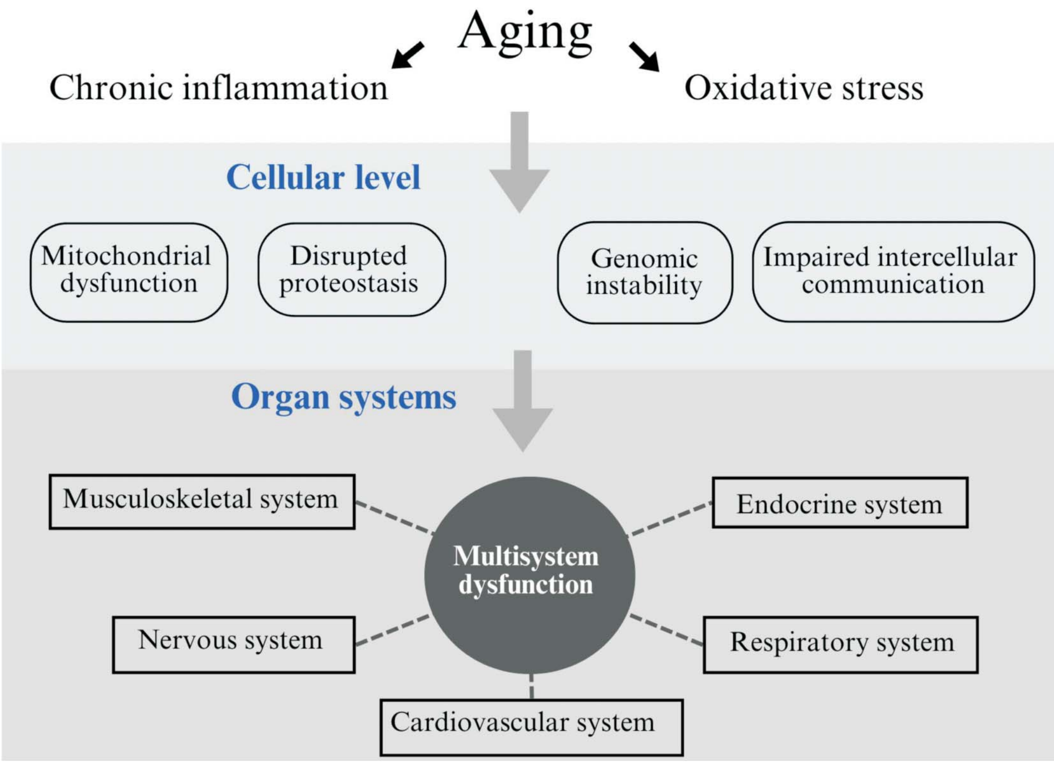

Figure 1. The pathophysiology of frailty. Aging is associated with the onset of chronic inflammation and oxidative stress, which disrupt protein synthesis, mitochondrial biogenesis, and genomic stability, as well as impair intercellular communication. These pathophysiological changes culminate in the dysfunction of multiple systems, including the musculoskeletal, nervous, cardiovascular, respiratory, and endocrine systems, thereby contributing to the development of frailty.

