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REVIEW ARTICLE

Electrical Muscle Stimulation in Heart Failure Patients: A Mini Review

Benjamin Vögeli[1], Vilson Kola[1], Maria Poltavskaya[2], Hugo Saner[3], Nisha Arenja[*,1]

[1] Department of Cardiology, Solothurner Spitäler AG, Bürgerspital Solothurn and Kantonsspital Olten, Switzerland
[2] Department of Cardiology, Functional and Ultrasound Diagnostics of N.V. Sklifosovsky Institute for Clinical Medicine, I.M.Sechenov First Moscow State Medical University, Moscow, Russian Federation
[3] ARTORG Center for Biomedical Engineering Research, University of Bern, Bern, Switzerland

*Correspondence nisha.arenja@spital.so.ch

ABSTRACT
This review serves as a synopsis of current knowledge about electrical muscle stimulation in patients with heart failure. It summarizes actual data, emphasizes the beneficial effects of electrical muscle stimulation in heart failure and tries to characterize a target population. Improvements of functional capacity and quality of life are knowingly achieved by variable stimulation protocols to the lower extremities. The population most likely to benefit from this therapy is of older age, has relevant comorbidities or reduced left ventricular ejection fraction. While short-term outcomes are mostly positive, there are few data on long-term outcomes that should be further investigated. Overall, electrical muscle stimulation can be considered a safe and efficacious therapy alternative to conventional physical exercise in patients with heart failure. Despite promising and increasing evidence for over two decades of scientific research on this topic, there are no recommendations in recent published guidelines concerning the use of electrical muscle stimulation in heart failure patients.

Abbreviations
AHF: acute heart failure
CIED: cardiac implantable electronic device
CHF: chronic heart failure
DASI: Duke Activity Status Index
EMI: electromagnetic interference
EMS: electrical muscle stimulation
HF: heart failure
HFpEF: heart failure with preserved ejection fraction
HFrEF: heart failure with reduced ejection fraction
ICD: implantable cardioverter-defibrillator
LVEF: left ventricular ejection fraction
MLHFQ: Minnesota living with heart failure questionnaire
QOL: quality of life
RCT: randomized controlled trial
SPPB: short physical performance battery
VO2max: peak oxygen uptake
6MWD: 6 minutes walking distance

1. Introduction

Heart Failure (HF) is one of the leading causes of hospitalization and thus associated with high morbidity and mortality. Patients hospitalized for acute HF (AHF) are at high risk for deconditioning and worsening of general condition due to bedridden and compromising symptoms such as dyspnea, fatigue or hemodynamic instability. Current guidelines from the European Society of Cardiology and the American Heart Association recommend physical exercise for all patients with chronic heart failure (CHF) in order to reduce morbidity and improve exercise capacity and quality of life (QOL) [1, 2]. According to those guidelines, a supervised, exercise-based cardiac rehabilitation program should be considered in frail patients with more severe disease or underlying comorbidities. Concerning elderly and frail patients, participation in cardiac rehabilitation programs is often limited due to sarcopenia, impaired hemodynamic status and limited mobility.

Electrical muscle stimulation (EMS) has proven to be a safe and efficacious method to counteract peripheral muscle wasting, thus improves exercise tolerance and QOL, and even decreases the need for inotropic support in patients with AHF.[3–6] Whereas in CHF EMS is already increasingly recognized as safe and effective therapy alternative to conventional physical exercise[7], more and more data is emerging, underlining the beneficial effects of EMS in AHF. Recent studies show consistent results with earlier publications, emphasizing the significant improvement of muscle strength, exercise capacity and NYHA functional class as well as QOL.[3,8–10] It is of note that multiple trials suffered from a low number of included participants, which impairs the generalization of the findings. On the other side data suggest in certain patients superiority of conventional physical exercise to EMS[11]. There are no recommendations targeting HF patients that are not able to perform physical activities or in the setting of acute and decompensated situation, despite increasing evidence of beneficial effects in this patient population. Furthermore, the specific HF population, which might benefit most, have not been described. Therefore, the definition of the population that is most likely to profit from EMS is of unmet clinical need.

This mini-review (1) gives an oversight of actual data on EMS in HF, (2) will highlight the impact of EMS on AHF and CHF in the in- and outpatient setting and (3) tries to characterize HF patients that are likely to profit from EMS.

