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Research Article

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The Relationship between Muscle Aging, Bone Tissue and Sports Activities

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ABSTRACT

Aim: This research was conducted with the aim of investigating the relationship between muscle aging, bone tissue and sports activities in 2024.

Methodology: Based on the nature of the data, this research is qualitative research, in terms of the purpose of applied research, and in terms of data collection tools, it is descriptive research. Due to the fact that the current research was conducted using the descriptive method of analysis and is based on library and documentary studies, therefore, the authentic document scanning tool was used to collect the information required for the literature section of the research. To answer the research question, the phenomenological method has been used. The phenomenological method can be used for research on any aspect of natural or social reality about which people have gained an understanding. The statistical population of the current research also includes men and women 50 years and older in Mashhad. The participants of this research are 30 people, 15 men and 15 women who were selected. In this research, the researcher has used purposeful sampling.

Results: The findings of this research show that the effects of heavy sports training on aging of muscle and bone tissue are combined. 8 weeks of resistance training in middle-aged women with metabolic syndrome, which is associated with low-level chronic inflammation, increases the systematic baseline amount of bone loss compared to the control group, and this indicates that heavy resistance training reduces the amount of bone loss. which has a positive effect on bone tissue. Aerobic resistance exercises for 8 months in a group of middle-aged women 30 to 68 years old had no effect on the amount of systematic rest bone loss. There are also other cytokines that affect bone tissue in different models of bone tissue. Alendronate-calcitriol has a negative relationship with the base bone of the back and a positive relationship with the concentration of parathyroid hormone.

Conclusion: Myostatin, which is considered a myokine and prevents muscle weakening, has a direct effect on bone resorption in a muscle model of rheumatoid arthritis, and inhibition of myostatin leads to preservation of bone tissue.

Keywords: Muscle age, Bone tissue, Sports activities

INTRODUCTION

In recent decades, the elderly population has been increasing with the spread of machine life, the improvement of the level of health and the subsequent increase in life expectancy. Old age is one of the sensitive periods of human life, which along with this event, the gradual process of destruction and weakness of body parts accelerates, and then the physical performance of a person faces a sharp decline. One of the most important changes that occur in the human body with increasing age is the breakdown and destruction of muscle mass and a significant decrease in the volume and size of skeletal muscle. Also, with increasing age, the protection of bones, joints and muscles becomes doubly important, these structures support the body and help to move. Keeping bones, joints, and muscles healthy can help us perform our daily activities and be physically active. Performing moderate to intense aerobic activities that strengthen muscles and bones can reduce the decrease in bone density caused by aging. Aging is associated with an increase in many

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non-communicating diseases and a significant decline in health, which occurs in the musculoskeletal system. Decline in skeletal muscle mass associated with aging is very common, and the prevalence of sarcopenia and osteoporosis is undoubtedly increasing among the elderly population. One of the effective factors in muscle and bone tissue breakdown over time is the change/dysfunction of the immune system, which is called age-related inflammation, which describes chronic reactions in many conditions and diseases. Sports training can be an effective measure [1].

Performing physical activities is vital to maintain bone mass and physical strength and helps people prevent fractures caused by osteoporosis. Some studies have shown a positive relationship between physical activities and bone mineral density, and some have shown the ineffectiveness of physical activities on bones. Therefore, a systematic study is needed to clarify these contradictions and determine the effect of sports activities on bone mineral density. Physical inactivity is one of the main health concerns for many diseases, and improving the level of physical performance, including more exercise as a lifestyle behavior, it is considered a beneficial factor in reducing the risk of developing chronic diseases as well as modifying the immune aging that occurs with age[5] This article applies to reducing the risk of developing skeletal muscle diseases such as sarcopenia and osteoporosis, as well as correcting immune aging that occurs with age. Most of the findings from various studies confirm the positive effect of sports activities on bone mineral density, reducing pain and improving the quality of life of people with osteoporosis. The findings of all the combined exercises used and the research conducted on young people (age range 25 to 50 years) have had a positive effect on the increase of bone density in the studied areas, while in the researches in which similar training courses are used on Elderly people (age range 60 to 92 years) have been used, they did not show a positive effect [7]. According to the points that were mentioned in the statement of the problem of the present research, the researcher in this research seeks to answer this basic question: Is there a significant relationship between muscle aging, bone tissue and sports activities?

