EFFICACY LOW FREQUENCY ELECTRICAL MUSCLE STIMULATION (EMS) TO TREAT SARCOPENIA IN ELDERLY

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ABSTRACT

Along with the increasing life expectancy and age of the population, on the other hand health problems are also increasingly complex. For this reason, efforts to maintain long-term health and well-being are becoming increasingly important. Sarcopenia is one of the health problems that often occurs with age in the form of a decrease in muscle mass and strength up to 60%. This literature review summarizes the results of studies relating to the use of electrical muscle stimulation (EMS) as a possible treatment for sarcopenia in elderly. We conducted separate searches of five electronic journal databases, namely PubMed, ScienceDirect, MEDLINE, EMBASE, and Google Scholar to find various scientific articles on the association or effect of EMS in elderly and elderly with sarcopenia. A total of seven articles were used in this review. The results showed that EMS can increase strength and muscle mass, so it is strongly suspected that EMS can be used to treat sarcopenia. Low-frequency EMS was more effective at increasing muscle strength, while high-frequency stimulation was more likely to support muscle mass gain. EMS also increases oxidative enzymatic activity and glucose uptake, thereby reducing postprandial blood sugar levels in diabetic patients and can cause changes in muscle fiber composition. In addition, EMS maintains the overall muscle fiber size that decreases with age, increases the rate of skeletal muscle protein synthesis, and prevents atrophy. The effects of EMS are similar to those of physical exercise. In molecular mechanisms, EMS regulates miR29 to prevent fibrosis accumulation, activates satellite cell-associated molecular markers such as myogenin, miR-206, and miR-1, activates IGF-1, and decreases myostatin gene expression and increases MyoD mRNA gene expression. It is hoped that this literature review can be used to consider therapeutic strategies for aging-related sarcopenia.

Keywords: electrical muscle stimulations (EMS), elderly, sarcopenia

INTRODUCTION

Sarcopenia, which is defined by muscle mass loss and other subsequent changes for example diminished muscular endurance and poorer functional capacity is one of the most noticeable alterations associated with aging[1]. It is subdivided into primary, age-related sarcopenia, and secondary sarcopenia, which is linked to several risk factors such as malnutrition, immobility, disease, and inflammation. In those aged 60 to 70, the prevalence of sarcopenia ranges from 5-13%. For people aged 80 and up, these prevalence estimates increase by 11-50%[2,3]. Observational research has discovered a high prevalence of sarcopenia in hospitalized patients, with up to 60% of patients critically ill for lack of muscle strength and performance. Importantly, patients with sarcopenia have a higher risk of death, a longer hospital stay, and a higher rate of readmission[4]. There is, however, no agreement on how to manage sarcopenic patients.

Effective interventions that improve lifelong well-being and health are now very important, as life expectancy and the proportion of the elderly population increase[5]. Physical activity is without a doubt one of the most efficient approaches for older persons to keep functional independence, and physical abilities, and lower their risk of developing numerous diseases and accidents[6]. Several interventions for sarcopenia management have been investigated. Early mobilization, for example, has been shown to reduce muscle wasting while also improving mood, quality of life, and mobility in patients recovering from critical illness[7]. Resistance exercise training (RT) appears to be the most effective method of preventing and treating sarcopenia when combined with nutritional interventions[8]. Falls are also a common issue among the elderly[9], and as such, they receive a lot of attention in terms of prevention. However, recent literature reviews have discovered numerous barriers to elderly' participation in exercise programs, including decreased physical ability, walking disability, a lack of companionship, and a lack of motivation[10].

Among various muscle strengthening interventions, the use of electrical muscle stimulation (EMS) to improve physical performance in young subjects has sparked considerable interest in the potential of using EMS to improve and prevent sarcopenia in the elderly population[11]. EMS has been shown to improve aging muscles' functional performance as well as to prevent muscle decline in old age [12,13]. Furthermore, EMS has been recognized as a practical intervention for elderly who have limited physical abilities or lack of motivation to exercise[14].

Based on previous research, this literature review centered on the use of EMS as a possible intervention for sarcopenia in elderly, include the cellular and molecular mechanisms of EMS to prevent muscle aging. Therefore, the objectives of this review literature are: a) to present scientific evidence on the benefits of EMS for the older elderly with sarcopenia, b) to discuss the effect of EMS on skeletal muscle structural changes and metabolic adaptation, c) to investigate the cellular and molecular mechanisms of EMS in the prevention of muscle aging, and d) to assess the safety of EMS.

