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REVIEW

The Effect of Neuromuscular Electrical Stimulation on Muscle Proteolysis, Muscle Mass and Strength, Cardiorespiratory Fitness, Functional Activity, and Quality of Life in Post-Cardiac Surgery Patients: A Narrative Review

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Abstract: Advances in medical and surgical practices, along with enhanced cardiac ICU services, have led to a substantial increase in cardiac surgeries (CS). Consequently, CS is now more frequently performed on older patients undergoing complex procedures, which results in higher rates of postoperative complications (POC) such as muscle proteolysis, prolonged hospital stays and worsened clinical and functional outcomes. These complications can delay early mobilization (EM) programs and exercise as core components of post-CS rehabilitation even though sometimes they fail to prevent functional decline. Neuromuscular electrical stimulation (NMES) has emerged as a physical modality to prevent muscle atrophy, improve muscle strength (MS), and enhance overall functional ability in post-CS patients with physical limitations. Therefore, NMES has been chosen for post-operative patients with physical limitations. This review aimed to describe the effects of NMES on muscle proteolysis, muscle mass (MM) and strength (MS), cardiorespiratory fitness (CRF), functional activity, and quality of life (QoL) in post-CS patients. Data were synthesized from PubMed, Google Scholar, and CINAHL using relevant keywords, and the review included six original articles and one systematic review. Findings indicate that perioperative NMES does not significantly affect proteolysis; however, postoperative NMES appears to increase metabolism and reduce protein degradation, thereby preventing muscle weakness. Although NMES has been shown to enhance MS, its impact on increasing MM remains insignificant. Similarly, improvements in the 6-minute walk distance (6MWD), a measure of CRF, were not statistically significant, even if they were clinically meaningful. Secondary outcomes related to functional activity and QoL also did not show significant improvements. In conclusion, post-operative NMES stimulates protein anabolism and insignificantly improves MS and MM without significantly enhancing CRF as measured by 6MWD. This may explain the lack of significant improvements in functional activity and QoL in post-CS patients.

Keywords: cardiorespiratory fitness, electrical stimulation, muscle weakness, proteolysis, quality of life

Introduction

Advances in medical and surgical practices and intensive care unit (ICU) services have substantially increased cardiac surgical procedures. Population aging has resulted in cardiac surgeries being performed in older patients with more

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complicated procedures resulting in increased post-operative complications (POC).[1] Cardiac surgery patients who experience POC are at higher risk for prolonged ICU care. The presence of POC, especially stroke, kidney failure, and pneumonia, decreases long-term survival.[1,2]

Major surgery causes a loss of 52% and 65% of muscle mass quantity and quality obtained from abdominal muscle computed tomography, respectively. Several factors have been known to be associated with surgical-related muscle mass loss such as older age, longer surgical time, open resection technique, and post-operative immobilization.[3] Inadequate protein intake postoperatively may contribute to this muscle mass loss.[4]

One of the mechanisms of muscle dysfunction after the cardiac surgical procedure is systemic inflammation-induced muscle proteolysis. Within 48 hours after cardiac surgery, there is an increase in protein catabolism that accelerates muscle proteolysis. Immobilization after cardiac surgery also stimulates muscle atrophy due to an imbalance between protein synthesis and degradation, further inducing a decrease in muscle strength (MS).[5–7] The incidence of POC was higher in patients who experienced muscle mass loss. On the other hand, the lowest survival rates were found in these patients.[3]

POC also prevents patients from immediately participating in active early mobilization (EM) programs. These complications resulted in prolonged length of hospital stays and worsened clinical and functional outcomes that can last for years after ICU treatment.[8,9]

EM and exercise are considered core components of the rehabilitation of surgical patients in the cardiac ICU but are sometimes inadequate to inhibit surgical-induced functional decline.[10]

Neuromuscular electrical stimulation (NMES) is a physical modality used as an adjunctive intervention to prevent muscle atrophy and improve MS and functional ability in post-cardiac surgery (PCS) patients.[11,12] This intervention was chosen because it can be used in patients with physical limitations after cardiac surgery due to critical illness conditions such as hemodynamically unstable patients, those with muscle weakness, and even those with mechanical ventilation.[5,13–16] Compared with traditional training, NMES is not superior in restoring muscle strength. However, this modality can be an option because it can be given in the early rehabilitation phase when voluntary contraction is impossible. In addition, NMES allows for a high training volume with minimal effort.[17]