Research method, statistical population, sample size and research data collection tools

Based on the nature of the data, this research is qualitative research, in terms of the purpose of applied research, and in terms of data collection tools, it is descriptive research. Due to the fact that the current research was conducted using the descriptive method of analysis and is based on library and documentary studies, therefore, the authentic document scanning tool was used to collect the information required for the literature section of the research. In the library method, by referring to Persian and Latin books and articles, part of the necessary information was collected, and in addition, the Internet was used as a source of current scientific information, and valid research articles were also used. To answer the research question, the phenomenological method has been used. The phenomenological method can be used for research on any aspect of natural or social reality about which people have gained an understanding [11]

The statistical population of the current research also includes men and women 50 years and older in Mashhad. The participants of this research are 30 people, 15 men and 15 women who were selected. In this research, the researcher has used purposeful sampling. In targeted sampling, a part of the society is selected based on the judgment and expert opinion of the researcher or the approval of the right people. This sample is selected in such a way that it has the characteristics of the real society as much as possible. In this research, the method and tool of data collection is through semi-structured interviews, each interview lasting between 45 and 60 minutes.The data was analyzed through the parallel comparative method and the results obtained from the interview were collected, recorded and interpreted in an interpretative way by compiling a guide table and extracting key points, open coding, component code and categorized in the form of major themes.

Discussion and review

With acute periods of exercise, whether aerobic or resilient exercise, there is a cellular immune response (leukocyte) that occurs in the systemic circulation also in essence (which is partially made up of cells such as monocytes/macrophages, neutrophils).and natural killer cells) and adaptive (which is composed predominantly of T cells and B cells) branches of the immune system. Within the innate immune response, there is generally neutrophilia (an increase in neutrophil numbers) which occurs immediately following exercise with a secondary increase hours later. There is a transient increase in monocytes, circulating dendritic cells, and natural killer cells (which are all different types of leukocytes, or white blood cells). In the adaptive branch of the immune system, there is a biphasic response of lymphocytes (T cells and B cells) to acute exercise. A transient increase in circulating lymphocytes occurs in response to exercise, which then declines below baseline (resting) levels [22]. Speculation exists that the transient decrease in lymphocytes may cause an "open-window" for opportunistic pathogens to infect the host, but the potential for lymphocytes to move to areas where pathogens may be encountered (like the gastrointestinal tract and lungs) seems highly probable, thus increasing the resistance to infections [2].

The leukocyte response to chronic exercise training is well documented. In general, if a trained individual is at true rest (ie, no exercise for the previous 24 hours), there does not appear to be any significant effect on leukocyte or lymphocyte counts in the systemic circulation. However,

there is debate about the effects of chronic exercise on the function of specific cells such as monocytes/macrophages, dendritic cells, and natural killer cells, (see Table 1 for a brief summary of the different types of leukocytes and their primary function in the immune system [4]. Low-grade chronic inflammation is defined as an increase of 2 to 4 times the level of inflammatory cytokines in circulation. It is possible to somewhat combat chronic low-grade inflammatory conditions by participating in regular exercise exercises. In particular, during an acute period of exercise, there is a significant increase in interleukin-6 (IL-6), a multifunctional myokine/cytokine, which may act in pre-and anti-inflammatory capacities. Skeletal muscle is able to produce myokines which are peptide/protein-based mediators that act in an autocrine, paracrine, and/or endocrine fashion to influence other tissues. In the context of acute exercise, IL-6 has been theorized to decrease the inflammatory cytokine tumor necrosis factor-α (TNF-α) and increase the levels of anti-inflammatory cytokines such as the IL-1 receptor antagonist. (IL-1ra) and IL-10 [3]. The "cross-talk" between the immune system and muscle and bone is possibly influenced by myokines and cytokines.

As mentioned above, chronic (regular) exercise training is associated with a reduction in low-grade inflammation, and both endurance (aerobic) and resistance training are associated with reductions in various biomarkers of systemic inflammation (such as IL-6, TNF-α, C-reactive protein (CRP), and serum amyloid A (SAA). Furthermore, one of the main mechanisms whereby chronic exercise training may decrease inflammation is through a reduction in fat mass (and especially visceral fat mass). The next sections of this review will address the influence of exercise on the immune response in relation to muscle and bone health [28]