METHODS

We conducted separate searches from five electronic journal databases, there are PubMed, ScienceDirect, MEDLINE, EMBASE, and Google Scholar to find various scientific articles about relationships or the effect of EMS on older elderly with sarcopenia. The criteria for scientific articles used as a reference source in this review are research articles conducted in the last 10 years (2012 - 2022). There are no language restrictions adopted, it can be an article in Indonesian or English, or even the language of another country if the article has very good information related to the review theme. The inclusion criteria used were: 1) respondents aged 55 years and over; 2) contains an explanation of the relationship between EMS and sarcopenia; 3) explain the mechanism of action of EMS as a treatment in sarcopenia. Total seven articles were used in this review.

RESULTS

Table 1. Effects of EMS on various study

Authors	**Design**	**Subjects**	**Interventions**	**Results**
Sillen et al., 2013	Systematic review	18 selected trials	Neuromuscular electrical stimulations (NMES) at a low frequency (<20 Hz) NMES at high frequency (>50Hz)	NMES at low freaquancy increases oxidative enzyme activity, NMES at high frequency increases skeletal muscle fiber type and muscle fiber mass
Kern et al., 2014	Interventional Study	8 males and 8 females (age: 73.1)	EMS at 60 Hz for 9 weeks	Increases muscle fibers size, increases IGF-1 gene expression and ECM type I, II, and III
Miyamoto et al., 2012	Repeated measures study	11 diabetic males (age: 57)	EMS at 4 Hz for 30 min	Decrease in post prandial glucose without an increase in insulin levels, induction of GLUT-4 translocation of muscle tissue
Wall et al.,	Repeated	6 eldery	EMS at 60 Hz for 60 min	Increase skeletal muscle protein

2012	measures study	man with diabetes mellitus type 2 (age: 70.3)		synthesis rates, decreased myostatin mRNA expression, increased MyoD mRNA expression
Dirks et al., 2015	Repeated measures study	6 illness patient with comatose (3 males, 3 females, age: 39-78)	EMS at 100 Hz for 30 min for 7 days	Prevent muscle atrpophy, decreased myostatin mRNA expression
Mosole et al., 2018	Cross sectional study	15 (8 males and 7 females, age: 71.8)	EMS at 60 Hz for 9 weeks (total 24 session (3x10 min each session)	Increase of MHC II/Serca mixed fibers, triggers calcineurin-NFAT and CaMKII pathway in muscle, promote muscle remodelling
Morbey et al., 2019	Repeated measures study	2 females subject with sarcopenia (62 and 56 years)	Whole-Body (WB-EMS) at 80 Hz for 16 session (each session not exceed 20 min)	Decrease the BF %, increase the MM %, increase the strength and muscle mass, improve the functionality of the muscle

DISCUSSION

EMS for sarcopenic elderly

Several studies have shown that EMS has an effect on motor nerve regeneration, prevention of denervation muscle atrophy, and muscle strengthening. Research results Mosole et al. on the effects of electrical stimulation (ES) on skeletal muscles in sedentary elderly people showed that neuromodulation by ES improves muscle quality so that it can fight fatigue and muscle weakness that interferes with daily activities of the elderly in healthy pathological conditions as well as in chronic conditions[15]. EMS causes contractions that act to reduce the effects of sarcopenia, making it an effective method for increasing or maintaining muscle mass, strength, and function. According to Morbey, EMS for the whole body can be very helpful for people with sarcopenia. In two sarponic female subjects aged 62 and 56 years, EMS was shown to cause weight loss through positive changes in body composition, particularly decreased body fat and increased muscle mass. The increase in strength and muscle mass as well as its functionality was indicated by an increase in the functional movement test (FMS) scores in both participants.[16]

EMS has been shown to produce a response similar to physical exercise in muscles[17]. EMS has also been shown to be effective in the treatment of muscle weakness in patients with advanced disease[18] and sarcopenia in elderly, even when combined with RT has an additive effect on morphologically healthy adults[19]. On the other hand, the effect of EMS on the functional performance of the elderly is less consistent[20].

EMS can be used as an alternative/complementary treatment option for sarcopenia and has been widely used in people who are unable to perform normal physical activity. When physical activity is not possible or parents are not motivated to do so, the adoption of EMS should be encouraged.