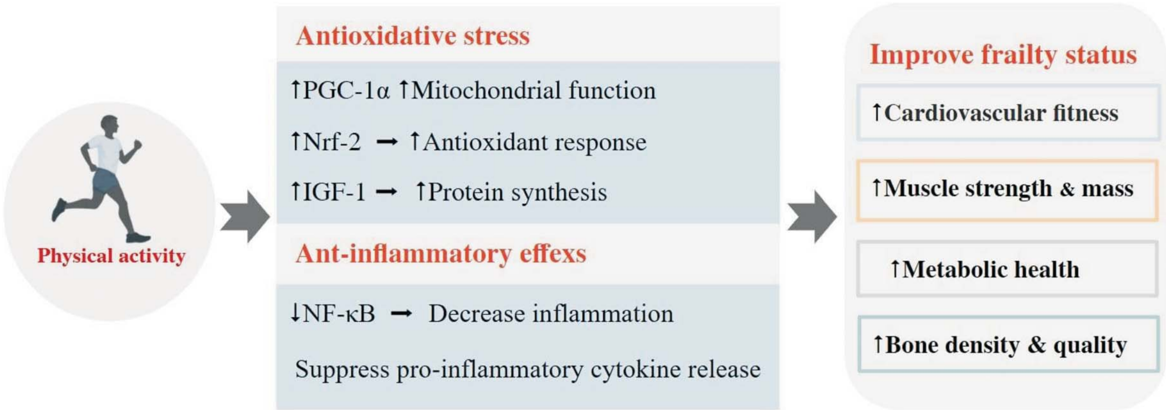

Figure 2. Physical activity effectively mitigates frailty-related physical decline through diverse molecular mechanisms. It enhances mitochondrial function by activating the transcription factor PGC-1α and improves antioxidant defenses by upregulating Nrf2 expression. Furthermore, it stimulates the IGF-1 signaling pathway, thereby promoting protein synthesis. Physical activity also reduces the release of pro-inflammatory cytokines and modulates NF-κB signaling. Collectively, these effects contribute to improved muscle structure and function, enhanced cardiovascular fitness, and overall metabolic benefits. IGF-1: insulin-like growth factor 1; NF-κB: nuclear factor kappa-light-chain-enhancer of activated B cells; Nrf2: nuclear factor erythroid 2-related factor 2; PGC-1α: peroxisome proliferator-activated receptor gamma coactivator 1-alpha.

proving muscle endurance, power, strength, and overall functional ability.[20] Different types of exercise uniquely contribute to mitigating chronic inflammation and addressing frailty mechanisms. Aerobic exercise improves endothelial function and arterial stiffness by reducing inflammatory and oxidative damage signaling in vascular tissue together with an increase in antioxidant enzymes and nitric oxide availability, globally promoting cardiovascular health.[21]

Resistance training has been demonstrated to enhance bone, muscle, and ligament strength, improve joint function, increase bone density and metabolism. In addition, resistance training is associated with reduced risk of low-grade inflammation related diseases such as atherosclerosis, obesity and insulin resistance. A systemic review[22] of 12 trials found that resistance exercise at a moderate level for 3 times/week with a duration of 6–12 weeks can significantly reduce inflammation markers. The findings contribute to providing suggestions for the elderly to participate in resistance training and reduce the concentration of inflammatory markers.

Flexibility and balance exercises are crucial for maintaining functional mobility, thereby reducing fall risk and alleviating joint stiffness. These programs have been found to improve static and dynamic stability, cognitive function, and quality of life.[23]

They can be combined according to need and prescribed as a multicomponent intervention. This multifaceted approach can stimulate and facilitate positive adaptations in various physiological systems involved in the development of frailty, such as the nervous, musculoskeletal, and cardiovascular systems. Individually tailored multicomponent exercise programs combined with adequate nutrition support are among the best ways to prevent and treat frailty-related physical impairment in the elderly.[24]

3. Physical activity/exercise intervention in frailty prevention and treatment

Physical activity is defined as any body movement produced by the skeletal system that increases energy expenditure. Exercise is a subset of physical activity that is planned and structured and whose objective is to maintain or improve physical fitness.[25] Sedentary behavior is a unique behavior from physical activity and is defined as low energy expenditure activities in a seated, reclining, or lying posture during awake hours.[26]

Many studies have found a significant association between sedentary behavior and the risk of frailty. In a cross-sectional study of 3238 community-living Chinese men and women, participants with sedentary behavior for > 8 hours/day were more likely to suffer from physical frailty than older adults with sedentary behavior for < 4 hours/day.[27] Similarly, a 3-year follow-up study of 7,480 Japanese older adults showed a significant positive dose–response association between sedentary time and the risk of frailty.[28] Regular physical activity participation can reduce the risk of developing of chronic disease and frailty. The English Longitudinal Study of Ageing (ELSA) showed that participants who performed in moderate to vigorous physical activity once a week significantly slowed the progression of frailty, compared to those who were sedentary during the 10-year follow-up.[29] A systemic review of 10 cohort studies showed that participants with the highest level of physical activity were associated with a 37% reduced risk of frailty when compared with participants with the lowest physical activity level. In a 20-year longitudinal study involving 5131 community-dwelling older people from the Taiwan Longitudinal Study of Aging (TLSA) database, Lin et al. investigated the relationship between physical activity trajectories and frailty. The study found that incline and decline physical activity trajectories are related to the lowest and highest frailty scores.[30] However, the combined association of physical activity and sedentary behavior with frailty is not yet clear in the literature. Some studies suggest that physical activity levels may not fully attenuate the detrimental association between high amounts of sedentary behaviors and frailty.[31] Some studies found that moderate to vigorous physical activity can offset the harmful effects of sedentary behavior.[32] Although two distinct behavioral aspects, combined insufficient physical activity level and excessive time spent in sedentary behavior may exacerbate the physiological alterations resulting from the aging process. These behaviors lead to a caloric overload and the accumulation of central adipocytes, which reduces the production of anti-inflammatory adipokines. This process may result in the development of chronic diseases, and, consequently, frailty in older adults. A cross-sectional study based on the National Health and Nutrition Examination Survey database found that reducing sedentary behavior by one hour/day with a concomitant increase of one hour/day of moderate-to-vigorous intensity physical activity potentiates the reduction of the risk for frailty.[33] These results indicated that increasing physical activity level or minimizing sedentary time helps prevent the risk of frailty.