Effects of Exercise on Immune Response and Skeletal Muscle

Chronic low-grade inflammation may contribute to the development of sarcopenia, and maintaining muscle mass and function throughout the aging process is viewed as a major health challenge [26]. The process of muscle hypertrophy and regeneration is highly regulated and involves communication between the immune system and muscle. As mentioned above, myokines are released from contracting skeletal muscle, and these myokines are likely to play an essential role in coordinating the "cross-talk" which occurs between the muscle and the immune system.The activated macrophages release chemokines that attract other leukocytes such as neutrophils to the region of muscle damage. The neutrophils' main function is to create a pro- inflammatory environment where pro-inflammatory cytokines such as IFN-γ and TNF-α predominate and attract further macrophages from the systemic circulation via extravasation (i.e., the movement of macrophages from the systemic circulation to areas within the tissue itself). These macro- phages are phenotypically distinct and are named the M1 type. The M1 type of macrophage is known as the proinflammatory phenotype, whereas the M2 type of macrophage is involved in creating an anti-inflammatory environment and is involved with muscle regeneration. Thus, depending on the stage of muscle injury or repair, either the M1 or M2 type of macrophage will predominate which allows for a coordinated response of the immune system in the muscle [8, 9].

The link between the regulation of the immune system, the associated inflammatory response, and muscle has recently started to become apparent. There are a few cytokines that play an essential role in linking the inflammatory response of the immune system with the muscle regeneration that occurs.

Table 1: Various types of leukocytes (white blood cells) and their main function in the immune system

Cell type	Main immune system function	Acute exercise	Chronic exercise
Neutrophils	Phagocytosis	↑	↔
Monocytes/macrophages	Phagocytosis, antigen presentation, cytokine, production, cytotoxicity	↑	↔
Dendritic cells	Antigen presenting cells	↑	↔
Natural killer cells	Cytotoxicity	↑	↔
T cells	Lymphocyte regulation, antigen recognition, B-cell proliferation	↑ then ↓ (biphasic)	↔
B cells	Antibody production, memory cell production	↑ then ↓ (Biphasic)	↔

↑, increase in circulating cell numbers systemically; ↓, decrease in circulating cell numbers systemically; ↔, no change in circulating cell numbers systemically. Adapted from reference

It includes IFN-γ, which acts to mediate the production of the macrophage type M1, but also controls the expression of the genes of the Trans-activating master gene Class II of tissue compatibility (CIITA) in myocytes. IFN-γ activates muscle satellite cells to express ciita target genes, which essentially links the immune system with skeletal muscles [10]. Furthermore, TNF-α is intricately involved in linking the inflammatory response due to muscle injury and muscle regeneration following injury. Here, the TNF-α cytokine is linked to suppression of proliferation, but promotion of differentiation of muscle satellite cells as well as the activation of NF-κB in myeloid cells and myocytes (inducing an inflammatory response and muscle atrophy respectively) [14]. Thus, it is evident that TNF-α plays multiple roles and influences the muscle and immune systems in a variety of ways. It is interesting to note that TNF-α is not released in substantial quantities into the systemic circulation with exercise but is increased at the gene level within skeletal muscle itself. This suggests that TNF-α acts in an autocrine manner within the muscle tissue but may also communicate with resident macro- phages in the muscle itself [19].

When M1 macrophages are transitioning to the M2 phenotype, there is concomitant increase in IL-10 (a cytokine that is predominantly considered to be anti-inflammatory). This cytokine is involved in both inflammatory modulations, via M1 to M2 phenotypic shifting, and regeneration of muscle following damaging injury by signaling myogenic satellite cells to transition from proliferation to differentiation (12 and 25). The IL-10 cytokine/myokine is also released in substantial amounts into the systemic circulation via exercise and is thought to play an essential role in producing the anti- inflammatory effects of exercise (Fig. 1) which may contribute to improving muscle health in those with chronic low-grade inflammation. Transforming growth factor-β (TGFβ) is another cytokine that is intricately involved in the muscle and immune compartments within regenerating muscle tissue. Here, TNF-α expression is suppressed, and TGFβ expression is increased which shifts the phenotype of macro-phages to the M2 type: this promotes muscle regeneration following damage or injury [20].