The Impact of EMS on Skeletal Muscle Structural Changes and Metabolic Adaptations

There are several factors that influence the therapeutic effect of EMS, including the frequency of flow used, duration of exercise, and period of exercise. EMS with a higher frequency (> 50 Hz) is known to cause an increase in muscle size, while a lower frequency (< 20 Hz) is known to increase oxidative enzymatic activity. Training durations also vary from 4 to 12 weeks, with an average of one to two hours

of training per day[21]. In healthy elderly populations, EMS has been reported to protect muscles from the effects of aging. Improvements in muscle torque and walking speed were obtained in EMS with 60 Hz given three sessions of 10 minutes per day. Training sessions were conducted twice a week for the first three weeks and three times a week for the last six weeks. In addition to its effect on muscle mass, in healthy young male subjects, EMS at a frequency of 100 Hz for 30 minutes twice daily was able to prevent muscle atrophy caused by temporary immobilization (leg casting for five days). In addition, the quadriceps muscle cross-sectional area (CSA) decreased by 3.5% compared to the control group and prevented a decrease in muscle strength by almost 10%. Analysis of muscle biopsies revealed a decrease in myostatin mRNA expression (a negative regulator of muscle mass in vivo) in the EMS intervention group[22]. EMS with a frequency of 100 Hz also prevented muscle atrophy in critically ill comatose patients. Meanwhile, in the control group, there was a significant decrease in CSA muscle fibers type I (16%) and type II (24%) after seven days of full sedation[23].
In the process of voluntary skeletal muscle contraction, in addition to a strong muscle structure, coordination and increased energy are required for cellular metabolism. In this regard, the body undergoes a number of physiological adaptations, including increased blood flow, accelerated heart rate, increased oxygen consumption (particularly by muscle tissue), and regulation of serum glucose levels to provide energy substrates. In this regard, EMS has also been shown to be capable of regulating physiological adaptations, albeit at a slower rate than reflex movements. Miyamoto et al. investigated the effectiveness of an EMS intervention in 11 elderly men with type 2 diabetes mellitus (T2DM). EMS at a frequency of 4 Hz was successful in reducing postprandial glucosuria without causing an increase in insulin for at least two hours in the postprandial period (up to one hour after EMS was turned off)[24]. In T2DM patients, EMS has been shown to improve glucose metabolism and functional performance. This finding proves that EMS has the potential to be an adjunct therapy modality besides physical activity training, to assist patients in overcoming their condition that is difficult to move[25].

The Cellular and Molecular Mechanisms of EMS in The Prevention of Muscle Aging

Electrical stimulation has been shown to boost muscle performance. Increased muscle strength was associated with increased muscle fiber and, more importantly, increased fast fiber, which was linked to an increase in skeletal muscle strength. Electrical stimulation was found to increase IGF-1 expression. Electrical stimulation stimulates anabolic pathways while also inhibiting muscle catabolism. The expression of collagen was also investigated. Remodeling occurs not only during physical exercise but also during electrical stimulation of the extracellular matrix (ECM). In electrically stimulated muscles, three different collagen forms (I, III, and VI) are upregulated. The researchers then investigated whether the increase in collagen stimulates fibrosis via one of the important fibrosis controllers, miR29. Electrical stimulation regulates miR29, which may prevent the accumulation of fibrosis. The number of satellite cells that can be activated by electrical stimulation was then determined. Electrical stimulation did increase the number of satellite cells, according to the findings. Furthermore, electrical stimulation was shown to increase molecular markers associated with satellite cells, such as Myogenin, miR-206, and miR-1[26,27]. Thus, EMS modulates similar factors associated with exercise for those who are unable to perform normal physical activity. This electrical stimulation will activate IGF-1, furthermore IGF-1 stimulates anabolic pathways, increasing protein synthesis while reducing protein degradation and activating satellite cells, which in turn will contribute to increased muscle performance.

EMS Safety

1. **EMS-caused muscle damage**

   Muscle damage caused by EMS is understandable because it causes contractions that are not inhibited by voluntary control. Subjects reported muscle soreness 24 hours after receiving EMS at frequencies of 75 Hz and higher, and creatine kinase plasma levels increased 48 to 72 hours after EMS. The most obvious clinical sign of muscle damage is a decrease in MVC strength following EMS, and the negative effects are exacerbated by electrically generated eccentric contractions[28]. As a result, it is thought that using low-frequency EMS for a shorter period of time is preferable to causing muscle damage. Furthermore, in older diabetic patients, a single treatment of EMS at 60 Hz for 60 minutes triggered a 25% higher rate of muscle protein synthesis compared to control. During the recovery period, myostatin mRNA expression was reduced two and four hours after treatment[29].