2. Current situation

2.1 Beneficial effects of electrical muscle stimulation

Beneficial effects of EMS in patients with CHF have been described in literature for about 20 years. Aforesaid effects include improvement of muscle strength, peak oxygen uptake (VO2max), endothelial function, QOL, and overall exercise tolerance, objectified by cardiopulmonary exercise testing, 6 minutes walking distance (6MWD), flow-mediated dilation and Minnesota living with heart failure questionnaire (MLHFQ).[12–21] Recent publications conclude similar results for patients in the acute phase hospitalized for acute or decompensated CHF.[3,6,8,9,22–24] Tanaka et al. presented a significant improvement of quadriceps isometric strength and short physical performance battery (SPPB) when compared add-on EMS to physical rehabilitation versus physical rehabilitation only, in a frail and old (> 75 years) population.[9] Poltavskaya et al. showed a significant improvement in 6MWD, Duke Activity Status Index (DASI) and MLHFQ in a sham-controlled pilot study within a population of 45 patients with reduced systolic left ventricular function (mean LVEF EMS-group: 32.3%, sham-group: 30.8%) treated with EMS early after hospital admission.[8]

All these studies demonstrate the beneficial effect of early intervention strategy to counteract muscle wasting in the most vulnerable phase of treating an AHF or decompensated CHF patient, to further favor convalescence in the outpatient setting or even to shorten length of hospital stay. In addition, Dirks et al. have described preventing of muscle wasting in critically ill patients.[4] This supports the idea of EMS even in the setting of intensive care medicine., which was evaluated by a randomized controlled trial (RCT) conducted by Forestieri et al..[5] The trial displayed a significant dose reduction of dobutamine in patients with AHF on continuous inotropic support receiving EMS compared to usual care.

These data support a promising therapy alternative or bridge to physical exercise with a wide range of applicability reaching from CHF patients in the outpatient setting to AHF patients during hospital stay and even in the field of intensive care medicine.

2.2 Target population

In a systematic review with meta-analysis, Gomes Neto et al. reported a better improvement of VO2max with conventional exercise training compared to EMS in HF patients. [11] Although feasibility of EMS in HF patients was shown in multiple studies[3,23,24], a possible explanation for inferiority of EMS might be low therapy adherence and early discontinuation, as shown by Poltavskaya et al. and Arenja et al..[3,8]

This arises the question of which patient population is likely to benefit most from EMS. As there are different settings where EMS can be of benefit, target population depends on the field of use. Focusing on acute medicine, patients that are not able to participate in physical therapy are often patients with following characteristics: (1) age > 75 years, (2) Fried Frailty-Score > 3, (3) comorbidities such as pulmonary disease (e.g. obstructive or restrictive ventilation disorders), diseases of the musculoskeletal system or cognitive impairment and (4) reduced left ventricular ejection fraction (LVEF <40%). According to aforementioned studies, this population is likely to profit from EMS in the acute phase, for example as bridge to conventional physical exercise. Numerous studies have shown that EMS is feasible in this patient population.[3,23,24] However, there is evidence supporting the fact, that early EMS in severely deconditioned HF patients leads to discontinuation of therapy.[3,8] This indicates that moderately deconditioned patients or patients after initial stabilization during hospitalization may be best eligible for early EMS.

In the outpatient setting the same population as mentioned above qualifies for EMS, adding patients or institutions with considerable limited resources (e.g. missing rehabilitation opportunities and/or prolonged waiting periods for rehabilitation programs or long distance to rehabilitation centers), as well as patients with lack of training motivation or poor training compliance.

A third target population might be patients already participating in a cardiac rehabilitation program, where EMS is used as an add-on therapy to improve training effects. However, existing data show inconsistent results whether add-on EMS is more beneficial than conventional physical exercise only.[25–27]

2.3 Appropriate stimulation protocol

According to multiple reviews to the subject[11,28,29], different EMS protocols came into use. In the vast majority of analyzed studies, EMS was applied to the legs, mainly bilateral stimulation of quadriceps and calf muscles, others added stimulation to the hamstrings and gluteal muscles. In terms of intensity, the usual goal was to either induce visible muscle contraction, get 25 - 30% of maximum voluntary contraction or application of highest tolerable amplitude. Time in minutes per EMS session was variable between 30 and 120 minutes. Concerning the frequency of EMS and total duration of therapy, protocols varied from two up to seven sessions per week and duration of two to 12 weeks respectively. With most of the used protocols, beneficial effects of EMS could be shown (see Table 1), suggesting that the choice of protocol is of secondary priority.[28] However, Gomes Neto et al. demonstrated in their meta-analysis that a total EMS application time of ≥ 30 hours showed a significant improvement in VO2max and 6MWD compared to total application time of < 30 hours.[11]

Wang et al. performed a subgroup analysis comparing HF patients with reduced ejection fraction (HFrEF) and HF patients with preserved ejection fraction (HFpEF). Both subgroups showed benefits of EMS, while patients with HFrEF exhibited greater improvements in functional capacity and QOL.[28] Considering general condition, stable CHF patients may tolerate more intense protocols compared to AHF patients. According to Arenja et al., an adjustment of protocol intensity should be considered in AHF patients to prevent discontinuation of therapy.[3]