NMES can be used in conjunction with exercise. A study that applied NMES combined with physical therapy consisting of exercises to improve range of motion, muscle strength, and functional status obtained functional improvements. This study found that low-frequency electrical muscle stimulation combined with conventional physical therapy was superior to physical therapy alone in improving knee extensor strength, muscle balance of the operated and non-operated limbs, and greater levels of independence compared to conventional physical therapy alone.[18] As resistance exercise, NMES shortened the treatment period, increased walking speed, stair climbing performance, and sit-to-stand test scores, as well as inhibited the decline in the cross-sectional area of the quadriceps muscle.[19] The mechanism of muscle mass maintenance with NMES is thought to be because electrical stimulation inhibits the breakdown of muscle protein and maintains its synthesis.[20] The increase in MS is suggested due to changes in muscle fiber types, stimulation of muscle protein anabolism and inhibition of muscle protein degradation, and muscle fiber recruitment synchronization similar to the effect of high-intensity resistance training.[7]

Research data on the application of NMES in PCS patients are limited. This review aimed to describe the use of NMES in patients who underwent cardiac surgery focusing on its effect on muscle proteolysis, muscle mass and strength, and functional abilities such as cardiorespiratory fitness (CRF), functional activity, as well as quality of life (QoL).

Methods

Data synthesis based on articles listed on PubMed, Google Scholar, and CINAHL was conducted up to February 2022. Search terms or keywords related to “neuromuscular electrical stimulation”, “muscle proteolysis”, “muscle mass and strength”, “cardiorespiratory fitness”, “functional activity”, “quality of life”, and “cardiac surgery” were combined. The inclusion criteria were original articles from any study that applied NMES in post-cardiac surgery patients and were freely accessible in PDF or HTML format. The review was limited to studies conducted in adult patients. Exclusion criteria were non-English or non-full-text articles, using NMES as a combined intervention with other modalities, and no relevant outcomes were measured.

The identical articles were identified first and then reviewed based on title, abstract, and keywords. Further synthesis was done by reading full-text articles. Data obtained were study designs, objectives, participants, protocols, outcome measures, and results. The outcome measures explored were muscle proteolysis, muscle mass, MS, CRF, functional activity, and QoL. Data collection was done by four reviewers and a critical review by the first author. Data are presented in the form of text and table.

Results

The article search was based mainly on the research objectives. Two articles were found relevant to explain the NMES effect on muscle proteolysis. As for muscle mass and strength, six articles (five randomized trials and one meta-analysis) were used to elaborate on the NMES effect. NMES effect on CRF was later explained by reviewing two original articles and one systematic review and meta-analysis article. Subsequently, three original articles were examined to explore the impact of NMES on functional activity. Finally, to explain the NMES effect on QoL, three original articles and one systematic review and meta-analysis article were used.

The included study is then summarized and presented as a narrative review that elaborates on NMES in post-cardiac surgery patients and its thorough aspects. Later, protocols of NMES for patients who underwent cardiac surgery were also presented from four previous studies and centers (Table 1).

Discussion

NMES in PCS Patients

NMES is a non-invasive electrical stimulation (ES) modality to induce adequate muscle contraction without the patient's effort.[24,25] The term NMES is often used interchangeably with ES, a modality that delivers higher frequencies (20–50Hz) quickly to produce tetany and voluntary muscle contractions to increase MS thereby supporting functional activities.[24,26]

In managing muscle atrophy after injury or disease, the use of NMES is widely accepted. There is no consensus on specific parameters to improve neuromuscular performance with NMES administration. Previous studies that aimed to determine the optimal NMES parameters to increase muscle mass did not show consistent results, but recent studies have shown that NMES successfully caused muscle hypertrophy. Therefore, NMES administration with an appropriate protocol is considered a potential modality to improve muscle function.[26]

The Rationale of NMES Administration

Cardiac surgical procedures lead to complex systemic pathophysiologic events that increase acute inflammatory response with increased production of myostatin and pro-inflammatory cytokines. Decrease protein synthesis and increased protein catabolism resulted from the acute inflammatory response leading to muscle proteolysis, especially within the first 48 hours after surgery.[11,22,27,28] Coronary artery bypass graft (CABG) surgery causes a decrease in muscle mass on the seventh postoperative day.[28] One study found that surgical stress and low pre-operative physical function affected post-operative muscle proteolysis. Therefore, patients who have catabolism-enhancing factors should be targeted for the rehabilitation interventions because, in this group of patients, the proteolysis will occur immediately after cardiac surgery.[29]