Effects of Exercise on Immune Response and Bone

As already mentioned, chronic inflammation with a low degree is strongly associated with the development of bone loss (osteopenia, osteoporosis) with age (13). Many of the inflammatory signaling pathways and molecular mechanisms responsible for inflammation are countered by participating in regular exercise. For instance, IκBα kinase (IKK) phosphorylates nuclear factor-κB (NF-κB) which is a transcription factor that plays a key role in immunity and inflammation via the production of many pro-inflammatory regulators (14). NF-κB is stimulated by the receptor activator of NF-κB ligand (RANKL) which binds with the receptor activator of NF-κB (RANK) on precursor osteoclast cells to eventually form osteoclast cells which results in bone resorption. Many pro-inflammatory cytokines such as interleukin-1 (IL-1), IL-6, IL-7, IL-17, vascular endothelial growth factor (VEGF), and TNF-α will promote osteoclast genesis as well as bone resorption via their stimulation of RANK through accumulative production of RANKL. Osteoprotegerin (OPG) is a cytokine decoy receptor that binds with RANKL and inhibits its ability to bind with RANK which results in less osteoclast differentiation and consequently less bone resorption. The drug denosumab, a monoclonal antibody to RANKL, binds to RANKL in a similar manner as OPG and is now used in the treatment of osteoporosis. The RANK receptor, which is typically associated with the immune system, clearly has profound influences on bone [26,27].

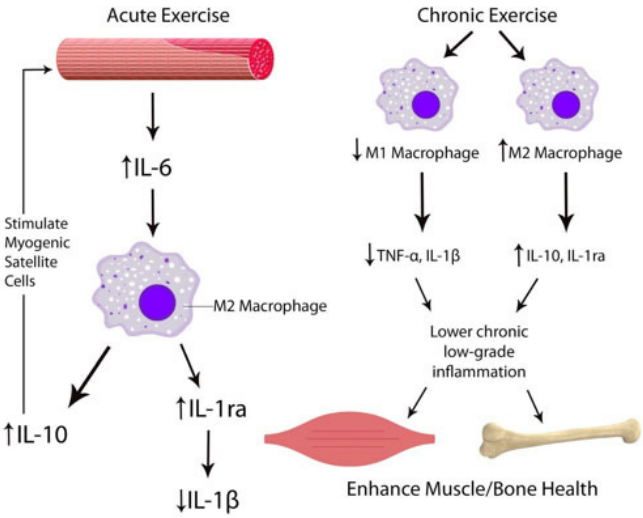

Figure 1: Acute and chronic effects of exercise on some inflammatory cells and cytokines. IL-6, interleukin-6; IL-10, interleukin- 10; IL-1ra, interleukin-1 receptor antagonist; IL-1β, interleukin-1 beta; TNF-α, tumor necrosis fac- tor alpha.

High-impact exercise (plyometric jumping) in girls, boys and young men greatly increases the systemic OPG, which suggests that exercise of this type may have a beneficial effect on bone. Systemic RANKL decreased after an acute plyometric training session in female children and adolescents. However, OPG remained unchanged in this group. In contrast, two days in a row of high-intensity metabolic ventilation (which included cardiovascular ventilation and resistance training) led to a significant drop in OPG 48 hours after exercise in a group of young adults. Further work indicated that an acute session of high- intensity interval exercise on a cycle ergometer was able to significantly increase immediate post-exercise concentrations of bone alkaline phosphatase (a biomarker of bone formation), OPG, and RANKL but the effect was only sustained for bone alkaline phosphatase at

1-h post-exercise. A biomarker of bone resorption (amino-terminal cross-linking propertied) was reduced 24-h post-exercise [6].

The effects of chronic exercise training on OPG/RANK/RANK-L are mixed. Eight weeks of resistance training in middle aged women with metabolic syndrome (which is associated with low-level chronic inflammation) was able to raise the basal systemic levels of OPG compared with that of a control group; this suggests that chronic resistance training is able to raise OPG levels which may have a beneficial effect on bone [15]. In contrast, aerobic-based endurance exercise for 8 months in a cohort of 30–65-year-old adults had no effect on the systemic resting levels of OPG. In a group of older women and men (mean age 68.2 years) who completed 32 weeks of 2 days per week of resistance training and 1 day per week of weight-bearing impact exercise training, there was a significant decrease in the inflammatory cytokines interferon-γ (IFN-γ) and IL-6 (in the men only) with no change in resting values of OPG, osteocalcin (a marker of bone formation), C-terminal telopeptide of type I collagen (a marker of bone resorption), or RANKL [16]. This type of exercise training may therefore be an effective anti-inflammatory modality; however, it may not have the desired chronic effect on bone biomarkers [17].