2. **An increase in blood pressure throughout the body**
   Intramuscular pressure and peripheral vascular resistance rise during isometric muscle contractions, causing systemic blood pressure to rise. Blood pressure should be monitored during EMS stimulation because it promotes sustained isometric contractions. A proposed solution to this problem is to combine EMS and electrocardiography, allowing muscle contractions to be triggered after cardiac ventricular systole, preventing systolic blood pressure elevation, and decreasing cardiac after load[30].

CONCLUSION

It can be concluded that EMS can slow aging-related functional decline, increase strength and muscle mass, maintain overall muscle fiber size that decreases with age, activate satellite cells, and improve muscle adaptation as well as physical exercise. Low-frequency EMS was shown to be more effective in strengthening, whereas high-frequency EMS was more supportive of muscle mass gain. In addition, EMS also increases oxidative enzymatic activity and glucose uptake, as well as changes in muscle fiber composition. EMS also does not cause muscle breakdown and activates molecular tissue in the same way as resistance training. The information in the literature review could be taken into consideration in the treatment of sarcopenia due to aging.

REFERENCES

1. Cruz-Jentoft AJ, Bahat G, Bauer J, Boirie Y, Bruyère O, Cederholm T, et al. Sarcopenia: Revised European consensus on definition and diagnosis. Age Ageing. 2019;48(1):16–31.
2. Kizilarslanoglu MC, Kuyumcu ME, Yesil Y, Halil M. Sarcopenia in critically ill patients. J Anesth. 2016;30(5):884–90.
3. Wang C, Bai L. Sarcopenia in the elderly: Basic and clinical issues. Geriatr Gerontol Int. 2012;12(3):388–96.
4. Peterson SJ, Braunschweig CA. Prevalence of sarcopenia and associated outcomes in the clinical setting. Nutr Clin Pract. 2016;31(1):40–8.
5. Cheng X, Yang Y, Schwebel DC, Liu Z, Li L, Cheng P, et al. Population ageing and mortality during 1990-2017: A global decomposition analysis. PLoS Med [Internet]. 2020;17(6):1–17. Available from: http://dx.doi.org/10.1371/journal.pmed.1003138
6. De Souto Barreto P, Rolland Y, Vellas B, Maltais M. Association of Long-term Exercise Training with Risk of Falls, Fractures, Hospitalizations, and Mortality in Older Adults: A Systematic Review and Meta-analysis. JAMA Intern Med. 2019;179(3):394–405.
7. Hodgson CL, Capell E, Tipping CJ. Early Mobilization of Patients in Intensive Care: Organization, Communication and Safety Factors that Influence Translation into Clinical Practice. Crit Care. 2018;22(1).
8. Marzetti E, Calvani R, Tosato M, Cesari M, Di Bari M, Cherubini A, et al. Physical activity and exercise as countermeasures to physical frailty and sarcopenia. Aging Clin Exp Res.

2017;29(1):35–42.

9. Cuevas-trisan R. Balance Problems and Fall Risks in the Elderly Balance Falls Older adults Risk factors. Phys Med Rehabil Clin N Am. 2017;28(117):727–37.

10. Yarmohammadi S, Saadati HM, Ghaffari M, Ramezankhani A. A systematic review of barriers and motivators to physical activity in elderly adults in Iran and worldwide. Epidemiol Health. 2019;41:1–11.

11. Filipovic A, Kleinoder H, Dormann U, Mester J. Electromyostimulation - A Systematic Review Of The Effects Of Different Electromyostimulation Methods on Selected Strength Parameters in Trained and Elite Athletes. J Strength Cond Res [Internet]. 2012;26(9):2600–14. Available from: doi: 10.1519/JSC.0b013e31823f2cd1.

12. Zampieri S, Mosole S, Löfler S, Fruhmann H, Burggraf S, Cvečka J, et al. Physical exercise in Aging: Nine weeks of leg press or electrical stimulation training in 70 years old sedentary elderly people. Eur J Transl Myol. 2015;25(4):237.

13. Mayr W, Krenn M, Hendling M, Haller M, Nepomucky T, Unger E, et al. Neuromuscular electrical stimulation for mobility support of elderly. IFMBE Proc. 2014;44(4):11–6.