Post-surgical immobilization and physical inactivity also result in muscle mass loss (atrophy). Physical inactivity induces muscle mass loss through myonuclear apoptosis acceleration and protein synthesis deceleration within muscle fibers, leading to decreased muscle function and strength.[7,11,27] Several factors that influence the development of POC lead to immobilization such as age, comorbidities, severity of the underlying disease, surgical stress, blood flow to end organs changes during cardiopulmonary bypass, and neuroendocrine changes.[11,22,27,28]

Post-surgical rehabilitation can prevent muscle atrophy and muscle weakness due to POC. In PCS patients, there is difficulty in performing activities immediately after surgery due to hemodynamic compromise and the presence of complications.[7,11] Among PCS patients, motivation to exercise is also lacking.[7] Knee immobilization for 5 days significantly decreased the cross-section area of the quadriceps muscle by 3.5% in healthy young males, representing the loss of muscle tissue of the immobilized leg of approximately 150 grams. Five-day leg immobilization also caused

Table 1 NMES in Patients Who Underwent Cardiac Surgery

Author, Study (Year)/ Study Design	Objectives	Participants	NMES Protocol	Outcome Measures	Result & Outcome
Rengo et al (2021)/A randomized controlled trial.[21]	To assess the utility of NMES as an adjunct to current rehabilitative care following post-surgical discharge and before entering outpatient CR on indices of physical function in patients undergoing CABG surgery	37 post-CABG patients with or without valve replacement were randomly assigned into CON with no intervention and NMES groups (19 CON vs 18 NMES)	• Duration Forty-five mins per day, 5 days/week • Intensity Based on the patient's preference to get maximum tetanic contractions with tolerable pain • Electrode Attached horizontally to the distal and proximal aspects of the quadriceps muscles, with the leg immobilized at 40° relative to full knee extension • Mode ○ Waveform: Biphasic ○ Frequency: 25 hz ○ Pulse duration: 400 µs duration at 25 hz, 10s on and 30s off)	• Physical functional capacity: a. SPPB b. 6MWT • Mental and physical health: MOS-SF36	• No between-groups differences in total SPPB score, its components, and 6MWT pre- and post-surgery discharge • A greater improvement in 6MWT distance and power output in the NMES group compared to CON • No between-groups differences in any MOS-SF36 domains and composite score pre- and post-surgery discharge
Iwatsu et al (2017)/A pre-post interventional study.[10]	To explore the efficacy of NMES postoperatively on muscle protein degradation and muscle weakness in post-cardiovascular surgery patients	102 total post-cardiovascular surgery patients were randomly assigned to the NMES group and non-NMES group (61 NMES vs 41 non-NMES)	• Duration Thirty to sixty minutes per session according to the patient's tolerance, once daily from POD 1–5 • Intensity The intensities were set to induce 10% and 20% of MVC. The repetitions of 10%-10%-20% MVC were set throughout the session • Electrodes Placed on the bilateral quadriceps femoris and triceps surae • Mode ○ Waveform: Biphasic symmetric square wave ○ Pulse duration: 0.4s on and 0.6s off. Each muscle was given 10 impulse trains with 30-second intervals during the session	• Primary outcome: 3-MH/Cre concentration in 24-hour urine from POD1 to 5 • Secondary outcomes: KEIS and HGS at POD 7	• Urinary 3-MH/Cre level peaked on POD 3 in the NMES group, and sustained increase until POD 4 in the non-NMES group • Compared to the baseline, KEIS decreased significantly in both groups at POD7. The value in the NMES group was significantly greater than that in the non-NMES group at POD7 • Compared to the baseline, HGS decreased significantly in both groups at POD7. The value in the NMES group was significantly greater than that in the non-NMES group at POD7