Recently, there has been a noticeable increase in exercise-based interventions to limit or reverse frailty in older adults. This is because it is becoming increasingly recognized that regular participation in physical exercise triggers many beneficial responses that contribute to healthy aging.[34]

For the pre-frail older adults, multicomponent exercise programs had the potential to slow down or prevent progression to frailty and adverse frailty outcomes. Serra-Prat et al.[35] randomly divided 172 pre-frail participants into an exercise intention group and a usual care group. The results showed the intervention group had fewer participants who had progressed to becoming frail, compared with the control group. Chen et al.[36] conducted a trial to investigate the effect of exercise training for pre-frail older adults. Participants were randomized to either 8 weeks of usual care or an exercise intervention consisting of three weekly supervised sessions of 45–60 min/session of elastic band strengthening exercises. After eight weeks, the intervention group had more participants who were no longer prefrail compared with the control group.

Several studies demonstrated significant changes in frailty status or reduced frailty prevalence with exercise training in frail older adults. Sadjapong et al.[37] enrolled 64 community-dwelling older adults with frailty to investigate the effects of a multicomponent exercise program on the frailty status over a 24-week period. The program regimen included aerobic training, resistance training, and balance training, with sessions occurring three days per week for 60 minutes each. The intensity of the sessions gradually increased from moderate to high, tailored to the participants' capabilities. The study demonstrated significant improvements in physical performance and frailty scores. Kim et al.[38] assessed 131 women randomized to 3-month interventions followed by a 4-month postintervention follow-up. The exercise intervention program consisted of 30 min of strengthening exercises and 20 min of balance and gait training, performed three times per week. At the 4-month follow-up, the intervention group had significantly more reclassified participants to either pre-frail or nor-frail status than the control group. A trial of 100 frail older adults who were randomized to supervised multicomponent exercise program group or control group. The multicomponent exercise program consisted of proprioception, aerobic, strength, and stretching exercises for 65 minutes, 5 days per week. The results showed that in 31.4% of the intervention group, frailty was reversed after the exercise training program, whereas no one in the control group reversed frailty after the 6-month period.[39] Recently, a systematic review and meta-analysis of 19 randomized controlled trials assessed the efficacy of the multicomponent exercise training for frail older adults and demonstrated significant improvement muscle strength, balance, and endurance function in frail older adults randomized to exercise training group.[40] Frailty in surgical patients is presumed to contribute to perioperative complications and slowed recovery.[41] Exercise prehabilitation has been shown to be beneficial for frail patients planning to total hip arthroplasty, and spinal surgery for degenerative lumbar spine disease.[42,43] These studies assessing the impact of exercise therapy on musculoskeletal conditions support its use in improving functional outcomes both before and following surgical procedures. Recently, virtual reality tools, robots, smart phone motivational program and a telemonitoring system have been increasingly applied to the care of frail older patients to increase physical activity level.[44,45] However, the methodological limitations of studies in this field have prevented generalizing data to real-world.