Table 1 *(data from 2016 and newer)*; EMS, electrical muscle stimulation; LVEF, left ventricular ejection fraction; mins, minutes; Hz, Hertz; Rehab, Rehabilitation; SPPB, short physical performance battery

Study	Group	Mean age	LVEF (%)	Stimulus position	Intensity	Frequency	Duration	Outcome
Groehs, 2016[6]	*EMS* *Sham EMS*	54 49	22 22	Quadriceps + Gastrocnemius	Visible muscle contraction	10 Hz	60 mins/d for 8-10 days	Significant improvement in QOL and exercise tolerance in EMS group
Iliou, 2017[27]	EMS + aerobic training Aerobic training	57.6 59.2	31.9 30.4	Quadriceps	Visible muscle contraction	10 Hz biphasic	20 min x 20 sessions during 4-8 weeks	No significant difference between groups
Ennis, 2017[24]	EMS Sham EMS	66.5 66.8	39 22	Quadriceps + hamstrings	Visible muscle contraction	4-5 Hz	60 mins/session, 5 sessions per week x 8 weeks	No significant difference between groups
Kadoglou, 2017[30]	EMS Sham EMS	72 70	27.7 28.9	Gastrocnemius	Visible muscle contraction	25 Hz	30 mins/d, 5 days per week x 6 weeks	Significant reduction of HF-related hospitalizations in EMS group
Palau, 2018[31]	EMS Control	72 75	68 66	Quadriceps + Gastrocnemius	Visible muscle contraction	10-50 Hz biphasic	45 mins/d, 2 days per week x 12 weeks	Significant improvement in QOL and exercise tolerance in EMS group
Poltavskaya, 2018[22]	EMS Bicycle Training	65.7 62.3	32.3 28.8	Quadriceps + hamstrings + anterior/posterior tibial muscles	Maximum tolerable contraction	25 Hz biphasic	45 mins/d, 5 days per week x 3 weeks	Significant improvement in QOL and exercise tolerance in EMS group
Arenja, 2021[3]	High intensity EMS Low intensity EMS Control	78.8 76 83.9	31.2 27.8 31.9	Quadriceps + hamstrings + anterior/posterior tibial muscles	Visible muscle contraction	Sound frequency 2500 Hz modulated with recantgular impulses with 50 Hz 25 Hz	30 mins/d, 5 days per week x 6 weeks	Significant improvement in QOL and exercise tolerance in EMS group
Tanaka, 2022[9]	Earyl Rehab + EMS Early Rehab	82.5 83.3	43.6 43.2	Quadriceps + hamstrings + anterior/posterior tibial muscles	Maximum tolerable contraction	20 Hz	30-40 mins/d, 5 days per week x 2 weeks	Significant improvement of quadriceps strength and SPPB
Poltavskaya, 2022[8]	EMS Sham EMS	64.5 68.9	32.3 30.8	Quadriceps + hamstrings + anterior/posterior tibial muscles	Maximum tolerable contraction	25 Hz biphasic	30-90 mins/d until discharge	Significant improvement in QOL and exercise tolerance in EMS group

2.4 Short and long-term outcomes

Most published studies conducted an EMS program over 12 weeks and recorded a short-term outcome at the end of the study, which was highly consistent with a positive effect of EMS (*see Table 1*). Data on long-term outcomes are limited to a few studies. For example, Kadoglou et al. reported a significant reduction in a combined endpoint (cardiac death and hospitalization for decompensated HF) after a mean follow-up of 383 days (maximum follow-up 580 days) in patients treated with EMS for six weeks.[30] Palau et al. showed a persistent rise in

VO2max six months after baseline following a 12-week program of EMS compared to usual care.[31] In contrast, Tanaka et al. reported no significant difference in the rate of hospital readmissions due to HF between the EMS and control group.[9]

The heterogeneous endpoints of the limited data do not allow a generalizable conclusion and indicate that further clinical investigation is needed. In addition, long-term outcome is highly influenced by subsequent treatment (eg. optimal medical therapy, regular physical exercise).

2.5 Safety aspects

Considering the impact of biphasic current applied to the legs via percutaneous electrodes, serious adverse events need to be ruled out in order to deem EMS as safe method. Besides expected muscle soreness or skin irritation unfavorable reports of increased cardiac afterload due to a rise in peripheral vascular resistance[32] or a concern for increased cardiac preload due to excessive venous return, which might worsen HF symptoms[33], have emerged. Multiple studies, taking safety aspects into account, did not show any serious adverse effects of EMS in HF patients.[9,19,23] These findings are supported by a literature review conducted by Ploesteanu et al., where out of 22 analyzed studies; none has reported serious adverse events.[29] Only in one of the analyzed studies, two patient dropouts caused by intolerance of EMS were reported. Patients with cardiac implantable electronic device (CIED), especially with cardioverter-defibrillator function deserve particular attention, as there were inappropriate ICD discharges reported.[34,35] Kamiya et al. investigated this issue and reported no electromagnetic interference (EMI) with CIED's in 27 patients hospitalized for decompensated HF, that were treated with EMS to the legs.[36] Those findings are supported by multiple reviews addressing this issue.[37,38] However, when treating CIED patients with EMS, individual risks, as well as regular treatment supervision by a physician and device examination after first use of EMS, to detect possible EMI, should be taken into consideration. Considering the actual data on adverse events caused by EMS demonstrate, that this method seems to be safe for patients with HF.