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Cerqueira et al (2018)/A randomized clinical trial.[5]	To investigate the effects of NMES on walking ability, muscle strength, functional independence, and quality of life in cardiac valve surgery patients in the immediate post-operative period	• 122 adult patients after cardiac valve reconstruction and/or replacement randomized to NMES and CON group • 59 patients assigned to the NMES group (26 patients included in the analysis) • 63 patients assigned to the CON group (33 patients included in the analysis)	• Duration Sixty minutes per session, twice a day • Intensity Intensity was increased gradually to achieve visible muscle contraction. Palpation of the stimulated muscle can be done to confirm muscle contraction • Electrodes Placed on quadriceps and gastrocnemius muscle bulks bilaterally • Mode ○ Pulse duration: 400 ms at 50 hz, 3 seconds on-time and 9 seconds off-time	Primary outcome: • Ambulation ability (6MWT and Walking Speed Test) Secondary outcomes: • Muscular strength (MRC scale) • Functional independence measure (FIM Questionnaire) • Quality of life (NHP)	• No statistically significant difference, with a small effect size, between the groups in the distance walked and walking speed • A decrease in upper-limb MRC values at POD3 compared to preoperative values in both groups. The value returned to baseline at POD5 in the CON group and tended to return to baseline values in the NMES group • No between-group differences, with only a small effect size, were found for muscle strength in the upper limb, lower limb, and total MRC scores • No reduction during the study or significant differences between the groups in FIM score (motor, cognitive, and total FIM) • No between-group difference, with a small effect size in the total NHP was found between the groups • The NHP score of the mobility domain increased at POD3 in both groups and recovered at POD5
Kitamura et al (2018)/A randomized controlled trial.[11]	To examine the effects of perioperative NMES on muscle proteolysis and physical function and to collect data for sample size calculation for future trials	• 119 eligible participants who underwent cardiovascular surgery were assigned to the CON group (n=70) and NMES group (n=60)	• Duration Ten times (3 days before and 5 days after the surgery), with 10 seconds of stimulation with an interval of 30 seconds given to each muscle for 30 minutes. • Intensity The intensities were set to induce 10% and 20% of MVC. The repetitions of 10%-10%-20% MVC were set throughout the session. The intensity was lowered to 10%-10%-15% of the maximum voluntary contraction if the previous intensity caused pain • Electrodes Placed on the triceps surae and medial- and lateral-vastus bilaterally • Mode ○ Waveform: symmetric and biphasic square ○ Pulse duration: 0.4s on and 0.6s off	Primary outcomes: • 3-MH/Cre from POD1 to POD6 • KEIS on POD 7 Secondary outcomes: • Usual walking speed (10-meter walk test) • HGS (digital dynamometer)	• No significant difference in the mean 3-MH/Cre after surgery between the NMES and CON groups • No significant difference in physical function measures (KEIS, usual walking speed, and HGS) between both groups at POD7

(*Continued*)

Table 1 (Continued).

Author, Study (Year)/ Study Design	Objectives	Participants	NMES Protocol	Outcome Measures	Result & Outcome
Sumin et al (2020)/A randomized controlled trial.[22]	To assess the effectiveness of NMES cardiovascular surgery patients with post operative complications	• 37 participants were assigned to the NMES group (n=18) and CON group (n=19)	• Duration Daily from POD 3 until discharge (12 sessions or more), 90 min per session • Intensity At 10%-10%-20% of the MVC. The intensity was lowered to 10%-10%-15% of the MVC if the previous intensity caused pain • Electrodes Located above the points of attachment of the quadriceps femoris • Mode ○ Waveform: rectangular pulses ○ Frequency: 45 hz ○ Pulse duration: 12s on and 5s off	Primary outcome: • Knee extensors strength Secondary outcomes: • HGS • Knee flexor strength • CSA of the quadriceps femoris	• A significantly higher right and left knee extensors strength at discharge in the NMES group • No significant difference of HGS, knee flexor strength, quadriceps CSA, and 6-minute walk distance • A significant increase in right and left knee extensor strength in both groups with a higher increased in NMES group at discharge • A similar increase in knee flexor strength and HGS in both groups at discharge • The increased in the quadriceps CSA was more in the NEMS group than in the CON from POD 3 to the time of discharge • No between group difference in the quadriceps CSA, knee flexor strength, and HGS at discharge
Fischer et al (2016)/ A randomized controlled trial.[23]	• To investigate the effect of NMES in preventing MLT loss and muscle strength • To observe the time variation of MLT and muscle strength from preoperative day to hospital discharge	• 54 critically ill patients were randomized into four strata based on the SAPS II score and given NMES	• Duration Twice a day, 7 days a week (2×30 minutes with an interval of at least 30 minutes • Intensity Highest tolerable intensity just below the pain threshold • Electrodes Attached at all parts of the quadriceps muscle at both thighs were electrically stimulated • Mode ○ Waveform: biphasic rectangular pulses ○ Frequency: 66 hz ○ Pulse duration: 0.4ms, 3.5s on and 4.5s off	Primary outcomes • MLT • Muscle strength Secondary outcomes: • Average mobility level • FIM score • Timed up and go test • SF-12 health survey	• No significant effect of NMES on MLT • Regained muscle strength 4.5 times faster in NMES group compared to CON • All participant regained preoperative levels of muscle strength, but not of MLT, preoperative mobility level, and FIM score at hospital discharge • The timed up and go test and mental and physical component scores of the SF-12 regained preoperative levels at hospital discharge • No between group difference in changes in all functional outcomes from preoperative day to ICU or hospital discharge