Collectively, strong evidence demonstrates that regular physical activity/exercise has health benefits for older adults, regardless of age, sex, race, ethnicity, and frailty status. Taking into consideration current evidence about the benefits of physical activity/exercise for frail older adults, several guidelines strongly recommend implementation of physical activity and exercise programs to prevent and reverse for older adults. The World Health Organization, 2020 guidelines[46] on physical activity suggest that adults 65 and older should engage in 150 minutes of moderate- or 75 minutes of vigorous-intensity aerobic activity and two or more days of muscle-strengthening activity per week. The US Department of Health and Human Services suggests that multicomponent exercises training that includes balance training as well as muscle-strengthening (at least 2 days a week) and aerobic activities of at least moderate-intensity performed 3 or more times per week for a duration of 30 to 45 minutes per session appears most effective to increase functional ability in older adults with frailty.[47]

Exercise adherence plays a crucial role in determining whether and how much the exercise intervention could be effective. It is important for healthcare providers to identify and address barriers and enablers to adherence when designing and implementing exercise interventions for pre-frailty and frailty older adults. Previous studies have identified common reasons for this lack of adherence, such as physical limitations, environmental barriers, and time constraints, lack of motivation and enjoyment of exercise have been recognized as significant factors influencing adherence.[48]

In clinical settings, designing exercise programs for frail older adults should prioritize individualized assessments and adaptations. Before prescribing exercise to frail older adults, clinicians must consider medical factors such as existing comorbidities, current medications, recent hospitalizations, and any history of falls or injuries. Patients must be informed about the possible risks and benefits of the exercise program. Before initiating an exercise program, the participant should be given a detailed description of the program. The description should include the frequency, intensity, time, type, volume, and progression of the exercise program. A clear description of the program helps maintain motivation and adherence. Among the exercises type suitable for frail elderly individuals, aerobic exercise serves as the foundation, while strength training constitutes the core. Flexibility training acts as an auxiliary component, and balance training, alongside virtual training, provides complementary support.[49] Participation in exercise programs may be reduced by lack of transportation, and time constraints. Thus, although supervised exercise programs seem to have better outcomes, home-based exercises may be alternative training programs. Video games-based interventions could be a good option to increase motivation to participate in exercise programs.[50] Notwithstanding, as the impact of social isolation on frailty is well established, group-based exercise enjoys the additional benefit of socialization.[51] Additionally, group-based exercise settings may provide social bonds, peer support and exercise learning, which is highly determinant for long-term physical activity maintenance in frail older adults. Lastly, supervised training appears to be essential and should be delivered by highly competent exercise specialists. Indeed, a lack of professional guidance was considered as a main barrier for older adults before participating in an exercise program.[52]

4. Conclusion

Enhancing physical activity intervention and concurrently addressing sedentary behavior play a crucial role in preventing and treating frailty in older adults. The pathophysiology of frailty includes inflammation, oxidative stress, and their effects on skeletal muscle, respiratory, cardiovascular, endocrine, and nervous systems. Physical activity/exercise has the potential to exert significant anti-inflammatory and anti-oxidative stress effects, facilitating the recovery of frailty-related physical impairments in the elderly. The prescription of a multicomponent exercise program, tailored to progressively include strength, balance, mobility, and endurance training, must shift from a casual recommendation to a central intervention in combating frailty in older adults. However, additional research is needed to further contribute to our knowledge about the optimal dose of individually fitted exercise programs by frailty status.