3. Future perspectives

Looking in the future of cardiac rehabilitation, multimodality cardiac rehabilitation programs consisting of conventional physical exercise, as well as other exercise types, such as high intensity interval trainings, inspiratory muscle training or EMS could be promising, although further research is needed.[39] To implement EMS in routine clinical practice in patients with AHF, it will be crucial to define the best possible timing, as well as the choice of a treatment scheme that is not too demanding to reach an optimal compliance of patients.

Concerning future developments in the use of EMS as medical therapy, promising data suggests an improvement of stroke volume and cardiac output when EMS is synchronized to the cardiac cycle.[40] Although this study was conducted in healthy volunteers, it gives an excellent outlook in which direction developments could be heading, to further improve the beneficial effects of EMS, when treating patients with HF.

4. Conclusion

EMS is an efficacious and safe therapy in AHF and decompensated CHF as well as in stable CHF to improve functional capacity and QOL. Target population is most likely old, frail and has significant comorbidities or a LVEF <50% (i.e. HFrEF and HFmrEF). Whenever possible conventional physical exercise should be the main strategy, whereas EMS should be considered for patients not eligible for physical exercise (see Image 1).

5. Conflicts of Interest

The authors have no conflicts of interest to declare.

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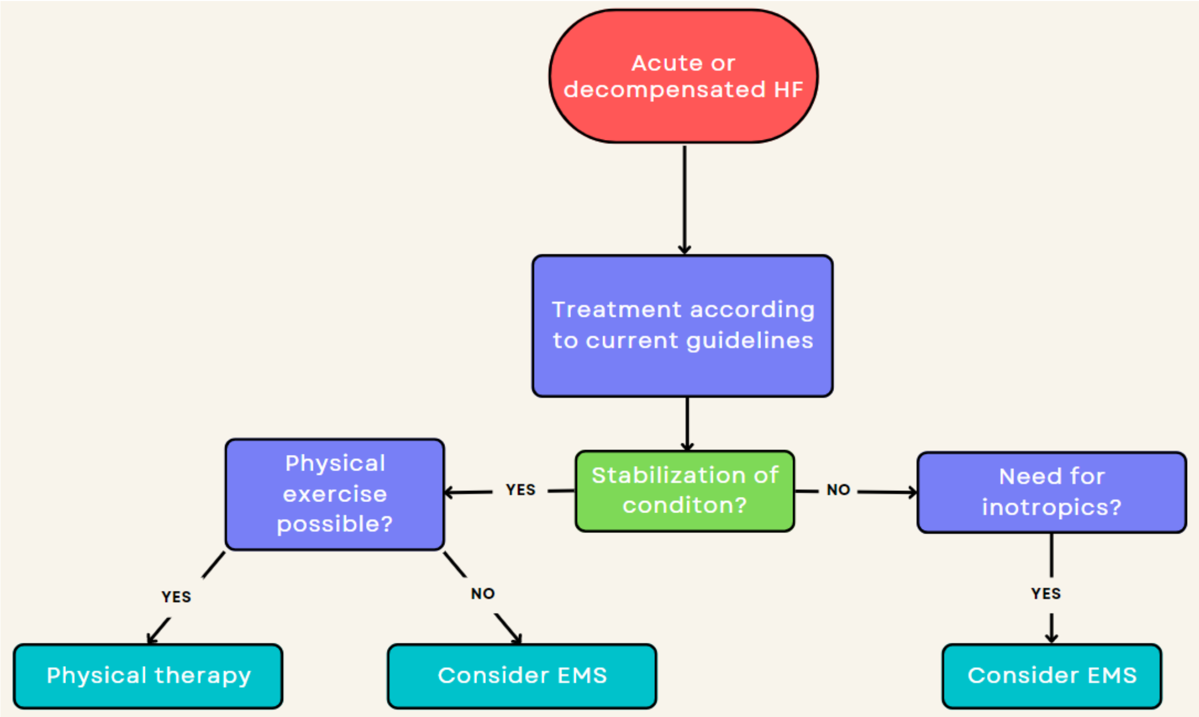

Image 1; decision-making flowchart

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