Abbreviations: 3-MH/Cre, 3-methylhistidine concentration corrected for urinary creatinine content; 6MWT, 6-minute walk test; CABG, coronary artery bypass graft; CON, control; CSA, cross-sectional area; CR, cardiac rehabilitation; FIM, Functional Independence Measurement, HGS, hand grip strength; KEIS, Knee extensor isometric muscle strength; MOS-SF36, Medical Outcomes Study 36-item Short Form; MLT, muscle layer thickness; MRC, Medical Research Council; NHP, Nottingham Health Profile; NMES, neuromuscular electrical stimulation; POD, postoperative day; SAPS II, Simplified Acute Physiology Score II; SPPB, Short Physical Performance Battery.

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a 9.0–2.2% decrease in MS. These findings become the basis for developing interventions to prevent atrophy of immobilized muscles.[30]

ICU care also causes muscle weakness known as ICU-acquired weakness (ICU-AW). ICU-AW was affected 24% to 77% of patients admitted to the ICU for more than 1 week. Sepsis, hyperglycemia, prolonged ICU stays, catecholamine use, and immobilization are considered risk factors for ICU-AW development.[5,23] Functional impairments due to ICU-AW include difficulty performing daily activities, prolonged hospitalization, muscle atrophy, weakness, and increased mortality.[9,22] ICU-AW usually describes bilateral relationships and symmetrical neuromuscular sequelae that occur during ICU care and are not associated with another specific etiology.[31] Several case reports showed that PCS patients with low MS at hospital discharge had a low six-minute walking distance (6MWD) at 3 to 24 months post-treatment and this effect was continued for up to 5 years. This suggests that PCS patients with low physical function might become a serious public health problem.[7]

NMES is proven to reduce protein catabolism in post-surgical patients. In patients with physical limitations, NMES is an effective intervention because it does not require cooperation from the patient. It can control muscle contraction automatically to achieve muscle training goals effectively.[7]

Previous studies have shown that NMES administration in patients with longer sedation, mechanical ventilation, and immobilization, who receive ICU care, and patients who cannot perform active rehabilitation including coma patients, resulted in positive results.[7,23] NMES administration decreased the time needed to mobilize patients and increased walking distance in patients with neurological complications.[5] NMES also prevents muscle atrophy but not MS loss during 5 days of knee immobilization. Daily NMES administration prevented immobilization-induced muscle atrophy.[30]

NMES Protocols

NMES protocols vary based on previous studies (Table 1). Variations in stimulation parameters can include session length, frequency, and overall intervention duration and intensity.[5,10,11,21] Not enough data are available to make NMES regimen recommendations for optimal functional improvement.[21] The protocols provided by Iwatsu et al gave better results. Although increases in the proteolysis marker and decreases in muscle strength did not differ between the NMES and non-NMES groups, the values of these two variables were better in the NMES group.[12] A similar result was obtained by Rengo et al, as an improvement in 6MWD and power output were greater in the NMES group compared to control.[21]

Based on Table 1, it is known that the effect of NMES on muscle proteolysis as seen from the levels of 3-methylhistidine concentration corrected for urinary creatinine content (3-MH/Cre) showed no significant difference in the levels of this marker between the two groups. However, within-group differences before and after the intervention showed that the peak levels of 3-MH/Cre in a study by Iwatsu et al reached on the third day after surgery and lasted until the fourth day. Kitamura et al found 3-MH/Cre level was high at day 6 after surgery in both groups. Both studies provide quite similar protocols except for the duration of total stimulation given. Iwatsu et al gave 30 to 60 minutes of stimulation, while Kitamura et al gave 30 minutes.[11,12]

The insignificant results obtained in these two studies may be related to the intervention protocol. Previous studies examining the effects of NMES on muscle proteolysis provided stimulation with 8 seconds on and 4 seconds off, obtained significant results.[32] The protocols of Iwatsu et al and Kitamura et al provided stimulation with 0.4s on and 0.6s off.[11,12] Although the markers of muscle protein degradation and synthesis were different, the difference in stimulation duration may influenced the results.