References

1. Dent E, Morley JE, Cruz-Jentoft AJ, et al. Physical frailty: ICFSR International Clinical Practice Guidelines for identification and management. *J Nutr Health Aging.* 2019;23:771–787. doi:10.1007/s12603-019-1273-z
2. Fried LP, Tangen CM, Walston J, et al. Frailty in older adults: evidence for a phenotype. *J Gerontol A Biol Sci Med Sci.* 2001;56:M146–M156. doi:10.1093/gerona/56.3.m146
3. Rockwood K, Song X, MacKnight C, et al. A global clinical measure of fitness and frailty in elderly people. *CMAJ.* 2005;173:489–495. doi:10.1503/cmaj.050051
4. Feng Z, Lugtenberg M, Franse C, et al. Risk factors and protective factors associated with incident or increase of frailty among community-dwelling older adults: A systematic review of longitudinal studies. *PLoS One.* 2017;12:e0178383. doi:10.1371/journal.pone.0178383
5. Cheng YJ, Tseng HK, Hu YJ. Association of clinical frailty scale with readmission and mortality rate in hospitalized older adults. *Int J Gerontol*. 2024;18:70–74. doi:10.6890/IJGE.202404_18(2).0002
6. Garatachea N, Pareja-Galeano H, Sanchis-Gomar F, et al. Exercise attenuates the major hallmarks of aging. *Rejuvenation Res.* 2015;18:57–89. doi:10.1089/rej.2014.1623
7. Angulo J, El Assar M, Rodríguez-Mañas L. Frailty and sarcopenia as the basis for the phenotypic manifestation of chronic diseases in older adults. *Mol Aspects Med.* 2016;50:1–32. doi:10.1016/j.mam.2016.06.001
8. Hubbard RE, O'Mahony MS, Savva GM, Calver BL, Woodhouse KW. Inflammation and frailty measures in older people. *J Cell Mol Med.* 2009;13:3103–3109. doi:10.1111/j.1582-4934.2009.00733.x
9. Piotrowicz K, Gasowski J. Risk factors for frailty and cardiovascular diseases: Are they the same? *Adv Exp Med Biol.* 2020;1216:39–50. doi:10.1007/978-3-030-33330-0_5
10. Ji Y, Li M, Chang M, et al. Inflammation: Roles in skeletal muscle atrophy. *Antioxidants (Basel).* 2022;11:1686. doi:10.3390/antiox11091686
11. Tan BL, Norhaizan ME, Liew WP, Sulaiman Rahman H. Antioxidant and oxidative stress: A mutual interplay in age-related diseases. *Front Pharmacol.* 2018;9:1162. doi:10.3389/fphar.2018.01162
12. McArdle A, Pollock N, Staunton CA, Jackson MJ. Aberrant redox signalling and stress response in age-related muscle decline: Role in inter- and intra-cellular signalling. *Free Radic Biol Med.* 2019;132:50–57. doi:10.1016/j.freeradbiomed.2018.11.038
13. Huang DD, Fan SD, Chen XY, et al. Nrf2 deficiency exacerbates frailty and sarcopenia by impairing skeletal muscle mitochondrial biogenesis and dynamics in an age-dependent manner. *Exp Gerontol.* 2019;119:61–73. doi:10.1016/j.exger.2019.01.022
14. Navarrete-Villanueva D, Gómez-Cabello A, Marin-Puyalto J, Moreno LA, Vicente-Rodriguez G, Casajus JA. Frailty and physical fitness in elderly people: A systematic review and meta-analysis. *Sports Med.* 2021;51:143–160. doi:10.1007/s40279-020-01361-1
15. Lee CH, Hsieh MT, Laio CY, et al. The effects of a physical activity program on quality of life and wellbeing among community-dwelling older people in Taiwan: empirical evidence from Taiwan long-term care system 2.0. *Int J Gerontol.* 2024;18:29–35. doi:10.6890/IJGE.202401_18(1).0006
16. El Assar M, Álvarez-Bustos A, Sosa P, Angulo J, Rodríguez-Mañas L. Effect of physical activity/exercise on oxidative stress and inflammation in muscle and vascular aging. *Int J Mol Sci.* 2022;23:8713. doi:10.3390/ijms23158713
17. Done AJ, Traustadottir T. Nrf2 mediates redox adaptations to exercise. *Redox Biol.* 2016;10:191–199. doi:10.1016/j.redox.2016.10.003
18. Angulo J, El Assar M, Álvarez-Bustos A, Rodríguez-Mañas L. Physical activity and exercise: Strategies to manage frailty. *Redox Biol.* 2020;35:101513. doi:10.1016/j.redox.2020.101513
19. Viña J, Salvador-Pascual A, Tarazona-Santabalbina FJ, Rodriguez-Mañas L, Gomez-Cabrera MC. Exercise training as a drug to treat age associated frailty. *Free Radic Biol Med.* 2016;98:159–164. doi:10.1016/j.freeradbiomed.2016.03.024
20. Jadczak AD, Makwana N, Luscombe-Marsh N, Visvanathan R, Schultz TJ. Effectiveness of exercise interventions on physical function in community-dwelling frail older people: an umbrella review of systematic reviews. *JBI Database System Rev Implement Rep.* 2018;16:752–775. doi:10.11124/JBISRIR-2017-003551
