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The application of neuromuscular electrical stimulation (NMES) in cancer rehabilitation: current prescription, pitfalls, and future directions.

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Abstract

The plethora of treatment complications associated with cancer can be offset by regular exercise participation; however, adherence to current guidelines is poor, in particular in those unable or not allowed to participate in voluntary exercise due to their underlying disease. Alternative therapies such as neuromuscular electrical stimulation (NMES) are promising although previous results in cancer survivors have been equivocal. This is likely in response to methodological issues such as inappropriate NMES prescription. Therefore, the aim of this commentary is to propose three key areas which should be addressed to increase NMES effectiveness in cancer rehabilitation; 1) NMES exercise should target both the neuromuscular and cardiovascular systems through low and high frequency modalities, 2) technological advancements such as mobile app based systems should be leveraged to improve at-home monitoring of home-based NMES exercise, and 3) prescription and progression should follow the fundamental principles of exercise to overcome the heterogeneity in daily physiological, functional and psychological factors faced by survivors. Addressing these three key areas in future studies may help improve NMES exercise effectiveness and accelerate patient rehabilitation.

Key Words: neuromuscular electrical stimulation, rehabilitation, physical function, technology

Annual cancer diagnosis rates (> 10 million per year) are estimated to rise by 50% by 2030 [1]. Current antineoplastic treatments are effective, with a year-on-year decline in cancer mortality rates reported in men (-8%) and women (-3%) since 2011 [2]. However, cancer treatments are associated with a plethora of side effects which negatively impact on activities of daily living and quality of life.

Exercise performed under regular medical supervision is currently recommended to help offset cancer treatment complications such as the loss of muscle strength and cardiorespiratory fitness (CF). Current exercise guidelines recommend 150mins/week of moderate intensity exercise coupled with 2-3 resistance training sessions per week for all cancer survivors [3]. However, only 35% of patients achieve these recommendations [4]. The reduced participation rates among cancer survivors are exacerbated by treatment complications which make voluntary exercise difficult [5] and some patients (e.g. brain and bone metastases) may be excluded from exercise if determined to be at risk of harm [6]

Alternative therapies such as neuromuscular electrical stimulation (NMES) have the potential to provide an exercise stimulus to such individuals. Studies in patients with advanced disease have demonstrated functional and strength benefits and concluded that NMES is safe and best suited to those unable to perform voluntary exercise [7]. As such, NMES can be performed under regular medical supervision, even in those with severe concomitant disease, with a recent report suggesting physician supervised NMES to be safe even in those with implantable cardioverter defibrillators when delivered to the lower limbs [8]. This makes NMES uniquely placed for cancer survivors.

Over the past decade there has been a paucity of research investigating the implementation of NMES into cancer rehbailitation. A case study involving a female patient with extensive metastatic cancer which contraindicated voluntary exercise participation, showed improvements in endurance capacity (+44%), functional muscle strength (+20%), self-confidence and independence [9]. However, studies that have implemented home-based NMES exercise have generally had low adherence rates and minimal improvements in functional and strength outcomes [10–12]. The reasons for these findings are unclear, but may be partially due to methodological issues such as inappropriate NMES prescription and a lack of appropriate monitoring. Therefore, the aim of this commentary is to propose key issues which if addressed may help to increase the effectiveness of NMES in these populations. As such, three key areas have been identified:

1. *The use of NMES to target the neuromuscular and cardiovascular systems (termed concurrent NMES)*: Research in cancer to date has only implemented high frequency NMES exercise (>50Hz) which is recommended for gains in muscle strength and size, but has negligible effect on CF [13]. Therefore, NMES exercise which can target both strength and CF is required to meet current exercise guidelines. Aerobic NMES exercise protocols incorporating continuous rhythmical contractions at low frequency (4Hz) have been shown to improve CF (VO_{2max}: +10%) in patient groups after 8 weeks [14]. In addition, concurrent protocols involving both a strength (30Hz, 15mins) and an aerobic (4Hz, 45mins) phase within a 60min session have led to improvements in muscle strength (15%) and aerobic exercise capacity (3.5%) over 8 weeks in the elderly [15]. By utilising both high and low frequency NMES exercise, this form of NMES prescription has the potential to meet exercise guidelines, ensure that an unmet clinical

need is addressed and possibly accelerate rehabilitation and patient return to voluntary exercise through improved muscle strength and exercise tolerance.

2. *Leveraging technology for effective home-based monitoring:* Supervised NMES exercise allows for the close monitoring of exercise adherence. However, self-management interventions may improve patient adherence. In addition, patient preferences lean towards home-based NMES exercise [5]. Current data on adherence during home-based NMES has previously been collected using self-report diaries, but a common limitation to this method is over-reporting of exercise levels [16]. Therefore, patients may receive an inadequate exercise dose, possibly masking the true potential of NMES exercise. Home-based NMES exercise could be improved if advancements in digital technology which have revolutionised how we now communicate, access, and monitor information [17] are implemented to help monitor and collect patient data, in addition to providing remote support to patients [18]. Combined with regular physician supervision which can minimise and avoid exercise side effects, technology has the potential to help provide safe, monitored home-based NMES exercise which can improve patient engagement with their own healthcare through self-management and improve patient outcomes.

3. *Personalised NMES prescription and progression:* A homogenous NMES prescription which is seen in most NMES exercise studies may mask its potential in some users due to the considerable inter-individual heterogeneity which exists between users. In voluntary exercise, four exercise principles (individualisation, specificity, progressive overload, and rest/recovery) have been outlined to improve exercise prescription in cancer [19] but are not conventionally applied to NMES exercise protocols. To target

these principles, voluntary exercise programmes systematically manipulate exercise variables (i.e. periodisation) to maximise adaptations [20]. In addition, autoregulation, defined as the ability to alter the magnitude of the exercise stimulus through manipulation of variables such as exercise volume and intensity to match the individual's daily readiness to train [21] has the potential to allow for better monitoring and personalisation of the daily exercise prescription [22]. Considering the heterogeneity in daily physiological, functional and psychological factors, cancer patients may benefit from a similar approach and more personalised NMES protocol design. Designing individually tailored NMES exercise based on these exercise principles may help improve the effectiveness, progression and adherence to NMES exercise.

In conclusion, to improve the delivery of NMES, it is proposed that we address the challenges mentioned in this commentary. Whilst current NMES exercise demonstrates efficacy in various pathologies, methodological issues in the current NMES/cancer literature combined with the heterogeneity of cancer patients potentially masks the true potential of NMES exercise in patients unable to exercise voluntarily or those in which active exercise is contraindicated. Digital technologies and the application of exercise principles may help significantly improve the clinical effectiveness of NMES and accelerate patient return to activities of daily living and voluntary exercise.

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