Knee extensor isometric strength was found significantly higher with NMES intervention in Iwatsu et al and Sumin et al studies.[12,22] These findings were not found in Kitamura et al study.[11] Similar findings were also being observed regarding muscle strength or handgrip strength in which study by Iwatsu et al showed significant greater value in the NMES group compared to control group which not found in other study. Another study by Fischer et al showed that subjects received NMES intervention regain muscle strength 4.5 time faster than the control group.[23] The protocols slightly differ in the duration and duty cycle. As for duration, Iwatsu's study conducts the intervention for 30–60 min per session and Sumin's study for 90 min per session, slightly longer than Kitamura's and Fischer's study which run the intervention for 30 min. For duty cycle, Iwatsu applied pulse with 0.4s on and 0.6s off which are shorter than other studies.[11,12,22,23] Only two studies observed muscle mass and both showed no significant difference in terms of muscle layer thickness and cross-sectional area of quadriceps.[22,23]

Regarding the effect of NMES on CRF in post-cardiac surgery patients, a study by Rengo et al showed significant greater improvement in 6MWD compared than two other studies by Cerqueira et al and Sumin et al which showed no improvement.[5,21,22] Rengo protocol applied longer on pulse duration with 10s on and 30s off compared to Cerqueira et al study (3s on and 9s off) but shorter than Sumin et al study (12s on and 5s off). All studies show no significance difference statistically in quality of life or functional activity in various assessment instruments.[5,21,23] However, Rengo et al stated that change between groups for total Short Physical Performance Battery (SPPB) score was clinically meaningful (change of 0.5 units).[21]

Safety Issues

Administration of NMES in PCS patients resulted in no intervention-related adverse events (AE). One study reported pleuritic pain experienced by one patient at hospital discharge assessment and no procedure-related event occurred.[21] Other studies reported that NMES can be safely implemented immediately after cardiac surgery.[7,10] NMES was well tolerated and improved functional outcomes such as functional capacity, MS, and QoL in stable heart failure (HF) patients. In these patients, the administration of NMES did not cause AE or noticeable changes in heart rate, blood pressure, and cardiac output.[10,33]

AE associated with NMES was reported in one study that applied NMES to the quadriceps muscle, where muscle soreness occurred in one patient. Another AE that had been reported was a temporary increase in blood pressure.[33] One study reported a significant increase in heart rate, systolic blood pressure, and pacemaker malfunction. In addition, side effects such as muscle pain also occurred. However, the incidence of these AE was low.[11]

A previous study reported increased heart rate (from 94 to 99 beats per minute) and systolic blood pressure (from 127 to 133 mmHg) during NMES administration in ICU patients. However, no excessive cardiovascular responses were reported in the administration of NMES during the acute post-operative phase, although given in patients who received inotropic or continuous vasopressor therapy. In patients who required a temporary pacemaker at the first session of NMES, no heart rate abnormality was found. The application of NMES in pacemaker users caused pacemaker failure or interference with electromagnetic fields, so some studies did not provide NMES in these patients.[10]

Another concern in NMES administration immediately after cardiac surgery was the risk of cardiac arrhythmias, especially atrial fibrillation. Although postoperative atrial fibrillation is not life-threatening, it was associated with hemodynamic compromise leading to prolonged hospitalization. NMES administration also did not cause AE in patients receiving beta-blocker therapy.[10]

NMES Effect on Muscle Proteolysis

Perioperative NMES administration did not affect the 3-methylhistidine concentration, the proteolysis parameter. This finding was due to the mobilization program effect that interfered with the NMES effect.[11] NMES administration in post-abdominal surgery patients has significantly increased metabolism and decreased protein degradation.[32]

Administration of NMES immediately after cardiac surgery effectively reduced muscle protein degradation and maintained MS. NMES administration for less than 1 week could maintain quadriceps strength in patients who experienced hypercatabolic status. These findings revealed that even if given in the short term, NMES was effective in preventing muscle weakness. The underlying mechanism was suggested due to a decrease in myofibril degradation and an increase in protein anabolism stimulation through growth factor excretion with adequate intensity (20% of MVC).[12]

NMES Effect on Muscle Mass and Strength

NMES administration immediately after cardiac surgery did not cause changes in muscle structure, as presented by no difference in the quadriceps muscle cross-sectional area at hospital discharge.[22] Short-term use of NMES was not enough to provide increased MS.[5,22] Administration of NMES with a duration of up to 4 weeks in healthy people increases the strength of the stimulated muscle without the occurrence of hypertrophy.[22]