21. Kozakova M, Palombo C. Vascular ageing and aerobic exercise. *Int J Environ Res Public Health.* 2021;18:10666. doi:10.3390/ijerph182010666
22. Cheng X, Yang Z. Effect of resistance training on inflammatory markers in middle-aged and older adults: A meta-analysis. *Arch Gerontol Geriatr.* 2024;126:105536. doi:10.1016/j.archger.2024.105536
23. Dunsky A. The effect of balance and coordination exercises on quality of life in older adults: A mini-review. *Front Aging Neurosci.* 2019;11:318. doi:10.3389/fnagi.2019.00318
24. Assar ME, Laosa O, Rodríguez Mañas L. Diabetes and frailty. *Curr Opin Clin Nutr Metab Care.* 2019;22:52–57. doi:10.1097/MCO.0000000000000535
25. Caspersen CJ, Powell KE, Christenson GM. Physical activity, exercise, and physical fitness: definitions and distinctions for health-related research. *Public Health Rep.* 1985;100:126–131.
26. Kehler DS, Theou O. The impact of physical activity and sedentary behaviors on frailty levels. *Mech Ageing Dev.* 2019;180:29–41. doi:10.1016/j.mad.2019.03.004
27. Zhou Y, Yuan Y, Wang X, et al. Sedentary behavior and physical frailty among rural older adults in China: The moderating effect of social isolation. *J Am Med Dir Assoc.* 2024;25:500–505.e1. doi:10.1016/j.jamda.2023.08.020
28. Seino S, Abe T, Nofuji Y, et al. Dose-response associations between physical activity and sedentary time with functional disability in older adults with or without frailty: a prospective cohort study. *Front Public Health.* 2024;12:1357618. doi:10.3389/fpubh.2024.1357618
29. Rogers NT, Marshall A, Roberts CH, Demakakos P, Steptoe A, Scholes S. Physical activity and trajectories of frailty among older adults: Evidence from the English Longitudinal Study of Ageing. *PLoS One.* 2017;12:e0170878. doi:10.1371/journal.pone.0170878
30. Lin YK, Chen CY, Cheung DST, Montayre J, Lee CY, Ho MH. The relationship between physical activity trajectories and frailty: a 20-year prospective cohort among community-dwelling older people. *BMC Geriatr.* 2022;22:867. doi:10.1186/s12877-022-03493-7
31. Kehler DS, Clara I, Hiebert B, et al. The association between bouts of moderate to vigorous physical activity and patterns of sedentary behavior with frailty. *Exp Gerontol.* 2018;104:28–34. doi:10.1016/j.exger.2018.01.014
32. Mañas A, Pozo-Cruz BD, Rodríguez-Gómez I, et al. Can physical activity offset the detrimental consequences of sedentary time on frailty? A moderation analysis in 749 older adults measured with accelerometers. *J Am Med Dir Assoc.* 2019;20:634–638.e1. doi:10.1016/j.jamda.2018.12.012
33. Blodgett J, Theou O, Kirkland S, Andreou P, Rockwood K. The association between sedentary behaviour, moderate-vigorous physical activity and frailty in NHANES cohorts. *Maturitas.* 2015;80:187–191. doi:10.1016/j.maturitas.2014.11.010
34. Delaire L, Courtay A, Humblot J, et al. Implementation and core components of a multimodal program including exercise and nutrition in prevention and treatment of frailty in community-dwelling older adults: A narrative review. *Nutrients.* 2023;15:4100. doi:10.3390/nu15194100
35. Serra-Prat M, Sist X, Domenich R, et al. Effectiveness of an intervention to prevent frailty in pre-frail community-dwelling older people consulting in primary care: a randomised controlled trial. *Age Ageing.* 2017;46:401–407. doi:10.1093/ageing/afw242
36. Chen R, Wu Q, Wang D, et al. Effects of elastic band exercise on the frailty states in pre-frail elderly people. *Physiother Theory Pract.* 2020;36:1000–1008. doi:10.1080/09593985.2018.1548673
37. Sadjapong U, Yodkeeree S, Sungkarat S, Siviroj P. Multicomponent exercise program reduces frailty and inflammatory biomarkers and improves physical performance in community-dwelling older adults: A randomized controlled trial. *Int J Environ Res Public Health.* 2020;17:3760. doi:10.3390/ijerph17113760
38. Kim H, Suzuki T, Kim M, et al. Effects of exercise and milk fat globule membrane (MFGM) supplementation on body composition, physical function, and hematological parameters in community-dwelling frail Japanese women: a randomized double blind, placebo-controlled, follow-up trial. *PLoS One.* 2015;10:e0116256. doi:10.1371/journal.pone.0116256
39. Tarazona-Santabalbina FJ, Gomez-Cabrera MC, Perez-Ros P, et al. A multi-