14. O'Connor D, Brennan L, Caulfield B. The use of neuromuscular electrical stimulation (NMES) for managing the complications of ageing related to reduced exercise participation. Maturitas. 2018;113(April):13–20.

15. Mosole S, Zampieri S, Furlan S, Carraro U, Löefler S, Kern H, et al. Effects of Electrical Stimulation on Skeletal Muscle of Old Sedentary People. Gerontol Geriatr Med. 2018;4:233372141876899.

16. Morbey R. The Effects of Whole-Body Electrical Muscle Stimulation on Electrical Muscle. 2019;(August):0–11.

17. Barberi L, Scicchitano BM, Musarò A. Molecular and cellular mechanisms of muscle aging and sarcopenia and effects of electrical stimulation in seniors. Eur J Transl Myol. 2015;25(4):231.

18. Jones S, Wdc M, Gao W, Ij H, Wilcock A, Maddocks M, et al. Neuromuscular electrical stimulation for muscle weakness in adults with advanced disease (Review). Cochrane Database Syst Rev. 2016;(10).

19. Evangelista AL, Teixeira CVLS, Barros BM, de Azevedo JB, Paunksnis MRR, de Souza CR, et al. Does whole-body electrical muscle stimulation combined with strength training promote morphofunctional alterations? Clinics. 2019;74:1–6.

20. Langeard A, Bigot L, Chastan N, Gauthier A. Does neuromuscular electrical stimulation training of the lower limb have functional effects on the elderly?: A systematic review. Exp Gerontol [Internet]. 2017;91:88–98. Available from: http://dx.doi.org/10.1016/j.exger.2017.02.070

21. Sillen MJH, Franssen FME, Gosker HR, Wouters EFM, Spruit MA. Metabolic and Structural Changes in Lower-Limb Skeletal Muscle Following Neuromuscular Electrical Stimulation: A Systematic Review. PLoS One. 2013;8(9).

22. Dirks ML, Wall BT, Snijders T, Ottenbros CLP, Verdijk LB, Van Loon LJC. Neuromuscular electrical stimulation prevents muscle disuse atrophy during leg immobilization in humans. Acta Physiol. 2014;210(3):628–41.

23. Dirks ML, Hansen D, Van Assche A, Dendale P, Van Loon LJC. Neuromuscular electrical stimulation prevents muscle wasting in critically ill comatose patients. Clin Sci. 2015;128(6):357–65.

24. Miyamoto T, Fukuda K, Kimura T, Matsubara Y, Tsuda K, Moritani T. Effect of percutaneous electrical muscle stimulation on postprandial hyperglycemia in type 2 diabetes. Diabetes Res Clin Pract [Internet]. 2012;96(3):306–12. Available from: http://dx.doi.org/10.1016/j.diabres.2012.01.006

25. Van Buuren F, Horstkotte D, Mellwig KP, Fründ A, Vlachojannis M, Bogunovic N, et al. Electrical myostimulation (EMS) improves glucose metabolism and oxygen uptake in type 2 diabetes mellitus patients - Results from the EMS study. Diabetes Technol Ther. 2015;17(6):413–9.

26. Kern H, Barberi L, Löfler S, Sbardella S, Burggraf S, Fruhmann H, et al. Electrical stimulation (ES) counteracts muscle decline in seniors. Front Aging Neurosci. 2014;6(JUL):1–11.

27. He Y, Huang C, Lin X, Li J. MicroRNA-29 family, a crucial therapeutic target for fibrosis diseases. Biochimie [Internet]. 2013;95(7):1355–9. Available from: http://dx.doi.org/10.1016/j.biochi.2013.03.010

28. Sanchis-Gomar F, Lopez-Lopez S, Romero-Morales C, Maffulli N, Lippi G, Pareja-Galeano H. Neuromuscular Electrical Stimulation: A New Therapeutic Option for Chronic Diseases Based on Contraction-Induced Myokine Secretion. Front Physiol. 2019;10(November).

29. Wall BT, Dirks ML, Verdijk LB, Snijders T, Hansen D, Vranckx P, et al. Neuromuscular electrical stimulation increases muscle protein synthesis in elderly type 2 diabetic men. Am J Physiol - Endocrinol Metab. 2012;303(5):614–23.

30. Sasaki K ichiro, Matsuse H, Akimoto R, Kamiya S, Moritani T, Sasaki M, et al. Cardiac cycle-synchronized electrical muscle stimulator for lower limb training with the potential to reduce the heart's pumping workload. PLoS One. 2017;12(11):1–12.