Results of studies investigating the effect of NMES on MS vary. A previous systematic review found that one of the reviewed studies found that NMES administration was effective in increasing knee extensor strength, but four other studies did not find a significant difference in knee extensor strength. The mechanism underlying the increase in MS is suggested due to an increased quantity of type 1 muscle fibers, which increases aerobic metabolism and muscle endurance, protein anabolism stimulation, and synchronization of muscle fiber recruitment that mimics the high-intensity training effect.[7]

Hand grip strength did not increase in the group given NMES. This was suggested due to the small sample size and inadequate NMES intensity. NMES intensity is linearly related to the therapeutic effect. The therapeutic intensity reported in the previous study (10–20%) of MVC did not affect arm MS.[7]

In athletes, to maximize the increase in MS, NMES was given with a fairly intense dose and long-term stimulation for at least 4 weeks. NMES administration for 5 days with less degree of exposure provided a limited effect in muscle hypertrophy and MS even though a little increase in the cross-sectional area was evident. Early activities that were performed by PCS patients who had no POC were also considered a cause of insignificant results. On the other hand, in PCS patients who experience complications, the effect of NMES in increasing MS was significant.[22]

A study that assessed the effect of peri-operative NMES on the isometric strength of bilateral quadriceps and triceps surae muscles found no significant result compared to the control group who received a standard postoperative rehabilitation program. This might be due to the effect of EM and physical activity after surgery which were not being controlled in this study.[11]

Another study found that knee extensor isometric strength 7 days after surgery was greater in patients who received NMES compared to the control group. In the group that did not get NMES, there was a decrease in knee extensor isometric strength by 35.1% and hand grip strength by 30.2% at 7 days after surgery. On the other hand, the decrease in knee extensor isometric strength was 5.3% in the group that received NMES therapy while the decrease in hand grip strength was 14.9%.[12]

The effect of isolated NMES was smaller than that of active exercise with conscious muscle contraction, so it is recommended to combine NMES with active exercise. The reason is that NMES provides additional activation to muscle fibers that are not involved in conscious muscle contraction, so it increases neural and muscular adaptations.[22] The increase in MS after NMES administration <4 weeks, occurs due to neural adaptation without muscle hypertrophy in healthy people.[12] Therefore, NMES interventions should not be given to replace physical activities.[7] It is recognized that NMES is not superior to active training for restoring MS; however, this intervention can be applied in the early rehabilitation phase when conscious contractions are not possible since this intervention allows a sufficiently high-volume exercise but with little or no effort.[34]

NMES can also cause a cross-education effect, an increase in strength in the contralateral muscle that is not exposed to stimulation due to changes in the nervous system. One study found no increase in unstimulated contralateral MS. This is due to the short period of NMES administration. To get this cross-education effect, a long enough stimulation is needed, because changes in the contralateral muscle appear after 3 weeks of exposure.[22]

Early administration of NMES was effective in preventing loss of muscle layer thickness and MS in ICU patients after cardiothoracic surgery. A study found that all patients regained pre-operative MS, but there was still residual functional impairment and decreased muscle layer thickness compared to pre-ICU admission. The use of sedation contributed to decreased MS from pre-operative to postoperative day 1.[23]

It should be considered that on postoperative day 1, there was an increase in muscle layer thickness that may be caused by surgical inflammation and the positive balance of intraoperative fluid. Muscle layer thickness then progressively decreased until discharge from the ICU but was still higher than preoperative. Edema can cause dissipation of the electrical current so that the current reaching the intramuscular motor nerve branches is not enough to produce muscle contraction and weaken the effect of NMES.[23]

NMES Effect on CRF

NMES applied to the quadriceps muscle for 4 weeks after hospital discharge improved functional recovery as indicated by the 6MWD within 1 month after discharge in patients who underwent CABG surgery. The increase in 6MWD was 73 meters in the NMES group, far exceeding the clinically significant difference of improvement (14–30 meters). The improvement obtained in the NMES-treated group at the time of entering Phase II cardiac rehabilitation (CR) was similar to that which could be expected to be achieved at the end of phase II CR in the control group.[21]

In heart-valve surgery patients, NMES use did not affect walking ability. This is due to the short duration of ICU care and sedation or mechanical ventilation use. In this group, it was suggested that obvious muscle dysfunction had not yet occurred, so NMES did not provide significant benefits.[5]