component exercise intervention that reverses frailty and improves cognition, emotion, and social networking in the community-dwelling frail elderly: A randomized clinical trial. *J Am Med Dir Assoc.* 2016;17:426–433. doi:10.1016/j.jamda.2016.01.019
40. Wang H, Liang Y, Wu H, Shi H, Hou R. Effect of multicomponent exercise intervention in community dwelling frail elderly: A systematic review and meta-analysis. *Arch Gerontol Geriatr.* 2024;126:105543. doi:10.1016/j.archger.2024.105543
41. Tanaka S, Kayamoto A, Terai C, et al. Preoperative sarcopenia severity and clinical outcomes after total hip arthroplasty. *Nutrients.* 2024;16:2085. doi:10.3390/nu16132085
42. Lindbäck Y, Tropp H, Enthoven P, Abbott A, Öberg B. PREPARE: presurgery physiotherapy for patients with degenerative lumbar spine disorder: a randomized controlled trial. *Spine J.* 2018;18:1347–1355. doi:10.1016/j.spinee.2017.12.009
43. Hermann A, Holsgaard-Larsen A, Zerahn B, Mejdahl S, Overgaard S. Preoperative progressive explosive-type resistance training is feasible and effective in patients with hip osteoarthritis scheduled for total hip arthroplasty--a randomized controlled trial. *Osteoarthritis Cartilage.* 2016;24:91–98. doi:10.1016/j.joca.2015.07.030
44. Kubicki A, Bonnetblanc F, Petrement G, Mourey F. Motor-prediction improvements after virtual rehabilitation in geriatrics: frail patients reveal different learning curves for movement and postural control. *Neurophysiol Clin.* 2014;44:109–118. doi:10.1016/j.neucli.2013.10.128
45. Persson HL, Lyth J, Lind L. The health diary telemonitoring and hospital-based home care improve quality of life among elderly multimorbid COPD and chronic heart failure subjects. *Int J Chron Obstruct Pulmon Dis.* 2020;15:527–541. doi:10.2147/COPD.S236192
46. Bull FC, Al-Ansari SS, Biddle S, et al. World Health Organization 2020 guidelines on physical activity and sedentary behaviour. *Br J Sports Med.* 2020;54:1451–1462. doi:10.1136/bjsports-2020-102955
47. Piercy KL, Troiano RP, Ballard RM, et al. The physical activity guidelines for Americans. *JAMA.* 2018;320:2020–2028. doi:10.1001/jama.2018.14854
48. Picorelli AM, Pereira LS, Pereira DS, Felicio D, Sherrington C. Adherence to exercise programs for older people is influenced by program characteristics and personal factors: a systematic review. *J Physiother.* 2014;60:151–156. doi:10.1016/j.jphys.2014.06.012
49. Izquierdo M, Merchant RA, Morley JE, et al. International exercise recommendations in older adults (ICFSR): Expert consensus guidelines. *J Nutr Health Aging.* 2021;25:824–853. doi:10.1007/s12603-021-1665-8
50. Vázquez FL, Otero P, Garcia-Casal JA, Blanco V, Torres ÁJ, Arrojo M. Efficacy of video game-based interventions for active aging. A systematic literature review and meta-analysis. *PLoS One.* 2018;13:e0208192. doi:10.1371/journal.pone.0208192
51. Katayama O, Lee S, Bae S, et al. The association between social activity and physical frailty among community-dwelling older adults in Japan. *BMC Geriatr.* 2022;22:870. doi:10.1186/s12877-022-03563-w
52. Bethancourt HJ, Rosenberg DE, Beatty T, Arterburn DE. Barriers to and facilitators of physical activity program use among older adults. *Clin Med Res.* 2014;12:10–20. doi:10.3121/cmr.2013.1171