While OPG has received a high degree of attention as a potential mediator of bone metabolism, and may be stimulated with acute exercise interventions, there are a number of other cytokines that have an influence on bone from a variety of different research models. As previously discussed, IL-6 is elevated in chronic inflammatory states and stimulates bone resorption by augmenting osteoclast differentiation via RANKL stimulation. In a group of post-menopausal women diagnosed with osteopenia, the systemic concentration of IL-6 negatively correlated with bone mineral density (BMD) and hand-grip strength at baseline. Furthermore, the decrease in IL-6 with 6 months of alendronate-calcitriol therapy negatively correlated with baseline lumbar BMD and positively correlated with parathyroid hormone concentration (PTH). This study concluded that the improvement in IL- 6 concentrations over the 6 months was associated with the severity of bone loss at baseline and higher levels of PTH. Muscle contraction (exercise) is known to stimulate the re- lease of the myokine/cytokine IL-6 into the systemic circulation but the increase is only a temporary response with concentrations usually decreasing fairly rapidly after the exercise session is complete [24]. It is likely that the beating nature of acute exercise's IL-6 response will help create an anti-inflammatory environment, while chronic IL-6 increases are considered pre-inflammatory with detrimental effects on a number of tissue types, including bone. Additional anti-inflammatory cytokines such as IL-1 receptor antagonist (IL-1ra) and IL-10 are released with acute periods of exercise. There is a theory that this systemic cytokine response creates an anti-inflammatory environment for people who participate in regular exercise [18].

There are a number of additional cytokines that may affect bone metabolism. IL-7 is a pleiotropic cytokine which has effects on both osteoclasts and osteoblasts, and thus, its re- mains a contentious issue as to what effects IL-7 has on bone metabolism. Osteoblasts produce RANKL which is stimulated by TNF-α which is induced by IL-15; therefore, IL-15 is involved in osteoclast genesis via the RANK/RANKL pathway. TNF-α is a major stimulator of osteoclast genesis and therefore bone resorption. Myostatin, which is considered a myokine that inhibits muscle hypertrophy, directly affects bone loss in a mouse model of rheumatoid arthritis and inhibition of myostatin resulted in preservation of bone. Seven days of unloading in myostatin knockout mice decreased osteoblast cell numbers, and bone loss was not prevented in this model. Finally, the myokine irisin is lower in post-menopausal women who had a previous fragility fracture when compared with those who had not had a fragility fracture. In mice, injection of low-dose recombinant irisin stimulates an increase in cortical bone mass, prevents trabecular and cortical bone mineral density loss during hind-limb suspension, and restores bone mass once hind-limb suspension ceases[21,23]. These cytokines and myokines demonstrate the cross-talk that the immune system has on bone as well as the cross-talk that may be occurring when skeletal muscle releases myokines that could influence bone. More research evaluating the effects of various cytokines and myokines on bone tissue may lead to better therapeutic approaches to diseases and the understanding of the cross-talk between various physiological systems.

CONCLUSION

While there is some understanding of the inter-relationship between the immune system, muscle, and bone in response to exercise, research is limited and additional work is warranted. Specifically, identifying the types, doses, intensities, and frequencies of various exercise modalities on influencing the immune system response and how this influences bone and muscle is an area apt for future research. Also, identifying the similarities or differences in the acute response of the immune system, and its cross-talk with muscle and bone, between an un-trained and trained state is of interest.

The findings of this research show that the effects of heavy sports training on aging of muscle and bone tissue are combined. 8 weeks of resistance training in middle-aged women with metabolic syndrome, which is associated with low-level chronic inflammation, increases the systematic baseline amount of bone loss compared to the control group, and this indicates that heavy resistance training reduces the amount of bone loss. which has a positive effect on bone tissue. Aerobic resistance exercises for 8 months in a group

of middle-aged women 30 to 68 years old had no effect on the amount of systematic rest bone loss. There are also other cytokines that affect bone tissue in different models of bone tissue. Alendronate-calcitriol has a negative relationship with the base bone of the back and a positive relationship with the concentration of parathyroid hormone. Myostatin, which is considered a myokine and prevents muscle weakening, has a direct effect on bone resorption in a muscle model of rheumatoid arthritis, and inhibition of myostatin leads to preservation of bone tissue.

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Conflict of Interest

According to the authors, this article has no conflict of interest.

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