A meta-analysis found no significant difference in 6MWD and walking speed in the group given NMES and the control group.[7] In patients with HF, there was no significant difference in the increase in 6MWD between the group that received NMES and the control group that received conventional exercise, although an increase in 6 MWD by 63.54 meters was obtained. This result is considered quite good because the minimum clinical difference of 6MWD expected in HF patients is 30.1 meters. Conventional exercise was more effective than NMES in improving peak oxygen uptake (VO2 peak). Compared to the control group that did not receive exercise, NMES was efficient in increasing VO2 peak and 6MWD. An increase in VO2 peak of >10% in patients undergoing a CR program represents a good outcome.[33]

The effectiveness of NMES in non-hospitalized chronic HF patients in terms of walking distance, CRF, MS, fatigue tolerance, decreased anaerobic enzyme levels, and fast-to-slow-type fiber transition was found in a previous study. Sixty minutes of NMES administration twice daily with an average of 16 days, increased the 6MWD.[5]

The prescription of NMES should also be considered properly because there is an association between functional ES volume and increased VO2 peak in HF patients. A meta-analysis found a significant increase in VO2 peak and an increase in 6MWD in studies that provided NMES interventions with a total time of ≥30 hours compared to <30 hours. The effect of NMES is affected by the intervention dose and dose-to-effect relationship, so these issues should be further investigated for the effectiveness of NMES in PCS patients.[32]

NMES Effect on Functional Activity

A study found no significant difference in physical function that was assessed with the SPPB between the NMES-treated and the non-NMES-treated groups. The difference in total SPPB score between the two groups was 1.2 units. However, the changes of 0.5 units SPPB total score were considered clinically meaningful. Measurement of physical function with SPPB in this study was done by the patients themselves, so it is possible that the patients did not realize an increase in activity.[21]

NMES administration also did not lead to changes in functional independence.[5] Improved physical activity and functional ability were determined by increased MS and 6MWD.[33] In one study, patients did not regain their pre-operative mobility level with a lower average mobility level and functional ability at hospital discharge. These functional limitations persisted months to 5 years later, although they regained MS.[23]

The use of NMES in patients undergoing routine post-operative cardiac care did not affect ambulation ability and functional independence. These findings might be related to the short period of sedation, mechanical ventilation, bed rest, and length of ICU stay. EM led to better functional outcomes and decreased susceptibility to atrophy and muscle weakness secondary to immobilization.[5] The positive effect of EM on functional outcomes was shown in another study, which found that physical therapy led to better functional outcomes at hospital discharge.[23]

NMES Effect on Quality of Life

In PCS patients, QoL is severely compromised due to surgery's impact on physical and mental functions. QoL is associated with CRF and improves significantly when patients engage in physical activity.[33] Studies found no significant difference in QoL scores between the group given NMES compared to the control group.[5,7] There was also no significant difference in QoL scores between the group that received NMES and the control group that received conventional exercise. Although there was an increase in VO2 peak, an increase in 6MWD, an important factor in determining the QoL improvement in patients with heart disease, was not found.[33]

Patients with lower MS at hospital discharge had lower physical components of QoL scores measured by the Short Form 36-Item (SF-36) and 6MWD at 3, 6, 12, and 24 months after ICU discharge. ICU survivors showed only an additional 3% of 6MWD and 90% of the sedentary time 2 months after ICU discharge. Patients with low 6MWD also had a lower SF-36 at 6 and 12 months after hospital discharge compared to normal predicted values. Five years after ICU discharge, the 6MWD and SF-36 scores were decreased. These results suggested that ICU-AW is a public health problem beyond hospital discharge, requiring prevention or therapeutic measures.[23]

Conclusion

The administration of NMES immediately after surgery stimulates protein anabolism but does not increase muscle mass and MS significantly. This is suggested because EM programs or physical activities performed by patients postoperatively confound the effects of NMES. An inadequate intervention dose is also considered to affect the results. In addition, the short ICU treatment period causes the muscles not to experience obvious dysfunction so the administration of NMES becomes ineffective. The same reason was found in explaining the insignificant effect of NMES on 6MWD. Since the improvement of physical function such as MS and CRF as the determining components of functional activity and QoL were not significant, previous studies that assessed functional activity and QoL did not get expected results. Future studies are expected to be conducted with adequate NMES protocols to inhibit proteolysis, decreased muscle mass, MS, and CRF. Further studies are also expected to eliminate bias in the results caused by the EM program by applying a uniform protocol of both interventions to assess the individual effects of NMES and EM.

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